A Functional Magnetic Resonance Imaging Study of Deliberate Emotion Regulation in Resilience and Posttraumatic Stress Disorder

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Background: Sexual violence is an important public health problem in the United States, with 13% to 26% of women reporting a history of sexual assault. While unfortunately common, there is substantial individual variability in response to sexual assault. Approximately half of rape victims develop posttraumatic stress disorder (PTSD), while others develop no psychopathology (e.g., trauma-exposed non-PTSD). In this project, we examined the neural mechanisms underlying differences in response to sexual violence, focusing specifically on the deliberate modification of emotional responses to negative stimuli.

Methods: Using functional magnetic resonance imaging (fMRI) blood oxygenation level-dependent (BOLD) response, we examined the neural circuitry underlying effortful modification of emotional responses to negative pictures in 42 women: 14 with PTSD after sexual trauma, 14 with no psychiatric diagnosis after sexual trauma, and 14 nontraumatized control subjects.

Results: In response to deliberate attempts to downregulate emotional responses, nontraumatized healthy control subjects were more successful than either trauma-exposed group (PTSD or non-PTSD) in downregulating responses to the negative pictures as measured by subjective rating and BOLD response in regions of prefrontal cortex (PFC). In contrast, after deliberate attempts to upregulate emotional responses, regions of PFC were activated by trauma-exposed non-PTSD subjects more than by healthy control subjects or PTSD subjects.

Conclusions: Successful downregulation of emotional responses to negative stimuli appears to be impaired by trauma exposure. In contrast, the ability to upregulate emotional responses to negative stimuli may be a protective factor in the face of trauma exposure and associated with resilience.

Key Words: Alexithymia, PTSD, resilience, sexual assault, trauma

Sexual assault is an important public health problem, with data suggesting that 13% to 26% of women in the United States have experienced a sexual assault (1–6). While unfortunately common, it is clear that there is substantial individual variability in response to sexual assault. Approximately half of rape victims develop posttraumatic stress disorder (PTSD), while others endure rape with minimal adverse sequelae (7). Little is known about what underlies the capacity to endure this sort of trauma without developing the crippling symptoms associated with PTSD.

Resilience has been defined broadly as a positive adaptation in the face of adversity or trauma (8,9). In the present study, however, we define resilience as the absence of PTSD after violent sexual assault. This definition provides a clear, clinically meaningful way of dividing our sample into potentially more and less vulnerable groups retrospectively.

A recent theory suggests that emotional disinhibition may be a risk factor for the development of PTSD following trauma exposure (10–12). This theory is based, in part, on functional brain imaging studies showing that in response to negative emotional stimuli, PTSD patients show less activity in brain regions involved in modulation of emotional responses (10,11,13–22). These studies, however, examined emotion regulation as a passive response to aversive stimuli. By contrast, recent work on emotion regulation in healthy individuals has focused on the ability to exercise voluntary control over emotional responses (23–25). The frequent use of this form of emotion modification has been linked to enhanced control of emotion, better interpersonal functioning, and psychological and physical well-being (26). Evidence that such a capacity may have positive effects led to the hypothesis that the ability to voluntarily modify emotional responses may be a protective factor in the face of trauma exposure (27–29).

Studies have shown that individuals can be instructed to modify their emotional responses to negative stimuli and thereby decrease psychophysiological measures of affective reactivity and self-reported emotional change (30–35). Functional magnetic resonance imaging (fMRI) studies exploring the neural circuitry underlying voluntary emotion regulation in healthy individuals suggest that healthy individuals recruit regions of prefrontal cortex (PFC), including orbital frontal cortex and anterior cingulate cortex (ACC), during downregulation of emotional responses (30–32,36–40). The deliberate effort to enhance emotional responses to negative stimuli has been studied less but appears to recruit a network of brain regions similar to that employed in downregulation of emotional responses (31,39,41,42). Functional magnetic resonance imaging studies have tended to show that as healthy volunteers modify emotional responses, regions of PFC are activated and the amygdala responds in the direction of that modification (e.g., decreased blood oxygenation level-dependent [BOLD] signal in the amygdala with downregulation) (25,31,32,38,41). The one clinical sample studied to date of voluntary emotion regulation showed that individuals with major depressive disorder (MDD) overactivate right mid-PFC when instructed to suppress responses to negative images (37).

While a number of studies have examined fMRI responses to negative stimuli in PTSD, the present study is the first to extend

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the work on deliberate emotion modification from healthy individuals to trauma-exposed individuals with and without PTSD. The only prior study of voluntary emotion regulation after trauma showed that among individuals who developed PTSD after missile attacks in Israel, a higher level of deliberate control of mental images of the trauma was associated with fewer re-experiencing symptoms (43).

