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Elevated amygdala activity during reappraisal anticipation predicts anxiety in avoidant personality disorder

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Abstract

Background—Avoidant personality disorder is characterized by pervasive anxiety, fear of criticism, disapproval, and rejection, particularly in anticipation of exposure to social situations.

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An important but underexplored question concerns whether anxiety in avoidant patients is associated with an impaired ability to engage emotion regulatory strategies in anticipation of and during appraisal of negative social stimuli.

Methods—We examined the use of an adaptive emotion regulation strategy, cognitive reappraisal, in avoidant patients. In addition to assessing individual differences in state and trait anxiety levels, self-reported affect as well as measures of neural activity were compared between 17 avoidant patients and 21 healthy control participants both in anticipation of and during performance of a reappraisal task.

Results—Avoidant patients showed greater state and trait-related anxiety relative to healthy participants. In addition, relative to healthy participants, avoidant patients showed pronounced amygdala hyper-reactivity during reappraisal anticipation, and this hyper-reactivity effect was positively associated with increasing self-reported anxiety levels.

Limitations—Our finding of exaggerated amygdala activity during reappraisal anticipation could reflect anxiety about the impending need to reappraise, anxiety about the certainty of an upcoming negative image, or anxiety relating to anticipated scrutiny of task responses by the experimenters. While we believe that all of these possibilities are consistent with the phenomenology of avoidant personality disorder, future research may clarify this ambiguity.

Conclusions—These results suggest that amygdala reactivity in anticipation of receiving negative social information may represent a key component of the neural mechanisms underlying the heightened anxiety present in avoidant patients.

Introduction

Avoidant personality disorder seriously and chronically impairs interpersonal and occupational functioning and is among the most prevalent personality disorders (Skodol et al., 2002; Torgersen et al., 2001). It is characterized by a pervasive pattern of avoiding interpersonal contact because of fears of criticism, disapproval or rejection. This leads to serious limitations in the ability to function in occupational settings and severely circumscribed interpersonal relationships. In particular, the prospect and anticipation of exposure to social situations generates high levels of anxiety in individuals with avoidant personality disorder (Hummelen et al., 2007).

Although a considerable body of work has addressed the phenomenology of avoidant personality disorder (Sanislow et al., 2012), few studies have probed its underlying neurobiology and in particular the neural mechanisms associated with the anxiety response and those that serve to regulate emotion. To our knowledge, the only published functional neuroimaging study of avoidant patients was a study by our group which examined the neural correlates of an implicit emotion regulatory mechanism, habituation (Koenigsberg et al., 2014). We found that avoidant patients did not habituate to repeated negative image presentation and did not increase dorsal anterior cingulate cortex activity, associated with

cognitive control and reduced affective instability, to the level of healthy volunteers, providing preliminary evidence that avoidant patients show anomalous implicit emotion regulation.

Another adaptive and commonly employed emotion regulatory mechanism is cognitive reappraisal (Gross, 1998). Unlike habituation, cognitive reappraisal is a deliberate and voluntary mechanism. It entails cognitively reframing an emotional stimulus so as to change one's response to it. In the case of an aversive situation, reappraisal can be used to render it less disturbing (Gross, 1998). Two commonly employed reappraisal tactics are situational reinterpretation and psychological distancing (McRae et al., 2012; Ochsner and Gross, 2008). In the former, a narrative is created for the aversive situation that portrays it more positively (e.g. a scene depicting a sickly looking man lying in a hospital bed is rendered less disturbing by imagining that he is beginning to respond to a highly effective treatment). In the latter, the individual adopts a perspective that fosters experiencing the situation as remote from the self (e.g. the emergency room physician employing clinical detachment to function effectively in the presence of disturbing stimuli).

Cognitive reappraisal and its neural correlates have been studied extensively in healthy populations (Buhle et al., in press; Ochsner and Gross, 2008; Ochsner et al., 2012). This work has identified the regions consistently recruited by reappraisal (i.e. associated with emotion *regulation*), including those associated with selective attention and working memory (e.g. dorsal anterior cingulate cortex and dorsolateral prefrontal cortex), mental state attribution (e.g. medial prefrontal cortex), and response selection and inhibition (particularly ventrolateral prefrontal cortex) (Ochsner et al., 2012). This reappraisal-related activity has been shown to modulate the activity of subcortical appraisal regions (i.e. associated with emotion *reactivity*), most crucially the amygdala (Wager et al., 2008), which has been associated with detection of arousing and potentially threatening stimuli (Buhle et al., in press; LeDoux, 2000; Ochsner et al., 2012).

