

Postpartum depressive symptoms moderate the link between mothers' neural response to positive faces in reward and social regions and observed caregiving

Judith K. Morgan, Chaohui Guo, Eydie L. Moses-Kolko, Mary L. Phillips, Stephanie D. Stepp, and Alison E. Hipwell

Department of Psychiatry, University of Pittsburgh, Pittsburgh, PA 15213, USA

Correspondence should be addressed to Judith K. Morgan, University of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213, USA.
E-mail: morganjk@upmc.edu

Abstract

Postpartum depression may disrupt socio-affective neural circuitry and compromise provision of positive parenting. Although work has evaluated how parental response to negative stimuli is related to caregiving, research is needed to examine how depressive symptoms during the postpartum period may be related to neural response to positive stimuli, especially positive faces, given depression's association with biased processing of positive faces. The current study examined the association between neural response to adult happy faces and observations of maternal caregiving and the moderating role of postpartum depression, in a sample of 18- to 22-year old mothers ($n = 70$) assessed at 17 weeks (s.d. = 4.7 weeks) postpartum. Positive caregiving was associated with greater precuneus and occipital response to positive faces among mothers with lower depressive symptoms, but not for those with higher symptoms. For mothers with higher depressive symptoms, greater ventral and dorsal striatal response to positive faces was associated with more positive caregiving, whereas the opposite pattern emerged for mothers with lower symptoms. There was no association between negative caregiving and neural response to positive faces or negative faces. Processing of positive stimuli may be an important prognostic target in mothers with depressive symptoms, given its link with healthy caregiving behaviors.

Key words: caregiving; ventral striatum; precuneus

Introduction

Positive caregiving, characterized by warm, sensitive and consistent responding to the needs of one's infant, is important for healthy child development (Sroufe, 2005). In particular, prior work has demonstrated that warm and sensitive parental responding during the early years of life predicts greater positive affect, affect regulation, empathy and physiological self-regulation in offspring across development (Feldman, 2007, Leclere et al., 2014). In contrast, early negative caregiving, characterized by hostile, harsh and intrusive responding, has been linked to greater affective and physiological dysregulation in

offspring (Egeland et al., 1993; Feldman, 2015). These elements of parenting appear to be especially important during the early years, a sensitive developmental period when infants depend on caregivers for all of their primary needs and when their physiological systems are developing quite rapidly (Feldman, 2015).

Recent work has demonstrated that a network of neural regions, "the caregiving brain" is involved in positive caregiving. The caregiving brain is concentrated in a cortico-striatal-thalamic loop that includes the prefrontal cortex, cingulate, striatum and thalamus, as well as the precuneus and amygdala

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(Swain, 2011; Swain et al., 2014). Function in these regions is thought to aid in increasing emotional arousal to, and salience of, infant cues (i.e. striatum, amygdala and insula), in promoting regulation of one's own affect in order to attend to these cues (i.e. prefrontal cortex), and in fostering empathy and mentalizing skills to understand how to respond sensitively to these cues (i.e. thalamus, precuneus, posterior cingulate) (Barrett and Fleming, 2011).

Multiple psychosocial and contextual factors may influence function within the caregiving brain (Barrett and Fleming, 2011). In particular, postpartum depression appears to interfere with adaptive function of these neural regions (Moses-Kolko et al., 2014). Specifically, a growing body of work has demonstrated that postpartum mothers with high depressive symptoms show blunted responding to infant distress in regions implicated in emotional salience and threat responding (e.g. amygdala, anterior cingulate), in reward and social bonding (e.g. striatum), in goal-directed behavior and self-regulation (e.g. cingulate, orbitofrontal cortex), and in social cognition (e.g. thalamus), suggesting they may have fewer neurobiological resources to respond sensitively to their distressed infant (Laurent and Ablow, 2012, 2013, Moses-Kolko et al., 2014). This depression effect on brain function, particularly brain function in regions that have been associated with caregiving, is not surprising, given evidence that depression is often associated with compromised caregiving (Lovejoy et al., 2000; Field, 2010). For example, postpartum depressive symptoms have been associated with more irritable and hostile mother-infant interactions (Field, 2010). Importantly, this depression-related effect on caregiving has a considerable public health impact. Approximately, 10–15% of new mothers experience postpartum depressive symptoms (Paulson et al., 2006) and the likelihood of these symptoms increases for mothers living in high-stress environments, for mothers with low socioeconomic status, and for mothers who are younger age or minority status (Segre et al., 2007), leaving the children of these mothers at even greater risk for negative child outcomes.

