A cry in the dark: depressed mothers show reduced neural activation to their own infant’s cry

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This study investigated depression-related differences in primiparous mothers’ neural response to their own infant’s distress cues. Mothers diagnosed with major depressive disorder (n = 11) and comparison mothers with no diagnosable psychopathology (n = 11) were exposed to their own 18-months-old infant’s cry sound, as well as unfamiliar infant’s cry and control sound, during functional neuroimaging. Depressed mothers’ response to own infant cry greater than other sounds was compared to non-depressed mothers’ response in the whole brain [false discovery rate (FDR) corrected]. A continuous measure of self-reported depressive symptoms (CESD) was also tested as a predictor of maternal response. Non-depressed mothers activated to their own infant’s cry greater than control sound in a distributed network of para/limbic and prefrontal regions, whereas depressed mothers as a group failed to show activation. Non-depressed compared to depressed mothers showed significantly greater striatal (caudate, nucleus accumbens) and medial thalamic activation. Additionally, mothers with lower depressive symptoms activated more strongly in left orbitofrontal, dorsal anterior cingulate and medial superior frontal regions. Non-depressed compared to depressed mothers activated uniquely to own infant greater than other infant cry in occipital fusiform areas. Disturbance of these neural networks involved in emotional response and regulation may help to explain parenting deficits in depressed mothers.

Keywords: depression; fMRI; mother; infant; cry

INTRODUCTION

An infant’s cry of distress sets in motion a cascade of emotional and behavioral responses in the caregiver that cements their bond and, ultimately, serves the survival of the species. However, deviations from this sequence occur, notably in cases of parental psychopathology. The growing field of parent–infant neurobiology has begun to identify components of parental response and what shapes them through neuroimaging, but the focus has remained on normative patterns. The present study was designed to shed light on ways maternal response may be compromised by major depressive disorder (MDD).

Parental response to infant cues requires an orchestration of multiple subcortical and cortical systems, many of which are involved in generating and organizing emotional response more generally (Kober et al., 2008). Across studies of infant images and sounds, parents have shown enhanced activation to their own infant (compared to unfamiliar infants) in striatal areas, as well as thalamus/hypothalamus, insula, orbitofrontal cortex (OFC) and anterior cingulate cortex (ACC) (see Swain et al., 2007). These activations are thought to underlie reward and motivational processes, as well as empathic and regulating elements, needed to build a sensitive parental response. Indeed, correlational analyses provide evidence for a role of nuclei within striatum and OFC in generating both positive (joyful) and negative (anxious) maternal feelings (Noriuchi et al., 2007), and studies specifically of cry sound highlight thalamocingulate and striatal loops in optimal maternal response (Lorberbaum et al., 2002; Swain et al., 2008). Still, little is known about which aspects are important throughout human infancy, and which become more/less relevant as the infant (and parent–infant relationship) develops. Maternal response circuits appear to shift across the first several months postpartum (Swain et al., 2007), yet response during the transitional toddler period when infants assert growing independence has yet to be addressed. Beyond normative developmental patterns, ambiguity surrounds aspects of maternal response compromised by psychopathology.

One of the most common forms of psychopathology disrupting maternal response at the behavioral level is major depression. Depressed mothers respond less sensitively to their infants in face-to-face interaction and engage in less positive interaction with their infants (Field, 2010), patterns linked to long-term negative consequences for child cognitive and social–emotional development (Murray and Cooper,
1997). Given the prevalence of clinically significant depressive symptoms in new mothers (Gavin et al., 2005) and the severity of the consequences, it is important to determine what drives depressed mothers’ insensitive responses, and how these may be ameliorated. We submit that a clearer understanding of these issues will come from exploring the nature and stability of depression effects on mothers’ neural processing of infant cues.

