Cognitive reappraisal in trauma-exposed women with borderline personality disorder

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ABSTRACT

Borderline personality disorder (BPD) is characterized by emotional dysregulation and a high prevalence of traumatic stress. Recent estimates suggest that 2–6% of non-clinical populations suffer from BPD. Despite this relevance, this is the first study considering the neural mechanisms underlying trauma-history and temporal features of cognitive reappraisal in non-clinical BPD patients using script-driven stimuli. Using functional magnetic resonance imaging (fMRI), we examined subjective ratings of negative emotional experience and brain activity following up- and down-regulation of emotional responses to standardized negative scripts in 43 women: 14 trauma-exposed BPD patients (BPD), 14 trauma-exposed healthy subjects without posttraumatic stress disorder (non-PTSD), and 15 non-traumatized healthy subjects (HC). Behaviorally, all groups were able to use cognitive reappraisal to up- and down-regulate negative emotions. HC subjects showed increased early activation in the prefrontal cortex (PFC) and the amygdala following up-regulation of emotions to negative scripts, whereas BPD and non-PTSD subjects showed early deactivation in the PFC. Additionally, the anterior cingulate cortex was more activated in HC subjects than in BPD and non-PTSD subjects during up- and down-regulation. No significant group differences were found between BPD patients and non-PTSD. BPD patients and healthy individuals with trauma history do not engage the cognitive control regions to the extent than HC subjects do when employing down-regulation of negative emotions. They also do not activate the brain regions associated with emotional up-regulation. These findings may reflect compensatory changes associated with trauma-exposure.

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Introduction

The ability to process emotionally salient events and to integrate emotional experiences into daily life is of considerable importance for mental health and well-being (Baumeister and Exline, 2000; Gross and John, 2003; Salovey et al., 1993). These skills often require the ability to intentionally regulate one's emotions. The borderline personality disorder (BPD) is a severe mental disorder that is primarily characterized by dysfunction of emotional regulation (Barnow et al., 2009; Barnow et al., 2010a; Lieb et al., 2004). BPD is the most common personality disorder diagnosed in both inpatient and outpatient settings (Widiger and Trull, 1993). In addition to its prevalence in clinical populations, estimates suggest that 2–6% of non-clinical population have BPD (Barnow et al., 2010b; Grant et al., 2008; Swartz et al., 1993).

According to the biosocial theory of Linehan (Linehan, 1993; Lynch et al., 2006), emotion dysregulation in BPD results from a combination of emotional vulnerabity and the inability to modulate emotional responses. Most previous studies have focused on emotional processing rather than on emotion regulation, showing inconsistent results dependent on the methods used for assessing emotional processing (Rosenthal et al., 2008). There are only two studies that examined neural correlates of emotion regulation in BPD (Koenigsberg et al., 2009; Schulze et al., 2011). In these studies, the authors focused on reappraisal of negative emotions. Reappraisal is a cognitive-linguistic strategy that alters emotional responses by changing one's interpretation of a situation (Gross, 2002; Gross and John, 2003). In reappraisal tasks, participants are instructed to deliberately enhance or decrease their negative emotions in response to aversive stimulation (Ochsner et al., 2004). According to Gross, cognitive reappraisal belongs to the antecedent focused strategies that refer to things we do before emotion response tendencies have become fully activated and change our behavior and peripheral physiological responding (Gross, 1998; Gross and Thompson, 2007).

Functional neuroimaging revealed that reappraisal involves frontal brain regions such as the dorsolateral prefrontal cortex (PFC), dorsomedial PFC, orbitofrontal cortex, and anterior cingulate cortex (ACC) (Ochsner et al., 2002, 2004; Phan et al., 2005). The recruitment
of these frontal brain regions is associated with goal-appropriate increases or decreases in amygdala activation (Ochsner et al., 2002, 2004; Urry et al., 2006).

In a study by Königsberg (Koenigsberg et al., 2009), BPD patients had to down-regulate their responses to negative pictures of the International Affective Picture System (IAPS) using a distancing technique, in which the subject had to increase the sense of objective distance. Compared to healthy control subjects, BPD patients showed decreased brain responses in the dorsal ACC and inferior parietal lobe and less deactivation in the amygdala. In another study, Schulze et al. (2011) applied a cognitive reappraisal task with up- and down-regulation also using IAPS pictures. Compared to healthy subjects, BPD patients showed decreased activation in the left orbitofrontal gyrus and increased activation in the insula following down-regulation. No group differences were found during up-regulation. These findings indicate that BPD patients do not engage the relevant cognitive control regions to the same extent as healthy subjects do when employing down-regulation.

