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Neural responses during emotional processing before and after cognitive trauma therapy for battered women ☆

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ABSTRACT

Therapy for combat and accident-related posttraumatic stress disorder (PTSD) has been reported to influence amygdala and anterior cingulate cortex (ACC) response during emotional processing. It is not yet understood how therapy influences different phases of emotional processing, and whether previous findings generalize to other PTSD populations. We hypothesized that cognitive trauma therapy for battered women (CTT-BW) would alter insula, amygdala, and cingulate responses during anticipation and presentation of emotional images. Fourteen female patients with PTSD related to domestic violence completed the Clinician Administered PTSD Scale (CAPS) and functional magnetic resonance imaging (fMRI) before and after CTT-BW. The fMRI task involved cued anticipation followed by presentation of positive versus negative affective images. CTT-BW was associated with decreases in CAPS score, enhanced ACC and decreased anterior insula activation during anticipation, and decreased dorsolateral prefrontal cortex and amygdala response during image presentation (negative–positive). Pre-treatment ACC activation during anticipation and image presentation exhibited positive and negative relationships to treatment response, respectively. Results suggest that CTT-BW enhanced efficiency of neural responses during preparation for upcoming emotional events in a way that reduced the need to recruit prefrontal-amygdala responses during the occurrence of the event. Results also suggest that enhancing ACC function during anticipation may be beneficial for PTSD treatment.

1. Introduction

Treatment for posttraumatic stress disorder (PTSD) usually includes psychotherapy, medication, or a combination of both (Foa, 2006; Stein et al., 2006). There is strong empirical support for cognitive-behavioral therapies (CBT) for PTSD, including prolonged exposure therapy (Foa, 2006) and cognitive processing therapy (Resick and Schnicke, 1992), among others. Cognitive trauma therapy for battered women (CTT-BW) is a CBT treatment developed by Kubany et al. (2004) to specifically target issues faced by women who developed PTSD after intimate partner violence (IPV). While response rates for CTT-BW (Kubany et al., 2004) and other CBTs are relatively high (50–80% of completers), there is still room for improvement, with 20–60% of patients either dropping out or not responding optimally (Schottenbauer et al., 2008). Neuroimaging techniques may be useful in determining mechanisms of healing and in offering insights into potential novel treatment targets.

Neuroimaging studies with PTSD patients have focused primarily on processing of trauma-related and emotional stimuli. In general, results suggest PTSD subjects have greater activation in amygdala and anterior insula regions and less activation of anterior cingulate cortex (ACC) and/or medial and lateral prefrontal cortex (PFC) (Etkin and Wager, 2007; Liberzon and Sripada, 2008; Shin and Liberzon, 2010) compared to non-PTSD subjects, though there have been some inconsistencies regarding directionality of findings (Etkin and Wager, 2007). While the amygdala is implicated in processing affective salience (Davis and Whalen, 2001; Morrison and Salzman, 2010), the insula is implicated in processing interoceptive signals (i.e., bodily responses) (Critchley et al., 2004; Craig,

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2011) and anticipating future events (Simmons et al., 2004; Knutson and Greer, 2008). The overall pattern of dysfunction in PTSD is thought to relate to difficulties appropriately engaging prefrontal regions to monitor and regulate amygdala and insula activation and the cognitive and behavioral responses to emotional stimuli (Liberzon and Sripada, 2008; Shin and Liberzon, 2010).

A few studies have used fMRI to investigate changes in neural response with PTSD treatment. Felmingham et al. (2007) and Roy et al. (2010) observed that exposure-based CBT for PTSD was associated with decreased amygdala and increased rostral and/or dorsal ACC response during emotional face processing and the affective Stroop task, respectively. These findings suggest therapy may (a) enhance function within cingulate regions important for conflict monitoring, inhibition, and cognitive-emotion regulation (Ochsner and Gross, 2005; Botvinick, 2007; Levine, 2009) and (b) reduce responsivity within the amygdala, perhaps reflecting a reduction in the salience attributed to presented stimuli (Davis and Whalen, 2001; Morrison and Salzman, 2010). A more recent fMRI study by Thomaes et al. (2012) reported decreased dorsal ACC and anterior insula activation during the affective Stroop task after group CBT for complex PTSD. This suggests that CBT treatment for PTSD may decrease insula as well as amygdala activation during certain tasks and that the directional relationship between treatment and ACC responses may be complex and influenced by either subject or paradigm factors that differ between studies.

Neuroimaging methodologies may also enhance our understanding of why certain individuals experience more or less benefit from treatment. Bryant et al. (2008) reported that greater pre-treatment activation within both ventral ACC and amygdala to backward-masked negative emotional faces was predictive of worse response to exposure-based CBT for PTSD. While the negative relationship between amygdala activation and treatment response was in the expected direction, the authors had theorized a positive relationship between ACC activation and treatment response. The authors suggested the directionality of the finding may have been due to the subconscious presentation of stimuli and hypothesized that greater baseline ACC response during conscious emotional processing may relate to better treatment response.

The current fMRI study investigated neural outcomes and predictors of CTT-BW using a task involving conscious anticipation (ANI, API) followed by presentation of negative (NI) and positive (PI) affective images. Enhanced emotional or physiological responses to cues or "triggers" of emotional events are an important aspect of PTSD diagnostic criteria. Anticipatory anxiety can also lead to avoidance behavior, which is another important aspect of PTSD that CBT often targets specifically (Foa, 2006). The task used in the current study was designed to enable investigation of neural processing during cued anticipatory processing. In previous work, women with IPV-related PTSD have exhibited enhanced activation within bilateral anterior insula and reduced activation activation within lateral regions of the prefrontal cortex (PFC) during emotional anticipation compared to women without PTSD (Simmons et al., 2008; Aupperle et al., 2012). However, the employed anticipation task also allows for investigation of neural responses during the experience of the emotional stimulus itself (Simmons et al., 2006). This paradigm therefore has potential for elucidating the relationship between treatment and both anticipatory and stimulus presentation phases of emotional processing.

