

An fMRI study of the brain responses of traumatized mothers to viewing their toddlers during separation and play

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This study tested whether mothers with interpersonal violence-related posttraumatic stress disorder (IPV-PTSD) vs healthy controls (HC) would show greater limbic and less frontocortical activity when viewing young children during separation compared to quiet play. Mothers of 20 children (12–42 months) participated: 11 IPV-PTSD mothers and 9 HC with no PTSD. During fMRI, mothers watched epochs of play and separation from their own and unfamiliar children. The study focused on comparison of PTSD mothers vs HC viewing children in separation vs play, and viewing own vs unfamiliar children in separation. Both groups showed distinct patterns of brain activation in response to viewing children in separation vs play. PTSD mothers showed greater limbic and less frontocortical activity (BA10) than HC. PTSD mothers also reported feeling more stressed than HC when watching own and unfamiliar children during separation. Their self-reported stress was associated with greater limbic and less frontocortical activity. Both groups also showed distinct patterns of brain activation in response to viewing their own vs unfamiliar children during separation. PTSD mothers' may not have access to frontocortical regulation of limbic response upon seeing own and unfamiliar children in separation. This converges with previously reported associations of maternal IPV-PTSD and atypical caregiving behavior following separation.

Keywords: maternal PTSD; early childhood; functional neuroimaging; emotion regulation; corticolimbic pathways; interpersonal violence

INTRODUCTION

Adults with posttraumatic stress disorder (PTSD) have difficulty regulating their emotions when new experiences remind them of one or more aspects of their trauma (New *et al.*, 2009). Neuromaging studies of PTSD patients have reported significant activation in brain regions implicated in the processing and regulation of emotions and arousal (Etkin and Wager, 2007; Bluhm *et al.*, 2009). These studies have shown that limbic responses to either positively or negatively valenced emotional stimuli, such as facial expressions or evocative verbal descriptions of interpersonal conflict, are exaggerated in adults who have interpersonal

violence-related PTSD (IPV-PTSD), even when the stimuli have no apparent direct connection to the traumatic events previously experienced (Shin *et al.*, 2005). Medial prefrontal cortical (mPFC) activation that is known to regulate limbic activity within the brain is, in contrast, diminished in PTSD patients compared with controls during the processing of similar stimuli (Gilboa *et al.*, 2004).

While there are no previously published neuroimaging studies of women with IPV-PTSD who are mothers in response to their children, behavioral studies indicate that the use of neuroimaging could help us to understand caregiving behavior that differentiates these women from healthy controls (HC) (i.e. 'atypical caregiving behavior'), and thus help address such behavior clinically. For example, mothers who have IPV-PTSD in comparison to healthy mothers show impaired reading of child affect, less empathic responsiveness and less availability for joint attention, particularly after a social stressor such as mother–child separation (Lyons-Ruth and Block, 1996; Schechter *et al.*, 2010). Specifically, following child separation, mothers' emotional availability to respond to child bids for engagement in joint attention to play was negatively correlated with their IPV-PTSD symptom severity (Schechter *et al.*, 2010). The present MRI study was, in fact, nested in that

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behavioral study. While, no previous MRI studies to our knowledge have directly examined the neural circuits that could underlie these in PTSD-mothers' atypical caregiving behavior, several imaging studies investigated neural activity among healthy parents in response to infant cries and faces (Swain *et al.*, 2007; Strathearn *et al.*, 2008). One study that used video excerpts of toddlers during play and separation reported activation of the mPFC in healthy mothers when viewing responses of their child during separation *vs* play (Noriuchi *et al.*, 2008). This study found specific coordinated neural activity in cortical (i.e. mPFC, anterior cingulate and insula) and subcortical (i.e. amygdala, anterior entorhinal and perirhinal cortex) regions that participate in the emotion processing in response to viewing the video excerpts.

We also assessed brain activity in these corticolimbic circuits, but in a sample of mothers with marked IPV-PTSD compared to those without IPV-PTSD within an inner-city community that is rarely recruited for neuroimaging studies. Our overall goal has been to understand the circuitry in a mother's brain that might hinder *vs* support her capacity to respond sensitively to her child's affective communication under stress. Our curiosity has been fueled by our study of maternal emotional availability for joint focus of attention as mentioned above (Schechter *et al.*, 2010), as well as by an additional observation of IPV-PTSD mothers' tendency to 'misread' child affective communication (Fraiberg *et al.*, 1975). With respect to this latter point, we previously studied clinically referred mothers with IPV-PTSD, who prior to video feedback, frequently misread their child's anxious facial expressions as angry and controlling, and only after therapeutic intervention were able to see and describe their child's separation anxiety and helplessness (Schechter *et al.*, 2006). In the present study, we therefore describe the functioning of neural systems that subservise emotional reactions by mothers with IPV-PTSD and non-traumatized comparison mothers while watching videos of their own and unfamiliar toddlers displaying distress responses during separation or when playing quietly.

Hypotheses

Mothers with IPV-PTSD as compared to HC will show in response to viewing their own and unfamiliar children in separation (stressful condition) as contrasted with play (non-stressful condition) the following:

- (1) greater activation of fear-response circuitry (i.e. amygdala, entorhinal and perirhinal cortices, and hippocampus). We expect that this response will be stronger for own than for unfamiliar children, but will be generalized also to unfamiliar children.
- (2) less activation of higher cortical areas [i.e. superior frontal gyrus (SFG)/MpfC] that are involved in down-regulation of the fear response (Shin *et al.*, 2006) and
- (3) greater self-reported stress on a post-MRI scan interview.