While no studies have examined the neural mechanisms of reappraisal anticipation or implementation in avoidant personality disorder, aberrant patterns of activity during reappraisal—particularly involving hyperactivity of the amygdala—have been noted in patients with other mood and anxiety disorders such as major depression (Johnstone et al., 2007), borderline personality disorder (Koenigsberg et al., 2009; Schulze et al., 2011), and social anxiety disorder (Goldin et al., 2009a; Goldin et al., 2009b; Klumpp et al., 2010; Marazziti et al., 2014) relative to healthy controls. Variable, though often substantial, comorbidity between social anxiety disorder (also known as generalized social phobia) and avoidant personality disorder has been reported (Reich, 2009), though avoidant personality disorder is thought to be the more serious of the two disorders in terms of functional impairment and symptom severity (Marques et al., 2012; Reich, 2009; Rettew, 2000; Sanislow et al., 2012). Importantly, in addition to during stimulus presentation, amygdala activity has been associated with anticipation of aversive events in social anxiety disorder patients (Boehme et al., in press; Lorberbaum et al., 2004) as well as in healthy participants (Herwig et al., 2007; Ueda et al., 2003), though the effects in social anxiety disorder patients have been shown to be significantly greater than those shown by healthy controls (Boehme et al., in press; Lorberbaum et al., 2004).

Avoidance of social situations, which is the hallmark of avoidant personality disorder, is predicated upon anticipatory anxiety (Hummelen et al., 2007). We therefore examined neural activity during the period when participants anticipated the reappraisal task, a situation in which they would expect their performance to be judged by the experimenters. Because the anxiety in avoidant personality disorder is associated with fears of public shame, disapproval and social rejection, it generalizes beyond previously used categories of stimuli such as fear of angry or contemptuous faces. We therefore sought to examine cognitive reappraisal in avoidant patients in response to images depicting an array of aversive interpersonal situations including loss, tragedy, and hostility. The neural correlates of anticipating reappraisal as well as reacting to and reappraising aversive social images were compared in avoidant patients and healthy participants using functional magnetic resonance imaging (fMRI). We predicted that avoidant patients would show exaggerated anxiety relative to healthy participants as measured by behavioral self-reports as well as elevated reactivity in the amygdala, particularly during anticipation of reappraisal.

Methods

Participants

23 avoidant and 24 healthy participants were recruited from outpatient clinics at the Mount Sinai Medical Center and the James J Peters VA Medical Center in New York City, as well as from newspaper and online advertisements. All participants provided written informed consent to participate after all procedures were fully explained according to the regulations of the Institutional Review Board at the Icahn School of Medicine at Mount Sinai. Six avoidant participants and 3 healthy participants were excluded for technical reasons (shown in supplement). Thus, the present results reflect data from 17 avoidant and 21 healthy participants. Sample characteristics are given in Table 1.

Screening and Sample Comorbidity

Participants in the avoidant group met DSM-IV criteria for avoidant personality disorder but not criteria for borderline or schizotypal personality disorder. Participants were excluded if they met DSM-IV criteria for past or present posttraumatic stress disorder, bipolar I disorder, schizoaffective disorder, substance dependence, organic mental syndromes, head trauma, central nervous system neurological disease, seizure disorder, substance abuse disorder in the previous 6 months, or current major depressive disorder. Participants with significant medical illness, contraindications to fMRI, pregnant women, and those with current suicidal ideation were excluded. Participants had to be free of psychotropic medications for 2 weeks (6 weeks for fluoxetine). Healthy participants did not meet DSM-IV criteria for any axis I or axis II disorder and met no other exclusion criteria as indicated above. Diagnostic assessments were made using the Structured Clinical Interview for DSM-IV–Patient Edition and the Structured Clinical Interview for DSM-IV Axis II Personality Disorders. As expected, there was a high comorbidity with social anxiety disorder in the avoidant sample. Seven avoidant participants met criteria for social anxiety disorder and 6 had specific social phobias. Prior axis I diagnoses included major depression in 3 participants, substance abuse in 2, panic disorder in 1 and eating disorder in 1 participant. Comorbid Axis II diagnoses in

the avoidant sample included 14 participants with obsessive compulsive personality disorder, 2 with paranoid personality disorder, and 1 with dependent personality disorder.

