Neural Correlates of the Use of Psychological Distancing to Regulate Responses to Negative Social Cues: A Study of Patients with Borderline Personality Disorder

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Background: Emotional instability is a defining feature of borderline personality disorder (BPD); yet, little is understood about its underlying neural correlates. One possible contributing factor to emotional instability is a failure to adequately employ adaptive cognitive regulatory strategies such as psychological distancing.

Methods: To determine whether there are differences in neural dynamics underlying this control strategy between BPD patients and healthy control (HC) subjects, blood oxygenation level-dependent (BOLD) functional magnetic resonance imaging signals were acquired as 18 BPD and 16 HC subjects distanced from or simply looked at pictures depicting social interactions. Contrasts in signal between distance and look conditions were compared between groups.

Results: Borderline personality disorder patients showed a different pattern of activation compared with HC subjects when looking at negative versus neutral pictures. When distancing versus looking at negative pictures, both groups showed decreased negative affect ratings and increased activation of the dorsolateral prefrontal cortex, areas near/along the intraparietal sulcus (IPS), ventrolateral prefrontal cortex, and posterior cingulate/precuneus regions. However, the BPD group showed less BOLD signal change in dorsal anterior cingulate cortex and IPS, less deactivation in the amygdala, and greater activation in the superior temporal sulcus and superior frontal gyrus.

Conclusions: Borderline personality disorder and HC subjects display different neural dynamics while passively viewing social emotional stimuli. In addition, BPD patients do not engage the cognitive control regions to the extent that HCs do when employing a distancing strategy to regulate emotional reactions, which may be a factor contributing to the affective instability of BPD.

Key Words: Cognitive reappraisal, emotion, emotion regulation, fMRI, psychological distancing, social cognitive neuroscience
(the distance reappraisal condition). Motivated by prior work, we hypothesized that BPD patients might exhibit abnormal activation in prefrontal, anterior cingulate, temporal, and parietal regions previously implicated in reappraisal in general and distancing in particular, in combination with a relative failure to decrease amygdala activation.

Methods and Materials

Subjects

Subjects were 18 BPD patients (mean age 32.6 ± 10.4 years; 10 female patients) and 16 HC volunteers (mean age 31.8 ± 7.7 years; 9 female volunteers) recruited from outpatient clinics at the Mount Sinai Medical Center and the James J. Peters Veterans Affairs (VA) Medical Center in New York City and advertisements in local newspapers and local postings. Borderline personality disorder subjects met DSM-IV criteria for BPD and had prominent affective instability as indicated by the presence of three of four DSM-IV criteria associated with affective instability, i.e., 1) affective instability due to a marked reactivity of mood, 2) chronic feelings of emptiness, 3) unstable and intense interpersonal relationships, and 4) identity disturbance.

Exclusion criteria applied to the BPD group were present or past bipolar I disorder, schizophrenia, schizoaffective disorder, substance dependence, organic mental syndromes, or substance abuse disorder within the previous 6 months. Healthy control subjects were excluded if they met criteria for any current or past DSM-IV Axis I or Axis II disorder or had first-degree relatives with an Axis I disorder. Histories of significant head trauma, central nervous system (CNS) neurological disease, or significant medical illness were exclusion criteria for all subjects. Subjects were free of psychotropic medication for at least 2 weeks (6 weeks in the case of fluoxetine) before the scan. Subjects with any free of psychotropic medication for at least 2 weeks (6 weeks illness were exclusion criteria for all subjects. Subjects were excluded if they met criteria for any current or past abuse disorder within the previous 6 months. Healthy control subjects were excluded if they met criteria for any current or past Axis II comorbidity was present, as is typical in BPD samples (Table S1 in Supplement 1).

Diagnostic assessment was obtained using the Structured Clinical Interview for DSM-IV Axis I Disorders-Patient Edition (SCID-I/P) for Axis I (40) and the Structured Interview for DSM-IV Personality (SIDP-IV) for Axis II diagnoses (41). In previous studies, we have documented an interrater reliability kappa = .81 for diagnosing BPD (42).

