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Pregnancy, childbirth and caregiving alter functional connectivity in response to infant faces

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Research Article

Keywords: Pregnancy, Postpartum, Maternal brain, Functional connectivity, Theory of mind, Oxytocin

Posted Date: November 1st, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11182414/v1

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Additional Declarations: No competing interests reported.

Abstract

Background

Maternal experiences, including pregnancy, childbirth and caregiving, profoundly shape neural responses to infant cues. To elucidate the underlying network mechanisms, this study used functional MRI to examine how such experiences modulate regional brain activity and functional connectivity (FC) in response to infant faces.

Results

Compared to never-pregnant women (n = 27), primiparous postpartum mothers (n = 29) demonstrated stronger FC between face perception areas and the theory of mind network via the anterior insular cortex while viewing unfamiliar infant faces, accompanied by enhanced activation in related regions. Viewing their own nurtured infant's image further strengthened FC among face perception, episodic memory and affective theory of mind networks, including regions of the dopamine reward system, although connectivity with the temporoparietal junction was weaker. Theory of mind- and reward-related regions also showed greater activation when viewing nurtured versus unfamiliar infant faces.

Conclusions

These findings suggest that maternal experiences amplify neural responsiveness to infant faces by engaging interconnected social cognition, memory and reward processing networks.

Background

Pregnancy, childbirth and infant care are transformative experiences essential for the survival of the human species. Because mothers cannot see the foetus during the roughly ten-month gestation, their first visual encounter with the infant's face occurs after birth. Even so, mothers are naturally inclined to care for the newborn from this first encounter, responding intuitively to facial features that are evolutionarily significant regardless of culture, gender or age [1, 2]. Lorenz [3] conceptualised this phenomenon as the 'baby schema' or 'Kindchenschema effect', a set of infantile physical characteristics that instinctively elicit caregiving behaviour.

Caregiving imposes substantial physiological and psychological demands, so successful initiation depends on the rapid emergence of robust caregiving motivation [4, 5]. Understanding the infant's needs is as essential as motivation itself: the capacity to infer others' needs and intentions, known as 'theory of mind', enables mothers to interpret subtle facial expressions and non-verbal cues indicative of the infant's internal states [6, 7]. Postpartum mothers report higher empathic concern than nulliparous

women, with pregnant women showing intermediate scores [8, 9, 10], suggesting that theory of mind is progressively strengthened by pregnancy and further by childbirth and postpartum caregiving.

Caregiving motivation is thought to involve the oxytocin system, the dopaminergic reward system and their interaction [11]. Oxytocin, synthesised in the hypothalamus and secreted by the posterior pituitary, is well known for inducing uterine contractions and milk ejection, but also contributes to social cognition, including trust, cooperation, facial emotion recognition, empathy, in-group preference and social and maternal bonding [12, 13, 14, 15, 16, 17, 18]. Oxytocin receptors are distributed across brain regions including the amygdala [19, 20], which receives projections from magnocellular oxytocin neurons in the hypothalamus [21]. The midbrain dopaminergic system, comprising the mesolimbic pathway (ventral tegmental area [VTA] to nucleus accumbens, amygdala and hippocampus) and the mesocortical pathway (to orbitofrontal and prefrontal cortices), is central to reward, motivation and learning. In mice, activating medial preoptic area projections to the VTA increased pup-directed behaviour [22], and postpartum rats show elevated oxytocin receptor expression in the VTA and medial preoptic area, with receptor antagonism disrupting maternal caregiving [4]. Oxytocin and dopaminergic signalling converge at numerous sites, conferring mutually reinforcing interactions [23].

Theory of mind comprises cognitive theory of mind (understanding others' beliefs and intentions) and affective theory of mind (understanding others' emotions), which are behaviourally distinct but supported by dissociable, interacting neural networks [24, 25]: dorsolateral and dorsomedial prefrontal cortices and dorsal anterior cingulate cortex for cognitive theory of mind, and VTA, amygdala, inferior lateral frontal cortex, ventromedial prefrontal cortex, orbitofrontal cortex (OFC), ventral anterior cingulate cortex and anterior insular cortex for affective theory of mind [24, 26], with the temporoparietal junction (TPJ) and precuneus shared between components [24]. Regions supporting affective theory of mind, including the anterior insula, partially overlap with the oxytocin and dopaminergic systems and are recognised as key to empathy and emotional understanding [27].