However, both studies (Koenigsberg et al., 2009; Schulze et al., 2011), like most BPD studies, did not consider the factor of trauma-exposure, although traumatic experience is very common in borderline patients (Barnow et al., 2005; Barnow et al., 2010a; Laporte and Guttmann, 1996; Zanarini et al., 2002) as well as in healthy subjects and may also change brain activity (Britton et al., 2005; New et al., 2009; Otte et al., 2005). For example, Ganzel et al. (2008) found lower gray matter volume in amygdala, insula, medial prefrontal cortex, and ACC and total gray matter volume in trauma-exposed individuals relative to non-traumatized individuals. In a recent functional imaging study, New et al. (2009) demonstrated that trauma-exposed persons, as compared with non-traumatized healthy controls, were less successful in down-regulating negative emotions (as manifested in their subjective ratings) and showed a decreased activation of the PFC during down-regulation and an increased activation during up-regulation of negative emotions. Furthermore, prior studies on emotion regulation included inpatients who actively asked for therapy (Schulze et al., 2011), or a mixed in- and outpatient sample (Koenigsberg et al., 2009). Thus, it remains unclear whether emotion dysregulation is a general phenomenon in BPD or is restricted to specific subgroups within borderline patients. Another problem in these studies is that the authors did not examine the timing of the neural correlates of emotion regulation. In healthy adults, the engagement of PFC regions is at its maximum during the first second and then diminishes (Goldin et al., 2008). Additionally, one of our own recent study has shown that comorbid posttraumatic stress disorder (PTSD) in BPD modulates emotional reactivity substantially during a script-driven task (Limberg et al., 2011). Thus, emotion regulation might also be modulated by PTSD and therefore, results should be controlled for PTSD diagnosis. For example, Schulze et al. (2011) found increased insular activity following down-regulation in BPD patients with PTSD compared to BPD patients without PTSD. This indicates differences in emotion regulation between BPD with and without PTSD. In the present study, we were primarily interested in borderline-specific effects. Therefore, BPD patients with comorbid PTSD have been explicitly excluded in order to avoid confounding effects due to PTSD.

The aim of the current study was to examine neural responses during up- and down-regulation of negative emotions in trauma-exposed BPD patients without PTSD, trauma-exposed non-PTSD subjects and healthy non-traumatized subjects. Temporal analysis investigated early (0–4 s) and late (8–12 s) peak blood oxygenation level-dependent (BOLD) responses during the 12-s time interval of cognitive reappraisal to investigate temporal dynamics and consequences of reappraisal of emotional responses (see Fig. 1). We used negative standardized scripts, which have been applied successfully in our previous study concerned with BPD patients (Limberg et al., 2011).

The three-group design allowed us to disentangle the effects of BPD diagnosis from those of the traumatic experience. (1) We expected that BPD patients would show an impaired ability to down-regulate emotional responses and that this would be manifested in behavioral as well as fMRI measures. More specifically, we expected a decreased activation in the ACC and orbitofrontal cortex and increased amygdala and insula activation in BPD patients following down-regulation compared to the healthy control group without trauma-exposure. (2) According to the findings of Schulze et al. (2011), we did not expect group differences in the up-regulation between BPD and healthy subjects without trauma-exposure. (3) Considering the findings of the above-mentioned study (New et al., 2009), we assumed that trauma-exposure would modulate emotion regulation in the trauma-exposed group without PTSD as well (e.g., decreased activation in the PFC following down-regulation and increased PFC activation following up-regulation).

Materials and methods

Participants

We examined eighteen healthy non-traumatized women (HC), sixteen trauma-exposed women without posttraumatic stress disorder (non-PTSD), and fourteen non-clinical trauma-exposed women with BPD. Data of three HC and two non-PTSD subjects were dismissed due to artefacts. In order to avoid gender effects in emotion regulation, all participants were female (e.g., Hamann and Canli, 2004). All participants were recruited via announcements posted on bulletin boards. BPD patients were free of medication for at least 2 weeks prior to the study and had no history of neurological disorder or other major medical conditions. They fulfilled at least five of nine DSM-IV-TR criteria for BPD and did not have a PTSD, history of schizophrenia-spectrum psychosis, bipolar type I affective disorder or current substance abuse. All non-PTSD and BPD subjects reported a history of criterion A trauma occurring 3 months or longer before participation. Exclusion criteria for HC subjects comprised of any personality disorder or Axis I disorder, current psychiatric treatment or history of a trauma criterion A (Table S1). All subjects gave written consent after receiving a detailed description of the study and were paid for their participation. The study was approved by the ethical
board of the University of Heidelberg according to the declaration of Helsinki.