Strikingly, the pathophysiology of depression involves dysregulation of neural circuits similar to those identified in parental response (Drevets et al., 2008). Depression is thought to arise from limbic hyperactivity and inadequate regulation by medial prefrontal networks, though detected changes may depend on the stage/severity of depression (Drevets, 2000). Whereas hypoactivity of dorsomedial prefrontal cortex (dmPFC) and posterolateral OFC emerges consistently, activity in vmPFC/subgenual ACC may appear elevated earlier in the depression course but suppressed over time. A meta-analysis confirms that depression diminishes activation to emotional stimuli in ACC, as well as posterior OFC and insula, whereas subcortical (striatum, thalamus) activity is increased (Fitzgerald et al., 2008). Yet observed depression effects may depend on the stimulus—investigation of reward-related response has shown decreased striatal (caudate and nucleus accumbens) activation in depressed patients related to level of anhedonia (Pizzagalli et al., 2009). Furthermore, perinatal depression may carry specific consequences; a pilot study of postpartum depression showed decreased neural response to emotional words not only in posterior OFC, insula and cingulate, but also in striatum and amygdala (Silverman et al., 2007).

These neurophysiological distinctions could help to explain deficits in depressed mothers’ response to their infants, but no studies have introduced cues from the mothers’ own infant to determine what is missing in the parental response. The one study relating depressive symptoms to mothers’ response to infant stimuli found increased medial prefrontal activation in depressed mothers relative to normative, and variations from the norm, at 18 months. A response beyond the immediate postpartum to define what is missing in the parental response with a clinically defined sample, this might not apply to severely depressed mothers. The present study was designed to directly address the question of how major depression impacts mothers’ neural response to their infant’s distress. First-time mothers from a high-risk community sample—half with no significant psychopathology and half with a history of major depressive episode/s (MDE) during the perinatal period—were exposed to a recording of their own infant’s cry sound and comparison stimuli while undergoing functional neuroimaging. Besides being the first to test depression-related differences in parental response with a clinically defined sample, this study extends previous research by exploring maternal response beyond the immediate postpartum to define what is normative, and variations from the norm, at 18 months.

We hypothesized that more depressed mothers—both in the sense of belonging to the MDD diagnostic group and reporting more severe current depressive symptoms—would show blunted neural response to own infant cry in core limbic (thalamus/hypothalamus, ventral striatum, amygdala) and paralimbic (insula, pOFC) networks, as well as medial prefrontal regulatory circuits (dACC, dmPFC). Although previous research supports both hypo- and hyperactivation of limbic regions in depression, we predicted the former based on the pilot study of perinatal depression described above. We expected these differences would emerge most strongly for response to own infant cry compared to a non-cry sound, but that depressed mothers would also tend to show reduced activation in these areas to own infant cry compared to unfamiliar infant cry.

**METHOD**

**Participants**

A community sample of primiparous mothers of 15- to 18-month-old infants was recruited from the Women Infant Children (WIC) program. Mothers who indicated interest by responding to a flier were contacted for further screening. After consenting to participate (per IRB-approved guidelines), they were screened for MRI contraindications and psychopathology using the Structured Clinical Interview for the DSM-IV (SCID). To be in the ‘depressed’ group, the mother had to meet criteria for MDE during the perinatal period and report ongoing symptoms at least at the level of minor depression. To be in the ‘non-depressed’ group, the mother could not meet criteria for any axis I disorder. All mothers found to meet criteria agreed to participate; however, the final sample \( (n = 22, 11\) per group) represents the subset of those screened into the study \( (n = 34)\) who were eligible to complete the study; reasons for discontinuation included new pregnancy and failure to complete a well baby visit or lack of infant cry at the visit.

The majority of mothers (77%) were Caucasian (14% African American, 9% Latina). Most had experienced a vaginal delivery (18% caesarian section). Although a substantial proportion (64%) had engaged in post-high school education, only 18% completed college. Mothers tended to be young \( (M = 24.1\) years, s.d. = 4.1\) and low SES (32% reporting household income <$10,000 per year, 36% $20,000–$40,000, 32% >$40,000). A minority (36%) were married. Non-depressed mothers did not differ from depressed mothers on any demographic variables, including marital status; however, non-depressed mothers were more likely to report being in a stable married or cohabiting relationship with the biological father of their infant \( [n = 8\) vs 3 of the depressed group, \( \chi^2(1) = 4.54, P = 0.03]\).