Pregnancy, childbirth and postpartum caregiving induce substantial structural brain alterations, including in anatomical connectivity [28, 29]. Hoekzema et al. [29] reported that the transition to motherhood is associated with grey matter volume reductions overlapping the theory of mind network (TPJ, medial prefrontal cortex, precuneus, anterior temporal lobes, inferior frontal gyrus) and with regions activated by viewing an infant's face postpartum. A meta-analysis of 12 studies of maternal brain responses to an infant's or child's face identified the VTA, amygdala and insula as consistently activated [30]. However, no study has directly compared brain activity in response to infant faces before and after pregnancy, and only two studies compared nulliparous and postpartum women, reporting greater activation in affective theory of mind regions—middle and inferior frontal gyri, middle temporal gyrus, posterior cingulate cortex—in postpartum women [8, 9]. These studies used emotional facial expressions as strong affective cues, leaving it unclear whether responses reflect emotional processing or general sensitivity to infant faces; moreover, because infants do not smile socially until around two months, responses to smiling faces are likely shaped by prior mother–infant interaction. Neutral infant faces are therefore more appropriate than emotional ones for assessing brain activity changes related to pregnancy and childbirth.

The immediate onset of caregiving motivation towards the newborn, despite mothers' inability to see the foetus's face during pregnancy, suggests a brain-based mechanism established during gestation. We hypothesised that pregnancy and childbirth produce functional changes in dopamine-, oxytocin- and theory of mind-related regions that enhance responses to unfamiliar infant faces, and tested this by comparing regional brain activity and functional connectivity (FC) while viewing unfamiliar and own infant faces between never-pregnant women and women in the early postpartum period.

Methods

Participants

We recruited 27 nulliparous women with no history of pregnancy (never-pregnant group) and 32 primiparous postpartum women (postpartum group) via notices posted on the National Centre of Neurology and Psychiatry (NCNP) website and in public areas near NCNP. All participants were of Japanese ethnicity. Inclusion criteria were female sex, age 20–34 years, self-reported right-handedness (Edinburgh Handedness Inventory; [31]), no psychiatric history, and no current use of psychiatric medication or female hormones. One postpartum participant was excluded for an ambidextrous laterality quotient. The postpartum group comprised primiparous women who had given birth to a singleton infant within one to three months of participation; pregnancies occurring at or above 35 years of age (advanced maternal age) were excluded, consistent with the age-20–34 inclusion criterion above. The Japanese version of the Edinburgh Postnatal Depression Scale [32] screened for postpartum depression (cut-off score 9); two participants scoring above cut-off (9 and 17) were excluded and referred for further evaluation. The final sample comprised 27 never-pregnant and 29 postpartum women.

Baseline characteristics are compared in Additional file 1, and perinatal details of the postpartum group are summarised in Additional file 2. The postpartum group was significantly older and entirely married, with no significant difference in BMI between groups. The Japanese Ten Item Personality Inventory ([33]; adapted from [34]) assessed Big Five traits; the postpartum group scored significantly higher in conscientiousness (Additional file 1). Among postpartum participants, 27 (93.1%) conceived naturally and one (3.4%) delivered via caesarean section (Additional file 2).

This study was approved by the Ethics Committee of the National Centre of Neurology and Psychiatry (approval number: B2021−075) and performed in accordance with relevant guidelines and regulations. Written informed consent was obtained from all participants following protocol approval.

Data acquisition

Subjective cognitive measures. We developed the Infant-affection VAS (Additional file 3), a 10-cm horizontal line anchored by 'maximum possible liking' and 'maximum possible disliking', on which participants marked their affection toward an imagined unfamiliar infant (score 0–10). Participants also

completed the Japanese Parental Care and Tenderness questionnaire (PCAT-pn; [35]), a 10-item measure of parental protection (4 items) and nurturance (6 items) on a five-point Likert scale, translated into Japanese for this study; subscale scores were calculated as the mean of the relevant items (range 1–5), with higher scores indicating stronger protective or nurturing motivation. Both questionnaires were self-administered at home in advance and brought to the MRI session.