**Diagnostic and clinical measurements**

The following diagnostic instruments were used: The German versions of the Structured Clinical Interviews for DSM-IV Axis I and Axis II Disorders (SCID-I) (Spitzer et al., 1992); German version of the Posttraumatic Diagnostic Scale (PDS) (Ehlers et al., 1996); German version of the Child Behavior Checklist for DSM-IV (CFI); German version of the Child Depression Inventory (Hautzinger et al., 2006); Emotion Regulation Questionnaire (ERQ) (Abler and Kessler, 2009) to obtain self-rating of cognitive reappraisal; Edinburgh Handedness Scale (EHI) (Oldfield, 1971).

**Subjective characteristics**

The three groups did not significantly differ in age, handedness, education, or marital status (Table 1). The BPD patients scored significantly higher in depressive symptoms (BDI) than the other groups. Also, BPD patients had significantly higher scores in the CTQ than HC subjects but not in comparison to the non-PTSD group. There were no differences in the self-report of cognitive reappraisal (ERQ) between the three groups. Axes I and II comorbidity was present, as is typical in BPD samples (Table S2).

**Stimulus material and procedure**

On the basis of our previous study (Limberg et al., 2011), three standardized negative and three neutral scripts from the Affective Norms for English Text (ANET) (Bradley and Lang, 2007) were used. All scripts were presented in a first-person narrative and consisted of 3–4 sentences. All scripts were rated with respect to arousal and valence using a Likert-type scale ranging from 1 (not aroused, very pleasant) to 5 (very aroused, very unpleasant) in a pilot study outside the scanner. This resulted in mean arousal 5.67, SD 2.14 (negative scripts) and 1.92, SD 1.22 (neutral scripts), and mean valence 2.83, SD 1.37 (negative scripts) and 6.12, SD 1.19 (neutral scripts). Being confronted with emotionally negative scripts, participants were instructed to either increase their sense of distance, to perceive the script’s contents from a detached, third-person perspective (e.g. as if they were viewing a film or reading a book). On obtaining the command “maintain” (the M condition), participants were instructed to respond emotionally to each script category without trying to alter their emotions (Fig. 1).

During scanning, participants completed three trials with three different scripts to ensure that they were comfortable with performing the task inside the scanner. Each instruction appeared at the screen for 2 s, followed by a script of 10 s. Following the script, participants had to perform the appraisal task for 12 s. Some previous studies also compared the negative and neutral stimulation but in the present study we were primarily interested in emotion regulation and not in emotional processing. Therefore, only responses to negative scripts presented in the UP, DOWN and M conditions were analyzed, whereas neutral scripts were used as fillers in the M condition exclusively.

After each trial, participants had to rate their current affect. Finally, they were instructed to relax before the next trial began (4–6 s). The different blocks were alternated in a pseudo-randomized order, with each category presented three times, always beginning with the negative-maintain condition. The carryover effects were avoided by using the filling neutral-maintain condition. The subjective rating data were analyzed by means of an ANOVA with a between-subject factor group (BPD, non-PTSD, HC) and a within-subject factor Task (UP, DOWN, M).

**fMRI data acquisition and analyses**

MRI data were acquired by use of a 3 T Siemens TRIO System equipped with a 12 channel head coil. Changes in blood oxygenation level-dependent (BOLD) T2* weighted MR signal were measured using a gradient echo-planar imaging (EPI) sequence (TR = 2300 ms, TE = 25 ms, FoV = 210 mm, flip angle = 90°, 64 x 64 matrix, 40 slices covering the whole brain, slice thickness 3 mm, no gap, voxel size 3 x 3 x 3 mm). A T1-weighted anatomical image was additionally acquired for each subject to allow anatomical localization (TR = 2300 ms, TE = 2.98 ms, 160 slices, voxel size 1.0 x 1.0 x 1.1 mm).