Affective instability was assessed with the Affective Lability Scale (ALS) (43), a self-report instrument shown to correlate with clinician-rated affective instability in patients with BPD (42). Depression was rated with the 21-item Hamilton Depression Rating Scale (HAM-D) (44), state and trait anxiety with the Spielberger State Trait Anxiety Inventory (STAI) (45), impulsivity with the Barratt Impulsiveness Scale-II (BIS-II) (46), anger with the Spielberger State Trait Anger Expression Inventory (STAXI) (47), and handedness with the Edinburgh Handedness Inventory.

Subject Characteristics

The BPD and HC groups did not differ in age, sex, or handedness (Table 1). As expected, the BPD patients scored higher (Table 1) in depression (HAM-D), affective lability (ALS), impulsiveness (BIS-II), and state and trait anger (STAXI). They scored lower in state anxiety (STAI-State) and did not differ in trait anxiety (STAI-Trait). None of the BPD patients met criteria for current major depressive disorder, two had generalized anxiety disorder, and two met criteria for current posttraumatic stress disorder (PTSD). As is typical of clinical samples of BPD patients, a history of depression or anxiety disorders was common, with 12 patients reporting prior major depression. One patient had past panic disorder, two had past generalized anxiety disorder, seven had past PTSD, and two had a past eating disorder. Axis II comorbidity was present, as is typical in BPD samples (Table S1 in Supplement 1).

Materials

Stimuli for the reappraisal task were pictures depicting aversive (negative) and neutral interpersonal situations from the International Affective Picture System (IAPS) (48). Since BPD patients are particularly emotionally responsive to interpersonal cues (2) and social and nonsocial emotions are processed differently in the brain (49–52), we chose to restrict our stimuli to social cues, specifically excluding nonsocial IAPS pictures that have been intermixed with social stimuli in prior reappraisal studies. Selected negative interpersonal scenes included pictures of people in situations depicting loss or grief, abuse, or physical threat. Neutral images depicted persons engaged in work or hobbies or attending public events. For the two instructional conditions described below, we selected two sets of negative images that were matched for valence [mean valence norm ratings 2.3 and 2.4, respectively, where 1 = most negative and 9 = most positive; t(45) = .95, ms] and two sets of neutral images also matched for valence [mean ratings 5.2 in each set; t(47) = .49, ns]. Images were also matched for arousal rating between conditions. Negative images were more arousing than neutral images [mean scores 6.1 and 5.7, respectively, for negative images, t(45) = 1.30, ns; and 3.8 and 3.5 for neutral images, t(47) = 1.22, ns, where 1 = least arousing and 9 = most arousing].

Experimental Design

Task Design.

The task consisted of 96 trials divided into 4 blocks of 24 trials each. The trial structure and timings are presented in Figure 1. In each block, the order of trials (negative-distance, negative-look, neutral-distance, neutral-look) was pseudo-random and this order was used for all subjects.

Training Procedures.

Training of the subjects in the reappraisal by distancing technique included initial instruction followed by practice as the investigator observed and shaped their technique, following the method of Ochsner et al. (14). Participants were specifically instructed not to look away from the images or to close their eyes. Once they had mastered the technique to the satisfaction of the investigator, they practiced it on a laptop computer for 20 trials, using the same protocol and
timings that would be used during the scan but different IAPS pictures. They were instructed to apply the distancing technique in response to the auditory instruction “suppress” and to look while responding naturally and not diminishing their emotional reaction when they heard a “maintain” instruction.