Facial stimuli. Four stimulus types were presented during fMRI: an unfamiliar infant's face, a nurtured (own) infant's face, a control (adult) face, and a dummy infant's face (Fig. 1). Two model infants (one boy, one girl, both under three months) served as unfamiliar-infant stimuli; each participant's own infant was separately photographed for the nurtured-infant condition. Two adult men and two adult women served as control-face stimuli. For the never-pregnant group, a different infant girl ('dummy infant') replaced the nurtured-infant condition. Informed consent was obtained from all adult models and infants' parents. Faces were recorded on video (Panasonic HC-V480MS) with neutral expressions and open eyes, capturing five angles (45° right, intermediate right, front, intermediate left, 45° left) to minimise habituation, then cropped and standardised against a 900 × 900-pixel grey background (Additional file 4) using Paint 3D. Image data were stored on a secure, network-isolated hard drive accessible only to the research team, and will be deleted five years after study completion.

fMRI task design. Each trial began with a jittered fixation point (4.8–7.2 s), followed by a face stimulus (2.4 s) and a 2.4-s response window during which participants identified the image (baby, man, woman) by button press. The postpartum and never-pregnant groups viewed identical unfamiliar-infant and control (adult) faces; only the postpartum group viewed their own infant's face, and only the never-pregnant group viewed the dummy infant's face. All participants achieved over 95% accuracy, indicating that they remained alert and engaged throughout data acquisition. Stimuli were presented in randomised order using Presentation software (Neurobehavioral Systems; Additional file 4). Each run included 10 unfamiliar-infant images (2 infants × 5 angles), 10 control-face images (2 adults × 5 angles) and 10 own/dummy-infant images (5 angles), with 30 images per block across four runs (120 stimuli per participant in total).

MRI acquisition. Neuroimaging data were acquired on a 3.0-Tesla MRI system with a 32-channel head coil (MAGNETOM Skyra FIT, Siemens) at the Integrative Brain Imaging Centre, NCNP. Functional images used a multiband gradient-echo EPI sequence (multiband factor 6, TR 1,200 ms, TE 34.2 ms, voxel size 2.0 × 2.0 × 2.0 mm^3, 72 trans-axial slices tilted 30° from the AC–PC plane), acquired in anterior-to-posterior and posterior-to-anterior phase-encoding directions, with two opposing-phase spin-echo EPI images for distortion correction. Structural images used a 3D T1-weighted MPRAGE sequence (TR 2,500 ms, TE 2.18 ms, inversion time 1,000 ms, voxel size 0.8 × 0.8 × 0.8 mm^3, 320 slices).

Pre-processing. Functional data underwent top-up distortion correction, rigid-body motion correction (alignment of all volumes to a single-band reference image), slice timing correction, spatial smoothing (4-mm FWHM Gaussian kernel), nonlinear normalisation to MNI152 space, denoising, high-pass temporal filtering (0.0067 Hz cut-off) and FILM pre-whitening [36] to correct autocorrelation. Denoising

used the CONN toolbox (v20.b) with anatomical component-based correction (aCompCor; [37]), regressing 24 noise sources (six white-matter/CSF principal components, six motion parameters and their first-order temporal derivatives), with task-related regressors retained. All steps except denoising used FSL v6.0.

Salivary oxytocin. Saliva was collected immediately before MRI following Salimetrics protocols and prior literature [38], after participants refrained from alcohol, smoking, dental treatment, caffeine and lipstick, and completed meals/tooth-brushing ≥1 hour beforehand. Collection occurred in a quiet room in three rounds (1 min pooling, 1 min collection, 30 s rest), with ≥1.8 mL collected per round via passive drool (12:35–15:40). Samples were frozen at −80 °C and analysed in duplicate by Airplants-Bio Corporation using a validated ELISA-based absorbance assay.