Image processing was carried out using SPM8 software package (Wellcome Department of Cognitive Neurology, London UK; http://www.fil.ion.ucl.ac.uk/spm). Pre-processing included realignment, co-registration, segmentation, spatial normalization (template of Montreal Neurological Institute, MNI) and 8 mm3 isotropic Gaussian spatial smoothing. A temporal high-pass filter with a period cutoff of 128 s was applied. This was followed by the application of the whole-brain voxel-based general linear model (Friston et al., 1995) at the single-subject level to estimate signal change associated with the conditions of interest.
interest (M, UP, DOWN) for the early (0–4 s) and late (8–12 s) time intervals. Contrasts between UP and M, DOWN and M were computed for each subject.

For the statistical analysis of fMRI data two different approaches were applied. For the whole brain, activation patterns in each group (HC, non-PTSD, BPD) were evaluated by means of one-sample t-tests, for each time interval (early, late) and condition separately. The probability threshold was set at p = 0.001, uncorrected. For a priori defined brain activations, regions of interests (ROI) were used, which are implicated in cognitive reappraisal (dorsolateral PFC, dorsomedial PFC, orbitofrontal cortex, ACC), top-down control of attention allocation (parietal cortex), and emotion (amygdala, insula) (Kalisch, 2009; Ochsner et al., 2002, 2004; Phan et al., 2005; Urry et al., 2006). Furthermore, groups were compared pairwise using t-tests. So as to take into account multiple comparisons, the alpha level for these tests was Bonferroni corrected.

Additionally, data from the ROI analyses were extracted using the rfxplot toolbox (Glascher, 2009) and analyzed in SPSS using a mixed-design ANOVA with the between-subject factor group (HC, non-PTSD, BPD) and within-subject factors condition (UP-minus-M, DOWN-minus-M), interval (early, late) and hemisphere (left, right). In contrast to the pairwise comparisons described above, the ANOVA was intended to reveal interactions between several factors (e.g., group, condition, and interval). In case of significant effects Tukey post-hoc tests were applied. To control for depressive symptoms, BDI was included as a covariate.

The ROI approach was used with p < 0.05, corrected for family wise errors (FWE). The minimum cluster extent (K) was set at 10 contiguous voxels. The regions were derived from the anatomical labelling atlas (aal) toolbox from the PickAtlas (Maldjian et al., 2003).

Results

The main effect of BDI as the covariate was not significant in any analysis, nor was any interaction between the covariate and other factors. Therefore, depression was not included in the following analyses.

Subjective reports

All participants reported that they followed the instructions as practiced before scanning.

Arousal and valence ratings demonstrated significant main effects of task [arousal: F(2,80) = 36.92, p < 0.001; valence: F(2,80) = 22.54, p = 0.001], which were largely due to a significant linear trend [arousal: F(1,40) = 16.99, p < 0.001; valence: F(1,40) = 4.55, p = 0.039]. This indicates successful UP-regulation and cognitive DOWN-regulation of negative emotion across all groups, as shown in Fig. 2, that is, the UP condition was related to higher arousal and more negative valence than the M condition and the DOWN condition was related to lower arousal and less negative valence than the M condition. Also, the group effects were significant [arousal: F(2,41) = 4.12, p = 0.024; valence: F(2,40) = 4.03, p = 0.025] but group × task interactions were not (p > 0.10). Post-hoc tests showed that non-PTSD subjects scored lower in arousal (p = 0.017) and valence (p = 0.016) than HC subjects. BPD patients did not significantly differ from any other group.

Imaging results

Brain regions demonstrating increased and decreased BOLD signal in early (0–4 s) and late (8–12 s) reappraisal are summarized in Table S3.

In the UP-minus-M contrast, HC subjects showed early brain activation in the left amygdala, left dorsomedical and left dorsolateral PFC. Late activations were obtained in the right ACC and the left middle temporal gyrus. Contrary, BPD patients showed deactivation in the left medial PFC, ACC and right precuneus during the early interval and activation in the left middle temporal cortex during the late interval. Similarly, the early deactivation in the dorsolateral PFC, left inferior parietal gyrus, left posterior cingulate gyrus and left precuneus were observed in the non-PTSD group. There was no response in the amygdala in both BPD and non-PTSD groups.

In the DOWN-minus-M contrast, HC subjects demonstrated early brain responses in the left dorsolateral PFC, left middle temporal gyrus, left superior parietal lobe, left supramarginal gyrus, left inferior parietal gyrus, right thalamus, left putamen and left precuneus.