Our study used fMRI to explore whether differences in deliberate emotion regulation differentiated women who, after severe sexual trauma, developed PTSD compared with those who developed no psychiatric illness. To do this, we examined BOLD signal change after instruction to decrease or increase responses to negative emotional stimuli in women with PTSD after sexual assault, in age-matched healthy women with no significant trauma history, and in women with a trauma history similar to the PTSD group but no psychiatric disorder. Our three-group design permitted us to consider trauma-related outcomes by comparing traumatized and non-traumatized control subjects and disorder-related outcomes by comparing PTSD with trauma-exposed non-PTSD. In light of work suggesting that the ability to deliberately regulate emotion may be a protective factor in the face of trauma, we hypothesized that women in the trauma-exposed non-PTSD group would evidence enhanced ability to downregulate negative emotional responses on behavioral and fMRI measures.

Methods and Materials

Subjects

Forty-two women recruited through advertisements in local newspapers (14 PTSD; 14 trauma-exposed non-PTSD; 14 non-traumatized healthy women) completed the study. Twenty-two healthy, 14 trauma-exposed non-PTSD, and 24 PTSD subjects were screened to obtain our sample. All subjects were medically healthy as confirmed by physical examination and basic laboratory tests, on no medications, and had no history of serious head injury, neurological disorder, or other major medical conditions. Nontraumatized control subjects had no current or lifetime Axis I disorder and no history of a criterion A trauma. All members of the trauma-exposed groups had an adult history (age >18) of violent sexual assault at least 3 months before entry. The PTSD group met criteria for PTSD related to this trauma but no other major Axis I disorder except for symptoms of depression beginning after the index trauma and viewed as secondary to the PTSD symptomatology. The trauma-exposed non-PTSD group had no current or lifetime Axis I disorder, including PTSD.

We excluded individuals who had developed PTSD but recovered and anyone with substance abuse or dependence within the past 6 months; the trauma-exposed non-PTSD and nontrauma control subjects had no history of substance abuse or dependence. This study was approved by the Institutional Review Board of the Mount Sinai School of Medicine. Written informed consent was obtained from each participant.

Diagnostic/Clinical Ratings

Axis I diagnoses were assessed with the Structured Clinical Interview for DSM-IV (44). Posttraumatic stress disorder symptom severity was assessed with the Clinician-Administered PTSD Scale (CAPS) (45). The sexual assault in all trauma-exposed subjects reached the threshold of a DSM-IV Criterion A trauma. We quantified trauma burden by frequency and impact of the events using the Trauma History Questionnaire (THQ) (46). The Beck Depression Inventory (BDI) (47) and the Positive and Negative Affect Scale (PANAS) (48) were used to measure affective symptoms, the Life Orientation Test-Revised (LOT-R) (49) was used to measure optimism, and the Connor-Davidson Resilience Scale (CD-RISC) (50) was used to assess the broader psychological construct of resilience.

fMRI Task

In an event-related paradigm lasting 40 minutes, neutral and negative pictures from the International Affective Picture Set (IAPS) (51) were presented. All pictures chosen for this study depicted human content, although they were not related specifically to sexual assault, as our study focused on nontrauma-specific emotional processing. During each trial, subjects received one of three auditory regulation instructions via headphones, to "diminish," "enhance," or "maintain" responses to negative pictures. To diminish, subjects were instructed to decrease the intensity of their affect by imagining a less negative outcome for the circumstances depicted in the picture. Conversely, when instructed to enhance, subjects were asked to imagine a more negative outcome. In the maintain condition, participants were instructed to maintain their responses. Pictures were randomly assigned to regulation conditions on a subject-by-subject basis. Before the intertrial interval (ITI), subjects provided a rating of emotional experience on a Likert-type scale on which they indicated how negative or positive they found the picture (1 = very negative; 2 = negative; 3 = neutral; 4 = positive; 5 = very positive). Positive-valence images were not included, therefore the scale functionally ranged from 1 to 3.

Each trial consisted of 1-sec fixation, 12sec picture period, a regulation instruction delivered 4 sec after picture onset, a 4-sec