Materials

The materials and task procedure for this study are similar to those described in an earlier report examining the neural correlates of reappraisal in borderline personality disorder patients, who have also been shown to exhibit pronounced emotion dysregulation in response to social situations, relative to healthy participants (Koenigsberg et al., 2009).

Task stimuli consisted of 64 negative and 32 neutral images drawn from the International Affective Picture System (IAPS; Lang et al., 1993). Given the importance of dysregulated responses to social cues in the phenomenology of avoidant personality disorder, we used only social images that included at least one person for both negative and neutral image sets. Additional stimulus details are provided in the supplement.

Procedure

Questionnaires—Prior to the experimental task, participants completed the State-Trait Anxiety Inventory (STAI; Spielberger et al., 1983), containing sub-scales measuring the frequency with which participants report feeling anxious (state-related anxiety) as well the extent to which they report being anxious in general (trait-related anxiety). Participants were further rated by a clinician for depression using the Hamilton Depression Rating Scale (HAM-D). STAI-State scores were not available for 2 avoidant and 4 healthy participants. STAI-Trait scores were not available for 2 healthy participants. HAM-D scores were not available for 2 avoidant and 9 healthy participants.

Reappraisal task training—Participants performed an image-based reappraisal task similar to one used extensively in prior work (Koenigsberg et al., 2009; Ochsner and Gross, 2008; Ochsner et al., 2004; Wager et al., 2008). There were two task instructions: on Look trials (cued by the word "maintain") participants were instructed to simply look and respond naturally to the upcoming stimulus. On Reappraise trials (cued by the word "suppress"), participants were instructed to employ psychological distancing in order to view the upcoming stimulus as a detached, objective, impartial observer (Ochsner and Gross, 2008). Participants were trained to employ distancing according to established techniques used previously (Koenigsberg et al., 2009; Ochsner et al., 2004). Participants were specifically instructed not to look away from the image or close their eyes during the entire time that the image was displayed. Once participants demonstrated mastery of the instructions, they completed 20 practice trials using example stimuli.

Reappraisal task—Each reappraisal task trial began with an auditory cue instruction (either "maintain" or "suppress"), followed by a jittered interval, a negative or neutral image presentation, subjective ratings of affect and detachment, and finally a jittered relaxation period prior to the onset of the next trial. This reappraisal task trial structure is shown in more detail in Figure 1.

The reappraisal task incorporated three different trial types during task implementation: "Look Neutral" (i.e. the "maintain" instruction paired with a neutral image), "Look Negative" (i.e. the "maintain" instruction paired with a negative image), and "Reappraise Negative" (i.e. the "suppress" instruction paired with a negative image). Ninety-six total trials were presented (i.e. 32 trials per trial type), divided into 4 functional runs of 24 trials each. Negative images were divided into two sets and counterbalanced across participants according to instruction (Look or Reappraise), with mean normative valence ratings of 2.3 and 2.4 and mean normative arousal ratings of 6.1 and 5.7 for each set, respectively, with no significant valence or arousal differences between negative image sets. Trials were presented in one of two pseudorandomized orders counterbalanced across participants, with 8 trials presented per trial type per run.

Image Acquisition and Analysis—fMRI data were acquired using a Siemens 3.0 T Allegra scanner (Siemens Medical Solutions USA, Malvern, PA) and parameters described previously (Koenigsberg et al., 2009). Acquisition and preprocessing parameters are described in the supplement.

General linear modeling (GLM) for each participant was carried out using Neuroelf software (neuroelf.net) by convolving task event vectors (defined below) with the canonical hemodynamic response function. Six vectors were specified in the GLM: two task anticipation vectors corresponding to the two unique instruction types (Look Cue and Reappraise Cue); three task implementation vectors during image presentation (Look Neutral, Look Negative, Reappraise Negative); and a combined rating vector modeling the 9 s presentation of the affect and detachment rating periods that was undifferentiated by trial type. Participants' six motion parameters were also included in the GLM. Data were high-pass filtered (cut-off = 130 s), and participant time courses underwent percent signal change transformation.