Despite the growing body of work evaluating parental neural response to negative stimuli (see Barrett and Fleming, 2011), relatively little work has evaluated how neural response to positive stimuli may predict caregiving patterns in postpartum mothers. Research has shown that depressed individuals are less likely to recognize positive affect in others (Joormann and Gotlib, 2006; Surguladze et al., 2004), and some work has demonstrated that depressed mothers show difficulty in identifying happy affect in their infant's facial expressions (Arteche et al., 2011). This is problematic because warm, sensitive caregiving requires accurately identifying the feelings of one's infant in order to respond appropriately to those cues. Indeed, depressed mothers show lower sensitivity and less contingent responding to the positive cues of their infants (Field et al., 2010; Feldman 2015), although not all depressed mothers show these caregiving disruptions. Understanding and identifying the emotions of others requires mentalizing and theory of mind skills, and multiple social regions including the precuneus and temporoparietal junction appear to be involved in these social-cognitive skills. Altered function in neural regions supporting social cognition may be related to difficulty identifying positive emotion expressions of others, including those of one's infant, in mothers with high depressive symptoms. In turn, this altered function in social regions could explain lower levels of warmth and responsiveness to the infant's positive cues.

Additionally, function in reward regions involved in motivation, pleasure and approach behavior, such as the ventral and

dorsal striatum, contributes to motivational components of engaging in positive social interactions with others. Reward neural circuitry function has been linked to positive parental caregiving in several prior studies. Atzil et al. (2011) reported that mothers with more synchronous parenting, as characterized by mutually focused and reciprocated parent-child exchanges, showed greater activation in the nucleus accumbens of the ventral striatum when viewing positive mother-infant interaction clips. Laurent and Ablow (2013) demonstrated that mothers with higher levels of postpartum depressive symptoms showed *diminished* responding to their infant's happy facial expressions in the orbitofrontal cortex, a region implicated in reward processing, whereas mothers with fewer depressive symptoms showed greater striatal responding to their infant's happy facial expressions (relative to their expression of distress). These findings highlight the importance of reward regions in positive maternal caregiving and provide a potential rationale for the observed differences in positive interactions in mother-infant dyads with a depressed mother (i.e. lower striatal activity). However, work is still needed to empirically link neural responding to positive stimuli to observed early caregiving in mothers with varying levels of depressive symptoms.

The current study evaluated how postpartum depressive symptoms may moderate the association between function in regions identified in the "caregiving brain", namely the prefrontal cortex, ventral and dorsal striatum, thalamus, cingulate and precuneus in response to positive face stimuli, and observations of early parenting. We hypothesized that more positive caregiving would be related to greater function in these regions, especially reward and social regions, given their role in understanding positive facial expressions, but that these associations would be attenuated for mothers with higher levels of postpartum depressive symptoms. Given that the quality of mother-infant interactions depends on a number of factors beyond maternal depression including infant temperament, infant age and level of maternal social support (i.e. having a spouse or partner), we evaluated the moderating effects of postpartum depressive symptoms above and beyond these important covariates. We also tested the specificity of our findings by evaluating the association between negative caregiving behaviors and maternal neural response to positive faces and the association between maternal positive and negative caregiving and maternal response to negative faces.

Materials and methods

Sample

The sample comprised 70 first-time mothers (18–22 years old, mean age = 19.86 years, s.d. = 0.92) assessed at 17.06 weeks (s.d. = 4.68 weeks) postpartum. Participants were selected from the Pittsburgh Girls Study, a multicohort prospective study that has followed a sample of 2,450 urban-living, racially diverse girls for 16 years since childhood (see Keenan et al 2010 for details). Pittsburgh Girls Study participants who were at least 18 years old were recruited into this neuroimaging sub-study, if they had delivered a healthy, first-born infant within the prior 6 months and provided at least 2 hours of childcare daily ($n = 155$). Young mothers were excluded if they were pregnant at time of scan ($n = 5$), met criteria for Bipolar Disorder ($n = 5$) or cannabis abuse ($n = 8$), had medical or neurological disorders ($n = 6$), used psychotropic medication daily ($n = 3$), had metal in the body ($n = 4$), were claustrophobic or unable to enter the scanner ($n = 1$), had an IQ < 65 ($n = 2$), or were living out of state

($n = 5$). In addition to these 39 excluded participants, 8 scan-eligible women (5%) refused participation and 13 were lost to follow-up (8%), resulting in a final sample of 95 completed scans. Of these 95 scans, 70 participants had usable data and were included in analyses for this article. Data were missing for these 25 participants due to excessive movement (>4 mm), poor coverage ($<60\%$ in subgenual anterior cingulate) and/or low behavioral responding during the task ($<60\%$). Of the 70 participants with usable scan data, 83% were Black/African-American and 17% were White/Caucasian. Further, 83% reported being single parents, 40% reported being on public assistance and 75.8% had a high-school education or equivalent. There were no significant differences between mothers with usable scan data and those without imaging data on maternal depressive symptoms, positive caregiving, negative caregiving, infant fussy temperament, maternal age, or infant age (F 's = 0.01–3.36, P 's = 0.07–0.94).

Procedure

Participants were interviewed at home at a 10-week postpartum home visit (mean age of infant at this visit = 12.97 weeks) and attended a research laboratory visit at about 4 months postpartum. At the home interview, mothers completed the Structured Clinical Interview for DSM-IV Axis I disorders (SCID; First et al., 1995). At this lab visit, mothers completed face-to-face mother-infant interaction tasks and underwent an fMRI scan at the Magnetic Resonance Imaging Center, University of Pittsburgh. All participants provided written informed consent as approved by the University of Pittsburgh Human Research Protection Office.

