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Postpartum depression and brain response to infants: Differential amygdala response and connectivity

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ABSTRACT

Recent evidence suggests that postpartum depression is associated with reduced amygdala (AMY) response to negative stimuli. However, given the anhedonic features of PPD, it is important to consider mothers' brain response specifically to positive infant and to other positive stimuli. Mothers with (n = 28) and without (n = 17) clinically determined PPD (n = 28) viewed smiling pictures of infants (Own and Other), and positive non-infant stimuli (Non-Infant). First, we examined group differences in AMY response across conditions. Next, psychophysiological interaction was used to examine group differences in AMY connectivity across conditions. Connectivity estimates were then correlated with measures of maternal mood and anxiety. PPD mothers, compared to non-PPD mothers, showed overall increased AMY response across conditions in the right AMY. Despite this, PPD mothers demonstrated decreased bilateral AMY–right insular cortex (IC) connectivity as compared to non-PPD mothers when they view Own–Other infants. Furthermore, decreasing AMY–IC connectivity was associated with increasing symptoms of depression and anxiety. These differences were evident only for infant stimuli and did not apply to all positively valenced stimuli. Thus, PPD mothers show altered brain response and connectivity in regions strongly implicated in the processing of socially and emotionally relevant stimuli, as well as interoception and the evaluation of subjective emotional experience.

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Postpartum depression (PPD) is the most common maternal birth complication (Ross, Dennis, Blackmore, & Stewart, 2005). For approximately 15% of mothers, this time period is accompanied by severe mood disturbance that meets the criteria for depression and includes symptoms such as irritability, uncontrollable crying, extreme sadness/hopelessness, and sometimes thoughts of harm to self and to the baby (American Psychiatric Association, 2000; Beck, 2001; Cox, Murray, & Chapman, 1993; Dennis, Heaman, & Vigod, 2012; Halbreich & Karkun, 2006; O'Hara & Swain, 1996). Despite its prevalence and pervasive impact on the developing infant (Halligan, Murray, Martins, & Cooper, 2007; Murray, 1992; Pawlby, Sharp, Hay, & O'Keane, 2008), our understanding of the neural bases of PPD relies on only a few recent studies (Moses-Kolko et al., 2010, 2011; Silverman et al., 2007, 2011; Moses-Kolko et al., 2012; Chase, Moses-Kolko, Zevallos, Wisner, & Phillips, 2013; Laurent & Ablow, 2013, 2012; see Barrett & Fleming, 2011; Swain et al., 2014; Moses-Kolko, Horner, Phillips, Hipwell, & Swain, 2014; for reviews). These studies have identified an inverse relation between PPD symptom severity and amygdala (AMY) response (Moses-Kolko et al., 2010; Silverman et al., 2011), and suggest that this AMY hyporesponsiveness may be pathognomonic for PPD.

With a known role in the processing of motivationally, emotionally, and socially relevant stimuli (Adolphs, 2003; Adolphs, Baron-Cohen, & Tranel, 2002; Cunningham & Brosch, 2012; Pessoa, 2010), it is not surprising that the AMY may play an important role in PPD and mothering, in general. Previous work in women *without* clinical depression has found that the AMY responds preferentially, or selectively, when mothers view their own compared to an unfamiliar infant (Barrett et al., 2012; Leibenluft, Gobbini, Harrison, & Haxby, 2004; Ranote et al., 2004; Seifritz et al., 2003; Strathearn & Kim, 2013). As such, it appears that healthy mothers have an AMY that responds selectively to their own baby. Thus, we predict that an AMY response that deviates from this pattern of response, especially to images of infants, may be problematic for

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childrearing. In fact, work with other mammals suggests that species-typical maternal behavior is dependent upon normative AMY functioning (Fleming, Vaccarino, & Luebke, 1980; Numan, Numan, & English, 1993). Furthermore, work from our lab (Barrett et al., 2012) has demonstrated that infant-related AMY function is related to maternal anxiety, levels of distress during parenting, and individual differences in attitudes toward mothering. The current study will characterize whether and how infant-related AMY functioning differs in human mothers with PPD as compared to nondepressed mothers, and whether in PPD mothers, the AMY is differentially engaged with other brain regions during the processing of infant cues.

To date, negative non-infant stimuli have primarily been used to examine the neural correlates of PPD (e.g., Moses-Kolko et al., 2011, 2010; Silverman et al., 2011, 2007). Laurent and Ablow (2012) used negative *infant* stimuli for the first time, choosing to examine the brain response in mothers with depressive symptomology in the late postpartum stage (15–18 months) to infant cries. Although this work provides important first insights, for most mothers, infants represent motivationally relevant, positive stimuli. Relatedly, PPD is characterized by an altered emotional, cognitive, and behavioral response toward a stimulus that is typically interpreted as rewarding (e.g., one's own infant). The impact that this disorder has on mothering abilities highlights the need to understand the neural response of mothers with PPD to *positive* infant stimuli, specifically in comparison to other positive non-infant stimuli. It is also important to understand whether the pattern of brain response is specific to their own, or generalizable to all infants. Examining this may have implications for the treatment of PPD.

One recent study (Laurent & Ablow, 2013) examined the brain response in mothers with late postpartum stage depression (15–18 months) to positive pictures of their own infant as compared to positive pictures of an unfamiliar infant. They identified no group differences (PPD vs. non-PPD). Numerous factors may explain these unexpected results. For example, PPD has a high rate of onset in the early postpartum period (Cox et al., 1993), and depressive symptoms tend to remain elevated throughout the first postpartum year (Dennis et al., 2012). It is possible that brain differences in mothers with PPD may change across the postpartum period and that the authors may have failed to capture these mothers at their most vulnerable stage. Furthermore, the authors used a whole-brain approach to data analysis rather than an a priori hypothesis-driven region-of-interest analysis. As much of the existing research indicates that there may be altered brain response in PPD in relatively small brain regions (e.g., the AMY), some of their results may have been masked due to the stringent corrections for multiple comparisons inherent to whole-brain analyses.

In contrast to the paucity of brain-related research on PPD, brain response differences in individuals with major depressive disorder (MDD) have been relatively well characterized. MDD is associated with negative biases in processing facial expressions and altered activity in emotion-related brain regions in response to emotional facial expressions (Anand et al., 2005; Arteche et al., 2011; Dannlowski et al., 2009; Gil, Teissèdre, Chambres, & Droit-Volet, 2011), especially in limbic structures. More specifically, there is greater AMY response to emotional faces in individuals with MDD, and this AMY hyperresponsiveness is primarily for negative stimuli (Hamilton et al., 2012; Suslow et al., 2010; Victor, Furey, Fromm, Öhman, & Drevets, 2010). Thus, although both MDD and PPD are classified as depression, there appears to be a stark contrast between the AMY *hyper*responsiveness to negative stimuli in studies of MDD and the *hypo*responsiveness to negative stimuli observed in existing studies of PPD (Moses-Kolko et al., 2010; Silverman et al., 2011). As of yet, we do not know whether this paradox in brain response to negative stimuli (e.g., decreased in PPD and increased in MDD) will carry over into research with positive stimuli (e.g., increased in PPD and decreased in MDD). Relative to MDD, our understanding of the neurobiology of PPD is still in its "infancy", and continued research into this contradictory AMY response is important given that the symptoms of the disorders overlap to such a large degree.

While previous work with nonclinical samples has suggested that the AMY may play a unique role in the processing of negative- or threat-related stimuli (see Phelps & LeDeoux, 2005), more recent work supports the notion that the AMY is also responsive to uncertainty (e.g., Whalen, 2007) and novelty (e.g., Balderston, Schultz, & Helmstetter, 2011), regardless of the emotional valence of the stimuli. Thus, the AMY may play a role in relevance detection (Sander, Grafman, & Zalla, 2003) based on the particular motivational state, goals, and/or needs of the observer (see also Cunningham & Brosch, 2012). Throughout pregnancy, the postpartum period, and continued motherhood, women are placed in a particularly unique motivational state to which infants and children serve as stimuli worthy of detection, sine qua non. Thus, we believe this proposed role for the AMY forms a particularly relevant foundation for reconciling the growing literature examining the brain response to various stimuli, infant and non-infant,

positive and negative, in mothers with and without mood changes.