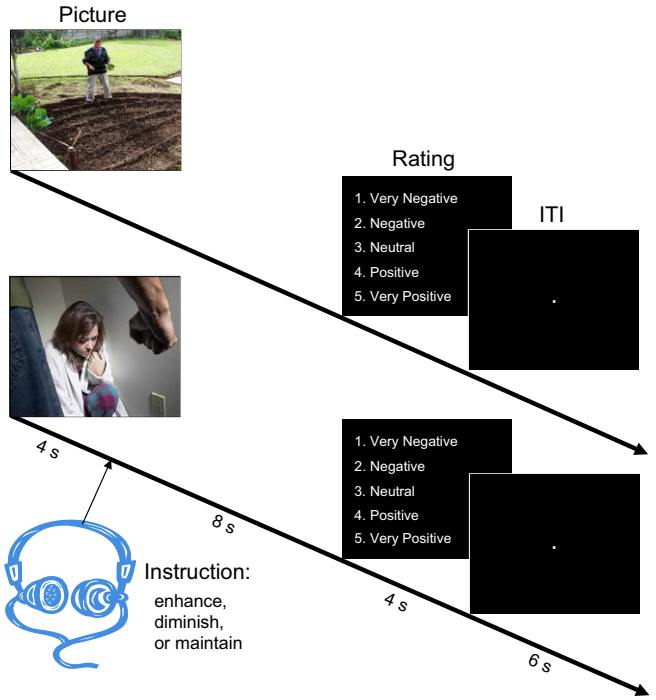

Figure 1. The emotion modification paradigm. This figure demonstrates our task design, with examples of two trials, one with the neutral picture and the other with the negative picture. We show here representative images similar to the IAPS image used in the task. We employed "diminish," "maintain," and "enhance" instructions. The bottom picture is an example of a negative image, similar to the IAPS image used in our task, to depict negative interpersonal interactions. For neutral pictures, subjects were asked only to "maintain" responses. IAPS, International Affective Picture Set; ITI, intertrial interval.

screen with a scale for subjective rating, and a 6-sec ITI (Figure 1; fixation period not shown). In each run, subjects viewed 5 neutral and 15 negative pictures. For the neutral pictures, subjects received only the maintain instruction. For the negative pictures, they received one of the three regulation instructions with five pictures for each condition. Negative pictures were matched for valence and arousal across regulation instruction conditions. Trials were presented in four runs of 20 pictures with the instructions presented in a pseudorandom order to maximize the fMRI model estimation efficiency. Prior to scanning, participants were trained to perform the emotion regulation. All scan sessions started and ended with a 24-sec fixation period to permit reliable estimation of BOLD response for the active versus baseline contrast in general linear modeling (GLM). We counterbalanced order to control for carryover effects from one trial to the next by intermixing the neutral-maintain condition as the reference for the other three instruction conditions (negative pictures: diminish, enhance, maintain).

fMRI Data Acquisition

Blood oxygenation level-dependent imaging was performed using an echo planar image (EPI) sequence (42 axial slices of 2.5 mm thick with a skip of .825 mm, repetition time [TR] = 3000 msec, echo time [TE] = 27 msec, flip angle = 85°, field of view [FOV] = 210 mm, matrix = 64 × 64) on a Siemens (Erlangen, Germany) Allegra 3 T magnetic resonance imaging (MRI) scanner. A T2-weighted structural scan with the same orientation and high in-plane resolution was acquired as an anatomical reference for realignment and spatial normalization of functional scans.

fMRI Data Analysis

Image preprocessing and statistical analysis were conducted using SPM2 (http://fil.ion.ucl.ac.uk.spm/) (52). Standard steps for preprocessing the EPI images were conducted, including correction for slice timing and head motion, registration to a high-resolution anatomical image, spatial normalization, and smoothing using a Gaussian kernel of 8-mm full-width at half maximum. A temporal high-pass filter with a period cutoff of 128 sec was also applied. The one-tag auto-correlation (1) was used to correct intrinsic temporal correlations. This was followed by the whole-brain voxel-based GLM at the single-subject level to estimate signal change associated with the conditions of interest (e.g., negative pictures during the diminish condition) with regard to the baseline condition, using six motion parameters as covariates of no interest. Specifically, one regressor was used to model the fixation period before the image using a boxcar function of 1-sec duration; two regressors were used to model the initial picture periods for negative and neutral images using boxcar functions of 4 sec; three regressors were used to model the three different sound instructions using 1-sec boxcar functions; four regressors using 7-sec boxcar functions were used to model the regulation periods for the negative-diminish, negative-enhance, negative-maintain, and neutral-maintain conditions; and one regressor was used to model rating responses using delta functions. For the group-level analysis, we employed random effects analyses for both within-group averaging and cross-group comparison. The intensity threshold for each voxel was set at $p < .01$ (uncorrected) and a minimum cluster extent threshold was set to 100 contiguous voxels resampled to $2 \times 2 \times 2$ mm^3 to correct for multiple voxel comparisons at $p < .05$, as