In the current study, we sought to determine (a) effects of CTT-BW on prefrontal-amygdala-insula responses during anticipation and presentation of affective stimuli and (b) what pattern of baseline prefrontal-amygdala-insula responses are predictive of CTT-BW treatment response. We hypothesized that CTT-BW would reduce activation in anterior insula during anticipatory processing and both amygdala and anterior insula during stimulus processing, but enhance ACC response during both anticipatory and stimulus processing. Further, we hypothesized that greater ACC activation and lower amygdala and/or anterior insula activation pre-treatment would relate to better treatment response.

2. Methods

2.1. Participants and measures

Women who had experienced IPV and were seeking treatment for PTSD symptoms were recruited for the study. Exclusionary criteria included substance abuse in the past year; history of >5 years of alcohol abuse; use of psychotropic medications within 4 weeks prior to the study, bipolar disorder or schizophrenia, irremovable ferromagnetic bodily material, pregnancy, or claustrophobia. Forty-one women with IPV-PTSD completed the anticipation task during fMRI and were offered CTT-BW (Kubany et al., 2004). Several of these participants were excluded due to not initiating or completing treatment or excessive movement during and lower amygdala description of exclusions). A total of 14 women with IPV-PTSD (mean [S.D.] age, 40.07 [7.44] years; mean [S.D.] education = 14.43 [1.99] years) were included in final analyses. These subjects represent a subset of a cohort for which pre-treatment fMRI results were reported previously (Aupperle et al., 2012).

All participants were seeking treatment for PTSD symptoms and met full ($N=11$) or partial ($N=3$) DSM-IV PTSD criteria, verified using the Clinician-Administered PTSD Scale (CAPS) (Blake et al., 1995). Treatment involved 90-minute weekly sessions of CTT-BW (mean number of sessions = 11.57, S.D. = 1.60). CTT-BW was developed by Kubany et al. (2004; Kubany and Ralston, 2008) and is a manualized, modular intervention designed to treat PTSD and functional impairment specifically for IPV victims. CTT-BW is based on cognitive behavioral principles and includes psychoeducation, skills training, exposure to reminders of trauma, and assessment and correction of irrational beliefs. CTT-BW focuses these intervention strategies on areas of distress most relevant to IPV survivors. See Supplementary Material for further of CTT-BW.

Subjects completed, among other measures, the CAPS (Blake et al., 1995), PTSD Checklist (PCL) (Blanchard et al., 1996), and Beck Depression Inventory version 2 (BDI-II) (Beck et al., 1996) pre- and post-treatment. The CAPS was additionally completed after treatment at 3-month follow-up. See Supplementary Material for IPV and full/partial PTSD definitions and exclusionary criteria.

After complete description of the study to the subjects, written informed consent was obtained at the initial study session. The study protocol was approved by the University of California—San Diego Human Research Protections Program and the Veterans Affairs San Diego Healthcare System Research and Development Office; all procedures were completed at these institutions.

2.2. fMRI data acquisition

The anticipation task was conducted pre- and post-treatment during fMRI scans sensitive to blood oxygenation level-dependent (BOLD) contrast using a Signa Excite (GE Healthcare, USA) 3.0 T scanner (T2*-weighted echoplanar [EPI] imaging, repetition time (TR) = 2000 ms, echo time (TE) = 32 ms, 64×64 matrix, 30 2.6-mm axial slices with a 1.4-mm gap, 290 scans). During each scan session, a high-resolution T1-weighted image (spoiled gradient recalled (SPGR), TR = 8 ms, TE = 3 ms, 172 sagittal slices with approximately 1 mm^3 voxels) was obtained for anatomical reference.

The anticipation task, conducted as previously described (Simmons et al., 2008) and as shown in Fig. 1, combines a continuous performance task (CPT) with interspersed presentation of positive (PI) and negative (NI) affective images. During the CPT, subjects were asked to press a 'LEFT' or 'RIGHT' button corresponding to the direction of an arrow on the screen. Simultaneously, a 250-ms long 500-Hz tone was presented every 2 s. During baseline conditions, the background screen was gray. Subjects were instructed prior to the task that when the background screen turned blue, accompanied by a 250-Hz tone, a positive image would appear on the screen, whereas when the background turned yellow, accompanied by a 1000-Hz tone, a negative image would appear. The trials in which the background was either blue or yellow represented the anticipation periods. The picture stimuli comprised 17 positive and 17 negative images taken from the International Affective Picture System (IAPS Lang et al., 2008). The positively and negatively valenced images were matched on level of arousal (as reported in the IAPS manual) to allow examination of valence effects specifically. The anticipation periods during the task lasted 6 s, and the image presentation lasted 2 s. The baseline CPT task was interspersed for variable duration averaging about 8 s in between trials. There was no inter-stimulus interval between anticipation and image presentation phase. The total duration of the task was 580 s. Response accuracy and reaction time were obtained for the CPT during baseline, anticipation of a positive image (API), and anticipation of a negative image (ANI) conditions. See Supplementary Material for further description of this task.