In addition to differences in mean-level AMY responsivity, it is becoming increasingly clear that brain networks underlie many cognitive processes, and differential connectivity is associated with many forms of psychopathology. For instance, resting-state connectivity between the prefrontal cortex and AMY is reduced in depression (Chase et al., 2013; Tang et al., 2013; Zhang et al., 2014). Only one study has examined task-dependent (during viewing of negative adult faces) functional connectivity of mothers with PPD in the immediate postpartum period (Moses-Kolko et al., 2010). This study found decreased top-down dorsomedial prefrontal cortex-AMY effective connectivity in mothers with PPD. Although functional connectivity has been examined with mothers who vary in maternal responsiveness (Atzil, Hendler, & Feldman, 2011), we do not yet understand, however, how task-dependent functional brain networks that covary with the AMY (Mayberg, 2003; Shafi, Westover, Fox, & Pascual-Leone, 2012) may be altered in mothers with PPD when they are viewing infant faces.

To address the above concerns, through fMRI, the current study will examine (1) AMY response to positively valenced infant stimuli of varying familiarity, and to positively valenced non-infant stimuli; (2) functional connectivity using the AMY as a seed of interest, during the viewing of infant and non-infant stimuli, in mothers with and without clinically determined PPD. First, in line with recent views that the normative functional role of the AMY includes assisting with both the identification of a salient stimulus and the convening of necessary resources for an adaptive response to said stimulus (Cunningham & Brosch, 2012), we predict that we will replicate the existing work that shows that non-PPD mothers show a preferential blood-oxygen-level dependent (BOLD) response in the AMY for their own, as opposed to another infant (Barrett et al., 2012; Leibenluft et al., 2004; Ranote et al., 2004; Seifritz et al., 2003; Strathearn & Kim, 2013). Second, we predict that this preferential BOLD response for one's own baby in the AMY in non-PPD mothers will be blunted in mothers with PPD. Third, we expect to see an altered pattern of task-based cortico-limbic connectivity in PPD compared to non-PPD mothers between the AMY and other brain regions important in affective processing or reward. As work with other species demonstrates that parity or maternal experience is known to influence many aspects of mothering, including brain response (Anderson, Grattan, Van Den Ancker, & Bridges, 2006; Featherstone, Fleming, & Ivy, 2000; Love et al., 2005; Scanlan, Byrnes, & Bridges, 2006), we will include this as a predictor in our analyses. We expect that multiparity, as compared to primiparity, will be associated with decreased AMY response (due to its proposed role in uncertainty detection), but overall enhanced connectivity between the AMY and other brain regions known to be important in affective or reward processing during the viewing of infant cues, as these connections may be strengthened with greater maternal experience.

Methods and materials

There were three phases in the study: (1) Diagnostic Interview and Photography Session, (2) fMRI Session, and (3) Home Visit. Of interest for the current study are Phases 1 and 2. A similar paradigm has been used successfully in previous work in our lab (Barrett et al., 2012). This study was approved by the Research Ethics Boards of St. Joseph's Healthcare (SJH), Hamilton, ON, Canada, and the University of Toronto at Mississauga (UTM), Mississauga, ON, Canada. Informed written consent was obtained from all participants.

Subjects

All participants were right-handed, English-speaking women, 20–40 years of age, with singleton, full-term babies. They presented with no contraindications to fMRI (e.g., metallic implants) and had corrected or normal vision. According to structured clinical interview (Composite International Diagnostic Interview-Venus (CIDI-V)(Martini, Wittchen, Soares, Rieder, & Steiner, 2009), all participants reported no serious medical or neurological condition, no substance dependence in the past year (except caffeine or nicotine), and no current or history of psychotic or bipolar disorder, according to Diagnostic and Statistical Manual fourth edition text revision (DSM-IV TR (American Psychiatric Association, 2000) criteria. Additionally, the Children's Aid Society was not involved in the care of the baby, and mothers did not present with suicidal, homicidal, or infanticidal risk. Mothers with no history of or current psychiatric illness (non-PPD, $n = 23$) were recruited from the maternity ward at SJH. Mothers who met DSM-IV TR criteria for major depressive episode, with perinatal onset (PPD, $n = 31$) were recruited from the Women's Health Concerns Clinic (WHCC) at SJH. A principal investigator (MS) provided clinical care to these participants. Since PPD mothers were recruited from an outpatient psychiatric clinic, some were receiving treatment in the form of selective serotonin reuptake inhibitors (SSRI use $n = 13$; no medication $n = 18$). Although these women were recruited based on a diagnosis of PPD at the time of their intake at the WHCC, they also completed a

diagnostic interview (CIDI-V) administered by a trained graduate student or research assistant approximately 1 week prior to the fMRI scan. To ensure a representative sample, these mothers were not excluded from the study and medication status was considered in all analyses. Symptom type and severity after the initial clinical diagnosis was assessed 1 week after diagnosis (and at the time of the scan) using the Edinburgh Postnatal Depression Scale (EPDS), a self-report measure of PPD severity and the State-Trait Anxiety Inventory, Trait version (STAI-T). These measures of mood reflect moment-to-moment changes in affect and are not necessarily consistent with the clinical diagnosis based on DSM-IV for major depressive episode with perinatal onset.

Mothers participated at 2–5 months postpartum. This range was chosen as this was the minimum age, based on our previous work (Barrett et al., 2012), at which positive (i.e., smiling) facial expressions were produced by infants in a relatively consistent manner. However, due to the often time-limited nature of PPD, keeping the time period under 5 months was ideal (Cox et al., 1993). Prior to the fMRI, mother–baby pairs attended a laboratory session at SJH, where a minimum of 50 positive infant facial expressions were photographed (by the first (KEW) and second (CBM) authors). Five observers then rated these images on a 9-point scale (1 = "not at all positive" and 9 = "extremely positive"). Twenty of the most positive infant face pictures (average rating of 5 or higher) were chosen for use in the fMRI protocol. The images were standardized for overall brightness, and framed and masked to present just the facial area. Own baby stimuli were matched by randomly choosing another baby from our stimulus set. For their participation, mothers were provided with $100 remuneration plus the cost of parking.

fMRI

Affect rating task

PPD and non-PPD mothers completed an affect rating task (ART) during an fMRI session at the Imaging Research Centre at SJH. The ART was presented using E-Prime 2.0 software (Psychology Software Tools, Pittsburgh, PA, USA), and timing was synchronized with the acquisition of functional images. During each ART run, three conditions were presented four times using a block-design: (1) smiling own infant face (Own); (2) smiling other infant face (Other); (3) positive non-infant stimuli (e.g., scenes, animals, food; Non-Infant). Prior to each condition-block, a 1.5 s visual cue was presented (Set A, Set B, Set C) followed by a 4 s fixation cross. Cue to condition-block assignment was randomized across participants. For each 40 s condition-block, five unique picture stimuli were presented randomly for 4 s. After this, mothers had 4 s to make a subjective rating of their emotional response to each stimulus ("How does this picture make you feel?"), made on a 9-point scale (1 = "not at all positive" and 9 = "extremely positive"). Each condition-block was followed by a jittered 8–10 s interstimulus fixation cross (see Figure 1). PPD mothers may interpret infant faces more negatively than non-PPD mothers (Arteche

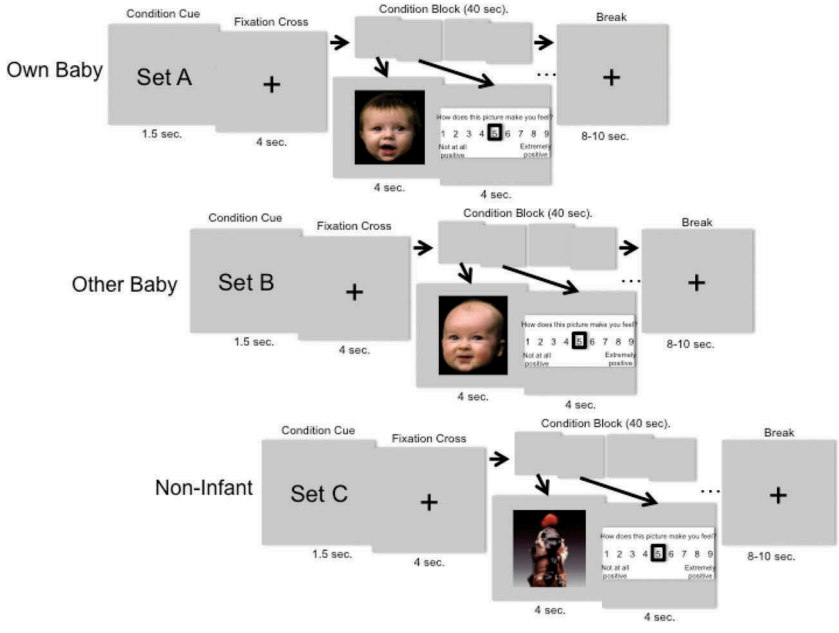

Figure 1. fMRI affect rating task (ART) design.