Table 1. Demographics/Clinical Information of Participants

Group	Healthy ($n = 14$)	Trauma-Exposed Non-PTSD ($n = 14$)	PTSD ($n = 14$)
Age (Years)	31.7 (10.3) range: 20–53	38.5 (10.8) range: 20–55	38.7 (11.2) range: 23–55
Race	4 H, 3 AA, 4 C, 1 A, 2O	4 H, 5 AA, 5 C	4 H, 4 AA, 4 C, 2 A
Employment	85.7% employed	85.7% employed	57.1% employed
Marital Status	21.4%M, 7.1%D	21.4%M, 35.7%D	21.4%M, 50.0%D
Education after High School (Years)	4.4 (2.3)	1.9 (2.5)[a]	2.7 (2.6)
CAPS	NA	5.9 (4.9)[b]	69.1 (17.6)
BDI	.8 (.9)[b]	2.1 (3.2)[b]	21.2 (12.5)
With Domestic Abuse	0/14[c]	3/14	5/14
THQ Sexual Assault Frequency	0 (0)[c]	5.2 (9.1)	13.9 (23.0)
THQ Impact of Sexual Assault	0 (0)[c]	16.4 (29.4)	68.3 (115.7)
THQ Total Frequency	6.1 (11.6)[b,c]	18.6 (23.2)[a]	44.6 (36.0)
THQ Impact of Trauma	12.7 (21.6)[b,c]	64.1 (90.8)[a]	190 (181.9)
CTQ Total	31.1 (5.8)[b]	39.6 (20.3)[b]	61.5 (24.4)
PANAS-Negative	12.6 (3.4)[b]	12.2 (2.7)[b]	24.7 (7.2)
PANAS-Positive	37.4 (5.7)[b]	42.5 (4.6)[b]	28.5 (10.1)
LOT-R Total Score	18.4 (3.2)[b]	17.9 (4.2)[b]	11.1 (5.5)
CD-RISC Total Score	80.4 (9.5)[a]	82.0 (17.7)[a]	62.3 (23.1)

Data shown: mean (SD).

A, Asian; AA, African American; BDI, Beck Depression Inventory; C, Caucasian; CAPS, Clinician Administered PTSD Scale; CD-RISC, Connor Davidson Resilience Scale; CTQ, Childhood Trauma Questionnaire; D, divorced; H, Hispanic; LOT-R, Life Orientation Test-Revised; M, married; O, other; PANAS, Positive and Negative Affect Scale; PTSD, posttraumatic stress disorder; THQ, Trauma History Questionnaire.

[a] $p < .05$ (statistically significant difference corrected for multiple comparisons between PTSD group and other groups).

[b] $p < .01$ (statistically significant difference corrected for multiple comparisons between PTSD group and other groups).

[c] $p < .001$ (resilient different from control subjects).

decided by a Monte Carlo simulation. The extent threshold and use of a random effects analysis limited the risk of false-positive findings due to multiple comparisons (53). For volume of interest (VOI) analyses, we selected regions by taking the peak voxel within the surviving clusters identified in across-group whole-brain analyses and extracted the average signal of voxels within 6 mm of each peak. Significant differences in terms of the main effect of conditions, of groups, and condition by group interactions were assessed in these regions.

Results

Subject Characteristics

Trauma severity in the trauma-exposed women was high, as we included only women with violent sexual trauma to enhance homogeneity of trauma histories. The trauma-exposed groups did not differ in sexual trauma frequency or impact but did differ in total trauma exposure frequency, including witnessing violence and victimization by petty crime (PTSD > trauma-exposed non-PTSD) [$F(1,26) = 5.1$, $p < .04$], impact [$F(1,26) = 5.4$, $p < .03$], and by the Childhood Trauma Questionnaire (CTQ) [$F(2,41) = 9.9$, $p < .001$; Fisher's least significant difference (LSD): resilient < PTSD, $p < .04$] (Table 1).

The groups did not differ significantly in age, marital status, or employment, but did in years of education [$F(2,39) = 3.37$, $p < .05$], with healthy control subjects more educated than trauma-exposed non-PTSD subjects but trauma-exposed non-PTSD not different from PTSD subjects (Table 1). The trauma-exposed groups did not differ in years since trauma exposure (trauma-exposed non-PTSD: 9.0 [SD = 5.9]; PTSD: 12.2 [SD = 9.9]). The PTSD group had significantly more PTSD symptoms, as expected, and more depressive symptoms than the other groups. The PTSD group also had less positive and more negative affect than the resilient and control groups. The control and trauma-exposed non-PTSD groups were higher in LOT-R score than the PTSD group. Forty-one subjects were right-handed, and one PTSD subject was left-handed. All above analyses controlled for trauma burden.

Subjective Rating

To match our fMRI contrasts, subjective ratings of negative pictures were analyzed in a group (PTSD, healthy control subjects, trauma-exposed non-PTSD) × condition (diminish-maintain, enhance-maintain) analysis of covariance (ANCOVA) controlling for trauma frequency, which revealed a significant group × condition interaction [$F(2,33) = 3.3$, $p < .05$]. Fisher's LSD tests showed that the healthy control group was more successful at decreasing negative ratings in response to the diminish compared with the maintain instruction than PTSD ($p < .03$) and tended to be more successful than the trauma-exposed non-PTSD group ($p < .07$). There were no significant post hoc group differences for enhance-maintain scores (Figure 2A and 2B). When examining the conditions separately in a group × condition multivariate analysis of covariance (MANCOVA) controlling for trauma burden, we found a main effect of condition [$F(2,29) = 1.20$, $p < .001$] but no group × condition interaction. That is, participants modified their subjective ratings of negative pictures in response to instruction to diminish, maintain, or enhance across groups but there was no difference between the groups in this effect (post hoc tests = ns). Adding education as a covariate did not alter results.

