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Impact of cognitive-behavioral therapy for social anxiety disorder on the neural bases of emotional reactivity to and regulation of social evaluation

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ABSTRACT

We examined whether Cognitive-Behavioral Therapy (CBT) for social anxiety disorder (SAD) would modify self-reported negative emotion and functional magnetic resonance imaging brain responses when reacting to and reappraising social evaluation, and tested whether changes would predict treatment outcome in 59 patients with SAD who completed CBT or waitlist groups. For reactivity, compared to waitlist, CBT resulted in (a) increased brain responses in right superior frontal gyrus (SFG), inferior parietal lobule (IPL), and middle occipital gyrus (MOG) when *reacting to social praise*, and (b) increases in right SFG and IPL and decreases in left posterior superior temporal gyrus (pSTG) *when reacting to social criticism*. For reappraisal, compared to waitlist, CBT resulted in greater (c) reductions in self-reported negative emotion, and (d) increases in brain responses in right SFG and MOG, and decreases in left pSTG. A linear regression found that after controlling for CBT-induced changes in reactivity and reappraisal negative emotion ratings and brain changes in reactivity to praise and criticism, reappraisal of criticism brain response changes predicted 24% of the unique variance in CBT-related reductions in social anxiety. Thus, one mechanism underlying CBT for SAD may be changes in reappraisal-related brain responses to social criticism.
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Introduction

Social anxiety disorder (SAD) is characterized by heightened fear of social evaluation in conjunction with a maladaptive pattern of emotion regulation (e.g., over-reliance on maladaptive emotion regulation strategies such as behavioral avoidance and expressive suppression (Stein & Stein, 2008; Werner, Goldin, Ball, Heimberg, & Gross, 2011)), and decreased self-efficacy when implementing cognitive reappraisal (Werner et al., 2011). Cognitive-behavioral models suggest that SAD (Heimberg, Brozovich, & Rapee, 2014) involves (a) distorted appraisals of social evaluation and (b) difficulty implementing adaptive emotion regulation strategies effectively in social situations.

Emotional reactivity in SAD

Studies of emotional reactivity in SAD highlight the importance of social-evaluative contexts that trigger exaggerated patterns of emotional reactivity and activate biases in attention (Schultz & Heimberg, 2008), self-focused beliefs (Blair et al., 2011), and interpretation (Amir, Prouvost, & Kuckertz, 2012). Experimental stimuli typically used to induce emotional reactivity in patients with SAD have primarily consisted of static displays of harsh faces (Goldin, Manber, Hakimi, Canli, & Gross, 2009), social criticism and praise statements (Blair et al., 2008), valenced words (Straube, Sauer, & Miltner, 2011) and negative self-beliefs (Goldin et al., 2013).

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Neuroimaging studies of emotional processing have shown that, compared to healthy controls, patients with SAD demonstrate greater activation of fear-related limbic regions (amygdala, insula, anterior cingulate cortex, parahippocampal gyrus), as well as prefrontal cortical regions (medial prefrontal cortex, orbitofrontal cortex, inferior frontal cortex), and posterior cortical regions (fusiform gyrus, posterior superior temporal gyrus) (Etkin & Wager, 2007). Most of these studies have used static stimuli to probe emotional processes. However, there is increasing interest in using potentially more powerful psychopathology-related, dynamic, ecological, and personally salient stimuli to probe emotional reactivity.

To date, three studies have used video stimuli to induce emotional reactivity in SAD patients. A positron emission tomography study (Van Ameringen et al., 2004) found *lesser* regional cerebral blood flow in right ventromedial frontal gyrus and right lingual gyrus in six male patients with SAD when viewing along with three confederates a video recording of themselves giving an impromptu speech (versus a socially competent stranger presenting). The results were interpreted to suggest lesser emotion regulation and greater diversion of attention away from anxiety-provoking visual stimuli. An fMRI study of 20 patients with SAD versus 20 matched healthy controls (Pujol et al., 2013) found that viewing six 30 s video recordings of themselves performing a verbal memory task along with a clinical psychologist evaluating their performance (versus viewing unknown others performing the same task) produced no between group differences. However, a less conservative uncorrected statistical threshold that revealed neural response *increases* in primary visual cortex and *decreases* in medial frontal cortex and anterior cingulate cortex in patients versus controls was interpreted to suggest visually induced emotional arousal with insufficient recruitment of cognitive control of negative emotion. A recent study (Ziv, Goldin, Jazaieri, Hahn, & Gross, 2013) of reactivity to videotaped social criticism in 67 adults with SAD and 28 healthy controls found greater whole-brain BOLD responses in left lingual gyrus, bilateral middle temporal gyrus and right parahippocampal gyrus, but no between group differences in *a priori* amygdala and anterior insula regions-of-interest. These three studies show no overlap in results, most likely due to different types of dynamic evaluative stimuli, neuroimaging methods, and data analytic approaches.