et al., 2011). Thus, prior to the onset of the task, mothers were verbally instructed to rate the infant faces for the degree of emotional intensity *they* felt internally when viewing them, rather than on the emotional intensity conveyed by the facial expressions. It is also possible that PPD mothers would display an altered response to all emotional stimuli. Consequently, each mother also viewed 20 Non-Infant, control images from the International Affective Picture System based on pre-chosen emotional subset categories defined by Mikels et al. (2005): amusement, contentment, and undifferentiated positive. Of note, all mothers practiced the same task outside of the scanner immediately prior to their scan, in which all of the babies were unfamiliar or "Other", in order to familiarize them with the task.

Acquisition

MRI scanning was conducted using a General Electric 3-T short-bore scanner with 32 parallel-receiver channels (General Electric, Milwaukee, WI, USA). BOLD response to infant faces was acquired using T2 weighted interleaved echo-planar imaging (EPI). A total of 256 volumes were obtained from each participant, consisting of 42 axial slices of 3 mm thickness (repetition time = 2.7 ms, echo time = 35 ms, flip angle = 90°, resolution = 64 × 64 over 24 cm field of view).

Preprocessing

The fMRI data processing was carried out using fMRI Expert Analysis Tool (FEAT Version 6.00), part of FMRIB's Software Library (FSL, www.fmrib.ox.ac.uk/fsl). Pre-statistic processing included: motion correction using MCFLIRT (Jenkinson, Bannister, Brady, & Smith, 2002); brain extraction using Brain Extraction Tool (Smith, 2002); spatial smoothing using a full width at half maximum 5 mm Gaussian kernel; grand-mean intensity normalization of the entire 4D dataset by a single multiplicative factor; highpass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma = 75.0 s). Participants were excluded from further analysis if they exhibited greater than 2 mm movement. The first four images were discarded to ensure the scanner had achieved steady state during image acquisition. Warped functional images were combined to create a mean study-specific template for coregistration with individual functional data. Registration to this template was carried out using FLIRT (Jenkinson et al., 2002; Jenkinson & Smith, 2001). Time-series statistical analysis was carried out using FILM with local autocorrelation correction (Woolrich). In the following description, "Own" refers to own baby pictures, "Other" refers to other baby pictures and "Non-Infant" refers to all positive nonbaby pictures. Ten experimental conditions were included as regressors: OwnSet (instructions for mothers), OwnView, OwnRate, OtherSet, OtherView, OtherRate, NonInfantSet, NonInfantView, NonInfantRate, and ThankYou (end of task message). BOLD response when the mothers were viewing infant faces (View = passive viewing of the faces) was modeled separately from the time they were making a subjective rating of the infant faces (Rate = rating scale on screen; mothers making response), as AMY activation can be inhibited by cognitive activity (Drevets & Raichle, 1998; Phan, Wager, Taylor, & Liberzon, 2002).

Region of interest analysis

An AMY region of interest (ROI) (Gil et al., 2011) was anatomically defined using the Harvard-Oxford anatomical atlas, at 70% probability threshold. We recognize that the human AMY is comprised of distinct subregions, each with their own afferents and efferents (Amunts et al., 2005; Ball et al., 2007; McDonald, 2003; Price, 2003). Subregions are also differentially involved in the processing of emotional face stimuli, especially in anxious individuals (Etkin et al., 2004; Etkin, Prater, Schatzberg, Menon, & Greicius, 2009). We chose to examine the AMY as a whole for comparison with the extensive work that uses this approach to examine the functional significance of the AMY in MDD. We examined the View conditions rather than the conditions during which mothers were actively using the response box to respond to the pictures (Rate). The mean time series of AMY ROI voxels was generated for OwnView, OtherView, and NonInfantView conditions in the right and left AMY (defined using the abovementioned anatomical mask). In order to examine both familiarity- and specificity-related differences, we examined AMY response to the following contrasts: OwnView–OtherView (familiarity) and OtherView–NonInfantView (specificity). To replicate our previous work (own positive–other positive contrast from Barrett et al., 2012), we first examined these contrasts in non-PPD and PPD mothers, separately. Next, we conducted group-level analyses in FSL, masked for the bilateral AMY, where *Z*-statistic images (Gaussianized T/F) were cluster thresholded ($z > 2.3$), and a cluster significance threshold of $p = 0.05$ was applied (Worsley, 2001). This represents a more sensitive alternative to voxel-based thresholding, where a *Z*-statistic is used to define contiguous clusters with an estimated significance level (from GRF-theory), which is then compared with the cluster probability threshold. For group-level analyses, we examined both contrast-level (OwnView–OtherView and OtherView–NonInfantView) and condition-level (e.g., OwnView, OtherView, and NonInfantView) effects, as well as the overall BOLD response across conditions (e.g., in

OwnView, OtherView, and NonInfantView, combined). To examine PPD and anxiety symptom severity, EPDS and STAI-T scores were entered into SPSS-21 for analyses with AMY mean signal change across contrast conditions. Medication status was used as a covariate in the group-level model.

Psychophysiological interaction

Again, in order to examine both familiarity and infant-related connectivity differences, separate psychophysiological interaction (PPI) models were conducted for OwnView–OtherView and OtherView–NonInfantView, respectively. Mean deconvolved time course was extracted from seed regions in the left and right AMY to serve as the psychophysiological variable. We restricted our bilateral AMY seed regions to those voxels within the anatomical ROI defined above that showed an overall enhanced BOLD response relative to baseline in all three of our conditions combined (OwnView, OtherView, and NonInfantView). PPI interaction terms were calculated as the cross product of the physiological variable and the task regressor. In each task model, separate analyses were computed for the right and left AMY with three regressors: task condition (OwnView–OtherView or OtherView–NonInfantView), PPI interaction term, and left or right AMY time course. Although not specifically of interest, all other task conditions were also included as regressors. The PPI interaction term was then brought to a second-level group analysis (non-PPD, PPD), with medication status entered as a covariate. *Z*-statistic(Gaussianized T/F) images were thresholded using clusters determined by $Z > 2.3$ and a (corrected) cluster significance threshold of $p = 0.05$ (Worsley, 2001). For any cluster of voxels identified as significantly connected with the AMY in non-PPD or PPD mothers, mean time series data was extracted and entered into SPSS-21 for analysis with covariates of interest using one-way ANOVA.

Analysis of other demographic and clinical data

Demographic and clinical variables were analyzed with SPSS using one-way ANOVA or chi-square test, where appropriate. We used Spearman correlations to examine the relationship between ART, clinical variables (EPDS and STAI-T), and parity with our fMRI contrasts (OwnView–OtherView and OtherView–NonInfantView) and conditions of interest (OwnView, OtherView, and NonInfantView). As these tests were considered exploratory, alpha level for significance was set at .05.

Results

Subject characteristics

Fifty-four mothers completed the study; however, nine mothers were excluded from analyses due to high movement during the fMRI (>2 mm); the current results represent data from 17 non-PPD mothers and 28 PPD mothers. Maternal age and education, as well as delivery method, parity, and breastfeeding status were not significantly different across non-PPD and PPD mothers (see Table 1). Other than parity (discussed subsequently), these variables did not contribute to the models discussed below, and were thus excluded from analyses. From a multivariate ANOVA, PPD mothers reported significantly higher depressive symptomology (EPDS ($F(1,43) = 14.403$, $p = .001$) and trait anxiety (STAI-T ($F(1,43) = 45.952$, $p = .001$); Table 1). Although 11 PPD mothers were taking SSRI medication, EPDS and STAI-T scores for PPD mothers did not differ based on medication status (SSRI vs. no medication; EPDS $F(1,26) = 1.180$, $p = .287$ and STAI-T $F(1,26) = .758$, $p = .392$).