fMRI BOLD Responses

A whole-brain analysis examining BOLD response in the diminish-maintain contrast across groups showed activation of lateral PFC (x, y, z: −44, 8, 48; $Z = 5.27$), ACC (x, y, z: 2, 20, 42; $Z = 4.89$), and intraparietal sulcus (IPS) (x, y, z: −32, −62, 42; $Z = 3.32$) (Figure 3A). A similar whole-brain analysis examining BOLD response in the enhance-maintain condition across groups showed activation of medial PFC, specifically the supplementary motor area (SMA) (x, y, z: −6, 15, 52; $Z = 4.26$) (Figure 3B), a region activated in healthy subjects during enhancement of responses to negative stimuli (31). A VOI analysis was done to explore patterns of brain activation with deliberate regulation (both upregulating and downregulating responses). The four regions surviving threshold for significance in the whole-brain across-group analyses were included in this analysis. Blood oxygenation level-dependent response was examined in a group × condition × region MANCOVA controlling for total trauma exposure. This analysis showed a significant group × condition interaction [$F(3,37) = 6.0$, $p < .006$], with trauma exposed

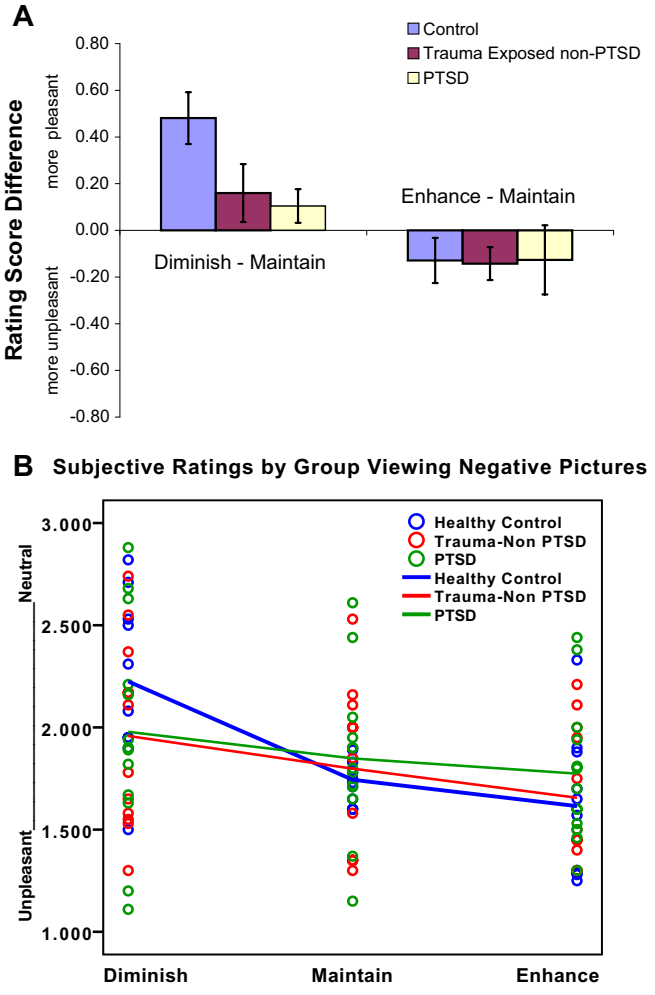

Figure 2. (A) Subjective behavioral response to instructions to "diminish" and "enhance" responses, compared with "maintain," to negative pictures. Subjects rated their responses to the pictures during the response period before the intertrial interval, after diminishing or maintaining their responses. There was a significant group difference showing that control subjects were able to adjust their response to a less negative valence significantly better than either the resilient or the PTSD groups. **(B)** Scatter plot of the behavioral responses for each group. PTSD, posttraumatic stress disorder.