Data analysis

Baseline demographic/clinical characteristics were compared using R (v4.2.3). Normality of continuous variables was assessed using the Shapiro–Wilk test and by visual inspection of histograms, and variables were then compared using Student's t-test (parametric) or the Wilcoxon rank-sum test (nonparametric), as appropriate; categorical variables were compared via χ^2 or Fisher's exact test. Infant-affection VAS validity was assessed via correlation with PCAT-pn scores (Pearson's or Spearman's, as appropriate). All tests were two-tailed, $\alpha = 0.05$.

fMRI analysis (unfamiliar infant's face). Task-related blood oxygen level-dependent (BOLD) responses were modelled with a general linear model (GLM) with four regressors (fixation, unfamiliar infant's face, control face, nurtured/dummy infant's face) convolved with the canonical haemodynamic response function. Group-level statistics were estimated using FSL's FLAME1 (FMRIB's Local Analysis of Mixed Effects, stage 1) mixed-effects model, and cluster-based correction for multiple comparisons used Gaussian random field theory (voxel-level threshold $p < 0.001$, cluster-level threshold $p < 0.05$). A voxelwise 2×2 mixed ANOVA (condition: control vs. unfamiliar infant's face [within]; group: never-pregnant vs. postpartum [between]) identified regions showing a significant positive group×condition interaction (voxel $p < 0.001$, cluster $p < 0.05$, corrected), indicating enhanced postpartum responsiveness to unfamiliar infant faces. Within-group activation was assessed via voxelwise paired t-tests. Correlations between baseline salivary oxytocin (log-transformed to approximate a normal distribution) and activity in postpartum-enhanced regions were tested via Pearson's correlation; group differences in log-transformed oxytocin were assessed via Student's t-test. For the three oxytocin-correlated regions, separate 2×2 ANOVAs (condition: control vs. unfamiliar infant's face; group: never-pregnant vs. postpartum) tested whether effects were specific to infant faces, with simple-effects Student's t-tests following significant interactions.

FC analysis. PPI analyses [39, 40] assessed task-related FC from the three seed regions (right dorsomedial prefrontal cortex, right anterior insular cortex, left cerebellar Crus II), using a GLM with five regressors (fixation, infant-versus-control-face response, seed BOLD time course, their interaction [PPI

term], and the other infant-face condition). Whole-brain group differences in PPI beta weights were assessed (voxel $p < 0.001$, cluster $p < 0.05$, corrected). Additional FC analyses used four ROIs: OFC (comprising anterior, posterior, medial and lateral orbital gyri) and amygdala, both from the Neuromorphometrics atlas in SPM12; TPJ, defined as 8-mm spheres at left (−53, −59, 20) and right (56, −56, 18) coordinates [41, 42]; and VTA, from a probabilistic atlas [43]. Mean ROI beta values were compared between groups via Student's t-test (ROI: $p < 0.05$). These ROI-based comparisons (here and in the nurtured-infant analysis below) were exploratory and were not corrected for multiple comparisons; results should be interpreted with this in mind.

fMRI and FC analysis (nurtured infant's face). Voxelwise paired t-tests (nurtured versus unfamiliar infant's face, postpartum group only) identified activated regions (voxel $p < 0.001$, cluster $p < 0.05$, corrected). Correlations with baseline oxytocin were assessed as above. FC used the same three seed regions and four ROIs, comparing nurtured versus unfamiliar infant's face conditions via paired t-tests (whole-brain: voxel $p < 0.001$, cluster $p < 0.05$, corrected; ROI: $p < 0.05$).

Use of AI tools. ChatGPT 5.2 (OpenAI) was used solely to improve the clarity, grammar and fluency of the text. The authors conceptualised and designed the study, performed data analysis, interpreted the results and structured the manuscript without AI assistance.

Results

Experiences of pregnancy and childbirth were associated with increased subjective fondness for unfamiliar infants

The final sample comprised 27 nulliparous women with no prior history of pregnancy (never-pregnant group) and 29 primiparous postpartum women (postpartum group). The postpartum group was slightly but significantly older and had a higher proportion of married individuals than the never-pregnant group, with no significant difference in BMI between groups (Additional file 1). The perinatal details of the postpartum group are provided in Additional file 2.