Additionally, we expect that mothers' self-reported stress in response to seeing their own and unfamiliar children in separation (*vs* play) and clinician-assessed PTSD symptom severity will both be associated with greater activation of fear-response circuitry and less activation of corticofrontal areas (i.e. mPFC) that are known to regulate limbic response when continuous analyses are applied across the entire sample. Given previous behavioral findings of less maternal emotional availability following separation, we might also expect less activation of brain regions associated with empathy (i.e. the insula) in PTSD *vs* HC mothers in response to viewing children during separation *vs* play (Decety, 2010). In testing these hypotheses, this is the first study ever to examine how IPV-PTSD, considered as a disorder of emotion regulation, affects mothers' neural response to viewing their own and unfamiliar preschool-age children in a situation that renders the child helpless and vulnerable. It newly examines how this neural response might correspond to subjective reports of parenting stress and observations of parental interactive behavior before and after separation such as we have described in previous articles (Schechter *et al.*, 2010). Specifically, this study will help characterize how IPV-PTSD mothers process young children's emotional communication in the context of maternal IPV-PTSD (as compared to HC) in response to seeing them in a stressful (separation) *vs* non-stressful (play) condition.

METHODS

Participants

Recruitment

We obtained informed consent from participants both for the non-MRI and nested MRI study reported here according to procedures approved by the Columbia University Medical Center's Institutional Review Board. Recruitment from pediatric community clinics is described in further detail in the Supplementary Materials (see also Schechter *et al.*, 2010). Twenty mothers who either had a diagnosis of IPV-PTSD (PTSD mothers) or who did not (HC) and who had both joined the larger mother-child study and were eligible for imaging (i.e. not pregnant) were scanned.

Sample characteristics

Mothers (19 right-handed, 1 left-handed) of 20 children (10 boys, 10 girls), 12–42 (mean 24 ± 8) months of age, participated. The single left-handed subject, when subtracted and then re-added to the sample, did not significantly alter results within or between groups.

Procedures

Procedures for visits prior to MRI scan

The protocol consisted of two 2-h videotaped visits following informed consent and screening (Schechter *et al.*, 2010). During an initial videotaped interview, PTSD and HC mothers underwent a variety of psychometric examinations to assess their life-events history and psychopathology. Most

importantly, lifetime and current diagnoses of PTSD was determined using the Clinician Administered PTSD Scale (CAPS) (Blake *et al.*, 1995—see Supplementary Data and Schechter *et al.*, 2010), which has extremely high interrater reliability (Cicchetti *et al.*, 2009). The diagnosis of current PTSD at the time of participation was confirmed by self-report using the PTSD symptom checklist-short version (PCL-S) (Weathers *et al.*, 1996—see Supplementary Data and Schechter *et al.*, 2010).

One to 2 weeks after the initial videotaped maternal interview, the mothers and their children returned for a videotaped interaction. The protocol used to structure this visit was the Crowell procedure (Crowell *et al.*, 1988) as modified by Zeanah *et al.* (2000). It consisted of two repetitions of the following mother–child interactions: (i) playing together as they did at home using a range of toys provided (8 min), (ii) separating (3 min) and (iii) reuniting (3 min). fMRI stimuli were drawn from interaction sequences (i) and (ii).

Stimuli

Mother viewed six different, silent, 40-s video excerpts of three different children, each during the two conditions: separation and play: (i) own child, (ii) unfamiliar boy and (iii) unfamiliar girl. The unfamiliar children were of similar mean age, drawn from a similar Hispanic and African–American inner-city community, and were filmed in a similar parent–child interaction protocol to ours, but at another institution.

Selection of stimuli

A research assistant who was blind to case–control status among mothers' own children selected the silent excerpts for the fMRI stimulus in play and separation: mothers viewed the play excerpt observed to show the most joy and reciprocally the separation excerpt with the strongest child emotional response.

Selection of separation video excerpts

The two separation segments during the videotaped interaction protocol were rated without sound on a 5-point Separation Distress Scale (SDS; Schechter and McCaw, 2005) by two graduate-student raters independently, who were both naïve to group membership (rating 0 = no observable distress, 4 = agitation). The consistency of the child's response to separation across the both episodes of videotaped separation, as a measure of test–retest reliability was robust (Cronbach's $\alpha = 0.82$). The episode in which the child was more distressed was shown in the scanner. Interrater reliability was excellent (ICC = 0.95, $P < 0.001$). For own child, raters found the mean stress on separation to be 2.31 (s.d. = 1.35; range 1.5–4.0); unfamiliar boy was rated '2' and girl '4'. Concordance between raters' and mothers' estimation of child distress was high (Cronbach's $\alpha = 0.83$). Both genders of unfamiliar children were included in an effort to control for gender mix among own-child stimuli.

Study design

The study design (Supplementary Figure S1) consisted of four runs, each lasting 11 min 12 s, and each containing two blocks during which mothers viewed six 40-s video excerpts per block, displayed in a pseudorandom order, counterbalanced within and across runs. Thus, mothers viewed each of the six 40-s film clips eight times. Eye tracking and vocal reminders by the technician to pay attention to the screen between runs were used to ensure that mothers were attending to stimuli.

Postscan interviews of mothers about their response to stimuli

A postscan interview developed by the authors assessed subjective (self-reported) 'stress' (displeasure) and 'fun' (pleasure) experienced in response to viewing each of the six excerpts on a 5-point rating scale from '0' as 'least' to '4' as 'most'.

Image acquisition and pre-processing

Briefly, imaging was performed under GE 3T scanner. Standard fMRI preprocessing procedures including slice timing and motion corrections, and spatial normalization and smoothing were performed under SPM and MATLAB. See Supplementary Data for details.