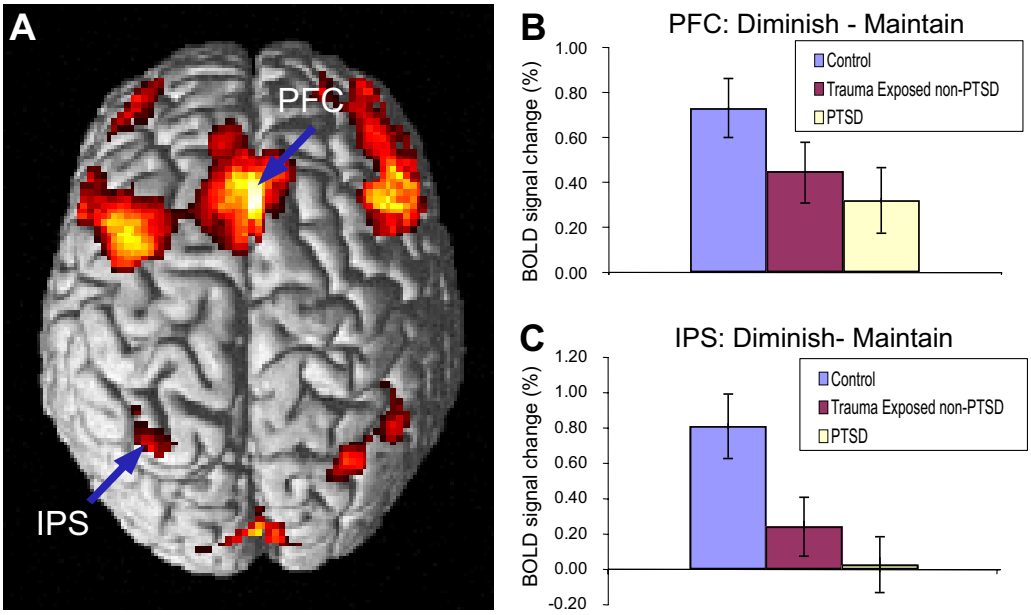

Figure 3. Brain responses related to voluntary emotion regulation to negative pictures. A whole brain contrast thresholded at $p < .01$ showing activation across groups in lateral PFC (x, y, z: −44, 8, 48; $Z = 5.27$) and in IPS (x, y, z: −32, −62, 42; $Z = 3.32$) during diminishment of responses to negative pictures **(A)**. A VOI-analysis for regions identified in the multivariate analysis showed group differences for "enhance" and "diminish" conditions in lateral PFC [x, y, z: −44, 8, 48; $F(2,39) = 5.0$, $p < .02$] **(B)** and SMA [x, y, z: −6, 15, 52; $F(2,39) = 3.3$, $p < .05$ **(C)**. BOLD, blood oxygenation level-dependent; IPS, intraparietal sulcus; PFC, prefrontal cortex; PTSD, posttraumatic stress disorder; SMA, supplementary motor area; VOI, volume of interest.

non-PTSD subjects more active than control or PTSD subjects during enhance-maintain, whereas resilient were similar to PTSD subjects during diminish-maintain. There was no significant group × condition × region interaction, as all the tested brain regions showed a similar pattern across groups.

As a follow-up test for the group differences in individual brain regions included in our multivariate analysis, we tested group differences for enhance-maintain and diminish-maintain in each region separately. Significant group × condition interactions were found in lateral PFC [$F(2,39) = 5.0$, $p < .02$] and SMA [$F(2,39) = 3.3$, $p < .05$] (Figure 3C and 3D). In ACC, there was no significant group × condition interaction [$F(2,39) = 1.8$, ns], and in IPS, there was only a trend level group × condition interaction [$F(2,39) = 2.6$, $p = .09$].

See Table 2 for pairwise group contrasts during diminish-maintain and enhance-maintain instructions. We noted that in the diminish-maintain condition, the control subjects were more active across regions of PFC than either PTSD or trauma-exposed non-PTSD subjects, whereas PTSD and trauma-exposed non-PTSD subjects showed minimal areas of difference in this condition. In the enhance-maintain condition, we noted that control subjects were also more active in frontal regions than the PTSD group, but the trauma-exposed non-PTSD group resembled the control group. The one area more active in trauma-exposed non-PTSD than control subjects in this condition was the ACC. Within-subject comparisons showed BOLD activation of medial and lateral PFC, including ACC in healthy subjects and resilient as seen in other studies employing an emotion modification task (31,39,41,42) (Table 3 in Supplement 1).

To explore amygdala activation, we examined the maintain-diminish contrast across groups and identified activation in a right periamygdaloid region (x, y, z: 34, 2, −16; $Z = 4.37$, cluster size = 159 voxels), demonstrating an effect of voluntary down-regulation of emotion, although no group differences in amygdala activation were seen.

We also tested group differences in the maintain condition that might contribute to the differences found in our VOI analysis. A group × region MANCOVA for BOLD response (controlling for trauma) in negative-neutral images after maintain instruction did not reveal a significant group or group × region interaction (post hoc tests, ns). Although the maintain condition was not the focus of this work, whole-brain analysis assessing group differences in the maintain condition was done for completeness. While some areas did show group differences, regions identified by our omnibus across-group analysis, and therefore included in VOI analyses, did not show group differences. No amygdala activity in the maintain condition survived threshold (Table 2 in Supplement 1). We acknowledge that even the maintain condition involves some degree of emotion manipulation, in that subjects extend the duration of their emotional responses.