Table 1. Subject characteristics.

	Non-PPD mothers (n = 17)		PPD mothers (n = 28)		Statistical analysis	
	Mean	SEM	Mean	SEM	$F(1,43)$	p-value
Demographic measures						
Age (years)	29.18	1.19	30.64	0.93	1.02	.317
Education (% high school)	5.88%		14.29%		$\chi^2 = 0.76$	.384
Delivery method (vaginal:ccesarean)	70.59%		75.00%		$\chi^2 = 1.05$	.746
Parity (primiparous:multiparous)	70.59%		64.43%		$\chi^2 = 0.19$	.664
Feeding method (breast:bottle)	70.59%		57.14%		$\chi^2 = 0.81$	.367
Clinical measures						
Edinburgh Postnatal Depression Scale	3.12	1.07	8.29	0.84	14.40	.001*
State-Trait Anxiety Inventory (Trait version)	27.82	1.98	44.86	1.54	45.95	.001*

Chi-square test (df = 1); PPD=Postpartum Depression, *indicates significant group difference at $p < .05$.

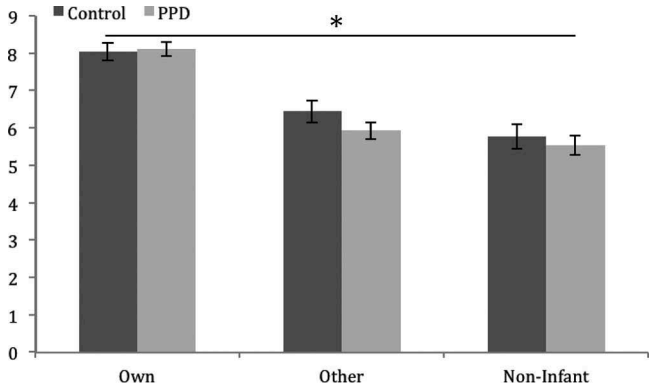

Figure 2. During the affect rating task (ART), all mothers reported feeling more positive when viewing their Own compared to Other infants or Non-Infant pictures ($F(1,43) = 75.405$, $p = .000$). There were no group differences in ratings across conditions ($F(1,43) = .733$, $p = .397$).

ART

During the ART, all mothers reported that they felt more positive when they viewed their own compared to other infants or non-infant pictures ($F(1,43) = 75.405$, $p = .001$). There were no group differences in this self-reported experience of positivity across conditions ($F(1,43) = .733$, $p = .397$; Figure 2); PPD mothers and non-PPD mothers all reported experiencing the same degree of positive affect when they viewed pictures of own, other, and non-infant stimuli.

ROI analysis

Non-PPD mothers

As shown in Figure 3a, average BOLD response in the bilateral AMY in mothers without PPD was greater for OwnView–OtherView (right AMY: 190 voxels, $p = 0.00473$, $z = 3.65$, peak $x = 24$, $y = -2$, $z = -14$; left AMY: 63 voxels, $p = 0.039$, z = 3.12, peak $x = -24$, $y = -4$, $z = -12$). There were no differences in AMY response to OtherView–NonInfantView.

PPD mothers

Average BOLD response in PPD mothers was greater for OwnView–OtherView only in the right AMY (87 voxels, $p = 0.0246$, $z = 3.76$, peak $x = 26$, $y = 0$, $z = -12$; see

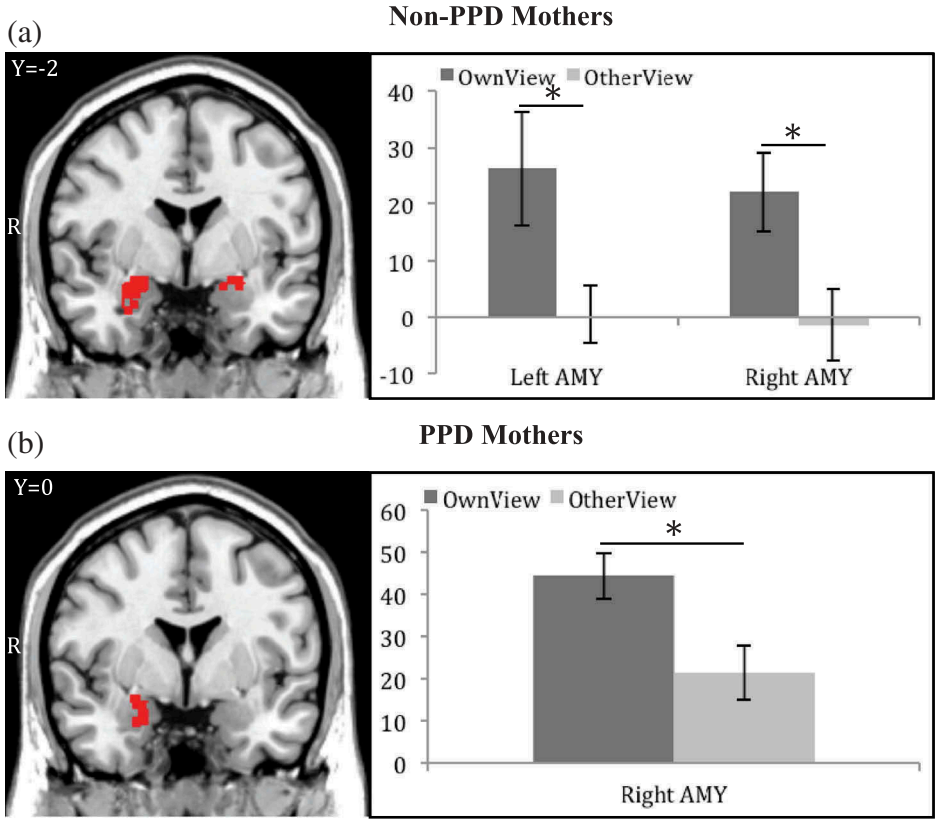

Figure 3. Average BOLD response in the amygdala (AMY) in non-PPD (3a) and PPD (3b) mothers. **3a**. Average BOLD response in the *bilateral* AMY was greater for OwnView compared to OtherView in non-PPD mothers (right AMY: 190 voxels, $p = 0.00473$, $z = 3.65$, peak $x = 24$, $y = -2$, $z = -14$; left AMY: 63 voxels, $p = 0.039$, $z = 3.12$, peak $x = -24$, $y = -4$, $z = -12$). There were no differences in AMY response to OtherView–NonInfantView. **3b**. Average BOLD response in the *right* AMY was greater for OwnView compared to OtherView in PPD mothers (87 voxels, $p = 0.0246$, $z = 3.76$, peak $x = 26$, $y = 0$, $z = -12$). There were no differences in *left* AMY response to OwnView–OtherView. There were also no differences in AMY response to OtherView–NonInfantView.

Figure 3b). There were no differences in AMY response to OtherView–NonInfantView.

Group-level

No group differences (e.g., both PPD > non-PPD and/or non-PPD > PPD) were observed for our contrasts of interest: OwnView–OtherView or OtherView–NonInfantView. With respect to condition-level differences, there were no group differences in average BOLD response for OwnView in non-PPD compared to PPD mothers. However, in comparison to non-PPD mothers, PPD mothers demonstrated *increased* BOLD response to OtherView (105 voxels, $p = 0.0173$, $z = 3.06$, peak $x = 24$, $y = -8$, $z = -18$; see Figure 4a) and to NonInfantView (54 voxels, $p = 0.0472$, $z = 3.24$, peak $x = 26$, $y = 0$, $z = -14$; see Figure 4b) in the right AMY. Thus, when BOLD response was collapsed across all conditions (OwnView, OtherView, and NonInfantView), PPD mothers showed an overall increased response in the right AMY (78 voxels, $p = 0.0291$, $z = 3.44$, peak $x = 28$, $y = -2$, $z = -12$; see Figure 4c). Medication status was used as a covariate in the model.