Fig. 2. (A) Subjective ratings of valence and arousal to instructions to “decrease”, “enhance”, and “maintain” for each group. HC, non-traumatized healthy subjects, non-PTSD, trauma-exposed non-PTSD subjects, BPD, borderline personality disorder. (B) Subjective ratings of valence and arousal to instructions to “decrease” and “enhance” compared to “maintain” to negative scripts. There was no group difference showing that all participants modified their emotion successfully.
During the late time interval, the left dorsomedial PFC, left middle temporal gyrus, and right parahippocampal gyrus were activated. BPD patients showed a differential activation in the left putamen, right middle and right superior temporal gyri. Late activation was found in the left middle temporal gyrus. Non-PTSD subjects engaged the right supramarginal gyrus, left inferior parietal gyrus, left middle temporal gyrus, right superior parietal gyrus and the cuneus during the early interval and the left middle temporal gyrus and precuneus during the late interval.

Pairwise between-group comparisons (Table 2) in the UP condition showed stronger early activations in the left ACC, the left medial and right dorsomedial PFC and the posterior cingulate gyrus (PCC) in the HC than in the BPD group. Likewise, HC subjects showed stronger early activations in the left dorsomedial and dorsolateral PFC than non-PTSD subjects (Fig. 3). In the DOWN condition, a trend toward a greater activation in the ACC in HC subjects compared to BPD patients was found during the early interval. Furthermore, HC subjects showed stronger activity in the left parietal cortex than non-PTSD subjects. No group differences attained significance during the late interval.

The ANOVA for selected ROI confirmed most of these effects. The significant hemisphere × condition × phase × group interaction [F(2,40) = 3.68, p = .034] for the dorsomedial PFC indicated that group differences were mainly restricted to the left hemisphere during early UP-regulation. Furthermore, a simpler phase × condition interaction was significant [F(2,40) = 4.90, p = .033], indicating a greater activation during UP- than DOWN-regulation in the early phase. The main effect of group was significant for the dorsomedial PFC [F(2,40) = 6.17, p = .005] and the ACC [F(2,40) = 5.18, p = .010]. Whenever the factor group or its interactions reached significance, post-hoc tests demonstrated greater activation in HC than in the other two groups (i.e., BPD and non-PTSD). However, no difference was found between the BPD and non-PTSD groups (p > .40).

Fig. 3. Group comparisons during early UP-regulation versus Maintain. Top: fMRI images comparing HC to BPD (A), HC to non-PTSD (B), non-PTSD to BPD (C). The display threshold is p < .05 (FWE-corrected). The color bar indicates t values. Bottom: quantitative BOLD signal changes in three regions of interest. ACC, anterior cingulate gyrus; PCC, posterior cingulate cortex; DMPFC, dorsomedial prefrontal cortex. HC, non-traumatized healthy controls; non-PTSD, trauma-exposed healthy controls; BPD, patients with borderline personality disorder. Note that although PCC activation significantly distinguished BPD patients from HC subjects, the group × condition interaction for PCC in the ANOVA was not significant.

Table 2
Significant differences in BOLD signal between groups during UP versus Maintain and DOWN versus Maintain.

<table>
<thead>
<tr>
<th>Brain regions</th>
<th>HC vs BPD</th>
<th>HC vs non-PTSD</th>
<th>non-PTSD vs. BPD</th>
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<tbody>
<tr>
<td></td>
<td>MNI coordinates</td>
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<td>MNI coordinates</td>
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<tr>
<td>Up vs. maintain</td>
<td>k x y z t</td>
<td>k x y z t</td>
<td>k x y z t</td>
</tr>
<tr>
<td>Dorsomedial frontal gyrus (10, 8)</td>
<td>52 3 56 1 3.69</td>
<td>44 −6 44 46 3.79</td>
<td></td>
</tr>
<tr>
<td>Medial frontal gyrus (10)</td>
<td>89 −3 53 −2 5.09</td>
<td>95 −45 41 7 4.24</td>
<td></td>
</tr>
<tr>
<td>Anterior cingulate cortex (32)</td>
<td>−3 44 −2 4.45</td>
<td>87 −36 50 13 3.85</td>
<td></td>
</tr>
<tr>
<td>Inferior frontal gyrus (9)</td>
<td>−3 35 10 3.80</td>
<td>247 −36 14 34 4.38</td>
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<tr>
<td>Inferior frontal gyrus (46)</td>
<td>52 −39 14 31 4.38</td>
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<tr>
<td>Middle frontal gyrus (10)</td>
<td>95 −45 41 7 4.24</td>
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<td>Middle frontal gyrus (9)</td>
<td>87 −36 50 13 3.85</td>
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<tr>
<td>Posterior cingulate cortex (23)</td>
<td>14 −3 −52 22 3.90</td>
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<tr>
<td>Down vs. maintain</td>
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<tr>
<td>Anterior cingulate cortex (32)</td>
<td>30 3 47 10 2.87</td>
<td>96 −51 −61 34 3.86</td>
<td>33 −27 −55 37 4.64</td>
</tr>
<tr>
<td>Angular gyrus (39)</td>
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<tr>
<td>Inferior parietal gyrus (39)</td>
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Notes: k = cluster size in 3 × 3 × 3 mm voxels, minimum cluster size, k > 10, BA = Brodmann Area, p < .05 (FWE corrected), *p < .001; **p = .088 (FWE corrected). The positive sign of t implies higher signal intensity in the group named first.
Discussion