Discussion

Our study extends the literature on neural correlates of deliberate emotion regulation from healthy individuals to trauma-exposed women with and without PTSD. We did not affirm the hypothesis that the ability to downregulate emotional response was associated with protection against psychiatric sequelae. We showed, instead, that nontraumatized healthy control subjects appeared to be more successful at decreasing emotional responses to negative stimuli than either trauma-exposed group, as indicated by more positive change in control participants' rating of negative pictures and a similar pattern of greater fMRI response in brain regions activated by the task in control subjects. Our second major finding is that trauma-

Table 2. Significant Differences in BOLD Signal Between Groups During Conditions of Voluntary Emotion Regulation to Negative Pictures

	Control–PTSD				PTSD–Control				Control–Non-PTSD				Non-PTSD–Control				Non-PTSD–PTSD				PTSD–Non-PTSD	
Regions	x	y		Z_{score}	x			Z_{score}	x			Z_{score}	x			Z_{score}	x	y		Z_{score}	x	Z_{score}
Diminish Minus Maintain																						
Posterior cingulate																						
Left (BA 29/31)	−6	−42	10	2.62																		
Right	14	−42	38	2.69					4	−24	26	3.76										
Lingual gyrus (BA 18)																	0	−60	2	3.26		
Left inferior orbital cortex																						
(BA 47)	−32	38	−8	2.56																		
Superior frontal gyrus																						
Left (BA 9)									−22	12	48	2.56					−18	46	32	3.25		
Right	20	20	50	2.80					14	26	48	3.03										
Left middle frontal gyrus																						
(BA 6)	−38	2	36	2.96					−34	16	56	3.97					−22	32	42	2.56		
Medial frontal gyrus																						
(BA 8)	−4	40	44	3.30																		
Left inferior frontal gyrus																						
(BA 44/47)	−36	30	−12	3.81	54	8	2	3.43														
Middle temporal gyrus																						
(BA 20/21)					−52	−58	0	3.48					50	−66	2	3.85						
Superior temporal gyrus																						
Left (BA 42)					−56	−8	10	3.76														
Right													56	10	0	3.52						
Precentral gyrus (BA 4/6)	−36	−6	36	2.60																		
Rolandic operculum																						
(BA 48)					54	−2	10	2.88														
Inferior pari lobe																						
(BA 7/40)	−42	−60	40	3.24					−34	−66	48	3.03										
Right caudate									10	6	16	3.23										
Left superior occipital																						
gyrus (BA 38+)													18	−84	40	3.93						
Inferior occipital gyrus																						
(BA 29)													38	−82	−4	3.08						
Enhance Minus Maintain																						
Left superior frontal gyrus																						
(BA 32)	−12	38	40	4.61																		
Right medial prefrontal																						
cortex/SMA (BA32/6)	10	22	50	4.10													−6	12	60	4.16		
Right middle frontal gyrus																						
(BA 8)	44	14	36	3.17													44	16	38	3.49		
Left middle frontal gyrus																	−40	10	44	3.37		
Anterior cingulate																						
(BA 24/32)													−4	2	42	2.93						
Superior parietal lobe																						
(BA 7)					14	−66	60	3.61														
Inferior parietal lobe																						
(BA 39)	−42	−62	52	2.86																		

Table 2. Continued

Regions	Control–PTSD			PTSD–Control			Control–Non-PTSD			Non-PTSD–Control			Non-PTSD–PTSD			PTSD–Non-PTSD		
	x	y	Z_{score}	x		Z_{score}	x		Z_{score}	x		Z_{score}	x	y	Z_{score}	x		Z_{score}
Superior temporal gyrus (BA 42)				−58	−30	18	3.32											
Inferior temporal gyrus (BA 20)																		
Lingual gyrus (BA 18)				20	−68	−8	3.07											
Parahippocampal gyrus (BA 36/20)																30	6	−30	3.34
																32	−22	−18	3.39

This table shows clusters that survived whole-brain between pairwise group comparisons for signal change in the "diminish" minus "maintain" and "enhance" minus "maintain" contrasts for aversive pictures. The random effects analysis was thresholded at $p < .01$, with a minimum cluster extent threshold of 100 contiguous voxels. *Z* scores reported for peak voxels. Locations are derived from the Montreal Neurologic Institute Atlas.

BA, Brodmann area; BOLD, blood oxygenation level-dependent; MNI, Montreal Neurologic Institute; PTSD, posttraumatic stress disorder; SMA, supplementary motor area.

exposed non-PTSD subjects activated PFC more after the enhance instruction than the PTSD group and tended to activate these regions somewhat more than the nontraumatized control subjects.