Contrast images for all participants were entered into random-effects between-subjects analyses using Neuroelf software. Three contrasts were of primary interest: Reappraise Cue > Look Cue (i.e. regions involved in *anticipating* reappraisal), Look Negative > Look Neutral (i.e. regions involved in emotion *reactivity*) and Reappraise Negative > Look Negative (i.e. regions involved in emotion *regulation*). Whole-brain family-wise error (FWE) multiple comparison correction thresholds were determined using Alphasim (Ward, 2000). For whole-brain analyses thresholds were p<0.01, uncorrected, and an extent threshold of 53 voxels (3mm isotropic), resulting in FWE correction at p<0.05. Amygdala results were masked using a bilateral Brodmann atlas-based anatomical boundary, and small volume-corrected FWE extent thresholds were determined via Alphasim. Anatomical labels were determined using an International Consortium for Brain Mapping (ICBM) to Talairach coordinate conversion (icbm2tal.m) and the Talairach atlas (Talairach and Tournoux, 1988). Reported coordinates are in MNI space. Behavioral data and extracted data from neural regions-of-interest (ROI's) were analyzed using linear mixed models incorporating fixed effects estimates for group (avoidant and healthy), condition (Look and Reappraise during anticipation; Look Neutral, Look Negative, and Reappraise Negative during image presentation), and their interaction, and a random effect consisting of an intercept for each participant.

Results

Self-reported Anxiety Scores and Sample Characteristics

Relative to healthy participants, avoidant patients reported more state as well as trait anxiety as measured by the STAI (see Table 1). State and trait anxiety scores were highly positively correlated in both groups (avoidant group: $r = 0.68$, p<0.01, two-tailed; healthy group: $r = 0.69$, p<0.01, two-tailed). HAM-D scores were comparable for both groups and indicated an absence of clinically significant depression.

Self-reported Affect Ratings

Self reports of affect made during the reappraisal task indicated a large main effect of condition, $F(2,72)=175.11$, p<0.01, with both groups showing a similar pattern of responses typical of successful reappraisal of negative images, with greater positive (i.e. less negative) affect reported during Reappraise trials relative to Look trials (Figure 2). There was no significant main effect of group nor a group-by-condition interaction. Planned simple comparisons confirmed our a priori hypothesis of significant reappraisal success (i.e. Reappraise Negative > Look Negative) in the healthy group (t(20)=4.60, p<0.01, two-tailed, d=1.00), but only a marginal effect in avoidant patients (t(16)=2.06, p=0.06, two-tailed, d=0.50). Subjective detachment ratings also did not show a significant main effect of group nor a group-by-condition interaction.

We also separately examined the subset of avoidant patients who were not comorbid for social anxiety disorder and found no significant difference in behavioral performance of this group compared to the comorbid sample, suggesting that avoidant patient responses were not accounted for by the social anxiety disorder comorbid subgroup.

Imaging Findings

Anticipation Period

Reappraisal Anticipation (Reappraise Cue > Look Cue): For the Reappraise Cue relative to the Look Cue, avoidant patients showed significantly greater activity in bilateral amygdala compared to healthy participants (left amygdala: 29 voxels, p<0.05, two-tailed, peak at [−21, −6, −15], FWE small volume-corrected, p<0.05; right amygdala: 68 voxels, p<0.05, two-tailed, peak at [24, −3, −18], FWE small volume-corrected, p<0.05; Figure 3A). We further found that left amygdala activity in anticipation of reappraisal was significantly correlated with state anxiety in avoidant patients (but not in healthy controls) in the independently-defined ROI indicated in Figure 3A–B (Figure 3C; $r = 0.70$, p<0.01, two-tailed).

Beyond our *a priori* interest in amygdala, we investigated whole-brain group differences in anticipatory activity (Reappraise Cue > Look Cue) and found only one whole-brain corrected result (p<0.01, k=53 voxels, FWE-corrected, p<0.05) in left lingual gyrus, where avoidant patients showed greater recruitment during reappraisal anticipation relative to healthy participants (133 voxels, peak at [−15, −90, −3]). Whole-brain montages for this contrast (Reappraise Cue > Look Cue) for each group separately are shown in Figure S1 and Table S1.