Measures

Mothers reported on their own age, infant age, relationship status and past year receipt of public assistance (e.g. WIC, food stamps, welfare). Mothers also completed questionnaires about their infants' temperament (at 10 weeks postpartum) and their own current depressive symptoms (at 4 months postpartum).

Infant difficult temperament. Mothers completed the Infant Characteristics Questionnaires (Bates et al., 1979), a 23-item measure of infant fussy/difficulty temperament. Items are rated on a seven-point Likert scale. A sample item from this measure includes "how many times per day, on average, does your baby get fussy and irritable—for either short or long periods of time". Reliability for this measure was adequate to good in the current sample ($\alpha = 0.72$).

Depression. Mothers completed the 10-item Edinburgh Postnatal Depression Scale (EPDS; Cox et al., 1987), which measures severity of depressed mood, anhedonia, guilt, anxiety and suicidal ideation experienced in the past 7 days rated on four point scales (0–3). An EPDS score of 10 or higher indicates "possible" depression (Gibson et al., 2009). This measure had good internal consistency in the current sample ($\alpha = 0.79$). Mothers also completed the SCID at the 10-week home interview with a trained and reliable clinical interviewer. DSM-IV diagnoses were determined by the study psychiatrist after comprehensive discussion with the interviewer. Because of our interest in evaluating depressive symptoms dimensionally as a measure of commonly experienced symptoms in the postpartum period, we opted to use total EPDS score in all models.

Observed maternal behavior. At 4 months postpartum, each mother-infant dyad was videotaped in face-to-face interaction during episodes of warm-up and toy play when the infant was

alert and not distressed. Mothers were first instructed to "talk to your infant in any way you want to" without the use of toys, followed by an episode of toy play when the mother was asked to "help your child to get interested" in a specific toy. The warm-up play interaction lasted for 2 minutes and the toy play interaction lasted for 3 minutes.

Caregiving behavior during the warm-up and the toy-play episodes was coded by graduate-level trained observers using time-sampled global ratings. The coders were unaware of all other information about the dyad, and the two episodes were also coded independently by separate coders. Prior research has demonstrated the validity of brief structural laboratory observations coded with similar global rating scales (Shaw et al., 1998; Leventhal et al., 2004). Maternal behavior of warmth, involvement, sensitivity, hostility/irritability and intrusiveness were coded using rating scales adapted from the Early Parenting Coding System (Shaw et al., 1998). Warmth was coded as positive affect (smiling, laughing) expressed toward the infant. Involvement was coded as the degree to which the mother attended to and engaged with the infant. Sensitivity was defined as responding appropriately and promptly to the infant's cues. Hostility/irritability was defined as negative expressions, including annoyance, critical comments, angry teasing and sharp or harsh tones of voice. Intrusive behavior was characterized as poking, pulling, lunging face or hands close to the infant's face, and loud/high-pitched vocalizations. Inter-rater reliability was determined by intra-class coefficients (ICCs) on a random sample of 24 mother-infant pairs: maternal warmth ICC = 0.84, maternal involvement ICC = 0.84, maternal sensitivity ICC = 0.82, maternal hostility/irritability ICC = 0.88, and maternal intrusiveness ICC = 0.91. A principal components analysis revealed two factors accounting for 68.2% of the variance: a factor labeled "positive caregiving" comprised warmth and positive involvement and a factor labeled "negative caregiving" consisted of high levels of hostility/irritability and intrusiveness, and low levels of sensitivity (see Hipwell et al., 2016 for more details). These two components were used in final models.

Dynamic Faces paradigm. In this 13-minute task, participants were presented with gray-scale images of emotional faces taken from the NimStim database (Tottenham et al., 2009) displaying happy, angry, fearful and sad expressions and with control stimuli (gray-scale ovals matched with lighting to face stimuli) using Visual Basic software. The task is a block-design with three, 12-image blocks for each of the four emotional face types and 12, six-image blocks of shapes. Trials were separated by a 2–3 second jittered inter-trial interval. During each of the face trials, the face changed emotional expression from neutral to emotional over 1 second in 5% increments. During shape trials, a dark oval was superimposed on a light gray oval and changed in size to parallel changes in the face stimulus trials. In the middle of each trial (between 200 and 650 ms), a colored semi-transparent oval (blue, orange, or yellow) overlaid the image. Participants were asked to identify the color of the oval and respond by button press. This task measures implicit emotion processing and has been demonstrated to reliably activate multiple regions implicated in emotion processing in prior work (see Perlman et al., 2012; Hafeman et al., 2014; Manelis et al., 2015). For our models, we used neural activity when viewing happy faces relative to shapes (Happy > Shapes) in order to assess parental neural response to positive facial expressions. Participants' accuracy of and reaction time of color identification were collected for each trial.