Hypothesis-driven analyses

The Blood Oxygen-Level Dependent (BOLD) response from each run was first assessed using a General Linear Model containing seven time-dependent functions representing each stimulus type (resting gaze fixation and six videos) and one constant (baseline BOLD signal). Contrast images representing the differential effect of the video presentations on voxel-wise BOLD signals were created for each subject. A contrast specifying 'separation *vs* play' was the difference in estimated neural activity during the viewing of the child in the separation condition compared with estimated activity during the viewing of the child during free play (condition). Results for this are not discussed but can be found in the Supplementary Table S3. To examine hypotheses 1 and 2 (see page 4), we performed paired-samples *t*-tests that compare BOLD activation in subjects with PTSD to the BOLD activation in HC when watching scenes of separation *vs* play, once for own children and once for unfamiliar children. To examine within-group differences in activation associated with the familiarity of the children (i.e. own *vs* unfamiliar), we performed paired-sample *t*-tests comparing activity when viewing their own child *vs* unfamiliar children for the separation relative to play contrast. We report significant changes in voxels using a $P \leq 0.025$ threshold (i.e. a two-tailed $P \leq 0.05$) together with the requirement that the activation occurred in an empirically derived spatial cluster greater than 25 adjacent voxels. This conjoint cluster-size requirement which is based on an approximation formula (Friston *et al.*, 1994), yields a conservative effective

$P < 0.000005$. The combined application of a statistical threshold and cluster filter reduces substantially the false-positive identification of activated voxels at any given threshold (Forman *et al.*, 1995).

Group differences with respect to maternal self-reported stress experienced when looking at their own and unfamiliar children during separation were tested using independent *t*-tests.

To investigate the neural correlates of this same variable of maternal self-reported stress, we entered into a regression model BOLD signal change, detected by the contrast of separation relative to free play as the dependent variable and as a predictor, the maternal self-rated stress score from the post-MRI interview. Similarly, to investigate the neural correlates of maternal PTSD symptom severity, we entered into a similar regression model as a predictor, a composite of *z*-scores based on the CAPS score from the initial interview with mother—and the maternal self-reported PCL-S that was administered during the scanning visit. These analyses also use a $P \leq 0.025$ threshold with a minimum cluster size of 25 voxels.

RESULTS

Characteristics of PTSD vs HC groups

The IPV-PTSD case group ($n = 11$) was rigorously defined by clinician rating on the CAPS and PCL-S scores (Supplementary materials; Schechter *et al.*, 2010): 11 PTSD mothers (30 ± 6 years old) and 9 HC mothers (31 ± 7 years old), 5 of whom had limited violence exposure that they did not rate as traumatic and to which they did not attribute

PTSD symptoms (one with prior domestic violence and four with histories of excessive corporal punishment for a defined period). These nine HC mothers had neither the diagnosis of PTSD nor subthreshold PTSD, and were not suffering from major depression.

As expected (Shea *et al.*, 2004), PTSD was significantly more often comorbid with major depressive disorder (MDD) and greater severity of depressive symptoms. Overall dissociative symptom scores (DESS) were similarly elevated for PTSD (27 ± 20) and minimal for HC (5 ± 1.5 ; $t_1 = 3.6$, $P < 0.01$). The degree of naively rated child distress on silent video excerpts depicting children during separation also did not differ between groups (Table 1).

PTSD and HC groups did not differ significantly in terms of child age or gender (Table 1). Cases differed only from controls on background variables with respect to lower household income and number of years of education ($P < 0.05$), despite no group difference in attainment of a high-school diploma or General Educational Diploma (GED) ($P > 0.3$). Consequently, we included household income and number of years of education as covariates in the model for neural activation during the viewing of separation *vs* play and noted no significant effects.

Imaging results

Mothers viewing their own children during separation vs free play

Neural activity when viewing their own children during separation *vs* free play ('separation-play') was compared across

Table 1 Demographic and clinical characteristics of subjects^a

	PTSD cases ($n = 11$)	HC ($n = 9$)	<i>t</i> -test and χ^2 statistics (df = 18)	
			<i>t</i> -value or χ^2	Significance (<i>P</i>)
Mean age of mother	29.5 (7.1)	30.4 (7.2)	0.31	0.76
Mean age of child (months)	25.4 (7.9)	21.9 (7.8)	-0.98	0.34
Number of boys	6	4	-1.34	0.20
Number of mothers with high school diploma or equivalent (GED)	6	7	1.17	0.37
Mean years of the mothers education	11.9 (1.4)	14.3 (3.4)	2.15	0.05
Mean income in \$1000 increments	25.5 (18.6)	54.4 (32.1)	2.53	0.02
Mean number of violent events	25 (17.4)	8.7 (8.9)	-2.71	0.02
Recent domestic violence (%)	64	0	-4.18	0.002
Mothers who attempted suicide (%)	45	0	-2.89	0.02
History of child protection involvement (%)	45	0	-2.90	0.02
PSI-SF mean score	47.6 (15.4)	20 (12.4)	3.38	0.006
CAPS mean score (lifetime PTSD)	88.5 (15.6)	18.3 (16)	-9.40	<0.001
Baseline mean PCLS (current PTSD)	43.3 (17.2)	19.9 (9.7)	-3.80	<0.001
Scan mean PCLS (current PTSD)	43.7 (13.5)	13.2 (10.2)	-5.58	<0.001
MDD diagnosis on MINI	7.0 (63.6)	0.0 (0.0)	5.87	0.02
Baseline mean BDI	18.7 (13.2)	5.2 (4.8)	-3.91	0.004
Scan mean BDI	16.2 (12.6)	3.3 (4.6)	-3.77	0.002
DES mean score	25.8 (21.4)	5 (5.2)	-3.12	0.009
Borderline personality screen (PDQ-IV)	3 (27.2%)	2 (22.2%)	0.27	0.54
Mean child distress (independently rated)	2.5 (1.4)	2.1 (1.3)	-0.56	0.58

^aMeans are reported with standard deviations; 19/20 subjects were right-handed.

PSI-SF, parenting stress index-short form; PCLS, post-traumatic stress symptoms checklist-short version; MINI, Mini International Neuropsychiatric Interview; BDI, Beck Depression Inventory; DES, Dissociative Experiences Scale; PDQIV, Personality Disorders Questionnaire.

two groups: for 11 PTSD mothers *vs* 9 HC (group-by-condition interaction, see Figure 1A).

PTSD mothers *vs* HC (Figure 1A and B) exhibited significantly greater activation in the bilateral anterior entorhinal cortex (AEC, BA34) and the left caudate.