Image Presentation Period

<u>**Reactivity (Look Negative > Look Neutral):**</u> *A priori* analyses indicated that avoidant patients also exhibited hyper-reactivity of a region of right amygdala relative to healthy participants during image presentation at a liberalized threshold (17 voxels, p<0.05, one-tailed, peak at [15, −9, −21], FWE small volume-corrected for right amygdala, p<0.05, Figure S2). Given the liberalized threshold, these results should be interpreted with caution as preliminary evidence for hyper-reactivity during image presentation in avoidant patients. As shown in Figure S2, this effect is driven by an exaggerated right amygdala response on the Look Negative trial type in avoidant patients. Additionally, we found that this right amygdala reactivity (Look Negative > Look Neutral) was significantly correlated with increasing trait anxiety in avoidant patients (but not in healthy controls) in this independently-defined region-of-interest (ROI) indicated in Figure S2A (Figure S2C; $r =$ 0.52, p<0.05, two-tailed).

Whole-brain analyses indicated that avoidant and healthy participants showed comparable patterns of reactivity overall (Figure S3 and Table S2; p<0.01, k=53 voxels, FWE-corrected, p<0.05). No whole-brain corrected regions of reactivity group difference emerged (p<0.01, k=53 voxels).

<u>**Regulation (Reappraise Negative > Look Negative):**</u> Avoidant and healthy participants engaged similar brain regions during reappraisal of negative images, including common recruitment of medial, dorsolateral and ventrolateral prefrontal cortex as well as dorsal anterior cingulate cortex (Figure S4 and Table S3; p<0.01, k=53 voxels, FWE-corrected, p<0.05). Again, no whole-brain corrected group differences emerged (p<0.01, k=53 voxels), and amygdala attenuation during reappraisal was comparable across groups.

Discussion

Here, in the first examination of the neural mechanisms underlying cognitive reappraisal in avoidant personality disorder, we found that, while showing broad similarities to healthy participants in the behavioral and neural mechanisms recruited during reappraisal of negative social images, avoidant patients showed heightened reactivity in the amygdala, a brain region particularly associated with negative emotional appraisal (LeDoux, 2000; Ochsner et al., 2012), particularly during anticipation of reappraising negative images. In addition, as expected, avoidant patients showed heightened self-reports of state and trait anxiety overall relative to healthy participants, and these reports were highly positively correlated across participants. Critically, in avoidant patients, the magnitude of amygdala hyper-reactivity during anticipation of reappraisal was shown to predict the extent of heightened reports of anxiety. The present results shed light on the neural mechanisms underlying the psychopathology of avoidant personality disorder, an important but underexamined personality disorder associated with pronounced fear and anxiety relating to anticipation of social rejection.

During reappraisal anticipation, avoidant patients showed pronounced hyper-reactivity in the bilateral amygdala in a manner consistent with prior work assessing the neural correlates of anticipatory anxiety in social anxiety disorder patients (Boehme et al., in press; Lorberbaum

et al., 2004). Indeed, avoidant personality disorder has much in common with social anxiety disorder, a condition characterized by a marked and intense fear of social settings in which the individual is exposed to possible scrutiny by others (American Psychiatric Association, 2013). The fear and avoidance of social situations predominates as a defining feature of social anxiety disorder, while the avoidant personality disorder construct emphasizes fear of social criticism, disapproval, and rejection as motivators for the social avoidance. Nevertheless, high comorbidities (ranging from 22% to 89%) have been reported for these disorders (Reich, 2009). While overlap in diagnostic criteria may account for some comorbidity between these diagnoses, there remains debate about whether the two disorders are distinct (Lampe and Sunderland, 2013; Sanislow et al., 2012). Some have argued that the two disorders lie on a continuum with no discrete dividing line (Chambless et al., 2008; Reich, 2009; Rettew, 2000; Sanislow et al., 2012) and others have suggested that they are distinct, but share common predisposing factors (Tillfors and Ekselius, 2009). We have further provided evidence that the magnitude of this hyper-responsivity in amygdala activity in avoidant patients during anticipation of reappraisal predicts the magnitude of self-reported anxiety, suggesting that such anticipatory amygdala reactivity may form a central element of the neurobiological basis of the exaggerated anxiety that is symptomatic of avoidant personality disorder.