Mothers in the depressed group all reported MDD onset prior to the perinatal period \( (M = 14.3\) years, s.d. = 2.9\); thus, they represent a group prone to recurrent depression, and symptoms were not unique to perinatal events. A range of chronicity/severity was evident—from two fairly limited MDE’s (two mothers) to too many to count (3)—and six reported significant (past) suicidality (four attempted, two planned). During the perinatal period, half had a MDE during pregnancy (3) or postpartum (3) only, with the
Depressed mothers’ activation to cry

Remainder depressed across both (5). In keeping with the less controlled but ecologically valid community sampling approach, depressed mothers were allowed to have comorbidities, though MDD had to be the dominant current complaint.

Closer to scanning (within 1 week), mothers reported on current depressive symptoms using the Center for Epidemiologic Symptomatic Depression (CESD) scale (Radloff, 1977). As expected, the depressed group scored significantly higher ($M = 24.18$ years, s.d. = 9.37) than non-depressed ($M = 7.45$ years, s.d. = 6.19). Yet a degree of intergroup overlap (‘non-depressed’ range 0–20, ‘depressed’ 10–32) suggested diagnostic status did not fully capture current depressive symptoms. Therefore, CESD scores were considered as an additional index of depression severity. At this assessment, three of the depressed mothers reported having begun antidepressant (SSRI) treatment (duration 2–4 weeks). Dropping these cases did not alter the pattern of results; in the interests of retaining balanced groups and reflecting a range of treated/untreated depression syndromes, they were kept in analyses.

Stimulus collection and presentation

Researchers attended participants’ 18-month well-baby visits and recorded infant cry sound following injections. Twenty-one seconds from the beginning of the first cry expiration were selected for the cry stimulus and maximum amplitude set to 1 dB. Comparison of depressed and non-depressed group cries revealed non significant differences in fundamental frequencies. In addition to participant-specific stimuli, cry sound from an unfamiliar infant was collected (using the same procedures) to be presented to all participants. A non-cry control sound was developed by editing a rising and falling tone to have a fundamental frequency within the range of normal infant cry ($400–600$ Hz; Zeskind and Lester, 1978) and 1 dB maximum amplitude.

The stimulus protocol was created as a block design to be presented via the Presentation 10.0 program and consisted of two 9-min runs. Each run contained six repetitions of own infant cry, other infant cry, control sound, and rest. Sound blocks were 23 s (2 s pause + 21 s sound), and rest blocks 21 s. Multiple presentation input files dictating different orders of blocks within runs were used to counterbalance stimulus presentation within and across participants. Participants were simply instructed to listen to the sounds to allow the most natural range of response to cry. Sound was presented via earphones in the scanner, and a sound check carried out before each scan to ensure audibility.

Scanning

MR imaging was carried out with a 3T Siemens Allegra 3 magnet. A standard birdcage coil was used to acquire data from the whole brain. Sessions began with a shimming routine to optimize signal-to-noise ratio, followed by a fast localizer scan (FISP) and Siemens Autoalign routine, then the two functional runs and anatomical scan.

Functional

$T2^*$-weighted gradient echo sequence, $64 \times 64$ voxel matrix, $\text{TE} = 30$ ms, $\text{TR} = 2000$ ms, flip angle = $80^\circ$, 32 contiguous slices thickness = $4$ mm; 273 volumes per run.

Structural

$T1$-weighted 3D MP-RAGE sequence, $\text{TI} = 1100$ ms, $\text{TR} = 2500$ ms, $\text{TE} = 4.4$ ms, 176 transverse slices $1.0$ mm thick, $256 \times 176$ matrix FOV = $256$ mm.

Post-scan ratings

Mothers rated each sound on Zeskind and Lester’s (1978) scales of subjective response to cry. Each sound was rated from 1 to 5 on the following qualities: urgent, grating, arousing, piercing, discomforting, aversive, distressing and soothing. Depressed mothers did not differ significantly from non-depressed mothers on any ratings.

Data analysis

Functional imaging data were analyzed with tools from the FMRIB Software Library (FSL v.4.1). Preprocessing steps included motion correction with MCFLIRT, non-brain structure removal with BET, spatial smoothing using Gaussian kernel 5-mm FWHM, intensity normalization using grand mean scaling and high-pass temporal filtering (sigma = 65 s). Within-subject time series data were analyzed using FILM with local autocorrelation correction, and boxcar models describing onset/offset of each sound stimulus were convolved with a double-gamma basis function. Functional data were registered to the participant’s own high-resolution structural image (six df) and to a standard brain (Montreal Neurological Institute template; 12 df) using FLIRT. All data were checked for excessive motion (>1 mm) and artefacts.