HC compared to PTSD mothers (Figure 1A and C) exhibited significantly greater activation in higher cortical regions (SFG; BA8,10) and bilateral superior parietal lobes (SPL; BA7).

Maps for separation *vs* rest ('separation-rest') and play *vs* rest ('play-rest') suggested that the group difference in these activations originated in response to separation rather than to play (Supplementary Figure S2).

In response to seeing their own children in separation *vs* play (Figure 1A), we noted apparent activation of the left insula (BA13) in the PTSD mothers compared to HC, which actually represents 'deactivation' among HC (i.e. activation while seeing their own child in play, which is also a control condition, as confirmed by separation *vs* rest and play *vs* rest maps (Supplementary Table S1 and Figure S2).

Mothers viewing unfamiliar children during separation vs with free play

PTSD *vs* HC mothers (Figure 1D and E) exhibited significantly greater activation in limbic regions: the right amygdala, bilateral AEC (BA34), left perirhinal cortex (BA35); as well as the left caudate and the L > R fusiform gyrus (BA37).

HC *vs* PTSD mothers (Figure 1D and F) when viewing unfamiliar children in separation *vs* play did not exhibit significantly greater activation in the SFG (BA8,10). However, PTSD mothers activated the L middle frontal gyrus (MFG; BA10) significantly more than HC.

Maps for separation *vs* rest and play *vs* rest suggested that this group difference originated in response to separation rather than to play (Supplementary Figure S2).

In response to seeing unfamiliar children in separation-play (Figure 1D), we noted activation of the left insula (BA13) in the PTSD *vs* HC mothers that was similar to that which we noted in response to mothers viewing their own child. The origin of this apparent activation is again a 'deactivation' among HC (i.e. activation in response to viewing play), as was true in response to mothers viewing their own child. Separation- and play-rest maps showed that HC mothers activated the insular cortex more than PTSD mothers when seeing their own and unfamiliar children play (Supplementary Table S2 and Supplementary Figure S2).

Within-group differences in viewing children in separation by own vs unfamiliar child

We assessed group differences in activation associated with the familiarity of the children (i.e. own *vs* unfamiliar) during

separation only as per our a priori hypothesis (familiarity-by-condition interaction) separately in PTSD and HC mothers (Figure 2).

Among PTSD mothers, activation differed significantly when viewing their own *vs* unfamiliar children (Figure 2C), with greater activation in response to viewing unfamiliar children as compared to own children in AEC and perirhinal cortices, as well as caudate and cerebellum, fusiform gyrus; as well as higher cortical areas (SFG [BA8,10]).

Among HC mothers, we noted greater activation in response to viewing unfamiliar children than own children in the higher cortical regions [bilateral SPL (BA7) and MFG (L > R (BA10))] (Figure 2C). This pattern of activity in HC mothers derived from more prominent deactivation when viewing their own children in separation compared to unfamiliar children (Figure 2F *vs* C).

In general, PTSD mothers activated more strongly to viewing unfamiliar children as compared to their own and HC mothers reacted more strongly to viewing their own children as compared to unfamiliar as supported by group comparisons (i.e. omnibus test) (Supplementary Table S2).

Postscan maternal interview data

The analysis of post-MRI interviews revealed a main effect of condition on the mothers' level of self-reported stress [$F(1,20) = 138.02, P < 0.001$], indicating that both groups experienced less stress when watching children (either their own or unfamiliar) during play than during separation. We also noted an interaction of group-by-condition [$F(1,20) = 11.37, P = 0.002$], which derived from significantly less stress in HC than in PTSD mothers when watching their own and unfamiliar children during separation but disproportionately greater stress in PTSD mothers when viewing their own child during separation as examined by independent *t*-tests [t -own child (1,18) = 2.59, $P < 0.05$; t -unfamiliar(1,18) = 2.15, $P < 0.05$], see Supplementary Table S4. These group differences cannot be accounted for by differences in independently rated child behavior during separation [$t(1,18) = -0.56; P = 0.58$].

To evaluate relations between self-report measures of stress and neuroimaging, we assessed correlations of within-group BOLD signal changes with post-MRI interview responses. In both HC and PTSD mothers, when seeing their own and unfamiliar children during separation (Figure 3), self-reported levels of stress correlated inversely with activation of dorsal SFG (BA10), and positively with activation of the caudate. The more stress HC mothers reported in response to seeing their own and unfamiliar children during separation the more they deactivated the bilateral AEC. PTSD mothers—who reported more stress than HC in the same conditions—differed significantly from this pattern of activation.

We also entered into a regression model BOLD signal change, detected by the contrast of separation relative to free play as the dependent variable, and as a predictor,