While we did find robust behavioral differences between avoidant and healthy participants in terms of self-reported anxiety, we did not find evidence of task differences in self-reported reappraisal efficacy across groups. While these results are the first reports of reappraisal performance in avoidant patients, they are consistent with prior findings on reappraisal in social anxiety disorder patients (Goldin et al., 2009a; Goldin et al., 2009b). As in those studies, we found that there was no significant group-by-condition interaction in behavioral reappraisal self-reports between patients and healthy controls. Further, we found that avoidant patients are broadly similar to healthy participants in terms of neural response profiles during reappraisal. In particular, we found no group differences in the activity of prefrontal areas typical of reappraisal implementation during reappraisal of aversive social scenes. This is consistent with prior work in social anxiety disorder (Goldin et al., 2009a), where prefrontal activity between social anxiety disorder patients and healthy participants was similar during reappraisal of violent scenes, with the exception of one dorsal prefrontal region (Brodmann area 9) where social anxiety disorder patients showed increased activity relative to controls.

In considering our finding of exaggerated amygdala activity during reappraisal anticipation, it is important to point out that this anticipatory activity could reflect anxiety about the impending need to reappraise; anxiety about the certainty of an upcoming negative image (given our design, based on a widely-used reappraisal task, where there is no "regulate neutral" condition due to its incongruity, the reappraise cue predicts that a negative picture will follow, whereas the look cue predicts either a neutral or negative picture); anxiety related to anticipated scrutiny by the experimenters of reappraisal task performance; or a combination of them. While we believe that all of these possibilities are consistent with the phenomenology of avoidant personality disorder, future work may continue to probe the nature of this anticipatory activity.