The ability to downregulate responses to negative experiences has face validity as one possible mechanism of resilience in the face of trauma exposure. According to this model, the ability to decrease emotional responses to negative stimuli would permit a positive adaptation to adverse events. By this model, we should have seen greater activation across regions of PFC and ACC in the trauma-exposed non-PTSD than the PTSD group and possibly the control group during emotion downregulation. Instead, during downregulation, the trauma-exposed non-PTSD group resembled the PTSD group in BOLD response, and both trauma-exposed groups showed less effective attenuation of responses to negative pictures regardless of the clinical outcome compared with nontraumatized control subjects. This raises that possibility that trauma exposure itself may impede the ability to decrease emotional responses to negative stimuli. The finding that the trauma-exposed groups in this task are similar is particularly noteworthy, given the remarkable differences in clinical outcomes after trauma between the two groups. The trauma-exposed non-PTSD participants are indistinguishable from the nontraumatized control participants in their low depression ratings, high levels of optimism, psychological resilience, and positive emotion, whereas the PTSD group had high scores of negative affect, low positive affect, low optimism, low resilience scores, and high levels of PTSD re-experiencing symptoms. In addition, we did not find evidence for an alternative functional mechanism by which trauma-exposed non-PTSD and PTSD might be more emotionally reactive, which could be seen in amygdala responsiveness; in fact, we found no group differences in amygdala response in the maintain condition viewing negative images. The absence of group differences in amygdala during downregulation, paired with the group differences found in PFC, leads us to consider that our groups employed different brain regions in regulatory strategies. For example, while control subjects may activate classical emotion regulatory regions, trauma-exposed groups may engage a more distributed cortical network in the control of emotion, which would likely not have reached threshold to be detected by our analysis.

Our second major finding, somewhat unexpected, is that trauma-exposed non-PTSD individuals resemble control subjects and not PTSD subjects in brain activation while deliberately increasing emotional response to negative images. How might the ability to magnify negative emotional responses relate to a protective factor in the face of trauma or resilience? One study showed that the deliberate enhancement of responses to fear-inducing stimuli is the most effective strategy in decreasing performance anxiety (54), suggesting perhaps that the ability to focus on negative emotions may help diminish the intensity of those emotions. Further support for this model comes from evidence that alexithymia is a risk factor for PTSD (55–57). These studies raise the possibility that the ability to focus on negative emotions permits the engagement of cognitive strategies for extinguishing negative emotional responses. In fact, female assault victims with high levels of initial engagement in the reimagining experiences during exposure therapy show the greatest symptomatic improvement (58). The specific region of the PFC activated during the deliberate increase of emotional responses was the SMA. Recent studies of the function of the SMA have suggested that it is preferentially recruited by emotional stimuli and is thought to be part of an emotion-related

sensorimotor network that may be involved in movement preparation (59,60). Interestingly, SMA has been viewed as part of the neural network underlying a "motor theory of empathy" (61).

Our study raises the possibility that resilience might relate to the capacity to focus intensively on negative emotional responses and to engage cognitive/linguistic areas of the brain to cope with the negative emotion. This may be adaptive because it may reflect an ability to manage negative emotions. Thus, while resilient individuals may not be able to decrease emotional responses to negative stimuli (perhaps related to their trauma histories), they may nevertheless cope with negative emotional stimuli through a capacity to tolerate emotional experiences. Indeed, the intensity of ACC activation, a brain region associated with emotion regulation, was significantly correlated with optimism in the trauma-exposed non-PTSD subjects.

Our study has a number of limitations. First, we did not demonstrate robust group differences in subjective ratings. This may be because of a floor effect and narrow range in our subjective ratings. The most negative rating possible was a "1" and our subjects rated the negative pictures very close to this floor even during the maintain instruction. In addition, while the PTSD group did not differ from the trauma-exposed non-PTSD group in sexual or physical assault histories, the PTSD group reported a higher number of total traumas. It is important to note, however, that we included only subjects who had experienced a violent sexual assault, a high threshold for trauma severity, and we controlled for total trauma exposure in our analyses. Furthermore, our findings on emotional downregulation do not support group differences in the trauma-exposed groups, making it unlikely that a difference in trauma exposure accounts for our finding. Finally, we did not fully explore in this report group differences in the maintain condition, although there were no significant group differences surviving threshold in the regions highlighted in our VOI analyses of emotion modification conditions.

Despite these limitations, the present study has important strengths. It is the first to examine deliberate emotion regulation in PTSD and trauma-exposed non-PTSD, extending the literature on neural correlates of emotion modification into the clinical realm in women who have been exposed to one of the most severe types of trauma, sexual assault. Our data draw attention to the possibility that downregulating emotional responses may be influenced by trauma history, whereas the ability to sustain attention to emotionally negative stimuli might be associated with better outcomes after trauma. These findings await replication in future studies. The seemingly counterintuitive finding that trauma-exposed non-PTSD and PTSD groups are similar in their ability to dampen down their emotional responses to negative stimuli, coupled with the finding that differences in brain activation differentiating PTSD from trauma-exposed non-PTSD women were observed only while increasing emotional responses, highlight the need for a more complex model of emotion regulation in future studies of risk and resilience to trauma.

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Supplementary material cited in this article is available online.

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