Image Acquisition and Analysis

As subjects performed the reappraisal task (Figure 1), blood oxygenation level-dependent (BOLD) images were obtained using a Siemens 3.0 T Allegra scanner (Siemens Medical Solutions USA, Malvern, Pennsylvania) with a gradient-echo echoplanar imaging (GE-EPI) sequence using the following protocol: 42 axial slices, 2.5 mm thick, skip = .825 mm, repetition time (TR) = 3 sec, echo time (TE) = 27 msec, flip angle = 84°, field of view (FOV) = 210 mm, matrix = 64 × 64. For anatomical localization, a high-resolution T2-weighted anatomical scan was acquired on an axial plane parallel to anterior commissure-posterior commissure (AC-PC) line with a turbo spin-echo pulse sequence.

Preprocessing and statistical analyses were carried out using SPM2 (Wellcome Department of Cognitive Neurology, London, England) standard workflow: motion correction of echo-planar images (EPIs) with realignment, co-registration of EPIs onto corresponding subjects’ high-resolution T2 scan, normalization to a standard template (Montreal Neurological Institute), and spatial smoothing with a Gaussian kernel (full-width at half maximum [FWHM] = 8 mm). General linear modeling (GLM) for each participant used the default statistical parametric mapping (SPM) basis function convolved with regressors of interest (53).

The linear combination of seven regressors was used to model the hemodynamic response (instruction cue: look or distance, as an event, picture viewing: negative-look, negative-distance, neutral-look, neutral-distance, as epochs; valence rating, as an event). Contrast images for all participants were entered into second-level random-effects group conjunction and contrast analyses as implemented in SPM2. The voxel level significance set to $p < .01$ and the minimum cluster extent threshold was set to $k = 85$ to correct for multiple comparisons to reach a corrected $p < .05$ as decided by a Monte Carlo simulation. Anatomical regions were identified using the anatomical automatic labeling algorithm (54). A conjunction analysis was carried out using the method of Friston et al. (55), which tests the global null using the minimum $t$ statistic with a global false-positive rate of $.01$ for the height threshold. This conjunction analysis makes the inference that the consistent effects are significant but not that the significant effects are consistent (55).

Results

Behavioral Results

In postscan debriefing, subjects reported that they implemented the distancing strategy as instructed and did not close their eyes or look away from the images during either the distancing or look conditions. Self-report affect ratings during the scan (Figure 2) demonstrated an overall image type (negative vs. neutral) × instruction (look vs. distance) interaction, as well as
main effects for image type and instruction. Interactions with diagnosis were not significant (for statistical test results, see Figure 2). There was no main effect of diagnosis. Planned comparisons revealed that for negative pictures BPD and HC subjects reported less negative affect (i.e., higher scores) following distancing as compared with looking [BPD: look \( t(14) = 1.99, p < .01 \); HC: look \( t(14) = 1.82, \) distance \( t(14) = 2.59, p < .01 \)]. For neutral pictures, affect ratings were close to the neutral value of 3.0 in both the look and distance conditions, although they were slightly higher in the look condition [BPD: look \( t(14) = 3.60, p < .01 \); HC: look \( t(14) = 5.73, p < .01 \)]. For neutral pictures, affect ratings were close to the neutral value of 3.0 in both the look and distance conditions, although they were slightly higher in the look condition [BPD: look \( t(14) = 3.60, p < .01 \); HC: look \( t(14) = 5.73, p < .01 \)].

We examined the variance in valence ratings, averaging over groups the within-subject variance for each image type and reappraisal condition, as an index of affective instability. There was a significant main effect of group with the BPD patients showing a greater variance in valence rating (BPD: \( \text{SS} = 53 \pm .42 \text{ vs. HC: } \text{SS} = .36 \pm .28 \)) and a main effect of condition in which there was less variance in the distance compared with look conditions (Figure 2). There was no main effect of image type and no group by condition by image type, group by image type, or group by condition interactions (for statistical tests, see Figure 2). Post hoc tests showed that when distancing from negative pictures BPD patients showed greater right superior temporal, middle and posterior cingulate cortex (DLPFC), right and left lateral and ventrolateral prefrontal cortex (right and left middle and superior frontal gyri [Brodmann area (BA) 10, 8]), extensive regions bordering the intraparietal sulci (IPS) bilaterally, right posterior cingulate cortex (PCC) extending into the precuneus, right parahippocampal gyrus, right insula, and the left superior temporal gyrus. In the look > distance contrast, both groups showed extensive activation in the cuneus, left inferior parietal lobule, and activation of the right postcentral gyrus and left supplementary motor area (Figure 3, Table 3).