The heightened amygdala activity in avoidant patients during and in anticipation of a reappraisal task involving negative social stimuli suggests that pharmacologic and behavioral interventions which down-regulate the amygdala in anticipatory social contexts may play an important role in the treatment of avoidant personality disorder. These interventions may involve existing therapies that have been shown to be beneficial in mood and personality disorders (e.g. cognitive-behavioral therapy), as has also been shown to improve behavioral and neural outcomes in social anxiety disorder (Goldin et al., 2013). The finding of little difference behaviorally or neurally between avoidant and healthy participants during cognitive reappraisal suggests that training in reappraisal skills may be less relevant in the treatment of avoidant personality disorder than in disorders such as depression (Johnstone et al., 2007) and borderline personality disorder (Koenigsberg et al., 2009; Schulze et al., 2011), where reappraisal is impaired. Additionally, the present work should be extended to directly compare samples of avoidant personality disorder and social anxiety disorder patients, exclusive of subjects comorbid for both, in order to help clarify whether these disorders are truly distinct.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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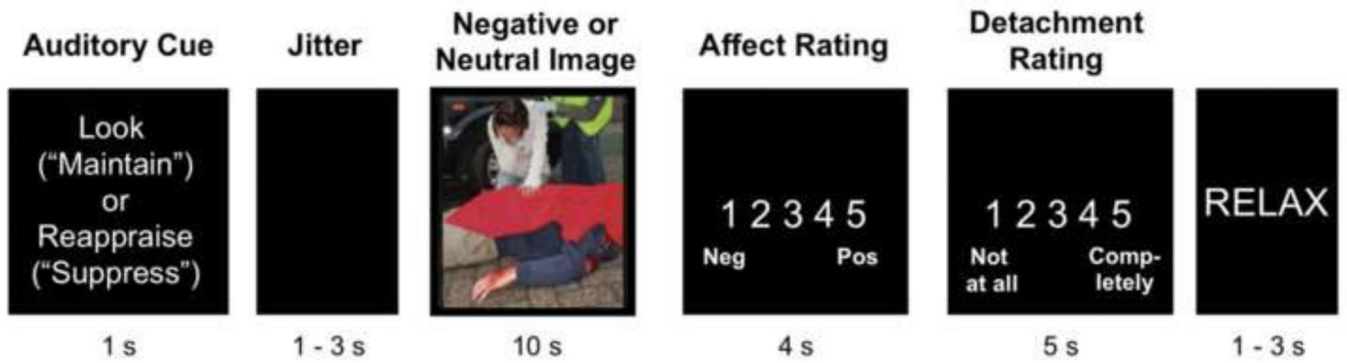
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Figure 1.
Trial structure. Each trial began with an auditory cue instruction (1 s duration) during which participants anticipated the upcoming trial. This was followed by a jittered interval of either 1 or 3 s. Next, a negative or neutral image was presented for 10 s, during which time the appropriate strategy (Look or