Emotion regulation in SAD

Among the variety of emotion regulation strategies that influence the magnitude or duration of emotions, reappraisal is considered one of the most effective strategies for actively modulating anxiety and promoting well-being (Gross, 1998). Reappraisal is a cognitive change strategy that uses cognitive-linguistic-attention processes in an integrated manner to inhibit automatic interpretations and reframe the meaning of an emotion-eliciting stimulus to up- or down-regulate emotional responses. Reappraisal has both immediate and longer-term beneficial effects on mental and physical health (Gross & Thompson, 2007). In SAD, there is evidence of overuse of maladaptive regulation strategies (e.g., avoidance, expressive suppression) and difficulties in implementing cognitive reappraisal (D'Avanzato, Joormann, Siemer, & Gotlib, 2013; Werner et al., 2011).

Neuroimaging studies have shown that, compared to healthy controls, patients with SAD have lesser activation of cognitive control (dorsolateral prefrontal (DLPFC), medial prefrontal cortex (MPFC)) (Buhle et al., 2013) and attention (medial precuneus, posterior cingulate, bilateral dorsal parietal cortex) (Fan, McCandliss, Fossella, Flombaum, & Posner, 2005) regions when reappraising social threat (harsh facial expressions) (Goldin, Manber, et al., 2009), as well as temporally delayed activation in MPFC, DLPFC, and ventrolateral prefrontal cortex (VLPFC), and less PFC-amygdala inverse functional connectivity (Goldin, Manber-Ball, Werner, Heimberg, & Gross, 2009). Deficits in reappraisal in patients with SAD may be specific to social threat and not physical threat (Goldin, Manber, et al., 2009). These brain patterns highlight problems with brain network recruitment, timing, and connectivity in the context of disorder-specific socio-emotional probes in SAD. Less is known, however, about whether and how clinical interventions modify these aberrant brain patterns in SAD.

Changes in reactivity and regulation during CBT for SAD

Cognitive-behavioral therapy (CBT) is the most effective psychosocial intervention for SAD (Gordon, Wong, & Heimberg, 2014), and CBT produces clinical improvements that are more enduring than those of pharmacotherapy (Canton, Scott, & Glue, 2012). Neuroimaging studies show that CBT modulates emotion processing brain networks (Clark & Beck, 2010; Porto et al., 2009). Using positron emission tomography, Furmark and colleagues (Furmark et al., 2002) were the first to demonstrate in 9 patients with SAD who responded to CBT or treatment with selective serotonin reuptake inhibitors (SSRIs) revealed post-treatment *reductions* in amygdala, hippocampus, and anterior/medial temporal lobe responses during a public speaking challenge. A functional magnetic resonance imaging (fMRI) study of 14 patients with SAD showed that CBT reduced elevated pre-treatment blood oxygen level dependent (BOLD) responses in right insula, medial orbitofrontal gyrus, and MPFC when reacting to angry (vs. happy) facial expressions in a forced-choice emotional face matching task relative to healthy controls (Klumpp, Fitzgerald, & Phan, 2013). In a companion to the present study using the same participants but a different fMRI experimental task (reappraising negative self-beliefs), we reported that CBT resulted in increased DLPFC and DMPFC activity, earlier temporal onset of DMPFC, and greater inverse functional connectivity between DMPFC and amygdala when reappraising patient-generated negative self-beliefs embedded in autobiographical social anxiety situations (Goldin et al., 2013). These studies provide initial evidence that CBT impacts brain responses related to *emotional reactivity* in limbic regions (amygdala, hippocampus, insula), *social cognition* (anterior temporal lobes, medial orbitofrontal gyrus, and MPFC), and *cognitive control* (DLPFC and DMPFC). These results suggest that CBT can modify the neural representations of affective, social, and cognitive processes that are important in SAD. The current study builds on these prior studies and extends our understanding by (a) using dynamic, ecological social evaluation videotaped stimuli (rather than static external faces or text) that have features that should more powerfully impact affective, social, and cognitive processes, (b) using a more conservative comparison of brain activity changes pre-to-post-CBT versus pre-to-post-waitlist control, (c) examining acute reactivity to both positive and negative social evaluation (rather than negative social cues only), (d) examining reappraisal to nomothetic (rather than idiographic) stimuli, and (e) directly testing whether pre-to-post treatment brain and self-rated emotional changes when reacting to and reappraising social evaluation predict CBT-related reductions in severity of social anxiety symptoms.

The present study

Our goals were to investigate the impact of CBT vs. a waitlist (WL) control group on self-reported negative emotion ratings and brain responses during reactivity to and reappraisal of dynamic social evaluation and examine whether pre-to-post-CBT changes in reactivity to and reappraisal of social evaluation would predict

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