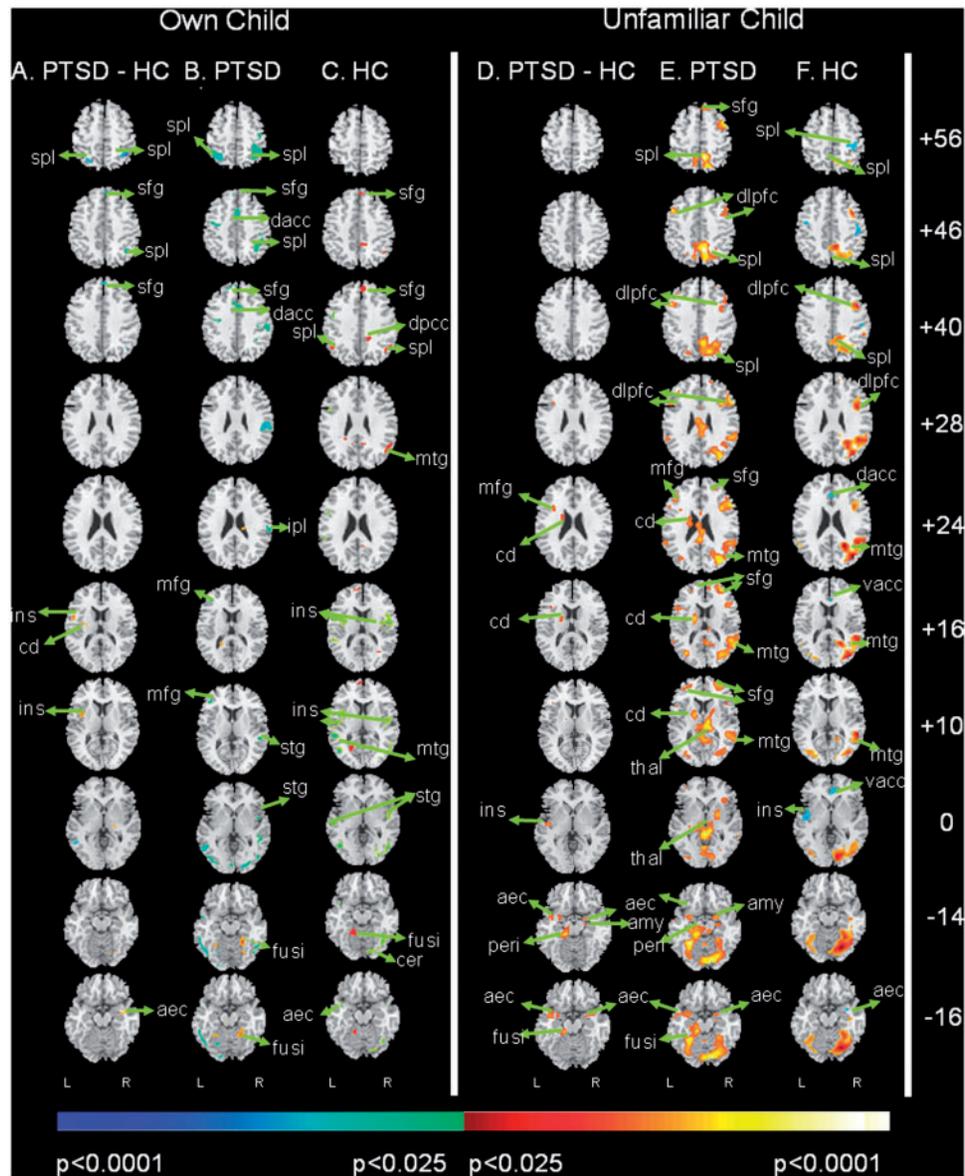


Fig. 1 Group comparisons of activation when mothers view their own and unfamiliar children during separation vs play. Two panels each containing three columns of contrast images are presented that test the a priori hypothesis that PIV-PTSD mothers exhibit reduced mPFC activation and greater limbic activation vs control mothers when viewing child mental states during separation vs during play, in both their own and in unfamiliar children. Each of the two panels is divided into three columns that represent the following: (A and D) group differences in fMRI signal with greater activation in PTSD mothers compared to controls in red and greater activation in controls in blue (i.e. the contrast of the activations in column B with the activations in column C. (B and E) group average fMRI signal in PTSD mothers when viewing separation compared with play and (C and F) HC mothers when viewing separation compared with play. For columns, B and E, and C and F, increases in signal while viewing separation relative to play are shown in red and decreases are in blue. The left-most three columns of this figure (A–C) show neural activity in PTSD and HC mothers while viewing their own children during separation relative to play. The right-most three columns (D–F) show neural activity in PTSD and HC mothers while viewing unfamiliar children during separation relative to play. These are transaxial views with Talairach z-coordinates shown to the far right of the row of corresponding slices, representing the slices positioned from superiorly to inferiorly (top to bottom). The left side of the brain (L) is displayed on the left side of the image. We report voxels using a P -value threshold <0.05 together with the requirement that the activation occurred in a spatial cluster >25 adjacent pixels, a conjoint requirement which, based on an approximation formula, yields a conservative effective $P < 0.000005$. The color bars depict P -values for the threshold of the respective statistical contrast without adjustment for the conjoint requirement of the special cluster. aec, anterior entorhinal cortex; amy, amygdala; cd, caudate; dacc, dorsal anterior cingulate cortex; dorsolateral prefrontal cortex; fusi, fusiform gyrus; ins, insula; peri, perirhinal cortex; mfg, middle frontal gyrus; mtg, medial temporal gyrus; sfg, superior frontal gyrus; spl, superior parietal lobe; stg, superior temporal gyrus; thal, thalamus; vacc, ventral anterior cingulate cortex.

a composite of z-scores based on the CAPS and PCL-S scores of the mother (Table 2). Across the entire sample, limbic regions were activated in response to viewing separation of mothers own and unfamiliar children (i.e. bilateral

amygdala, perirhinal, AEC and hippocampus), as well as motor planning areas (i.e. bilateral caudate and cerebellum). Scatter plots were checked to ensure that no outliers had skewed these results.