Reappraise) was to be implemented. Afterward, participants rated their current affect on a scale of 1 to 5, with 1 being most negative and 5 being most positive, during a 4 s rating period. Then, in a subsequent 5 s rating period, participants indicated to what degree they had subjectively detached, using a 1 (not at all) to 5 (completely) scale. Finally, participants saw the instruction to relax prior to the onset of the next trial during a jittered 1–3 s intertrial interval.
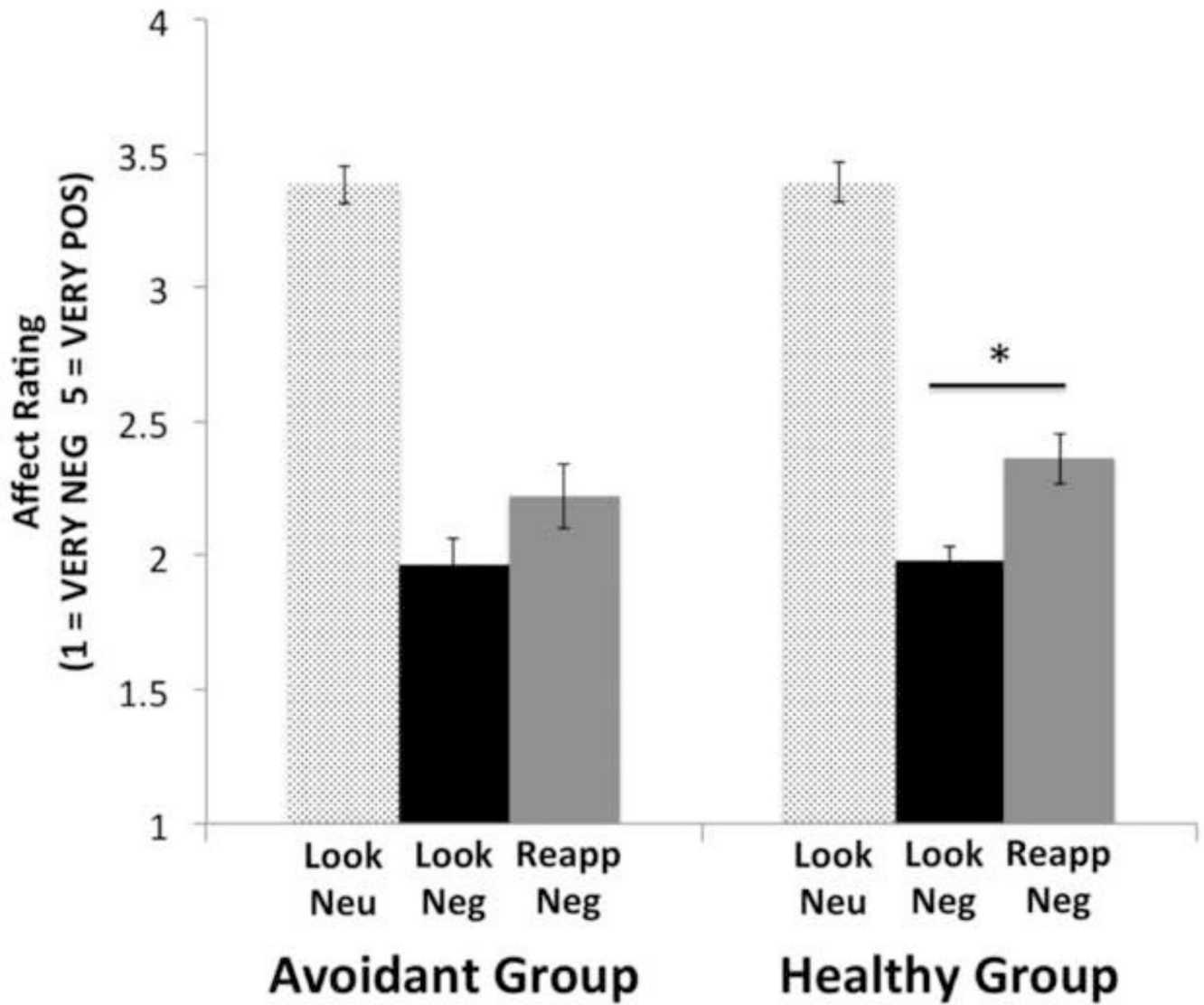
Figure 2.
Self-reported affect ratings made following image presentation. * represents a significant within-group difference, p<0.05, two-tailed.
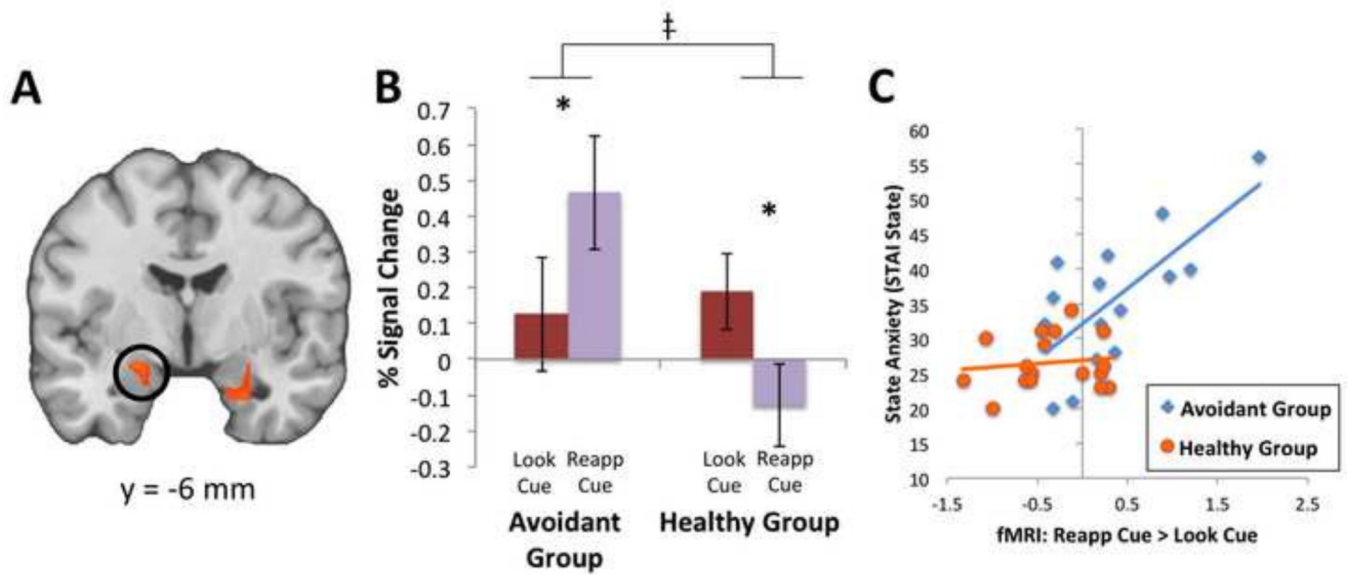
Figure 3.
Hyper-reactivity in amygdala in avoidant patients during reappraisal anticipation. (A) Left amygdala ROI (shown within circle). (B) Extracted beta weights for each condition during the anticipation period for the ROI shown in (A). (C) Correlation between reappraisal anticipation activity (Reappraise Cue > Look Cue) and state anxiety scores for each group for the ROI shown in (A). ‡ reflects a significant group-by-condition interaction, $F(1,36)=13.00$, $p<0.01$. Main effects of group and condition were not significant. * represents a significant within-group difference, $p<0.05$, two-tailed.

Table 1

Sample Characteristics

	Avoidant Group	Healthy Group	Avoidant Group versus Healthy Group
N	17	21	
Mean Age	29.59 (7.16)	29.00 (6.71)	$t(36) = 0.26$, n.s.
Gender (F/M)	8/9	11/10	$x^2 = 0.74$, n.s.
STAI State	35.60 (9.61)	26.53 (3.78)	$t(30) = 3.22^{**}$, $d=1.18$
STAI Trait	39.35 (8.45)	28.74 (5.68)	$t(34) = 4.25^{**}$, $d=1.46$
HAM-D	4.20 (3.03)	2.08 (3.63)	$t(25) = 1.61$, n.s.

[*] $p < 0.05$, two-tailed

[**] $p < 0.001$, two-tailed

Standard deviations are given in parentheses.