Parity

There was a marginal Parity × Group interaction for bilateral AMY response to OwnView (right AMY: $F(1,41) = 3.72$, $p = .061$; left AMY: $F(1,41) = 3.315$, $p = .076$; see Figure 5). While there was no group

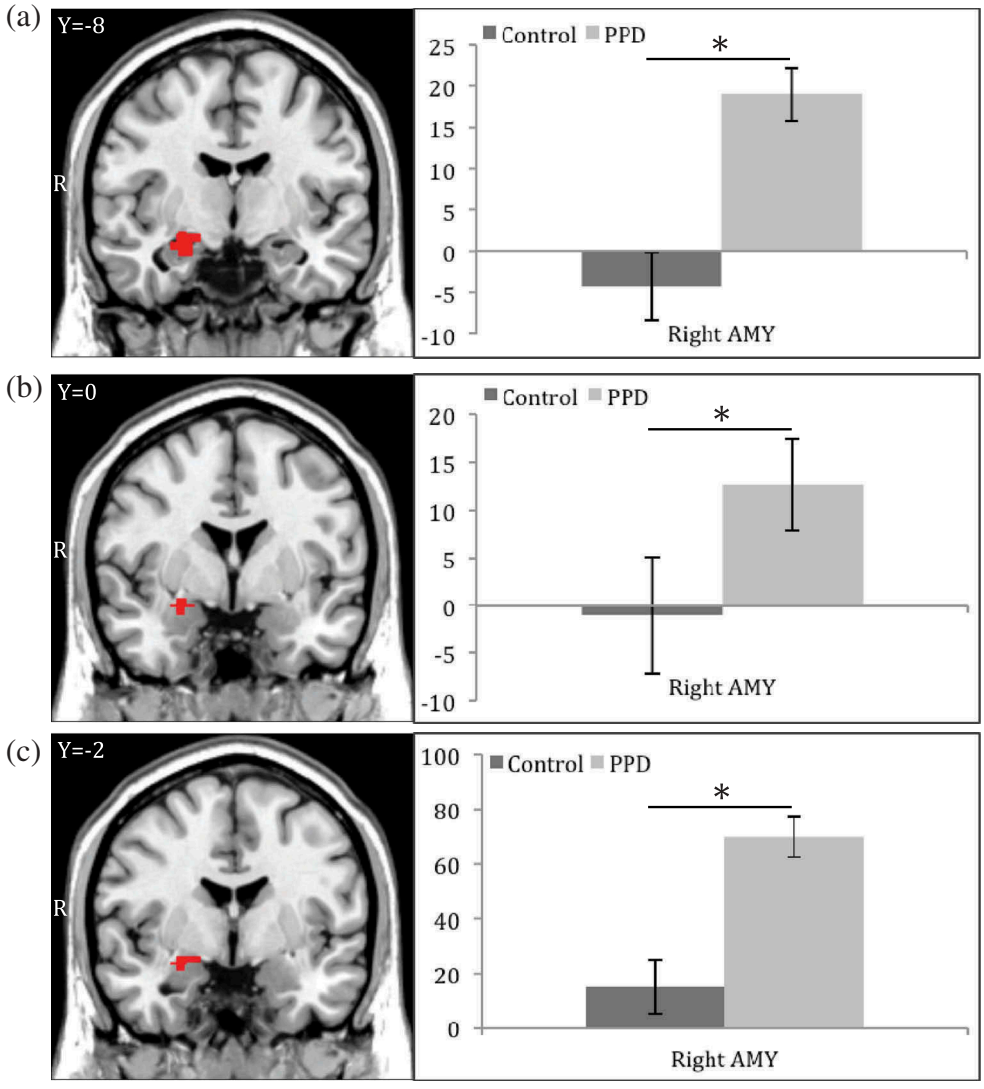

Figure 4. Group-level differences in average BOLD response in the amygdala (AMY) in non-PPD as compared to PPD mothers. **4a**. In comparison to non-PPD mothers, PPD mothers demonstrate increased BOLD response to OtherView in the right AMY (105 voxels, $p = 0.0173$, $z = 3.06$, peak $x = 24$, $y = -8$, $z = -18$). **4b**. In comparison to non-PPD mothers, PPD mothers demonstrate increased BOLD response to Non-InfantView in the right AMY (54 voxels, $p = 0.0472$, $z = 3.24$, peak $x = 26$, $y = 0$, $z = -14$). **4c**. Average BOLD response in the right AMY across all conditions is greater in PPD compared to non-PPD mothers (78 voxels, $p = 0.0291$, $z = 3.44$, peak $x = 28$, $y = -2$, $z = -12$).

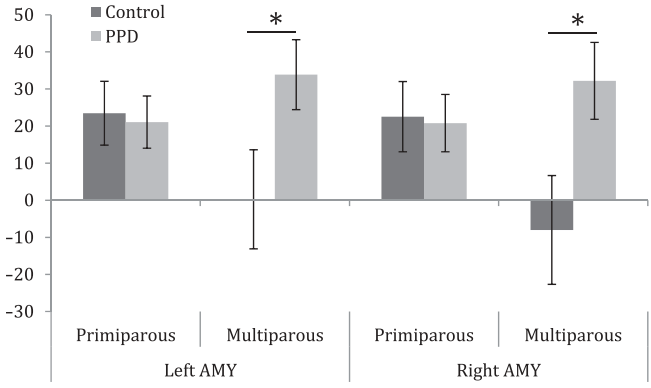

Figure 5. Marginal Parity × Group interaction for bilateral amygdala (AMY) response to OwnView (right AMY: $F(1,41) = 3.72$, $p = .061$; left AMY: $F(1,41) = 3.315$, $p = .076$). While there was no group difference in AMY response in primiparous mothers, multiparous PPD mothers had greater bilateral AMY response than non-PPD multiparous mothers; AMY response appears to decrease with experience in non-PPD mothers, but increase with experience in PPD mothers. There were no group differences in AMY response to OtherView or NonInfantView by maternal experience.

difference in AMY response in primiparous mothers, multiparous PPD mothers had greater bilateral AMY response than non-PPD multiparous mothers. In other words, AMY response appears to decrease with experience in non-PPD mothers, but increase with experience in PPD mothers. There were no group differences in AMY response to OtherView or NonInfantView by maternal experience. These findings should be considered exploratory, as they are derived from a small sample of multiparous (non-PPD $n = 5$, PPD $n = 10$) relative to primiparous (non-PPD $n = 12$, PPD $n = 18$) women, in the non-PPD sample, in particular.

Connectivity analysis

Group level

Although we observed group-level ROI differences in the right AMY, but not the left AMY, BOLD response differences do not always predict connectivity differences. Furthermore, our a priori hypothesis did not predict this laterality effect. As such, we proceeded to examine both right and left AMY connectivity differences with PPI. During OwnView–OtherView, at cluster-corrected $p < .05$ ($z = 2.3$), controlling for medication status, non-PPD mothers showed *increased* connectivity between the bilateral AMY and the right insular cortex (IC), whereas PPD mothers showed *decreased* AMY–IC connectivity (right AMY–right IC: 933 voxels, $p = 0.000244$, $z = 3.83$, peak $x = 54$, $y = -10$, $z = 4$; left AMY–right IC: 534 voxels, $p = 0.0239$, $z = 3.29$, peak $x = 34$, $y = 8$, $z = 14$; see