Table 1 presents the subjective fondness ratings for unfamiliar infants in both groups, assessed using the Infant-affection visual analog scale (VAS) (Additional file 3) and the Parental Care and Tenderness questionnaire (PCAT-pn) protection, nurturance and total scores. The total Infant-affection VAS scores and PCAT-pn nurturance subscale scores were significantly higher in the postpartum group than the never-pregnant group (Infant-affection VAS: 7.4 ± 2.1 vs. 8.6 ± 1.2, $U = 268$, $p = 0.03$; Nurturance subscale: 3.9 ± 0.6 vs. 4.3 ± 0.3, $t = -2.43$, $p = 0.01$). The Infant-affection VAS score was positively correlated with the nurturance subscale score (Additional file 5, $R = 0.7$, $p < 0.001$), supporting the construct validity of this newly designed VAS.

Table 1: Subjective fondness values for an unfamiliar infant face by never-pregnant and postpartum women.

	Never-pregnant group, mean (SD) (n = 27)	Postpartum group, mean (SD) (n = 29)	Statistical method	Statistics	Degrees of freedom	P value
Infant-affection VAS	7.4 (2.1)	8.6 (1.2)	Wilcoxon rank-sum test	U = 268	NA	0.03*
PCAT-pn Protection subscale	3.2 (0.7)	3.2 (0.7)	Student t-test	t = −0.35	54	0.72
PCAT-pn Nurturance subscale	3.9 (0.6)	4.3 (0.3)	Student t-test	t = −2.43	54	0.01*
PCAT-pn Total	3.6 (0.5)	3.9 (0.3)	Student t-test	t = −1.8	54	0.07

Statistical significance at *P < 0.05. NA: not applicable, SD: standard deviation.

Experiences of pregnancy and childbirth were associated with altered regional brain activity patterns while viewing unfamiliar infant faces

The visual stimuli and task conditions during fMRI scanning are shown in Fig. 1 (see Materials and methods) and Additional file 4.

Whole-brain analyses revealed significantly stronger fMRI signals during viewing of an unfamiliar infant's face relative to control faces in seven brain regions of the postpartum group compared to the never-pregnant group (Fig. 2): right dorsomedial prefrontal cortex, right inferior frontal gyrus, right anterior insular cortex, right dorsolateral prefrontal cortex, right angular gyrus, right precuneus and left cerebellar Crus II (Additional file 6). Within-group analyses also revealed significant activation in the anterior cingulate cortex, middle cingulate cortex and fusiform gyrus of both groups during viewing of an unfamiliar infant's face and control face (Additional file 7; Additional files 8 and 9).

Salivary oxytocin levels did not differ significantly between groups (never-pregnant: 6.50 ± 0.67 ln(pg/mL); postpartum: 6.61 ± 0.53 ln(pg/mL); t = −0.687, p = 0.494), but in the postpartum group, salivary oxytocin level was positively correlated with activity in the right dorsomedial prefrontal cortex (R = 0.39, p = 0.034) and right anterior insula (R = 0.45, p = 0.014) during viewing of unfamiliar infant faces (Fig. 3), while no such correlations were observed in the never-pregnant group. Conversely, in the never-pregnant group, a significant negative correlation was found between salivary oxytocin and activation of the left cerebellar Crus II (R = −0.46, p = 0.015), whereas this association was not present in the postpartum group. No significant group differences in activation were found for these three regions during control face viewing (Additional file 10). These regions may therefore be selectively modulated by

pregnancy and childbirth to enhance maternal caregiving motivation, and were selected as seed regions for subsequent FC analyses.

Experiences of pregnancy and childbirth were associated with altered FC while viewing unfamiliar infant faces

We defined the right dorsomedial prefrontal cortex, right anterior insular cortex and left cerebellar Crus II as seed regions for FC analysis (Fig. 4A) and conducted whole-brain psychophysiological interaction (PPI) analysis. The postpartum group showed significantly greater FC between the right anterior insula and right fusiform gyrus than the never-pregnant group while viewing unfamiliar infant faces (Fig. 4B; Additional file 11); no significant group differences in FC were found for the right dorsomedial prefrontal cortex or left cerebellar Crus II.