Post-scan task

Following completion of the fMRI scan, participants completed an emotion labeling task (Ladouceur et al., 2013). Participants labeled facial emotional expressions from greyscale images of male and female actors expressing happiness, anger, fear, disgust, sadness, or neutral expressions (Lundqvist et al., 1998). Participants were asked to select the appropriate emotion label by button click and rate the intensity of each expression on a 1–10 scale (with 10 being the most intense). Participants' percent accuracy and intensity of happy emotion identification were calculated.

fMRI acquisition and preprocessing

Each participant was scanned using a Siemens 3T Trio scanner with a 12-channel head coil. Before BOLD fMRI scanning, a T2-weighted and FLAIR MRI scans were acquired to rule out neuro-morphological abnormalities. A 160-slice high-resolution sagittally acquired T1-weighted anatomical image was acquired for co-registration and normalization of functional images (repetition time (TR) = 2300 ms, 256 × 256 acquisition matrix, number of excitations, 1, flip angle = 9). Before the collection of fMRI data for each participant, we acquired a reference echo planar imaging scan that we visually inspected for artifacts (e.g. ghosting) and for good signal across the entire volume of acquisition. BOLD functional images were acquired with a gradient echo planar imaging sequence and covered 38 slices (3 mm thick) encompassing the entire cerebrum and the majority of the cerebellum (voxel size = 3.2 × 3.2 × 3.1 mm, TR/TE = 2000/28 ms, field of view (FOV) = 205, flip angle = 90). All scanning parameters were selected to optimize the quality of the BOLD signal while maintaining a sufficient number of slices to acquire whole-brain data.

Preprocessing and whole-brain image analyses were completed using statistical parametric mapping software (SPM8; <http://www.fil.ion.ucl.ac.uk/spm>). Functional image preprocessing included spatial realignment to the first volume to correct for head motion and unwarping to correct for static inhomogeneity interactions. Realignment and unwrapped images were then coregistered with participant's anatomical image. The anatomical image was then spatially normalized into standard stereotaxic space (Montreal Neurological Institute template) using a nonlinear transformation and segmented into separate tissue types. BOLD images were then transformed into the same space via the parameters from the structural image segmentation, resample to 2 × 2 × 2 mm³ voxels, despiked (using Automated Functional Neuro-imaging, AFNI; <http://afni.nimh.nih.gov>) and spatially smoothed with a 6 mm full-width at half-maximum Gaussian filter to minimize noise and individual differences in anatomy. Preprocessed data were analyzed using first-level random effects models that account for scan-to-scan variability. Motion parameters from the realignment phase were entered as covariates to control for participant movement in first-level models. Second-level random effects models that account for participant-to-participant variability were then conducted to determine task-specific regional responses. All 70 participants had movement <4 mm in each plane.

Data analytic strategy. To test our hypotheses, we first examined neural response to happy faces > shapes using within-sample t tests. Next, we investigated brain-behavior associations, specifically the association between maternal depressive symptoms (as a continuous variable), maternal positive caregiving and the two-way multiplicative interaction of maternal depressive symptoms and positive caregiving on BOLD response

using multiple regression models conducted in SPM8. Given that we hypothesized that this task would activate multiple neural regions, we used whole brain analyses to test our models. We report findings that are significant at $P < 0.001$ and corrected for multiple comparisons using family-wise error (FWE) at $P < 0.05$. Two additional regression models were conducted in SPM8 to explore the specificity and robustness of our findings. These models included positive caregiving and its multiplicative interaction with maternal depressive symptoms, along with negative caregiving and its interaction with depressive symptoms as predictors of positive faces > shapes and negative faces > shapes. For significant interactive effects, simple slope analyses were conducted to evaluate the association between neural response and observed caregiving when adding/subtracting 1 s.d. from mean depressive symptoms (Preacher et al., 2006). We controlled for maternal age, infant age, infant fussy temperament and single parenthood for all three models. Maternal education level and use of government assistance/poverty were highly correlated with single parenthood in the current study, and thus were not included in models in order to reduce multicollinearity and to limit the number of variables in the model.

Results

Fifty of the 70 (71.4%) mothers did not meet current criteria for any Axis I disorder, 17.2% met criteria for an Anxiety disorder (Specific Phobia, Social Phobia, Generalized Anxiety Disorder, Obsessive Compulsive Disorder), and 7.1% met criteria for MDD or Depressive Disorder NOS. Likewise, six of the 70 participants (8.6%) reported depressive symptoms at the level of 'possible depression' (score of 10 or higher) on the EPDS, with two of those participants also meeting criteria for depression on the SCID. Given this relatively low base rate and our interest in examining the moderating role of depressive symptoms on the caregiving brain, depression severity on the EPDS was used as a continuous variable in all of our models. Bivariate correlations (see Table 1) revealed mothers showed greater negative caregiving and less positive caregiving with older infants (r 's = 0.24 and -0.27 , respectively, P 's < 0.05). Unexpectedly, postpartum depression severity was not associated with positive or negative caregiving ($r = 0.02$, $P = 0.88$ and $r = 0.17$ respectively, $P = 0.17$) (see Table 1).