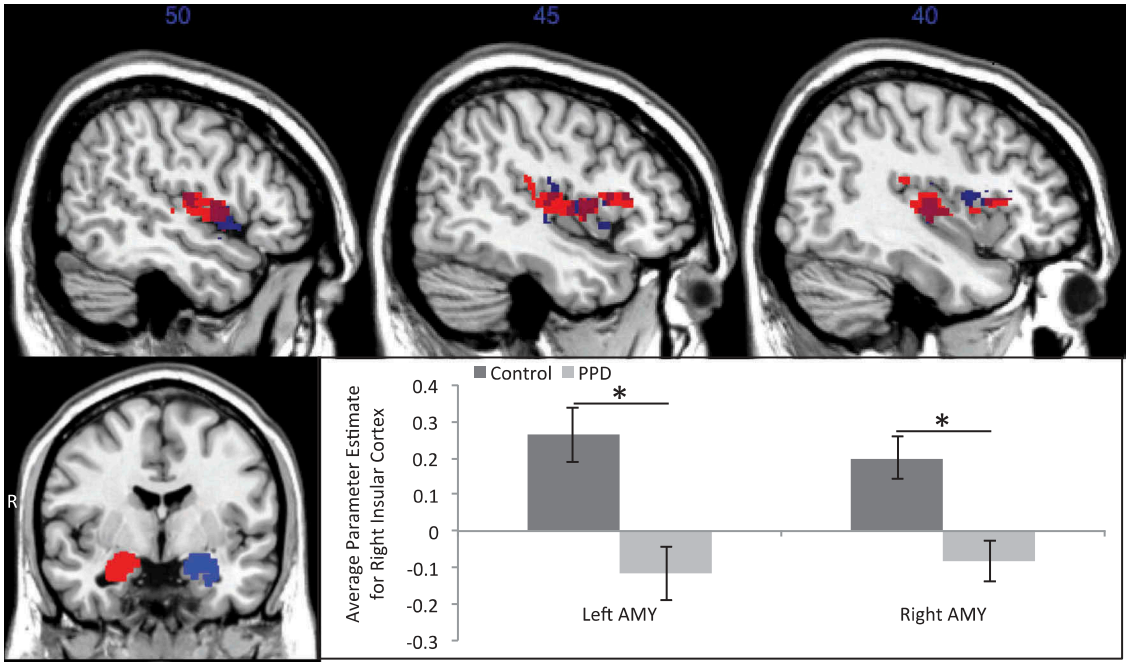

Figure 6. During OwnView–OtherView, *non-PPD mothers* showed *increased* connectivity between bilateral amygdala (AMY) and the right insular cortex (IC), whereas *PPD mothers* showed *decreased* AMY–right IC connectivity (right AMY–right IC: 933 voxels, $p = 0.000244$, $z = 3.83$, peak $x = 54$, $y = -10$, z = 4; left AMY–right IC: 534 voxels, $p = 0.0239$, $z = 3.29$, peak $x = 34$, y = 8, $z = 14$). Blue = left AMY–right IC connectivity, Red = right AMY–right IC connectivity. There were no group differences in connectivity with the left or right AMY during OtherView–NonInfantView.

Figure 6). There were no group differences in connectivity with the left or right AMY during OtherView–NonInfantView.

Parity

From a repeated measures ANOVA with group (non-PPD vs. PPD) and parity (primiparous vs. multiparous) as between-subjects factors and bilateral AMY to IC connectivity as within-subject factor, an interaction between group and parity was observed ($F(1,41) = 5.617$, $p = 0.023$). Although AMY–IC connectivity was low in PPD mothers, regardless of the amount of parenting experience they had (e.g., low in both primiparous and multiparous mothers), in non-PPD mothers, AMY–IC connectivity increased with maternal experience (e.g., multiparous > primiparous; see Figure 7). These findings should be considered exploratory, as they are derived from a small sample of multiparous (non-PD $n = 5$, PPD $n = 10$) relative to primiparous (non-PPD $n = 12$, PPD $n = 18$) women, in the Non-PPD sample, in particular.

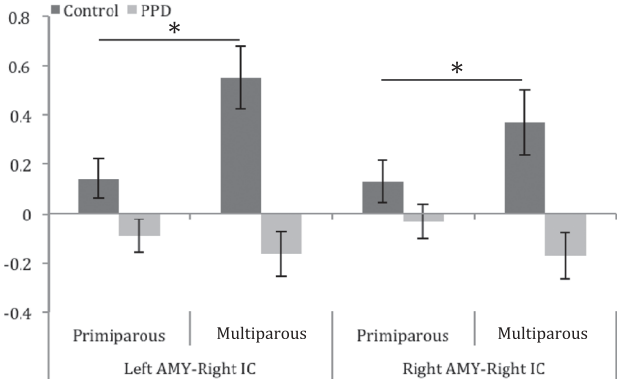

Figure 7. In non-PPD mothers, AMY–right IC connectivity increases with experience (e.g., multiparous > primiparous). However, in PPD mothers, AMY–right IC connectivity is low in both primiparous as well as multiparous mothers. Interaction between group and parity: $F(1,41) = 5.617$, $p = 0.023$.

Correlations

Non-PPD mothers

As can be seen in Table 2, EPDS scores were negatively correlated with left AMY response to OtherView–NonInfantView ($r = -.59$, p = .013) and positively correlated with left AMY response to NonInfantView ($r = .71$, $p = .001$). STAI-T scores were also negatively correlated with left AMY response to OtherView–NonInfantView ($r = -.59$, $p = .013$). In other words, more anxious mothers within the non-PPD group tended to show reduced Other Infant–NonInfant differences in BOLD response in left AMY. We also observed a negative correlation between STAI-Trait and left AMY response for OwnView ($r = -.54$, $p = .026$) and OtherView ($r = -.50$, $p = .039$). Hence, greater trait anxiety was associated with reduced left AMY response to babies (both own and other) in non-PPD mothers. There were no significant correlations between right AMY response to our conditions of interest and EPDS or STAI-T.

ART ratings made by non-PPD mothers during the fMRI for their own infant were not significantly correlated with bilateral AMY response to OwnView or OwnView–OtherView. However, ART ratings for other infants were positively related to bilateral AMY response for the contrast OwnView–OtherView ($r = .49$, $p = .046$). This suggests that mothers who showed a larger differential AMY response to their own infant (e.g., greater own-other difference in the AMY) reported higher positivity ratings for "other" infants.

PPD mothers

As shown in Table 2, EPDS scores were positively correlated with left AMY response to NonInfantView ($r = .39$,

Table 2. Significant correlations between amygdala ROI conditions of interest and clinical variables. Note, if there were no significant correlations between clinical and fMRI measures, they are not represented in this table.

	All mothers ($n = 45$)		Non-PPD mothers ($n = 17$)		PPD mothers ($n = 28$)	
	r-value	*p*-value	*r*-value	*p*-value	*r*-value	*p*-value
Left AMY						
OwnView (STAI-T)			−.54	.026[a]		
OtherView (STAI-T)			−.50	.039[a]		
NonInfantView (EPDS)	.49	.001[a]	.71	.001[a]	.39	.043[a]
OwnView–OtherView (ART Other Infant)	.49	.046[a]				
OtherView–NonInfantView (STAI-T)			−.60	.010[a]		
OtherView–NonInfantView (EPDS)			−.59	.013[a]		
Right AMY						
OtherView (STAI-T)	.30	.045[a]				
NonInfantView (EPDS)	.45	.002[a]				

[a]indicates significant correlation ($p < .05$).

p = .043). There were no other significant correlations between EPDS or STAI-T and bilateral AMY response to our contrasts or conditions of interest. There were no significant correlations between ART ratings of Own or Other infants and AMY response in mothers with PPD.

All mothers

EPDS scores were positively correlated with right AMY (r = .45, p = .002) and left AMY (r = .49, p = .001) response to NonInfantView. We also observed a positive correlation between STAI-T scores and right AMY response to OtherView (r = .3, p = .045). There were no significant correlations between ART ratings of Own or Other infants and AMY response in mothers with PPD.

Connectivity analysis

AMY–right IC connectivity parameters were negatively correlated with both EPDS (right AMY–right IC: r = −.339, p = .023; left AMY–right IC: r = −.411, p = .005; Figure 8) and STAI-T (right AMY–right IC: r = −.501, p = .001; left AMY–right IC: STAI-T r = −.548, p = .001; Figure 8); increasing depressive symptomology and trait anxiety were related to decreasing AMY–right IC connectivity. AMY–right IC connectivity was not correlated with ART scores.

Discussion

The first goal of the current study was to replicate our and others' previous work showing preferential AMY responsiveness to one's own as compared to another infant's face (Barrett et al., 2012; Leibenluft et al., 2004; Ranote et al., 2004; Seifritz et al., 2003; Strathearn & Kim, 2013). Indeed, we identified enhanced bilateral AMY response when non-PPD mothers view their own versus other infants. This effect has been replicated in similar studies that demonstrate enhanced AMY response to personally relevant faces (e.g., partner faces (Taylor et al., 2009)). The AMY is a brain region known to play a critical role in socioemotional processing (Adolphs, 2003; Adolphs et al., 2002; Pessoa, 2010) and maternal behavior (Barrett & Fleming, 2011; Fleming et al., 1980). Recently, Cunningham and Brosch (2012) have conceptualized the AMY as an early part of an affective system responsible for identifying important environmental stimuli and facilitating appropriate responding to said stimuli. One's own infant represents a particularly salient environmental stimulus for the recently postpartum mother. This saliency appears to be manifest at the neural level through enhanced AMY response.