FC analyses with these seed regions were also conducted for four regions of interest (ROIs)—the OFC, amygdala, TPJ and VTA—based on their known associations with the dopamine reward system, oxytocin system and theory of mind network. These analyses further revealed significantly enhanced connectivity between the right anterior insula and both the amygdala and TPJ, and between the left cerebellar Crus II and the amygdala, in postpartum group women (Fig. 4C).

Nurturing experience increased brain activity in regions related to theory of mind and dopamine reward while viewing the nurtured infant's face

In the postpartum group, whole-brain analysis revealed stronger fMRI signals while viewing the nurtured infant's face than an unfamiliar infant's face (Fig. 5) in regions including the bilateral OFC, anterior insular cortex, anterior cingulate cortex, dorsomedial prefrontal cortex and left precuneus (Additional file 12). Unlike the unfamiliar infant condition, there were no significant correlations between baseline salivary oxytocin and brain activity in the right dorsomedial prefrontal cortex, right anterior insular cortex or left cerebellar Crus II while viewing the nurtured infant's face (Additional file 13).

Nurturing experience increased FC while viewing the nurtured infant's face

Using the same three seed regions, whole-brain PPI analysis compared FC between unfamiliar infant and nurtured infant viewing conditions (Fig. 6A). Viewing the nurtured infant's face significantly increased FC between the right anterior insula and several regions, including the right fusiform gyrus, hippocampus, precentral gyrus and periaqueductal grey, compared to the unfamiliar infant's face condition (Fig. 6B). Analysis of FC between the seed regions and predefined ROIs further revealed stronger connectivity of

the right anterior insula with the OFC and VTA while viewing the nurtured versus unfamiliar infant's face (Fig. 6C). In contrast, FC between the right anterior insula and the TPJ was significantly weaker during nurtured infant's face viewing than unfamiliar infant's face viewing ($p = 0.015$). No significant connectivity differences were observed for the right dorsomedial prefrontal cortex or left cerebellar Crus II. Further details are in Additional file 14.

Discussion

Postpartum women showed higher subjective affection towards unfamiliar infant faces than never-pregnant women, together with greater activity in the right anterior insular cortex, dorsolateral and dorsomedial prefrontal cortices, angular gyrus, precuneus and cerebellar Crus II. Salivary oxytocin correlated positively with dorsomedial prefrontal and anterior insular activation only in postpartum women. FC was greater between the right anterior insular cortex and the fusiform gyrus, amygdala and TPJ, and between the left cerebellar Crus II and amygdala, while viewing unfamiliar infants' faces. Viewing one's own nurtured infant's face elicited stronger activation in the OFC, anterior cingulate cortex and anterior insular cortex than viewing an unfamiliar infant's face, with FC also enhanced—particularly between the right anterior insula and the fusiform gyrus, OFC, hippocampus and VTA. Together, these findings indicate that pregnancy and childbirth enhance emotional and brain responses to unfamiliar infant faces, and that infant nurturing further enhances activity and connectivity among regions implicated in reward processing, episodic memory and affective theory of mind—changes that may support motivation, awareness and empathy for infant care.

Pregnancy and childbirth enhance positive emotional responses to infants' faces

The Infant-affection VAS and PCAT-pn nurturance subscale scores were higher in the postpartum group than the never-pregnant group and were positively correlated, supporting the validity of the newly developed VAS. This positive emotional response extended to unfamiliar infants. Lehmann et al. [44] similarly reported that mothers rate infant faces more favourably than childless women, and suggested that caregiving experience may heighten responsiveness to others' offspring, or that more infant-responsive individuals are more likely to become parents. Because both studies relied on subjective measures susceptible to personal preference, cultural background and socially desirable responding, our findings are consistent with heightened maternal responsiveness but cannot rule out that positive attitudes toward motherhood pre-date pregnancy.