**Differentially Activated Regions.** To identify differences in patterns of neural activation between BPD patients and HC subjects when viewing negative pictures in the distancing versus looking contrast, we constructed SPM interaction maps of the double differences in BOLD activation: BPD (distance − look) − HC (distance − look) and the reverse (Figures 4, 5, and 6; Table 4). The graphs in Figures 4, 5, and 6 depict the change in activation from baseline (beta weights) to the look or distance conditions for the volumes of interest.

**Imaging Results**

We first compared the activation between groups in the look condition when viewing negative compared with neutral pictures. The BPD patients showed greater right superior temporal, anterior, and posterior cingulate and left cerebellar activation than the HC subjects, while the HC subjects showed greater activation in the fusiform gyrus and prefrontal regions (Table 2).

**Table 2. Activation Foci that Differed Between the Groups When Looking at Negative Versus Neutral IAPS Pictures**

<table>
<thead>
<tr>
<th>Region</th>
<th>k</th>
<th>x</th>
<th>y</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy Control Subjects &gt; Borderline Patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R fusiform (BA 18)</td>
<td>96</td>
<td>26</td>
<td>−80</td>
<td>−2</td>
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<tr>
<td>L lingual gyrus (BA 19)</td>
<td>105</td>
<td>−26</td>
<td>−64</td>
<td>−8</td>
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<tr>
<td>L inferior temporal gyrus (BA 20)</td>
<td>114</td>
<td>−58</td>
<td>−24</td>
<td>−16</td>
</tr>
<tr>
<td>R fusiform (BA 20)</td>
<td>121</td>
<td>40</td>
<td>−16</td>
<td>−22</td>
</tr>
<tr>
<td>L frontal inferior gyrus (BA 45)</td>
<td>159</td>
<td>−50</td>
<td>28</td>
<td>16</td>
</tr>
<tr>
<td>R superior medial frontal gyrus (BA 9)</td>
<td>281</td>
<td>10</td>
<td>44</td>
<td>36</td>
</tr>
<tr>
<td>L superior frontal gyrus (BA 9)</td>
<td>92</td>
<td>−18</td>
<td>54</td>
<td>28</td>
</tr>
<tr>
<td>Borderline Patients &gt; Healthy Control Subjects</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L cerebellum</td>
<td>106</td>
<td>−4</td>
<td>−68</td>
<td>−18</td>
</tr>
<tr>
<td>R superior temporal gyrus (BA 48)</td>
<td>208</td>
<td>56</td>
<td>−34</td>
<td>22</td>
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<tr>
<td>Posterior cingulate (BA 23)</td>
<td>1679</td>
<td>4</td>
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<td>46</td>
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<tr>
<td>Anterior cingulate (BA 32)</td>
<td>439</td>
<td>0</td>
<td>8</td>
<td>46</td>
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</table>

Notes: k = cluster size in \( 2 \times 2 \text{ mm} \times 2 \text{ mm voxels}, p < .01 \), minimum cluster size, \( k = 85 \).

Table S3 in Supplement 1 showed that when distancing from negative pictures BPD patients showed greater right superior temporal, middle and posterior cingulate cortex (DLPFC), right and left lateral and ventrolateral prefrontal cortex (right and left middle and superior frontal gyri [Brodmann area (BA) 10, 8]), extensive regions bordering the intraparietal sulci (IPS) bilaterally, right posterior cingulate cortex (PCC) extending into the precuneus, right parahippocampal gyrus, right insula, and the left superior temporal gyrus. In the look > distance contrast, both groups showed extensive activation in the cuneus, left inferior parietal lobule, and activation of the right postcentral gyrus and left supplementary motor area (Figure 3, Table 3).