For the first time, this study investigated whether emotion regulation in BPD is modulated by trauma-exposure. We assessed subjective ratings and neurophysiological responses during early and late time intervals in three female groups (BPD patients with a history of trauma; healthy individuals with traumatic experience; non-traumatized healthy controls) during cognitive regulation of negative emotions.

Subjective reports

Subjective ratings did not reveal deficits in emotion regulation in BPD compared to HC. This finding is in line with the results of previous studies indicating no differences in self-reports of affective responses to IAPS pictures notwithstanding differential brain responses (Koenigsberg et al., 2009; Schulze et al., 2011). A possible explanation might be that BPD patients underestimate the intensity of their emotions, perhaps because of their higher levels of alexithymia (Herpertz et al., 2001; Lang et al., in press).

Imaging data: general

In line with the findings of previous studies (Domes et al., 2010; Eippert et al., 2007; Kim and Hamann, 2007; Ochsner et al., 2004), HC subjects demonstrated successful UP-regulation of emotional response with increased activation in the left amygdala, dorsomedial PFC, left dorsolateral PFC, ACC and left middle temporal gyrus during UP-regulation. During DOWN-regulation, HC subjects engaged the left dorsolateral PFC, dorsomedial PFC, left middle temporal gyrus, superior parietal gyrus, thalamus and putamen, regions previously identified in similar conditions (Kalisch, 2009; Ochsner et al., 2004). Contrary to HC subjects, BPD patients and non-PTSD subjects showed early deactivation in the PFC and ACC during UP-regulation. There was no increased amygdala activation. During DOWN-regulation, BPD patients showed activation in the right middle temporal gyrus and superior temporal gyrus while non-PTSD subjects demonstrated greater bilateral activation in the middle temporal gyrus and parietal cortex.

In accordance with previous findings (Goldin et al., 2008, 2009), brain activations in the present study were mainly found during the early time interval (0–4 s) across all groups, indicating that responses related to emotion regulation are rather brief. This finding aligns well with the view of Gross (Gross, 1998; Gross and John, 2003) that cognitive reappraisal is an antecedent focused strategy, which occurs early in the emotion-generative process without the need for sustained effort over time. The most stable effect during the late phase was the activation of the left middle temporal gyrus. Whereas the early activation probably reflects the antecedent process, the late activation might be speculated to manifest post-hoc conceptualisations and verbalization of already applied strategies. One may putatively relate this hypothetical process to the fact that in the present study, contrary to the previous ones, emotions were elicited by verbal scripts.

Imaging data: BPD versus HC

BPD patients showed diminished ACC activation during UP-regulation compared to HC subjects and decreased early activation in the dorsomedial PFC and PCC. This finding stands in strong contrast to the recent study of Schulze et al. (2011) who did not find differential brain activations between BPD patients and HC subjects during UP-regulation. Possible reasons for these divergent results will be discussed below. In line with Koenigsberg et al. (2009), a generally decreased activity in the ACC was found in BPD compared to HC during DOWN-regulation. Additionally, the group differences in emotion regulation were independent of the level of depression. However, in contrast to Koenigsberg et al. (2009) and Schulze et al. (2011), we did not find enhanced activity in the amygdala or insula in BPD patients relative to HC subjects.