Experiences of pregnancy and childbirth increase FC while viewing an unfamiliar infant's face

FC was significantly greater in the postpartum group between the right anterior insular cortex and the right fusiform gyrus, amygdala and TPJ, and between the left cerebellar Crus II and amygdala. Hoekzema et al. [29] reported that the transition to motherhood reduces grey matter volume within the theory of

mind network, potentially reflecting microstructural changes in synaptic density, glial or neuronal composition, dendritic architecture, vascularisation or myelination. A longitudinal case study spanning preconception to two years postpartum similarly found pronounced decreases in grey matter volume and cortical thickness alongside increases in white matter microstructural integrity and ventricular volume, with few regions unaffected [28].

Our findings indicate that pregnancy and childbirth are associated with FC alterations within critical networks during infant face viewing, potentially reflecting underlying neuroplastic processes. The anterior insular cortex, amygdala, TPJ and cerebellar Crus II are strongly implicated in theory of mind—the anterior insula and amygdala primarily in its affective component [7, 26], and the TPJ and cerebellar Crus II in both cognitive and affective components [24, 45, 46]. The fusiform gyrus is a central mediator of face perception and identification [47, 48, 49], strongly dependent on anatomic connections to occipital visual regions [50, 51]; the insular cortex is also involved in face perception, particularly of emotional content, although no direct anatomical link with the fusiform gyrus has been identified [52]. Our findings suggest that neuroplasticity during pregnancy and childbirth enhances FC between face perception areas and the theory of mind network, and between the affective and cognitive components of theory of mind via the anterior insula.

Experiences of pregnancy and childbirth enhance regional brain activity in response to an unfamiliar infant's face

Several theory of mind-related regions showed increased activation to unfamiliar infant faces in the postpartum group: dorsomedial and dorsolateral prefrontal cortices and angular gyrus (cognitive theory of mind; [24]; [53]), anterior insula and inferior frontal gyrus (affective theory of mind; [7]; [26]), and precuneus and cerebellar Crus II (both components; [7]; [45]; [46]). Only two prior studies compared regional activity between postpartum and nulliparous women in response to an unfamiliar infant's face, both using emotional (rather than neutral) infant faces, and both reported greater activation in theory of mind regions—middle frontal gyrus, inferior frontal gyrus, middle temporal gyrus, posterior cingulate cortex—in postpartum women [8, 9]. We observed a similar pattern using neutral infant faces and simple viewing instructions, suggesting theory of mind processes are recruited even under minimal task demands, and that pregnancy and childbirth enhance brain responsiveness to infant faces independent of emotional content. Our sample was also assessed earlier postpartum (mean 48.1 ± 16.1 days) than in prior studies (3.5–6 months), suggesting our results more directly reflect changes attributable to pregnancy and childbirth themselves.

Baseline salivary oxytocin correlated positively with activity in the anterior insula and dorsomedial prefrontal cortex only in the postpartum group while viewing unfamiliar infant faces; in the never-pregnant group there was instead a negative correlation with cerebellar Crus II activity. Elevated plasma oxytocin during the postpartum period has been linked to maternal gaze, vocalisation, positive affect and affectionate touch [54]. The dorsomedial prefrontal cortex expresses oxytocin receptors and is implicated in anxiety reduction upon oxytocin administration in rodents [55]; the insular cortex is

innervated by oxytocinergic neurons [56] and is central to socio-emotional and empathic processing [27, 26], with oxytocin infusion increasing neuronal excitability and social-affective behaviour in rats [57] and intranasal oxytocin enhancing insular responses to infant cries in women [58]. We speculate that oxytocin signalling contributes to the enhanced dorsomedial prefrontal and anterior insular activity we observed during pregnancy and childbirth, though direct evidence for this mechanism is lacking.

The cerebellar Crus II, involved in both cognitive and affective theory of mind [45, 46] as well as broader non-motor cognitive functions [59], expresses oxytocin receptor genes [60] and showed a negative oxytocin correlation only in the never-pregnant group. The absence of this correlation postpartum, together with increased Crus II–amygdala FC, suggests that pregnancy and childbirth may reorganise oxytocin-related regulation of this region.