Main effect of task

There was a significant main effect of the task for the Happy > Shapes condition on bilateral amygdala [227 voxels (−18, −6, −16), $t = 6.87$, $pFWE < 0.01$; 149 voxels (30, 4, −20), $t = 5.87$, $pFWE < 0.03$] and temporo-parietal junction [TPJ; 615 voxels (46, −80, 0), $t = 7.24$, $pFWE < 0.01$] (see Table 2).

Table 1. Means, s.d., and intercorrelations of mother and infant variables

Variable	Mean (s.d.)	1	2	3	4	5
1. Mother age	19.86 (0.92)	–	–	–	–	–
2. Infant age	17.06 (4.68)	0.10	–	–	–	–
3. Fussy temperament	24.47 (6.62)	−0.14	0.06	–	–	–
4. Depressive symptoms	2.83 (3.63)	−0.02	0.05	0.01	–	–
5. Positive caregiving	0.09 (0.91)	0.06	−0.27*	−0.05	0.02	–
6. Negative caregiving	−0.09 (0.84)	−0.14	0.24*	0.09	0.17	0.01

Table 2. Within-sample and regression models on neural response to positive faces

Region	x, y, z	t	Cluster size	pFWE
<i>Within sample t-test</i>				
<i>Effect of task</i>				
Amygdala, parahippocampal gyrus, left (+)	-18, -6, -16	6.27	227	0.000
Amygdala, parahippocampal gyrus, right(+)	30, 4, -20	5.87	149	0.021
Temporal lobe, BA 39, right (+)	46, -80, 0	6.30	615	0.000
Temporal lobe, BA 39, left (+)	-40, -70, 18	6.57	360	0.000
Medial prefrontal cortex, BA 9 & 10 (+)	2, 62, 20	5.22	592	0.000
Superior, middle frontal gyrus, BA 8 (+)	-20, 30, 50	4.85	331	0.000
Precuneus, parietal lobe (+)	6, -62, 30	4.57	166	0.013
Lingual, parahippocampal gyrus (+)	-12, -32, -4	5.09	155	0.017
Lingual gyrus, posterior cingulate	12, -56, -4	4.57	123	0.044
Lingual gyrus, parahippocampal gyrus	14, -34, -4	4.56	187	0.013
Occipital lobe, cuneus (+)	18, -78, 30	4.16	203	0.005
Occipital lobe, cuneus (+)	-14, -64, -2	4.79	247	0.017
Occipital lobe, cuneus (-)	26, -94, 8	5.07	122	0.045
<i>Multiple regression model</i>				
<i>Depressive symptoms</i>				
Putamen, lentiform nucleus (-)	-22, 8, -10	4.92	149	0.021
Precuneus, parietal lobe(+)	-12, -58, 48	4.69	195	0.006
Temporoparietal junction, left (+)	-34, -48, 16	5.64	238	0.002
<i>Positive caregiving</i>				
Precuneus, parietal lobe, left (+)	-14, -60, -48	4.92	193	0.006
<i>Depressive × positive caregiving</i>				
Ventral striatum, putamen, hippocampus (+)	-28, -20, -10	5.94	736	0.000
Dorsal striatum, caudate, putamen (+)	8, 0, 10	5.54	166	0.013
Precuneus, parietal lobe, left(-)	-14, -60, 48	7.87	1016	0.000
Precuneus, parietal lobe, right (-)	12, -62, 44	4.60	127	0.039
Occipital lobe, cuneus (-)	-20, -74, 16	4.36	153	0.018

Note. (+) denotes positive association, (-) denotes negative association. BA= Brodmann area.

Maternal depression and caregiving and BOLD response

Findings from our original regression model revealed that maternal postpartum depressive symptoms were associated with lower face-related putamen activity [149 voxels (-22, 8, -10), $t = 4.92$, $pFWE < 0.03$] and higher face-related precuneus [195 voxels (-12, -58, 48), $t = 4.69$, $pFWE < 0.01$] and TPJ activity [238 voxels (-34, -48, 16), $t = 5.64$, $pFWE < 0.01$]. Observed positive caregiving was associated with greater activation in the precuneus [193 voxels (-14, -60, 48), $t = 4.92$, $pFWE < 0.01$].

Interaction of maternal depression and caregiving on BOLD response

In the original regression model, there was a significant interactive effect of maternal depressive symptoms and positive caregiving on bilateral precuneus [1016 voxels (-14, -60, -48), $t = 7.87$, $pFWE < 0.01$; 127 voxels (12, -62, 44), $t = 4.60$, $pFWE < 0.04$], ventral striatum [736 voxels (-28, -20, -10), $t = 5.94$, $pFWE < 0.01$], dorsal striatum [166 voxels (8, 0, 10), $t = 5.54$, $pFWE < 0.02$] and occipital lobe [153 voxels (-20, -74, 16), $t = 4.36$, $pFWE < .02$] in response to happy faces.¹ Simple