The non-consistent findings as compared to previous studies might be related to differences in the methods used by Koenigsberg et al. (2009) and Schulze et al. (2011). In both studies, IAPS pictures were employed that selectively relate to social cues, whereas the present study used verbal stimuli (negative scripts). However, social and non-social emotions are processed differently in the brain (Britton et al., 2006; Harris et al., 2007; Van den Bos et al., 2007). Furthermore, verbal stimuli might capture more attentional resources for reappraisal and might therefore engage prefrontal and temporal areas in a larger extent and the amygdala in a lesser extent than emotional pictures. Another difference between the present study and the previous ones is related to the selection of the sample. As we were particularly interested in the effects of trauma experience, we excluded BPD patients without trauma history as well as those with PTSD. The sample was acquired per announce rather than among in- or outpatients, which might have result in a group of relatively compensated patients who did not actively look for therapeutic help. As can be seen in our supplementary material (S1), the BPD sample had less comorbidities than typically observed in other BPD studies.

Trauma effects

The differences between trauma-exposed non-PTSD and HC subjects were quite similar to those between BPD and HC. Non-PTSD subjects showed a generally decreased ACC activation during UP- and DOWN-regulation and a decreased early activity in the dorsomedial and dorsolateral PFC during UP-regulation. It is very likely, therefore, that the group differences in brain activity between BPD and HC are not specific to BPD, but rather related to trauma-exposure per se. The non-specificity is further confirmed by the fact that there were no group differences in brain activation in any area between BPD and non-PTSD subjects.

Returning to the above-mentioned issue of attention demands, particularly related to the use of complex verbal scripts in the present experiment, a number of studies can be mentioned that showed a relationship between deactivation of prefrontal brain structures and abnormal attention to negative emotions (e.g., Shulman et al., 1997; Simpson et al., 2001).

Such abnormal attention in the trauma-exposed subjects (both BPD patients and non-PTSD individuals) may be interpreted as a potential risk factor. The ability to down-regulate responses to negative experiences is postulated as one possible mechanism of resilience in the face of trauma-exposure (Olff et al., 2005; Southwick et al., 2005). According to this model, the ability to decrease negative emotional responses permits a positive adaptation to harmful events. The fact that non-PTSD subjects resembled BPD patients rather than the HC subjects indicates that trauma-exposure itself may impede the ability to down-regulate negative emotional responses.

The dorsomedial PFC and ACC are typically involved in cognitive UP-regulation of negative emotions (Eippert et al., 2007; Kim and Hamann, 2007; Ochsner et al., 2004) and other emotional tasks (Etkin et al., 2011; Fan et al., 2005; Han et al., 2009; Lang et al., 2011; Pessoa, 2008). The ACC is implicated in selective attention (Gross, 1998) and executive functions including cognitive reappraisal (Fan et al., 2005; Kerns et al., 2004; Ochsner et al., 2004). The general decrement of ACC activation, independent of time-interval and task instruction, might be related to problems of selective attention in participants who were exposed to trauma. The PCC is also relevant for self-referential processing (Ochsner et al., 2004; Vogt et al., 2006). The deactivation in these brain regions, which was found in BPD and non-PTSD groups following UP-regulation, concurs with the data of a previous study using trauma-scripts in BPD patients and non-PTSD individuals (Schmah et al., 2004). The prefrontal deactivation might reflect an active attempt to deal with distress by the inhibition of emotional brain regions, although the exact
physiological meaning of BOLD signal decreases remains uncertain (Gusnard and Raichle, 2001). The findings agree well with a study by Ganzel et al. (2008), who reported structural and functional changes in multiple brain regions including the medial frontal gyrus and ACC in trauma–exposed healthy adults.

The severity of the trauma was not matched between the BPD and non-PTSD groups, which can be regarded as a serious limitation of the present study. Nevertheless, it is worth mentioning that even though BPD patients had experienced more severe trauma than non-PTSD individuals, we found remarkable similarities in these groups’ patterns of emotion regulation. Furthermore, we followed previous studies using self-reports as indicators of successful cognitive reappraisal. Future studies should also include psychophysiological measures as markers of emotional state.

Conclusions

The present study extended previous research on neural correlates of cognitive emotion regulation considering trauma-exposure in healthy subjects as well as in BPD patients. The findings indicate that trauma-exposure per se modulates UP- and DOWN-regulation of negative emotions. Further research is necessary to explore why non-PTSD subjects do not develop severe psychopathology though their brain activity patterns during reappraisal were very similar to those in BPD patients.

Conflicts of interest statement

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at doi:10.1016/j.neuroimage.2011.08.061.

References