Within-participant and group-level analyses were carried out using FEAT v.5.98. For each participant, three explanatory variables (EVs) modeled signal associated with own infant cry, other infant cry and control sound; zero for all three stimulus EVs corresponded to rest. Contrasts of parameter estimates (COPEs) for own cry > control sound and own cry > other cry tested primary hypotheses regarding response to own infant cry (own cry > rest contrast was also tested to describe signal change relative to baseline). First-level COPE images were averaged across runs using fixed-effects analysis. These served as inputs to higher level group analyses, conducted using FLAME to model random-effects components of mixed-effects variance. AlphaSim was used to determine cluster size needed, in conjunction with intensity threshold $P < 0.005$, to achieve a false discovery rate (FDR) of 0.05 for whole-brain analyses (Cox, 1996). Using these criteria, activation clusters exceeding 16 voxels, or 615 mm$^3$, were considered significant in group analyses.
Group-level analyses comprised progressively more fine-grained tests of effects of depression on brain response. First, response to own infant cry (>control sound, >other cry) was examined separately for non-depressed and depressed groups to assess convergence with previously identified regions of parental response. Then, tests directly comparing response between groups—non-depressed > depressed, depressed > non-depressed—were conducted. Finally, centered depressive symptom (CESD) scores were entered as a continuous predictor of brain response in the entire sample to investigate the explanatory power of current subjective depression, as opposed to diagnostic grouping (based more on history of clinical syndrome). Given concerns about interpreting brain response within regions defined solely by individual difference correlations (Vul et al., 2009), a mask defining regions activated by the sample as a whole was applied, and only CESD-related activations within masked areas were considered further. Finally, to visualize the data driving continuous depression effects, but not to perform new statistical tests (Poldrack and Mumford, 2009), spherical ROI’s (r=3 mm) centered on activation peaks were used to compute percent signal change associated with sound stimuli (compared to rest) and generate illustrative figures.

RESULTS
Response to own infant cry in non-depressed and depressed mothers

As a group, non-depressed mothers responded to own infant cry greater than control sound within networks previously implicated in parental response (Figure 1, yellow clusters). Specifically, mothers showed bilateral activation of lateral paralimbic areas—anterior insula, OFC—and core limbic subcortical regions including striatum, thalamus and midbrain (substantia nigra/ventral tegmental area, periaqueductal gray). They also displayed bilateral activation in dorsal subcortical regions—mediolateral superior frontal gyrus (SFG) extending to dACC—and a set of posterior activations including left angular gyrus, posterior cingulate cortex and cerebellum (Table 1, panel 1; see Supplementary Table S2 for more specific description of regional sub-clusters). Compared to unfamiliar infant cry, non-depressed mothers showed greater response to own infant cry in a more limited set of areas including dACC, right insula, right occipital fusiform to lingual gyrus and left posterior supramarginal gyrus (Figure 2, yellow clusters; Table 1, panel 4; see also Supplementary Table S3). Depressed mothers as a group failed to show a significant response to own infant cry greater than either control sound or other infant cry.

Depressed vs non-depressed group differences

The direct test of group differences in response to own infant cry greater than control sound revealed that non-depressed mothers activated more strongly than depressed mothers in a subcortical cluster involving the striatum (caudate, nucleus accumbens) and medial thalamus (Figure 1, red cluster; Table 1, panel 2). This response difference was predominantly right sided, but extended into left striatum. Examination of signal change in this cluster relative to resting baseline confirmed that depressed mothers showed diminished (ns) response to own infant cry, compared to non-depressed mothers’ clear activation to the stimulus (neither group showed significant signal change to control sound; Figure 3, panel A). Other areas activated in non-depressed mothers but not depressed mothers failed to show significant group differences because of greater variability within the latter group (i.e. some showed activation, whereas others showed non-significant change or deactivation). The group comparison of response to own infant cry greater than other cry revealed that non-depressed mothers activated more in a cluster involving mostly right-sided occipital fusiform and lingual gyri (Figure 2, red cluster; Table 1, panel 5). Signal change in this area associated with own infant cry was in opposite directions for non-depressed vs depressed groups; whereas the former showed activation (compared to baseline), the latter showed deactivation (signal change to other cry was non-significant in both groups, though the difference between depressed and non-depressed mothers was significant; Figure 3, panel B).