**Imaging Results**

We first compared the activation between groups in the look condition when viewing negative compared with neutral pictures. The BPD patients showed greater right superior temporal, anterior, and posterior cingulate and left cerebellar activation than the HC subjects, while the HC subjects showed greater activation in the fusiform gyrus and prefrontal regions (Table 2). Imaging findings for the negative pictures are the focus of this article because our hypotheses address differences in the neural dynamics of BPD and HC subjects when attempting to down-regulate negative emotion.1 For each group separately, we identified regions that were activated when viewing negative pictures in the distance > look and look > distance contrasts (Table S3 in Supplement 1). We then compared and contrasted the two groups to identify regions that were commonly or differentially activated by BPD and HC subjects when distancing versus looking.

**Commonly Activated Regions.** The conjunction analysis revealed that for the distance > look contrast both BPD patients and HC subjects together engaged the dorsolateral prefrontal cortex (DLPFC), right and left lateral and ventrolateral prefrontal cortex (right and left middle and superior frontal gyri [Brodmann area (BA) 10, 8]), extensive regions bordering the intraparietal sulci (IPS) bilaterally, right posterior cingulate cortex (PCC) extending into the precuneus, right parahippocampal gyrus, right insula, and the left superior temporal gyrus. In the look > distance contrast, both groups showed extensive activation in the cuneus, left inferior parietal lobule, and activation of the right postcentral gyrus and left supplementary motor area (Figure 3, Table 3).

**Differentially Activated Regions.** To identify differences in patterns of neural activation between BPD patients and HC subjects when viewing negative pictures in the distancing versus looking contrast, we constructed SPM interaction maps of the double differences in BOLD activation: BPD (distance − look) − HC (distance − look) and the reverse (Figures 4, 5, and 6; Table 4). The graphs in Figures 4, 5, and 6 depict the change in activation from baseline (beta weights) to the look or distance conditions for the volumes of interest.

For the distancing minus looking contrast, HC subjects demonstrated greater activation than BPD patients in the dorsal anterior cingulate cortex (dACC) (BA 32), bilateral IPS region, right middle occipital gyrus, and right fusiform gyrus. To separate the effects of group and instruction condition upon activation in the dACC and IPS—two regions related to control—we examined the regression weights (betas) quantifying signal change for each group in each condition over all voxels in a 6-mm radius sphere centered on the local maximum for the above contrast in each region. In both dACC and IPS, HC subjects activated more strongly (relative to baseline) in the distance condition compared with the look condition, while the BPD patients showed less activation (Figure 4A and 4B). For these volumes of interest, the

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1For completeness, we have provided in Table S2 in Supplement 1 activation foci contrasting BPD and HC subjects when attempting to distance from neutral pictures, showing greater engagement of the insula and superior/middle frontal gyri bilaterally in BPD compared with HC subjects.
Borderline personality disorder subjects showed greater distancing versus look activation than the HC subjects in various regions, including the superior temporal sulcus (STS), right superior frontal gyrus (BA 8), and right amygdala (Figure 5, Table 4). The extracted beta weights for the volume of interest (Figure 5) indicate that relative to baseline HC subjects showed less activation in the amygdala when distancing compared with looking [post hoc $F(1,15) = 4.41$, $p = .05$], while the reverse was true for BPD patients [post hoc $F(1,17) = 6.01$, $p = .03$]. In the look condition, BPD patients showed less amygdala activation relative to their baseline than the HC subjects [post hoc $F(1,32) = 8.78$, $p = .006$]. For both the STS and right superior frontal gyrus (SFG) (Figure 6), the extracted beta weights for the volumes of interest showed group $\times$ condition effects [STS: $F(1,32) = 14.59$, $p = .0006$; SFG: $F(1,32) = 9.00$, $p = .005$]. In both regions, the BPD patients showed greater activation in the distance compared with look condition [post hoc STS: $F(1,32) = 22.12$, $p = .00005$; SFG: $F(1,32) = 14.73$, $p = .0006$], while there was little difference between conditions for the HC subjects [STS: $F(1,32) = .67$, ns; SFG: $F(1,32) = .25$, ns].