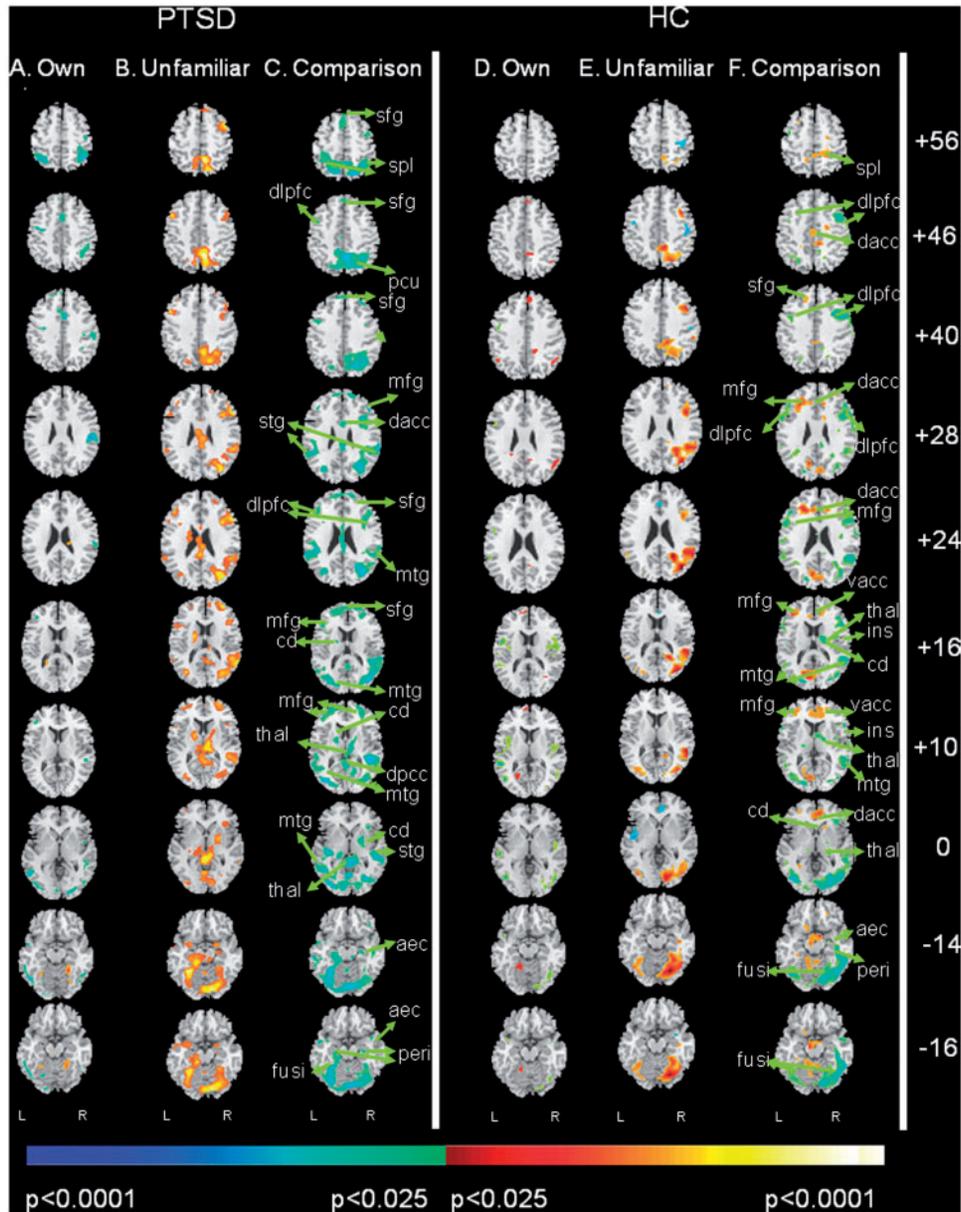


Fig. 2 Within-group comparison of activation when mothers view their own and unfamiliar children. This figure shows group differences in activation associated with the familiarity of the children (i.e. own vs unfamiliar) during separation compared with play (i.e. testing a familiarity-by-condition interaction) separately in PTSD and HC mothers. Two panels each containing three columns of contrast images are presented that test the a priori hypothesis that PTSD mothers compared to HC would display greater neural activation in response to unfamiliar children in separation vs play. The two panels representing these separate comparisons are: (A) PTSD and (B) HC. Each panel is subdivided into three columns: (A and D) own child in separation vs play, (B and E) unfamiliar children in separation vs play and (C and F) own child in contrast to unfamiliar children in separation vs play. Increases in signal while viewing own child relative to unfamiliar children are shown in red and decreases are in blue. Orientation and statistical thresholding are the same as in Figure 1. aec, anterior entorhinal cortex; amy, amygdala; cd, caudate; dacc, dorsal anterior cingulate cortex; dlpc, dorsolateral prefrontal cortex; fusi, fusiform gyrus; ins, insula; mfg, middle frontal gyrus; mtg, medial temporal gyrus; pcu, precuneus; peri, perirhinal cortex; sfg, superior frontal gyrus; spl, superior parietal lobe; stg, superior temporal gyrus; thal, thalamus; vcc, ventral anterior cingulate cortex.

DISCUSSION

Most mothers would say that viewing their child placed in a vulnerable situation such as separation from mother in the laboratory would not be a pleasurable experience. Yet what we have found in this study is that mothers with IPV-PTSD find it particularly stressful to view young children during separation; while they differed less than HC when viewing

young children during play. IPV-PTSD mothers compared to HC respond to seeing both their own and unfamiliar toddlers during separation with significantly greater (i) activation of specific fear circuit-related regions [for own child (Figure 1A): AEC; for unfamiliar children (Figure 1D): amygdala, AEC and perirhinal cortex] and (ii) self-report feeling stressed (Supplementary Table S4). Support for our