Self-reported depressive symptoms

Within brain regions showing response to own infant cry greater than control sound in the sample as a whole, mothers with higher CESD scores showed decreased response in the right-sided subcortical cluster (striatum and thalamus) noted above, as well as in left OFC extending to ventral striatum, and in dorsal mPFC (right dACC, left medial SFG) (Figure 1, blue clusters; Table 1, panel 3). Plots of signal change in these areas associated with own infant cry (Figure 4) revealed considerable variability within groups of mothers classified as ‘depressed’ or ‘non-depressed’; however, the latter activated more consistently to own infant cry in each region compared to baseline, whereas the former tended to show non significant change or even deactivation. The parallel analysis for own infant cry greater than other cry again demonstrated that mothers with higher depressive symptoms showed reduced activity in occipital fusiform-lingual gyri (Figure 2, blue cluster; Table 1, panel 6).

DISCUSSION

This study demonstrated depression-related differences in the way mothers’ brains respond to their infant’s cry. Whereas mothers with no history of major depression responded across multiple emotional response and regulation circuits implicated in previous parenting research, depressed mothers as a group failed to respond to their infants. Blunted response in subcortical limbic regions most consistently differentiated depressed from non-depressed mothers, and more severe symptomatology additionally predicted...
diminished prefrontal activations. Non-depressed mothers also activated more strongly to the identity of their infant (compared to an unfamiliar infant) in occipital fusiform areas. This fits with previous research showing hypoactive response to emotional stimuli in postnatally depressed mothers, but demonstrates differences specifically in the way mothers process their infant’s distress signals. Below, we consider the significance of these differences in the context of neurobiology of parental response, depression and social–emotional functioning more generally.

Depressed mothers’ failure to engage striatal (caudate, nucleus accumbens) and thalamic response networks points to a core deficit in limbic activation to infant cues that may underlie motivational and social bonding difficulties in the mother–infant relationship. Although ventral striatum is most closely associated with reward processing, both dorsal and ventral caudate have been found involved in motivation (Delgado et al., 2004), and reduced caudate/nucleus accumbens response to gains appears to contribute to anhedonic symptoms of depression (Pizzagalli et al., 2009). Striatal activation emerges consistently across parental response studies, but animal research suggests that deficits in the mother’s own caregiving history can interfere with nucleus accumbens response to infant cues, reducing motivation to care for offspring (Champagne et al., 2004). Intact medial thalamic activity has also been found critical for organizing mothering behaviors in rats (Slotnick, 1967) and may be an important marker of the degree of cortical–subcortical ‘traffic’ driving motivated responses. Together, hypoactivation in these areas may speak to depressed mothers’ difficulty...
experiencing a sense of reward and motivation to approach their crying infants, as well as fundamental difficulty organizing a response repertoire during infant interactions. This pattern is likely self-reinforcing, in that impaired interactions amplify negativity in the mother–infant relationship, increasing maternal anhedonia and withdrawal from infant cues. The fact that this group-level distinction emerged despite overlap in current symptomatology suggests this is a relatively stable marker of maternal depression with far-reaching impacts.

When current self-reported depression severity was considered, more depressed mothers showed reduced activation to their infant’s cry in prefrontal regions known to receive input from and/or modulate above limbic areas. Posterolateral OFC plays an important role in evaluating and titrating a response to emotional stimuli by coding valence and controlling emotional expression (i.e. via amygdala input), and its activity is inversely related to depression severity (Drevets, 2007). Intact left OFC function, particularly, appears protective against depression, and may be needed to override automatic responses in the service of social goals; left lateral OFC activation found when participants had to approach angry faces (Roelofs et al., 2008) could parallel efforts required for mothers to approach their crying infants. Research relating left-sided OFC activity to positive emotions concerning one’s infant (Noriuchi et al., 2007) suggests this hyporesponse in more depressed mothers could block

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Note: Clusters met thresholding criteria (>615 mm³, P < 0.005) based on whole-brain FDR 0.05. Coordinates based on Montreal Neurological Institute template. BA = putative Brodmann’s area; ACC = anterior cingulate cortex; SN = substantia nigra; VTA = ventral tegmental area; PAG = periaqueductal gray.

