Short Report

Changes in Anterior Cingulate and Amygdala After Cognitive Behavior Therapy of Posttraumatic Stress Disorder

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Posttraumatic stress disorder (PTSD) may develop from impaired extinction of conditioned fear responses. Exposure-based treatment of PTSD is thought to facilitate extinction learning (Charney, 2004). Fear extinction is mediated by inhibitory control of the ventromedial prefrontal cortex (vmPFC) over amygdala-based fear processes (Phelps, Delgado, Nearing, & LeDoux, 2004; Quirk, Russo, Barron, & LeBron, 2000). Most neuroimaging studies of PTSD reveal reduced vmPFC activity (particularly in rostral anterior cingulate cortex, or rACC; Lanius et al., 2001; Shin et al., 2005), and some find increased amygdala activity during threat processing (Shin et al., 2005). In addition, increased amygdala activity during fear conditioning and reduced vmPFC activity during extinction have been reported in PTSD (Bremner et al., 2005).

Although PTSD patients show increased orbitofrontal and medial prefrontal activity following treatment with serotonin reuptake inhibitors (SSRIs; Fernandez et al., 2001; Seedat et al., 2004), no studies have investigated neural networks before and after exposure-based treatment of PTSD. We report the first such study. We hypothesized that symptom reduction would be associated with increased rACC activity and reduced amygdala activity during fear processing.

METHOD

Eight individuals (5 females) with PTSD following assault (n = 4) or car accidents (n = 4) were recruited from the Westmead PTSD Unit, New South Wales, Australia. Average time post trauma was 65 months (SD = 64.0), and the subjects’ mean age was 36.8 years (SD = 8.8). Subjects were assessed using the Clinician-Administered PTSD Scale (CAPS; Blake et al., 1990) and the Structured Clinical Interview for DSM-IV Axis 1 Disorders (First, Spitzer, Gibbon, & Williams, 1997). Four subjects had comorbid major depression. Two subjects were medicated with SSRIs during the period when the testing sessions took place. Subjects were excluded if they had a history of neurological condition, psychosis, borderline personality disorder, or substance abuse. After giving informed written consent, participants received eight once-weekly sessions of imaginal exposure and cognitive restructuring (Bryant, Moulds, Guthrie, Dang, & Nixon, 2003). Patients underwent scanning prior to and 6 months following treatment.

Magnetic resonance imaging (MRI) scans were performed on a 1.5-T Siemens Vision Plus Scanner using an echoplanar protocol. Subjects viewed 120 fearful and 120 neutral standardized facial expressions (Gur et al., 2002) presented in a pseudorandom sequence of 30 blocks (8 fearful faces and 8 neutral faces per block). Stimuli were presented for 500 ms, with a 768-ms interstimulus interval. Ninety functional T2-weighted volumes were acquired (6.6 mm thickness; time of repetition,
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RESULTS

Treatment Outcome
The mean CAPS score was 78.1 at pretest (SD = 20, range: 55–120) and was reduced to 28.9 at posttest (SD = 20.3, range: 2–52). All subjects revealed at least a 30% reduction in total CAPS score.

MRI
The ROI analyses revealed significantly greater activation in bilateral rACC after treatment than before treatment, left hemisphere: \( t(7) = 2.03, p = .021 \) (Montreal Neurological Institute, MNI, coordinates: \( x = -4, y = 52, z = 2; 10 \) voxels), right hemisphere: \( t(7) = 1.79, p = .036 \) (\( x = 4, y = 44, z = 0; 36 \) voxels). There were no significant activations in amygdala before or after treatment. Whole-brain analysis revealed significantly greater activation before than after treatment in right postcentral gyrus, \( t(7) = 4.18 \) (\( x = 66, y = -16, z = 32; 172 \) voxels); right middle temporal gyrus, \( t(7) = 3.59 \) (\( x = 50, y = -62, z = 6; 29 \) voxels); and left superior temporal gyrus, \( t(7) = 3.48 \) (\( x = -60, y = -4, z = 4; 41 \) voxels). In contrast, activation was greater after than before treatment in left middle temporal gyrus, \( t(7) = 3.94 \) (\( x = -52, y = -18, z = -12; 213 \) voxels); right inferior frontal gyrus, \( t(7) = 3.75 \) (\( x = 60, y = 26, z = 2; 57 \) voxels); left parietotemporal gyrus, \( t(7) = 3.74 \) (\( x = -56, y = -62, z = 32; 47 \) voxels); and right hippocampus, \( t(7) = 3.23, p = .001 \) (\( x = 34, y = -24, z = -12; 6 \) voxels).

A significant positive correlation was found between change in total CAPS score and change in right rACC activity (\( r = .8, y = 36, z = 8 \)) from before to after treatment (\( r = .84, p < .01 \); see Fig. 1). A negative correlation was found in bilateral amygdala (\( x = 18, y = 4, z = -16 \)) and change in total CAPS score (\( r = -.35, p < .01 \); see Fig. 1). Therefore, as CAPS scores improved, rACC activity increased and amygdala activity decreased during fear processing.

DISCUSSION

This study provides the first evidence that successful exposure therapy for PTSD is associated with increased rACC and reduced amygdala activation during fear processing. This pattern is consistent with evidence of vmPFC involvement in fear extinction (Quirk et al., 2000). This study requires replication in research using larger samples, employing a wait-list control condition, and examining responses to trauma-related stimuli. The current data indicate that the neural correlates of fear processing after improvement in PTSD symptoms accord with evidence that amygdala and rACC activity underlie the acquisition and extinction of conditioned fear.

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