Next, we sought to examine whether this specificity effect was conserved in mothers with PPD. For the first time, we found that PPD mothers did, in fact, show a preferential response in the right AMY to their own as compared to an unfamiliar infant. As such, all mothers, regardless of depression status, showed greater BOLD response in the AMY for their own infant compared to an unfamiliar infant. This increased BOLD response for one's own infant in the AMY is interesting in the context of findings by Kim et al. (2010), which identified increased AMY volume across the early postpartum period as associated with enhanced positive perception of one's baby. Although these findings may appear contrary to existing fMRI studies that find blunted activation in the AMY in PPD mothers (Moses-Kolko et al., 2010; Silverman et al., 2011), the current study differs in a notable way. Rather than using negative stimuli (e.g., words, adult faces), we utilized stimuli that are positively salient and specific to the motivational state for the observer: positive

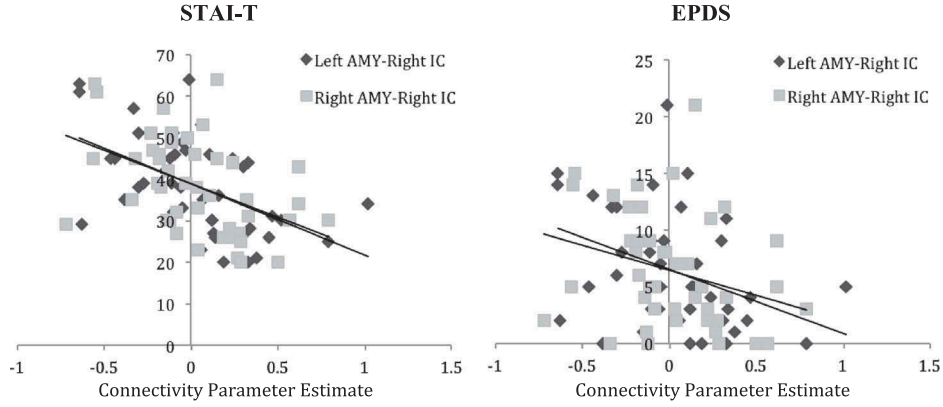

Figure 8. AMY–IC connectivity was not correlated with ART scores; however, AMY–IC connectivity was significantly correlated with both clinical measures: EPDS (right AMY–right IC: r = −.339, p = .023; left AMY–right IC: r = −.411, p = .005) and STAI-T (right AMY–right IC: r = −.501, p = .000; left AMY–right IC: r = −.548, p = .000).

pictures of babies—specifically, one's own baby. Facial expressions are a primary means of communicating emotion for a developing infant, and they are known to elicit infant-directed gaze from the mother (Colonnesi, Zijlstra, Van Der Zande, & Bögels, 2012; Klaus, Trause, & Kennell, 1975; Yale, Messinger, Cobo-Lewis, & Delgado, 2003). This relationship indicates that infant visual stimuli elicit maternal arousal and may reflect maternal motivation. In line with recent theories of AMY functioning as being involved in novelty (Balderston et al., 2011), uncertainty (Whalen, 2007), and relevance detection based on the particular motivational state, goals and/or needs of the observer (Cunningham & Brosch, 2012), it is possible then, that negative stimuli are not motivationally salient enough to engage the AMY in a PPD population.

Interestingly, from group analyses, while we observed no differences between PPD and non-PPD mothers in their AMY BOLD response to their own infant, we did see an overall enhanced response to both other as well as non-infant stimuli in the right AMY in PPD mothers. In other words, while the unique response to own infant was preserved in mothers with PPD, they showed a ramping up of AMY response to all other positive stimuli, both infant and non-infant. It is possible that the enhanced right AMY response we observed in mothers with PPD to all stimuli represents a generally enhanced or even dysregulated arousal/vigilance for salient stimuli. Although this study was designed to examine differences between clinical and nonclinical depression, anxiety is also a prominent feature of PPD. Importantly, in addition to depressive symptomology, the mothers in our PPD group also reported elevated trait anxiety, as compared to non-PPD mothers. Future studies should seek to tease apart the degree to which these findings may be related to symptoms of depression, anxiety, or both.

During the fMRI, mothers in the current study were instructed to think about and rate how they felt when viewing pictures of infants and other positive stimuli. All mothers, regardless of depression status, reported feeling most positive when viewing their own infant. Thus, the increased AMY we observed in the current study occurred in the absence of self-reported differences during the rating task. Notably, BOLD response does not necessarily map onto behavioral response; we cannot assume that increased signal in a particular brain region will be associated with behavioral changes. In fact, from our ART results, we did not observe a correlation between ratings in the scanner and BOLD response in the AMY. Rather, we observed the opposite in non-PPD mothers: the more positive they rated pictures of *other* babies, the more preferential their BOLD response was for their *own* baby in the left AMY. Thus, in non-PPD mothers, the specificity of the response (high for own baby, low for other baby), rather than the average activation, appears to relate to self-reported positive affectivity when viewing the pictures. This relationship was absent in PPD mothers. Further studies should seek to clarify whether the increased BOLD response to all positively salient stimuli in PPD mothers is reflected in other behavioral measures, such as those obtained from mother–infant interactions. Knowing how a depressed mother's brain responds to infant stimuli is critical, as the symptoms of PPD impact the mother–infant dyad and often involve excessive worry or guilt surrounding parenting abilities (Ross et al., 2005). Relatedly, mothers with PPD typically display an altered pattern of behavioral interaction with their infants (e.g., more intrusive and irritated and less sensitive and contingent (Murray, Fiori-Cowley, Hooper, & Cooper, 1996; Cohn, Campbell, Matias, & Hopkins, 1990; Stanley, Murray, & Stein, 2004; Fleming, Ruble, Flett, & Shaul, 1988)). Knowing this, it will be important for future studies to investigate how these differences relate to brain response to infants in mothers with and without PPD.

The second major goal of the current study was to investigate whether the pattern of connectivity between the AMY and other brain regions was altered in mothers with PPD. Using task-based AMY connectivity in PPD and non-PPD mothers, we found that AMY–right IC functional connectivity, brain regions with strong reciprocal anatomical connections, was enhanced when no-PPD mothers are viewing their own compared to another infant, but decreased in PPD mothers. Furthermore, this connectivity pattern was positively correlated with both depressive symptomology and trait anxiety. The dorsal posterior IC has been conceptualized as the primary interoceptive cortex, responsible for representing the physiological sense of one's body (Craig, 2002). The right anterior IC is important for representing one's internal state (Craig, 2009) and is activated in tasks that measure subjective emotional awareness, in particular, studies that assess recall of sadness (Mayberg et al., 1999), anger (Damasio et al., 2000), anxiety (Benkelfat et al., 1995), pain (Ploghaus et al., 1999), disgust (Phillips et al., 1997), and other aspects of emotional awareness (see Craig, 2002 for summary). Researchers have proposed that the representation of the physiological condition of the body in the IC serves as the neural substrate for these subjective feelings and emotions (Craig, 2002, 2009). This role of the IC is of particular relevance to PPD, as self-perceived maternal health was recently identified as the strongest risk factor for persistent PPD (Dennis

et al., 2012), and anxiety and parenting stress are common postpartum (Miller, Pallant, & Negri, 2006). It is also interesting in the context of the current study instructions ("think about how you feel when viewing these pictures"). Non-postpartum mood disorders have been associated with decreased anterior IC volume (Takahashi et al., 2010), decreased IC activity during interoception (Avery et al., 2014), and altered IC BOLD response following a variety of treatments (see McGrath et al., 2013). Additionally, altered connectivity between the IC and limbic structures, important for fast processing of emotional stimuli, such as the AMY (Manoliu et al., 2014; Ramasubbu et al., 2014), and more prefrontal regions thought to be important in guiding motivated actions, such as the anterior cingulate cortex (Connolly et al., 2013), has been identified in individuals with MDD (see Drevets, Price, & Furey, 2008 for review).