Fig. 2 Depression effects on brain areas activated by own infant cry greater than other infant cry. Note: Activations thresholded at whole-brain FDR 0.05. Non-depressed mean map (yellow–occipital cluster largely overlapping with subsequent maps) overlaid with non-depressed > depressed map (red), then CESD-related map (blue). Complete map of CESD-related activation shown.
positive associations with infant interaction, further diminishing motivation to engage.

Another component of the maternal response stream attenuated by depressive symptoms was dACC, which may provide a critical link from emotional inputs to thoughtful response selection. The area active in mothers reporting low depressive symptomatology belongs to the more ‘cognitive’ division of ACC but is likely to interact with lateral OFC regions involved in emotion processing (Margulies et al., 2007). Further evidence for dACC’s involvement in emotional judgment includes activation during recognition of ambiguous emotional facial expressions (Nomura et al., 2003) and functional connectivity with anterior insula as part of a network detecting emotional salience (Taylor et al., 2009). Additionally, cingulate activity is regularly involved in empathy, which requires integration of multiple sources of felt and cognitively processed information (Decety and Meyer, 2008). Again, this region is activated in normative parental response but underactive in depression, suggesting that depressed mothers’ difficulty judging and responding to their infant’s needs has to do in part with ACC dysfunction.

A final link in the chain of maternal response compromised by depressive symptoms was medial SFG (including pre-SMA), part of a cognitive–motor loop involved in selecting and energizing behavioral responses to emotional stimuli (Kober et al., 2008). Pre-SMA activation to arousing non-verbal vocalizations is thought to reflect involvement in a communicative ‘mirror’ network that enhances empathic response (Warren et al., 2006). SFG is also involved in effortful regulation of both positive and negative emotions (Mak et al., 2009), with deterioration related to depression severity (Shah et al., 2002). Hypoactivity among more depressed mothers may reflect an overtaxed regulatory system unable to productively deal with their infant’s cry. Given functional connections between pre-SMA and other PFC/ACC, as well as subcortical (caudate, anterior thalamus) areas, these regional differences point to a systemic response/regulation deficit that intensifies with maternal depression severity.

Fewer depression-related distinctions were found for response specifically to own infant identity (compared to other infant cry), with the most consistent difference in an occipital region including fusiform gyrus. Although activation in parts of fusiform gyrus has been found in parental response research and decreased in depression (Fitzgerald et al., 2008), the significance of activation in this visual processing area to sound cue remains unclear. It could be that the sound of their infant’s cry evoked a larger sensory–emotional response in non-depressed mothers that involved visualizing their infant (O’Craven and Kanwisher, 2000). Depressed mothers, on the other hand, showed deactivation to their infant’s cry, perhaps a sign they were blocking further processing of sensory associations with their infant.

Altogether, these results suggest that major depression blunts motivational responses to one’s infant, with ongoing symptoms impairing higher order regulatory circuits that could overcome initial aversion to a crying infant. The fact that the latter hypoactivations related to increasing severity of current self-reported depression, but not to group diagnostic differences, suggests these prefrontal networks are more amenable to change and could be a route by which maternal functioning is improved. Given the apparently greater stability of striatal hypoactivation in depressed mothers, it would be important to determine when this profile starts (i.e. immediate postpartum or after a period of depressed motherhood), what its immediate consequences are for mother–infant functioning, and whether it can be altered by psychotherapeutic and/or medication interventions. It should be noted that observed differences may have to do not only with depression, but also with related psychosocial constructs predictive of mood dysregulation. Strikingly, the current results mirror findings that mothers with secure adult attachment, but not those with insecure/dismissing attachment, showed ventral striatal response to affectively negative infant cues (Strathearn et al., 2009). It is quite possible that differences in depressed mothers’ own attachment histories, as well as in the stability/security of current romantic relationships—suggested by the low
likelyhood of an ongoing relationship with the biological father of their infant—contributed to both depressive symptoms and impairment of attachment-relevant neural circuits. Future research should address the relative contributions of attachment history, current attachments, and social support more generally to maternal depression and neurohormonal profiles with their infants.