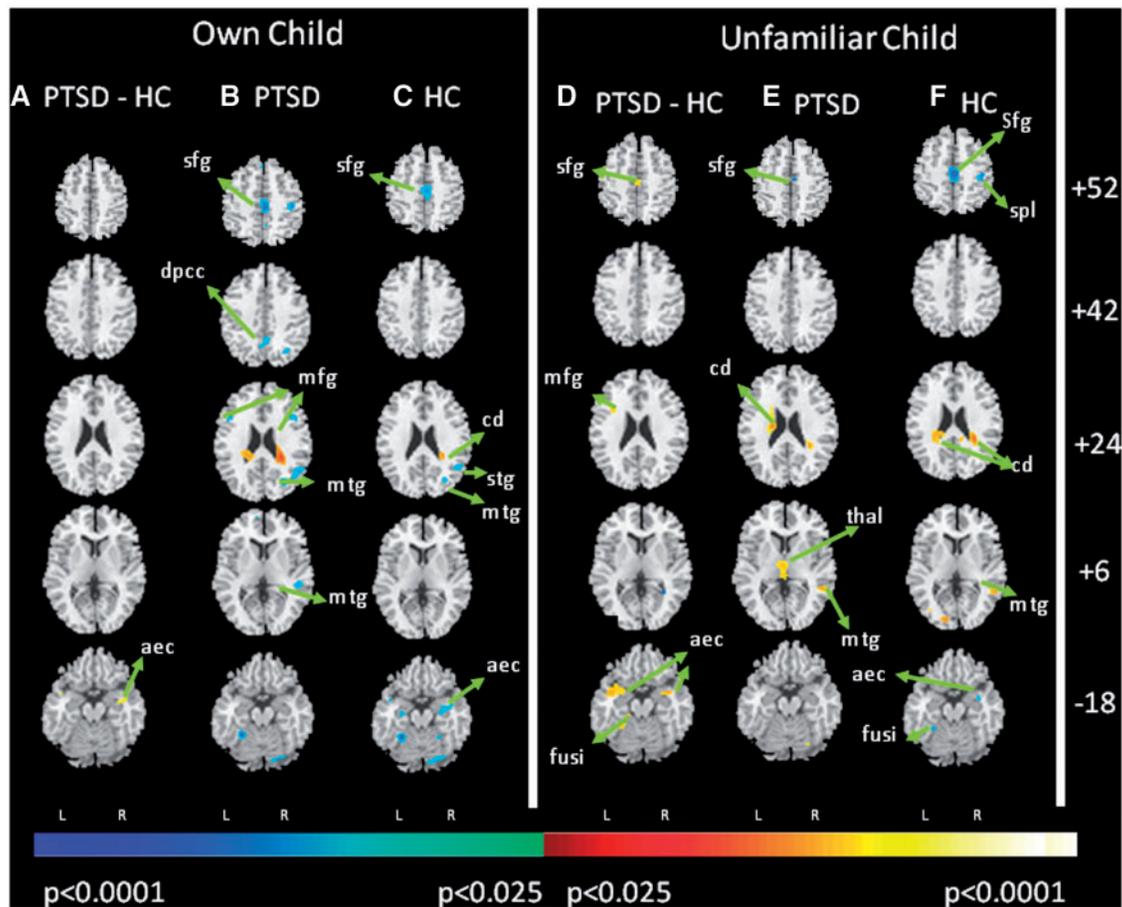


Fig. 3 Neural correlates of mothers' self-reported stress in response to separation. The figure displays the maps of correlations of the mothers' self-reported level of stress with neural activation when viewing their own and unfamiliar children during separation-play in control and PTSD groups. Red indicates a positive correlation and blue indicates an inverse correlation. The correlations are compared across the two diagnostic groups in the right-most columns. Orientation and statistical thresholding is the same as in Figure 1. aec, anterior entorhinal cortex; amy, amygdala; cd, caudate; dlpfc, dorsolateral prefrontal cortex; fusi, fusiform gyrus; dacc, dorsal anterior cingulate cortex; ins, insula; mfg, middle frontal gyrus; mtg, medial temporal gyrus; peri, perirhinal cortex; sfg, superior frontal gyrus; spl, superior parietal lobe; thal, thalamus; vacc, ventral anterior cingulate cortex.

a priori hypotheses as per these group findings is strengthened by the results of the continuous analyses in which maternal self-reported stress during separation was also associated with failure to deactivate the AEC in PTSD mothers compared to HC (Figure 3). Continuous standardized maternal PTSD symptom severity scores were also correlated with activation of the fear circuit-related regions: amygdala, AEC, perirhinal cortex and hippocampus in response to viewing both own and unfamiliar children during separation (Table 2.).

Only HC mothers showed activation of the SFG (i.e. mPFC) in response to seeing their own children during separation (Figure 1A). Thus, PTSD mothers displayed greater activation of fear circuit-related regions with less top-down regulation by the SFG. This finding also converges with higher levels of maternal self-reported stress among PTSD mothers in response to separation and may provide the neural underpinnings for our prior behavioral observations; namely, mothers' emotional availability for coordinated

joint attention during play upon reunion after separation negatively correlated to the severity of their IPV-PTSD symptoms (Schechter *et al.*, 2010).

We speculate that the present neuroimaging study's findings as well as those of our previous behavioral study may be, in part, explained by 'the polyvagal theory' (Porges, 2007), which postulates that the subject goes into a 'survival' mode rather than 'affiliative' mode when confronted with a traumatic reminder (i.e. for an IPV-PTSD mother—as we have speculated, viewing her own and other toddlers left alone and helpless). In the 'survival mode', the brain and sympathetic nervous system focus on the preparation for fight or flight—including related motor planning (i.e. caudate and cerebellum activation) at the expense of social-emotional availability and parasympathetic nervous system activity (Schechter *et al.*, 2005; Austin *et al.*, 2007).

As an alternative hypothesis, this activation pattern may also represent a difference of the degree of normative hyper-vigilance that is observed among mothers of infants and very

Table 2 Interactions of familiarity (own vs unfamiliar children) by condition (separation vs free play) by group (PTSD vs controls)

Region of interest	Side	Brodmann's area	MNI coordinates			t-value	z-score	P	Origins
			x	y	z				
Cortical regions									
STG, temporal pole	Left > Right	38,22,21	-44	0	-24	3.46	2.99	0.001	Separation
Limbic areas									
Amygdala, entorhinal cortex	Left/Right	34,28	-28	2	-16	2.81	2.52	0.006	Separation
Hippocampus, perirhinal cortex	Left > Right	28,35	-16	-8	-12	2.68	2.43	0.008	Separation
Other regions									
Cerebellum	Left > Right		0	-44	-44	2.86	2.57	0.005	Separation

young children—which in exaggerated form has been hypothesized to be associated with parental anxiety disorders (Leckman *et al.*, 2004). We think that such potentially exaggerated hypervigilance might be related to increased maternal emotion dysregulation among the PTSD mothers that is triggered by seeing the child in a helpless position during separation. This state of mind may be reminiscent of traumatized mother's state of mind during interpersonal violence exposure. It has been shown in multiple studies that individuals with IPV-PTSD have difficulty downregulating their own fear and helplessness in the face of negative and arousing emotional stimuli (Gilboa *et al.*, 2004; New *et al.*, 2009; Jovanovic and Ressler, 2010; Schechter *et al.*, 2010). The findings of increased activation in fear circuitry-related areas (i.e. limbic), motor planning areas (i.e. caudate) and facial emotion processing areas (i.e. fusiform gyrus) among PTSD mothers compared to HC, when viewing own and unfamiliar children during separation, support this interpretation. Decreased activation in the SFG among PTSD mothers in the same conditions further supports this view.