1 One participant had significantly higher ($z > 3$) activation in the precuneus in response to positive faces and significant lower ($z < 2$) activation in the VS in response to positive faces relative to the remaining sample. After removing this participant from analyses, findings remained significant for the VS cluster ($pFWE = 0.011$) but were no longer significant for the precuneus, dorsal striatum, or occipital lobe clusters. We present findings with this participant included based on her high depressive symptoms score (EPDS=12) that exceeds the cutoff for

slope analyses revealed that higher levels of positive caregiving were related to greater activation in the precuneus in response to happy faces for mothers with lower depressive symptoms (left precuneus, $\beta = .42$, $t = 6.66$, $P < 0.001$; (see Figure 1) right precuneus, $\beta = 0.40$, $t = 5.01$, $P < 0.001$). There was no association between positive caregiving and precuneus response for mothers with higher levels of depressive symptoms (P 's = 0.05 and 0.17). Likewise, higher levels of positive caregiving were related to higher occipital lobe response to happy faces for mothers with low depressive symptoms ($\beta = .24$, $t = 4.68$, $P < 0.001$), but were not significantly related to occipital lobe response for mothers with higher depressive symptoms ($P = 0.21$) (see Figure 1).

Unexpectedly, simple slope analyses also revealed that higher levels of positive caregiving were related to lower ventral striatal ($\beta = -0.35$, $t = 7.52$, $P < 0.001$) and lower dorsal striatal ($\beta = -0.33$, $t = 5.27$, $P < 0.001$) response to positive faces for mothers with lower depressive symptoms, but higher response in the ventral ($\beta = 0.11$, $t = 2.63$, $P < 0.02$) and dorsal striatum ($\beta = 0.15$, $t = 2.59$, $P < 0.02$) for mothers with higher depressive symptoms.

In final models to test for specificity and robustness of effects, findings for positive caregiving, depressive symptoms and their two-way interaction remained the same. Results showed no significant main effect of negative caregiving or interactive effect of negative caregiving and maternal depressive symptoms on neural response to positive faces. Results also showed no significant main effect of positive caregiving, negative caregiving, maternal depressive symptoms and no interactive effect

possible depression and that may explain her differential pattern of brain responding to positive faces.

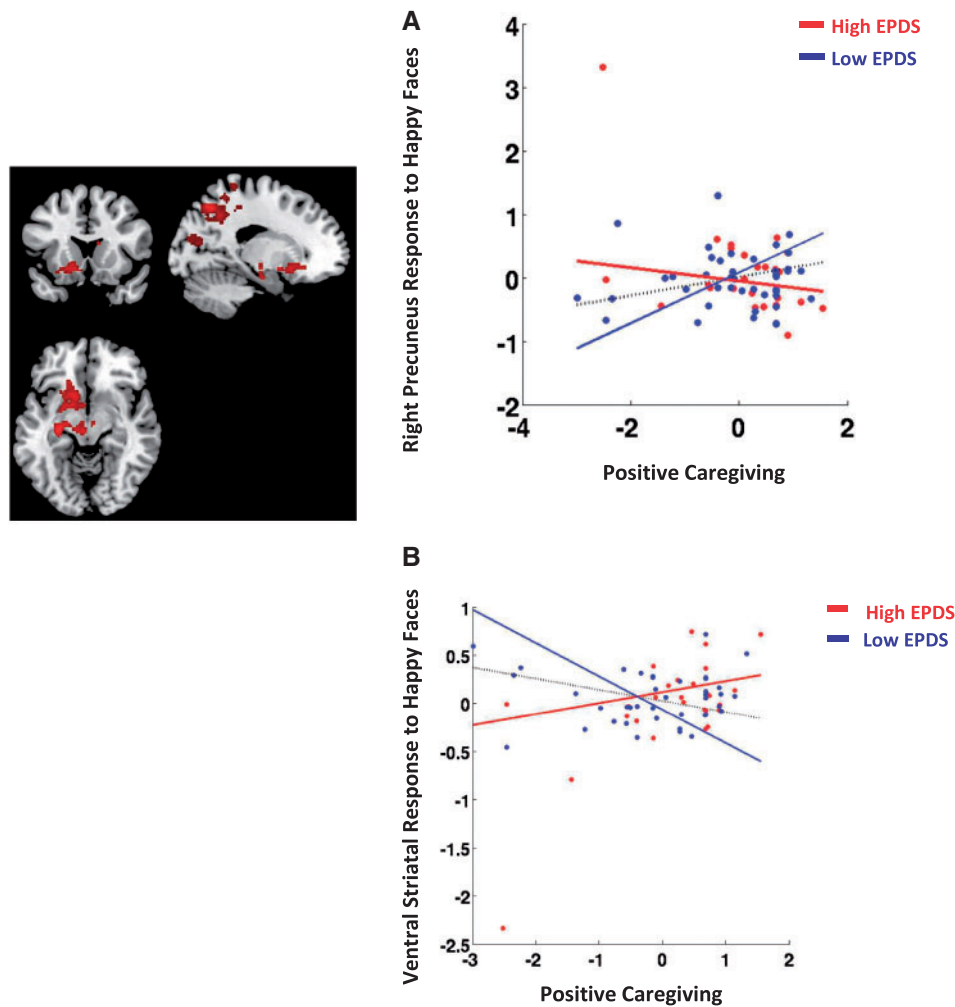


Fig. 1. Postpartum depressive symptoms moderate the association between positive caregiving and neural response to positive faces in the (A) precuneus, (B) striatum, and occipital lobe.

of maternal depressive symptoms with positive caregiving or negative caregiving on negative face processing. Controlling for maternal age, infant age, infant temperament and single parenthood in our models did not change our findings.