In addition to the neural circuits showing clear depression-related differences, non-depressed mothers responded to their infants’ cry in areas that some, but not all, depressed mothers displayed. These included anterior insula and periaqueductal gray, foci of emotional response highlighted repeatedly in parenting and emotion research. It may be that some depressed mothers experienced intense emotional reactions to their infants’ cry, but these were more negatively valenced (and underregulated) compared to emotionally responsive non-depressed mothers. Evidently, factors other than depression diagnosis/severity alone explain variability in neural response in these regions, and further investigation is needed to identify which aspects of a mother’s mental health profile interfere with which aspects of response. Heterogeneity of depressed mothers in the current sample introduced sources of variability that could be relevant. A relatively small sample did not allow for a breakdown by all possibly relevant characteristics, but future research within homogenous subgroups based on timing of depression (pre-natal only, post-natal only, both) and comorbidity (e.g. with PTSD or another anxiety disorder, history of specific substance dependence) may yield overlapping but distinct findings to those presented here.

Considered in light of previous parental response research, these findings extend what is known about normative maternal response to cry in both time (beyond the first post-natal year) and population base (to high risk, low SES mothers). Continuity with previous findings demonstrates that mothers experiencing high-socioeconomic stress are still responsive to their infants in expected ways. Furthermore, many response circuits found to emerge in the first few weeks to months postpartum remain relevant. At the same time, divergent results from prior cry research—particularly, lack of amygdala and hypothalamus activation—may have to do with developmental changes. By 18 months, infants have become more independent through physical mobility and verbal communication, and

**Fig. 4** Signal change (compared to resting baseline) associated with own infant cry in areas showing CESD-related differences. Note: Markers (black diamond = depressed, gray triangle = non-depressed groups) depict mothers’ mean signal change to own infant cry within 3 mm spheres centered on sites of peak CESD-related differences. (A) x = 10, y = 29, z = 24; (B) x = −12, y = 32, z = 55; (C) x = −29, y = 12, z = −17; (D) x = −11, y = 10, z = −9).
may not require the same degree of vigilance and hormonal activation from the mother. The fact that mothers failed to show amygdala activation to video of their distressed infants at 16 months (Noriuchi et al., 2007) suggests this element of limbic response habituates, at least for the range of infant cues mothers were exposed to in these studies. Longitudinal assessments of mothers’ changing response to a range of infant stimuli would clarify which elements become less important, and which enhanced, as the mother–infant relationship develops.

Even as this research answers questions about factors shaping maternal response, it raises others about when and how observed depression-related differences arose, and what these mean for mother–infant functioning. It may be that limbic hyperactivity early in the mother’s experience with her infant gave way to blunting, and there is a window in which teaching better emotion regulation skills would allow depression-prone mothers to remain responsive to their infants’ cry. The contribution of structural changes to observed hypoactivity in brain areas impacted by depression requires further clarification, and an important direction for future research is to combine structural and functional analysis of depressed mothers’ brains to disentangle contributions of neural integrity and relative activity to functional outcomes. We also cannot determine whether effects found here have to do with perinatal depression specifically, as opposed to recurrent (and ongoing) maternal depression. Unique effects of depression during particular perinatal periods should be further explored to clarify sensitive periods and guide intervention recommendations. Finally, the significance of depression-related differences at the neural level must be confirmed by testing associations with mothers’ subjective experience of parenting and behavioral sensitivity with their infants.

These limitations notwithstanding the present study shines light on what depression does and does not do to a mother’s ability to respond to her infant’s distress. Rather than eradicating the entire structure of normative response, depression appears to upset the balance by weakening elements of a complex response/regulation system. It may not be the presence of a strong negative response, but rather a void where a naturally rewarded response should be, that derailed the interactive sequence by which mother and infant re-inforce one another.

SUPPLEMENTARY DATA
Supplementary data are available at SCAN online.

Conflict of Interest
None declared.

REFERENCES