We repeated the analysis excluding BPD subjects with histories of PTSD and confirmed that the significant group differences in the distance versus look contrast described above remained for the regions described above: the dACC, IPS, right STS, right superior frontal gyrus, and right amygdala.

**Table 3.** Conjunctive Activation by Both Groups When Distancing Versus Looking at Negative IAPS Pictures

<table>
<thead>
<tr>
<th>Region</th>
<th>BA</th>
<th>$k$</th>
<th>$x$</th>
<th>$y$</th>
<th>$z$</th>
<th>MNI Coordinates</th>
<th>Z</th>
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</thead>
<tbody>
<tr>
<td>Distance &gt; Look</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L inferior parietal lobule</td>
<td>40</td>
<td>1538</td>
<td>$-54$</td>
<td>$-50$</td>
<td>46</td>
<td>6.51</td>
<td></td>
</tr>
<tr>
<td>R inferior parietal lobule</td>
<td>40</td>
<td>3131</td>
<td>46</td>
<td>$-52$</td>
<td>46</td>
<td>5.30</td>
<td></td>
</tr>
<tr>
<td>R precuneus</td>
<td>7</td>
<td>3254</td>
<td>6</td>
<td>$-66$</td>
<td>44</td>
<td>4.89</td>
<td></td>
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<td>$-38$</td>
<td>14</td>
<td>3.69</td>
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<tr>
<td>R parahippocampal gyrus</td>
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<td>122</td>
<td>18</td>
<td>$-6$</td>
<td>$-24$</td>
<td>3.42</td>
<td></td>
</tr>
<tr>
<td>R middle frontal gyrus</td>
<td>10</td>
<td>1314</td>
<td>38</td>
<td>56</td>
<td>4</td>
<td>4.72</td>
<td></td>
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<tr>
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<tr>
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<td>12</td>
<td>50</td>
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<tr>
<td>L middle frontal gyrus</td>
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<td>241</td>
<td>$-30$</td>
<td>28</td>
<td>52</td>
<td>3.38</td>
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<tr>
<td>R insula</td>
<td>48</td>
<td>87</td>
<td>34</td>
<td>$-16$</td>
<td>18</td>
<td>3.32</td>
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<tr>
<td>Look &gt; Distance</td>
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<td></td>
</tr>
<tr>
<td>R cuneus</td>
<td>17</td>
<td>8081</td>
<td>14</td>
<td>$-96$</td>
<td>14</td>
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<td>$-48$</td>
<td>54</td>
<td>4.52</td>
<td></td>
</tr>
<tr>
<td>L supplementary motor area</td>
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<td>159</td>
<td>$-4$</td>
<td>$-6$</td>
<td>54</td>
<td>3.53</td>
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<tr>
<td>R postcentral gyrus</td>
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<td>285</td>
<td>58</td>
<td>$-10$</td>
<td>32</td>
<td>3.51</td>
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</tbody>
</table>

Notes: $k$ = cluster size in $2 \times 2 \times 2$ mm voxels; $p < .01$, minimum = 85.

BA, Brodmann area; IAPS, International Affective Picture System; L, left; MNI, Montreal Neurological Institute; R, right.

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Discussion

The purpose of the current study was to further understanding of affective instability in BPD by determining whether the neural bases of one kind of reappraisal—known as distancing—were disturbed in BPD.