Next, we conducted bivariate correlations using extracted values from significant clusters associated with caregiving and EPDS (i.e. ventral striatum, dorsal striatum, bilateral precuneus and occipital lobe) and behavioral face data. There was no significant association between neural response to positive faces and accuracy or intensity ratings of happy emotion expressions post-scan (r 's = -0.19 to 0.14 , P 's = 0.12 – 0.95).

Discussion

The goal of our study was to evaluate the association among postpartum depressive symptoms, maternal neural response to positive facial stimuli, and positive caregiving in a sample of young, postpartum mothers. Our findings demonstrate that postpartum depressive symptoms moderate the association between early caregiving and neural response to positive facial stimuli in regions characterizing the "caregiving brain", particularly reward-related and social-cognitive regions. In particular, we found that the precuneus, a region implicated in mentalizing about others' emotions, in self-representation and in

episodic memory (Cavanna and Trimble, 2006), was directly associated with warm and involved caregiving in new, postpartum mothers. However, we also found that this effect was moderated by postpartum depressive symptoms, such that higher precuneus response was only associated with greater positive caregiving for mothers with low depressive symptoms. In this case, greater ability to engage in social processing that involves mentalizing about others' emotions may aid healthy new mothers in picking up on their infant's cues and considering what their infant may be feeling and needing in that moment. Further, given the precuneus' role in self-awareness and episodic memory (Cavanna and Trimble, 2006), greater response in this region to positive faces in healthy postpartum mothers may suggest a stronger ability to identify with the positive emotions of others and elicit positive memories of prior interpersonal interactions that ultimately extend to interactions with their infants. Likewise, for mothers with lower depressive symptoms, but not for those with higher symptoms, we found that greater occipital lobe responding to positive faces was also associated with more positive caregiving. Combined with our precuneus finding, this suggests that greater visual processing of happy faces may aid mothers in visually identifying their infants' emotions and responding appropriately to their positive feelings. However, we note that it is also possible that activity in

these regions may simply reflect greater social and visual processing in general, and caution should be taken in interpreting these findings using reverse inference.

For mothers with higher levels of postpartum depressive symptoms, a different association between positive caregiving and neural response in the precuneus and occipital lobe to happy faces emerged. Specifically, for mothers with more depressive symptoms, there was no significant association between positive caregiving and the precuneus or occipital lobe activity to faces, indicating that these neural regions may not be functioning appropriately to aid mothers in identifying their infants' positive emotion expressions or in remembering or considering their infants' needs. Given prior findings that depression is associated with difficulty identifying positive emotion expressions (Joormann and Gotlib, 2006), including those of their own infant (Arteche et al., 2011), and with biased responding to positive stimuli, events and autobiographic memories (Joormann and Gotlib, 2006; Bergouignan et al., 2008), it appears that the precuneus may be less responsive to positive stimuli in mothers with depressive symptoms. Indeed, we also found that, independent of caregiving, higher depressive symptoms were unexpectedly directly associated with *greater* response in the precuneus and the temporo-parietal junction, social processing regions implicated in mentalizing and theory of mind, respectively (Samson et al., 2004; Cavanna and Trimble, 2006). This falls in line with recent findings that postpartum depression is associated with increased amygdala response to positive infant stimuli (Wonch et al., 2016). Together, these findings suggest that postpartum mothers with higher depressive symptoms may need to engage in *greater* social-cognitive processing to understand and make sense of positive facial expressions, but that this degree of social-cognitive processing does not appear to aid them in caring for their young infant (as it does for healthy, postpartum mothers).

Similar to prior work (e.g. see Surguladze et al., 2005; Epstein et al., 2006), we also found that higher levels of depressive symptoms were associated with lower activity in the striatum (i.e. putamen) to positive faces. The ventral and dorsal striatum have been implicated in appetitive motivation and in subjective pleasure of positive events (Haber and Knutson, 2010), thus our findings and prior research suggests that depressive symptoms are related to blunted reward function in response to rewarding stimuli and low motivation and pleasure for positive events and interactions. Along these lines, we also found that the relationship between striatal response to positive stimuli and positive caregiving differed for mothers with higher levels of depressive symptoms relative to those with low or no symptoms.