The SFG has been implicated previously in the regulation of fear and anxiety states in response to viewing negatively valenced, arousing emotional stimuli (Numan and Insel, 2003; Leckman *et al.*, 2004; Shin *et al.*, 2005; Marsh *et al.*, 2009). The absence of SFG activation in response to negative arousing emotional stimuli has also been associated with the presence of increased anticipatory anxiety, alexithymia and dissociative phenomena, and reduced self-awareness (Gilboa *et al.*, 2004; New *et al.*, 2009). These explanations do not account for the group difference between responses to own vs unfamiliar child during viewing of separation among mothers with PTSD as compared to HC. The amount and intensity of activation to viewing unfamiliar vs own children during separation were greater particularly among IPV-PTSD mothers. We wondered whether this might be due to greater child distress in at least one of the unfamiliar children than in most of the mothers' own children.

In an effort to address this potential confounder, we controlled for the different levels of child distress among the unfamiliar children during separation (boy with score distress score of '2' and girl with '4') by repeating the contrasts

post hoc with each child separately. Results concerning the brain regions involved in our hypotheses were remarkably similar. Thus, we think that the novelty of seeing the unfamiliar children contributed to this greater overall activation, with certain specific brain areas affected in relation to the recognition of the unfamiliar children as novel stimuli particularly among the PTSD mothers as follows: upon viewing unfamiliar children, PTSD mothers access the MFG (BA10) likely in the service of autobiographical memory retrieval perhaps to differentiate novel from familiar stimuli (Burianova and Grady, 2007).

HC as compared to PTSD mothers deactivated the insular cortex upon viewing their own and unfamiliar children in play vs separation. While beyond the scope of this article, this observation raises a question that merits further study; namely, how the two groups differed in recruitment of emotional processing circuitry in response to play, as a likely nonstressful child stimulus that evokes positive affect (Strathearn *et al.*, 2009).

Limitations

This study has several limitations. These include a relatively small sample size and the inherent limitations in statistical power that follow. Of note, this inner-city sample of violence-exposed mothers with PTSD is rarely represented in the affective neuroscience literature and is difficult to recruit into a multivisit study including neuroimaging.

An additional limitation included unexpected group differences with respect to household income and number of years of maternal education—despite no significant group differences with respect to mothers' having completed a high school education or its equivalent. We covaried these sociodemographic factors with no significant change in results. However, it is clearly beyond the scope of this study to test whether these sociodemographic factors are predictive of PTSD caseness and/or whether having PTSD increases impairment that in turn limits the affected individual's likelihood of social, economic and academic success. Larger epidemiologic studies have shown that poverty and poor education can be both risk factors for and effects of chronic violence exposure and related PTSD (Koenen *et al.*, 2007).

Another important limitation pertains to the stimuli used. The naturalistic video clips of subjects own children, while having the advantage of providing more ecologically valid stimuli that were individualized for each mother, contained differing levels of distress across children. Even though naïve raters found no significant group differences in levels of child distress during separation, greater rigor could be applied to creating the unfamiliar child stimuli and in further constraining the breadth of ages among own and unfamiliar children. And as mentioned above, the levels of distress among the two unfamiliar children differed significantly from one another. Despite our post hoc analyses to control for this potential confounder, we cannot fully dismiss the possibility that these differing distress levels altered the results with regards to response to child separation stimuli.

The present study demands replication and expansion both with a larger sample and with two control groups: one with IPV exposure but no PTSD and one with neither PTSD nor IPV exposure (Adenauer et al., 2010). Additionally, given the characteristic failure among IPV-PTSD patients to extinguish hyperarousal in response to evocative stimuli, further studies might also test whether IPV-PTSD mothers habituate less to video-stimuli depicting their own and unfamiliar children in separation as compared to play (Wessa and Flor, 2007).

CONCLUSIONS

This article reports findings from the first study ever to characterize neural activation of violence-exposed parents with PTSD compared to HC in response to viewing very young children during separation as compared to free play. The study suggests that IPV-PTSD mother's viewing their own and unfamiliar children during this interpersonally stressful condition of separation triggers patterns of neural activation that are similar to those triggered in response to traumatic reminders among adult PTSD patients (Francati et al., 2007; New et al., 2009). Namely, activation of the amygdala and surrounding input and output regions (i.e. AEC and perirhinal cortex) in response to seeing very young children in separation is associated with greater PTSD symptom severity. While the SFG was not recruited by IPV-PTSD mothers in response to viewing their own child in separation, it was, in response to viewing unfamiliar children. The opposite was true for HC (i.e. the SFG was activated when seeing own children but not when seeing unfamiliar ones). The latter group activated this region in response to viewing their own children but not unfamiliar children. Given these findings, this study may help to clarify the neural underpinnings of atypical maternal behavior of IPV-PTSD mothers during interactions with their young children following interpersonal stressors such as separation (Fraiberg et al., 1975; Lyons-Ruth et al., 1999; Schechter et al., 2010). Understanding the neural basis for parental stress and its impact on caregiving behavior is particularly important given that longitudinal

follow-up studies have suggested that the children of IPV-PTSD mothers are at risk for long-term disturbances in their capacity to self-regulate their emotions, arousal and behavior (Lieberman et al., 2005; Schechter et al., 2007; Dutra et al., 2009).

SUPPLEMENTARY DATA

Supplementary Data are available at SCAN online.

Conflict of Interest

None declared.

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