Behavioral Observations

As expected, subjects reported less negative affect after distancing as compared with just looking at negative images, but not neutral images. Interestingly, these affect ratings did not differentiate the groups, which runs counter to the expectation that BPD patients would respond more intensely than HC subjects to negative images and would downregulate these responses less effectively. It is consistent, however, with prior reports of no differences between BPD patients and HC subjects in their self-reported affective responses to IAPS pictures despite differences in neural activation (24). One possible explanation is that subjective ratings reflect momentary intensity rather than the chronic instability of affective experience that characterizes BPD (7). This fits with the finding that BPD and non-BPD personality disorder patients differ in ratings of affective instability but not subjective affective intensity (42). In fact, examining the variance in valence ratings as an index of affective instability, we found a higher variance in BPD patients than HC subjects when distancing from negative pictures. Another possibility consistent with our finding and that of Herpertz et al. (24) is that in BPD patients there is a disconnect between the subjective experience of emotion and the physiological emotional response.

Neural Dynamics of Passive Looking

When looking at negative social emotional images compared with neutral images, borderline patients showed a different pattern of neural activation compared with healthy volunteers, indicating that borderline patients process emotional images differently than control subjects. The BPD patients showed greater activation in the superior temporal gyrus, posterior cingulate, anterior cingulate, and cerebellum than the HC subjects. We did not find the increased amygdala and fusiform activity reported by Herpertz et al. (24). This difference may be due to the fact that we employed exclusively social emotional pictures in both the negative and neutral conditions, whereas in the Herpertz et al. (24) study, faces appeared in the negative but not in the neutral pictures, which were all inanimate objects. Since faces are strong activators of the amygdala and fusiform,
we would expect greater activation when the effect of faces is not subtracted out in the contrast.

**Neural Dynamics of Reappraisal By Distancing**

**Common Features in Borderline Patients and Healthy Control Subjects.** Borderline patients activated many of the same networks as healthy control subjects during distancing, including networks implicated in executive function, goal maintenance, and the representation of social intentions (the DLPFC) (56); top-down control of attention allocation (the DLPFC/IPS network) (57–59); and self-other perspective taking (the precuneus/PCC) (60–66). Notably, DLPFC and IPS (67), but not precuneus/PCC, activity has been reported in prior work on reappraisal (for reviews, see [11,15]), possibly because this region is activated only in response to distancing from social cues, which have not been examined specifically until now. The look versus distance contrast identified primary visual regions whose activity diminished during reappraisal. This finding is consistent with prior reports (e.g., Ochsner et al. [16]) and the idea that distancing involves an inward focus of attention.

**Differences between Borderline Patients and Healthy Control Subjects.** Beyond the above commonalities, BPD patients showed a distinctly different pattern of activation compared with HC subjects in a set of regions related to control and emotional responding. Specifically, during distancing compared with looking, BPD patients showed less activation relative to baseline in the dACC and IPS and greater activation in the right superior frontal gyrus (BA 8) and STS, whereas HC subjects showed the reverse. Both groups showed comparable activation in the look condition. Unlike HC subjects, BPD patients increased amygdala activation relative to baseline during distancing compared with looking (Figure 5). In addition, during look trials, BPD patients showed less activation than HC subjects relative to their respec-

**Figure 5.** Coronal, sagittal, and horizontal sections illustrating greater activation in the amygdala of BPD patients compared with healthy control subjects when distancing and plot of regression weights for each group in right amygdala. The BOLD signal appears in yellow and the anatomic locus of the amygdala is shown in blue. BOLD signals are displayed overlaid on the Montreal Neurological Institute SPM canonical anatomic template. The display threshold is $p < .01$. The color bar indicates $t$ values. BOLD, blood oxygenation level-dependent; BPD, borderline personality disorder; HC, healthy control; SPM, statistical parametric mapping.