For mothers with higher levels of depressive symptoms, *greater* response in the ventral and dorsal striatum was associated with *more* positive caregiving, but surprisingly, the reverse appeared to be true for mothers with lower depressive symptoms. In this case, these new, young mothers with higher depressive symptoms may require *more* responding in the ventral and dorsal striatum in response to positive stimuli, relative to young mothers with lower symptom levels, in order to engage in warm and positive interactions with their infants, given depression's strong and consistent association with loss of pleasure, interest and motivation (Surguladze et al., 2005; Epstein et al., 2006; Zhang et al., 2013). Along these lines, although depression is often associated with compromised caregiving, including lower levels of warmth (Lovejoy et al., 2000), not all depressed parents experience these caregiving disruptions (Frankl and Harmon, 1996). Indeed, in our study, postpartum depressive symptoms were unrelated to positive caregiving. Perhaps our

findings suggest that postpartum mothers with greater function in reward circuitry are those who are also able to establish and maintain warm and nurturing relationships with their infants in spite of psychiatric symptoms. Further, we note that we had limited variability in depression severity (with six participants reporting possible clinical levels of depression), although the proportion of mothers with elevated symptoms (8.6%) is somewhat similar to epidemiological rates of postpartum depression (Paulson et al., 2006). Nevertheless, this low level of variability may have contributed to the non-significant association with positive caregiving.

Taken together, our findings suggest that the neurobiology of positive caregiving may be altered for mothers experiencing postpartum depressive symptoms, particularly in regard to social-cognitive and reward processing. Our findings were specific to positive caregiving, rather than negative (i.e. hostile and intrusive) caregiving, and to positive facial stimuli, but not to negative faces. Thus, quite intuitively and commensurate with conceptual models that suggest that positively and negatively valenced experiences are distinct, albeit related, it appears that the way in which mothers respond neurally to positive emotional cues, but not negative cues, reflects their ability to engage in warm interactions with their offspring, and both are unrelated to a tendency to engage in intrusive or hostile mother-infant interactions. Although we posit that the association between greater precuneus response to positive faces and higher levels of positive caregiving may be due to better socio-cognitive processing of positive stimuli, it is important to note that we did not find a significant association between neural response to positive faces and happy face identification post-scan. Furthermore, our findings suggest that strong reward circuit engagement to happy faces may serve as an important protective factor for positive caregiving for postpartum mothers with higher depressive symptoms, but not necessarily for those without these symptoms. One possibility, given that these stimuli were of strangers' faces and our sample included mothers of young infants, is that healthy, new mothers may be responding preferentially to infant stimuli, showing less motivation and preference for unfamiliar adults compared to their new infant. Prior work has shown that mothers show preferential responding to their own child relative to another child or in response to a non-infant control (i.e. adult) in regions implicated in emotional responding and in caregiving (Bartels and Zeki, 2004; Leibenluft et al., 2004; Barrett and Fleming, 2011), but that postpartum depression may interfere with this preferential responding (Wonch et al., 2016). Specifically, Wonch et al. (2016) demonstrated that postpartum depression was associated with diminished connectivity between the amygdala and the right insula, regions implicated in emotional salience, to positive stimuli from their own infant relative to an unfamiliar infant. Building on this, future work should evaluate postpartum mothers' response to positive facial stimuli of their own infant, a familiar infant, an unfamiliar infant and a non-infant control (i.e. adult) and associate this responding to caregiving patterns in order to disentangle patterns of emotional responding to own child relative to others.

Future work should also evaluate other important factors pertinent to positive caregiving, including one's own caregiving history and past psychiatric illness and affective functioning. Given that young maternal age may be related to elevated stress, psychiatric symptoms and different caregiving patterns (Luster and Haddow, 2005), it will be important to evaluate these associations in older postpartum mothers in future work. Studies that include longer duration mother-infant observation

tasks may also provide opportunities to observe certain caregiving behaviors (e.g. impatient or hostile caregiving behaviors). Also, studies that include mothers who meet diagnostic criteria for postpartum depression relative to those who do not may also provide more information about parenting-related neural differences not observed in our study, especially given our relatively low base rate of mothers with clinically significant levels of depression. Although our work evaluated how current symptoms may moderate the association between neural response and caregiving, we also note that in the current study, psychiatric diagnoses were assessed at the 10-week postpartum visit, whereas the neuroimaging assessment was conducted at 4 months postpartum. It is therefore possible that depression status may have changed in the short interval, although EPDS and fMRI data were assessed at the same time point.

Our study has many strengths including (i) evaluation of brain-behavior associations using a widely used fMRI task and independent observations of mother-infant interactional behavior, (ii) use of a low SES, racially diverse sample larger than most existing studies and (iii) confirmation of the specificity and robustness of results based on evaluation of both positive and negative caregiving, both positive and negative face processing, and other contextual factors. Findings are important for understanding neural mechanisms that may place some postpartum mothers at risk for displaying compromised caregiving and protect others from these disruptions. In particular, postpartum mothers who, regardless of exhibiting depressive symptoms, express motivation for and pleasure in positive events in their everyday life may be protected against depression's impact on caregiving and may instead be able to maintain warm and involved relationships with their infants. Identification of factors that can promote or hinder positive caregiving is important because of its potentially lasting effects on child physiological and self-regulation, social competence and prosocial behavior (Sroufe, 2005). In this regard, mothers who endorse higher depressive symptoms along with a loss of interest and pleasure in positive events or with difficulty identifying positive expressions in others may be at greatest risk for caregiving difficulties and may benefit most from interventions aimed at fostering warm, sensitive and empathic caregiving (e.g. see Cooper et al., 2005, Sadler et al., 2013).

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