The IC has been proposed as a brain region involved in the physiological pathway underlying the negative or overly catastrophic evaluations of the sensations in one's body, often observed in anxiety disorders (Paulus & Stein, 2006). More specifically, Paulus and Stein (2006) propose that there may be a mismatch between observed and expected body states in individuals with anxiety disorders, which can result in cognitive and behavioral compensatory mechanisms (e.g., worrying and avoidance, respectively), and that this process may be related to IC functioning. As aforementioned, while the goal of this study was to examine clinical depression, anxiety is also common in the postpartum period and is a prominent feature of PPD. Furthermore, the PPD and no-PPD mothers in this study reported significant differences in levels of trait anxiety. Preliminary analyses (Wonch et al., in prep) indicate that a similar pattern of findings are observed if individual differences in anxiety are used to predict connectivity, rather than PPD diagnostic grouping. Given the striking differences in AMY–right IC connectivity observed here in the context of increased self-reported trait anxiety, future studies should seek to clarify the unique influence of both depression as well as anxiety.

Interestingly, we also found that AMY–right IC connectivity increased with maternal experience in non-PPD mothers, a pattern that was not observed in PPD mothers. Although this finding was not anticipated, it is consistent with our conceptualization of AMY–IC functionality. If the AMY is thought to play a role in rallying together appropriate recourses to respond to emotionally salient or intense environmental stimuli (Cunningham & Brosch, 2012), one could hypothesize that increasing connectivity between this brain region and the IC, important for representing the physiological state of the body to guide subjective emotional experience (Craig, 2002), would increase with parental experience. Interestingly, we observed this in the context of a marginal difference based on parity in overall BOLD response in the AMY; while there was no group difference in AMY response in first-time mothers, multiparous PPD mothers had marginally greater bilateral AMY response as compared to multiparous non-PPD mothers. In other words, despite increased overall BOLD response in the AMY in multiparous PPD mothers, they did not show increased AMY–right IC connectivity. To our knowledge, this is the first report of altered response and functional connectivity in mothers as a function of their parity status. However, it is important to note that the current study was not designed to test this hypothesis directly. Further studies should continue to investigate the role of the AMY in maternal experience in mothers with and without PPD. For example, by examining unique contributions of AMY subregions (see, for example, with anxiety (Etkin et al., 2009)).

As research with MDD indicates that AMY hyperresponsivity to negative stimuli may be a trait-like characteristic of the disorder (Price & Drevets, 2010), studies with PPD postulate that AMY hyporesponsiveness to negative stimuli may be pathognomonic of PPD (Silverman et al., 2011). Although this is the first study to examine AMY response to positive stimuli in PPD, recent studies with MDD suggest that AMY response is decreased in response to positive stimuli (Stuhrmann et al., 2013). It is interesting, then, that we again found the opposite pattern of AMY responsivity in PPD (increased to positive stimuli in the right AMY rather than decreased, similar to what is seen with MDD). The present findings add to the literature examining the brain response of PPD mothers to emotional stimuli. They also support the notion that PPD may be phenotypically distinct from MDD. Future research should seek to compare directly how the AMY and other brain regions important in monitoring affective stimuli (e.g., the salience network and/or affective network (Menon & Uddin, 2010; Price & Drevets, 2010), respond to both positive as well as negative stimuli, infant and non-infant, in mothers with PPD.

There are a few potential limitations that cannot be addressed by the current study. For example, disturbances to the sleep-wake cycle are hallmark symptoms of MDD (American Psychiatric Association, 2000). However, under normal circumstances, the postpartum period is characterized by disrupted sleep and in some cases, extreme sleep disturbances, leading some researchers to postulate that disrupted circadian rhythms, which we did not measure, may be part of the pathogenesis of PPD in vulnerable women (Park, Meltzer-Brody, & Stickgold, 2013; Ross et al., 2005). Additionally, PPD is a

heterogeneous condition with wide variations in time of onset (e.g., pregnancy (which trimester?) vs. postpartum) and previous history of MDD or PPD. Some suggest that there may be phenotypic variation in uniquely "postnatal" depression, rather than antenatal (Cooper & Murray, 1995; Phillips, Sharpe, Matthey, & Charles, 2010). Although there are benefits to having strict inclusion criteria, the wide variations in symptomology, onset, history, and course of PPD are often not captured by such rigidity. Our study did not attempt to impose such criteria, thereby enhancing the ecological validity and generalizability of our findings to the greater population of women with PPD. A variety of other factors may influence how the brains of new mothers respond to their infants. For example, an association was identified between BDNF Met66 carrier status and development of PPD symptoms, only when mothers delivered during autumn/winter (Comasco et al., 2011). Ideally, future studies should adopt a multidimensional approach when assessing maternal behavior in relation to brain response in PPD mothers.

Despite neuroimaging evidence that brain regions showing decreased activation in individuals with MDD show increased activation following treatment with SSRIs, and vice versa (Fitzgerald, Laird, Maller, & Daskalakis, 2008; Price & Drevets, 2010), as noted, we did not see differences in AMY response with SSRI use in PPD mothers. It is possible that with stronger controls (e.g., specific type of SSRI, duration of use, dose, etc.) and a study designed specifically to target this relationship, we may see an association between brain response in PPD mothers and medication use. Future studies should do this, as controversy surrounding medication use during pregnancy and during breastfeeding still exists (Nulman et al., 2012; Steiner, 2012; Weissman et al., 2004).

In our study, the average EPDS scores for the mothers in our PPD group were not above the widely cited cutoff score of 12 at the time of the scan (Cox, Holden, & Sagovsky, 1987). While we recognize that this is below standard clinical cutoffs on this measure, due to both the repeat nature of our testing (e.g., clinical interview conducted approximately 1 week before fMRI scan) and the potentially fluctuating nature of PPD symptomology, we are not surprised that scores on this measure varied within mothers; it is possible that some women may have begun to compensate for their depressive symptomology by the time of the scan. Interestingly, a recent meta-analysis identified wide variation in the sensitivity and specificity of the EPDS as a screening measure for PPD (Gibson, McKenzie-McHarg, Shakespeare, Price, & Gray, 2009). In another study, using EPDS cutoff scores to classify mothers with or without a history of PPD failed to identify a relationship between child outcomes at 11 years and PPD, yet when they examined group differences based on diagnostic criteria from a standardized clinical interview, they identified significant differences (Pawlby et al., 2008). This indicates that EPDS may not adequately distinguish mothers with and without PPD, when compared to a diagnostic interview. Thus, the design of our current study is preferred, where mothers were grouped by diagnostic criteria rather than scores on a nondiagnostic mood measure.

As mentioned throughout, depression is not the only mental health concern faced by mothers during pregnancy and/or the postpartum period; many mothers also experience clinically relevant symptoms of anxiety, substance abuse, and/or trauma (see Moses-Kolko et al., 2014 for review). Studies that examine the pattern of brain activity in mothers with other forms of maternal psychopathology have also identified altered AMY responsivity. For example, Kim, Fonagy, Allen, and Strathearn (2014) identified decreased AMY response to infant distress cues in mothers with unresolved trauma. Important future insights may come from studies that measure overlapping symptomology of these disorders and examine how these relate to brain function in regions known to be important for regulating affect, reward, and even memory.

As previously mentioned, top-down effective connectivity between the prefrontal cortex and AMY during the viewing of negative adult faces has been shown to be decreased in PPD mothers (Moses-Kolko et al., 2010). Thus, it is interesting that we also observed decreased functional connectivity between the IC, a region so strongly implicated in interoception and subjective emotional awareness (Craig, 2002), and the AMY, specifically when PPD mothers view pictures of their own infant. Given this, together with previous reports of decreased AMY response to threatening words (Silverman et al., 2007), future research should examine how the brains of mothers with PPD process both threatening and rewarding infant and non-infant stimuli, and relate this to actual mothering behavior. Future studies should also seek to clarify whether the decreased AMY–IC connectivity observed here in PPD mothers reflects increased or dysregulated bottom-up influence of the AMY on the IC. The frequency with which PPD occurs as well as the potential for negative consequences for the developing infant underscore the need for continued research into its neurobiological substrates.

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Disclosure statement

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