**Figure 6.** Coronal, sagittal, and horizontal sections illustrating greater activation in the superior frontal gyrus (SFG) of BPD patients compared with healthy control subjects when distancing and plot of regression weights for each group in right SFG. BOLD signals are displayed overlaid on the Montreal Neurological Institute SPM canonical anatomic template. The display threshold is $p < .01$. The color bar indicates $t$ values. BOLD, blood oxygenation level-dependent; BPD, borderline personality disorder; HC, healthy control; SPM, statistical parametric mapping.
to monitor reappraisal processes within the scanner. Self-reports limitation of this study and future studies should make an effort psychophysiological measure indexing the reappraisal task is a reports that they carried out the task as directed. The lack of a other studies of cognitive reappraisal, we relied upon subjects’ patients, it is important to acknowledge its limitations as well. As in tone baselines. A possible explanation for these paradoxical differences in the look condition is that at baseline, BPD patients had higher levels of amygdala activation than HC subjects and their activation decreased as they focused on the task of looking at pictures, while for the HC subjects, activation increased from a low baseline when they looked at the pictures. The decrease in activation in the HC subjects in the distancing condition is consistent with a downregulation of the amygdala when distancing. What remains unclear is what accounts for the increased amygdala activation in BPD patients during distancing.

The regions showing differential activation between BPD and HC subjects have been implicated in various control and affective functions relevant to BPD. Theories of cognitive control postulate the dACC and DLPFC work hand-in-hand to signal the need for control and to implement control processes, respectively (68–70). The IPS has been implicated in top-down attentional control (57–59) and the STS has been implicated in representing social cues of the intentions of others (52,71–75).

Our finding of differences in neural activation between border-line patients and healthy control subjects during reappraisal by distancing must be considered in the context of our finding of differences in activation in the passive viewing condition as well. Thus, we cannot rule out the possibility that the different activation patterns in the reappraisal condition arise from a more general difference in overall emotion processing and not from differences in the mechanism of reappraisal per se. Nevertheless, our findings allow us to reject the null hypothesis that in explicit emotion regulation BPD patients and HC subjects do not differ in neural activation. Moreover, with respect to the IPS and dACC, the BPD versus HC differences during reappraisal do not appear to be a consequence of differences in passive emotion processing, since activation (regression weights) in the look condition did not differ between the groups.

**Limitations of the Present Study**

Although this study is the first to our knowledge to examine the neural dynamics of cognitive reappraisal in borderline patients, it is important to acknowledge its limitations as well. As in other studies of cognitive reappraisal, we relied upon subjects’ reports that they carried out the task as directed. The lack of a psychophysiological measure indexing the reappraisal task is a limitation of this study and future studies should make an effort to monitor reappraisal processes within the scanner. Self-reports of affective response may be influenced by demand. Redirection of eye gaze away from emotionally charged regions in the pictures could play a role in downregulation of the emotional response and is associated with differences in BOLD signal when reappraising versus looking (76). Eye gaze is regulated by both bottom-up and top-down control networks (77) and may be an intervening mechanism in reappraisal implemented differently in BPD patients and HC subjects. While the present study could not determine the extent to which eye gaze redirection was employed to downregulate emotion in each group, it demonstrates clear differences in the neural dynamics of distancing in BPD patients versus healthy volunteers. We cannot eliminate the possibility that contrary to our instructions some subjects closed their eyes or looked away from the pictures.

We cannot exclude the possibility that group differences could be explained by socioeconomic or cognitive differences. The BPD group was heterogeneous in terms of comorbidity and prior psychiatric history and further studies are called for to replicate these findings in more homogeneous samples. While group differences in depression as measured by the HAM-D were present, no correlations between HAM-D score and activation were detected.

**Implications for Borderline Pathology and Directions for Future Research**

The finding that borderline patients do not downregulate amygdala activity as healthy control subjects do and do not recruit the networks that healthy subjects employ in cognitive reappraisal by distancing suggests that BPD patients may be impaired in their ability to cognitively regulate their emotions, an impairment which may in turn contribute to the affective instability of borderline patients. To reduce task heterogeneity, the present study examined the single strategy of distancing, selected as one likely to distinguish BPD from HC subjects. Future studies should examine other commonly employed reappraisal strategies such as reinterpretation and response-focused strategies (12,14). Further studies are called for to replicate and to extend the findings of this study to other psychopathological groups, to help determine whether the results reported here are specific to borderline pathology.

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