Nurturing experience increases FC and brain activity while viewing the nurtured infant's face

FC was greater during nurtured than unfamiliar infant's face viewing, particularly between the anterior insular cortex and the fusiform gyrus, OFC, hippocampus and VTA, and activation was greater in the OFC, anterior cingulate cortex and anterior insular cortex. We are aware of no prior study examining FC while viewing one's own infant. Prior longitudinal studies reported reduced hippocampal grey matter volume from pre- to post-pregnancy that partially recovers within two years [29], alongside transient increases in white matter microstructural integrity [28]. The OFC and VTA are implicated in both affective theory of mind [24] and the dopaminergic reward system [61], while the hippocampus supports episodic memory. Although our participants were only in the early postpartum period, over a month of caregiving experience is likely to have fostered a strong emotional bond and accumulated episodic memories of the infant, making the infant's face a particularly salient stimulus. The dopamine reward system is critical for caregiving motivation [11], while theory of mind supports interpretation of subtle infant facial cues. Our findings suggest that caregiving experience enhances FC between face perception, episodic memory, affective theory of mind and dopamine reward networks, with the anterior insula acting as a central hub. Unlike the unfamiliar-infant condition, oxytocin did not correlate with brain activity during nurtured-infant viewing, suggesting that episodic memory and reward-related processes may exert a stronger influence on brain activity following caregiving experience than oxytocin signalling alone.

In contrast to these increases, FC between the right anterior insula and the TPJ was weaker while viewing the nurtured infant's face than the unfamiliar infant's face. The TPJ has been shown to mediate the incorporation of self-referential (metacognitive) information into inferences about others' mental states during mentalizing, with disruption of this region weakening such self–other integration [62]. We speculate that when viewing an unfamiliar infant, whose individual cues and needs are not yet known, mothers may draw more heavily on this self-information-based inferential process to interpret the infant's state. For their own nurtured infant, sustained caregiving experience may instead have furnished mothers with infant-specific experiential knowledge, plausibly reducing reliance on self-information-based inference while increasing reliance on retrieval of infant-specific memories—consistent with the

concurrent strengthening of insula connectivity with the hippocampus. This mechanistic hypothesis—a relative shift in the information mothers draw upon to infer their infant's state, from self-derived inference towards infant-specific stored experience—would require direct testing (for example, relating hippocampal connectivity to explicit measures of infant-specific recognition) and is offered here as a plausible interpretation of the present pattern rather than a demonstrated mechanism.

Although viewing one's own infant necessarily confounds genetic relatedness with caregiving experience, converging evidence suggests that caregiving experience itself, rather than biological relatedness per se, is a primary driver of infant-directed neural and attentional responses in mothers: birth mothers and non-biologically related (foster/adoptive) mothers show similarly enhanced early attentional processing of their own child's face relative to other children's faces [63], and virgin, non-parous rodents can be induced to display pup-directed caregiving through activation of the same neural circuitry engaged by biological mothers [22]. We therefore interpret the present findings—both the enhanced FC and activation described above and the altered insula–TPJ connectivity—as most plausibly reflecting caregiving experience accumulated over the postpartum period rather than genetic kinship per se, although the present design cannot formally dissociate these factors.

Pregnancy, childbirth and nurturing enhance maternal brain responses and mother–infant bonding

Maternal–infant bonding begins during pregnancy, despite the invisibility of the foetus's face, and intensifies through postpartum interaction; its quality significantly influences infant psychological development [64]. Our findings suggest that pregnancy and childbirth enhance FC and activation in face perception and affective theory of mind networks—processes essential for interpreting infant emotional cues—forming part of the brain's foundational mechanisms supporting mother–infant bonding initiated during pregnancy. The additional enhancement observed when mothers viewed their own nurtured infant's face likely reflects further neural adaptation reinforced through caregiving, together constituting part of the neural basis of the maternal reproductive process.

Limitations of the study

This study has several limitations. First, its cross-sectional design precludes causal inference about pregnancy- and childbirth-related brain changes; a longitudinal design would offer stronger evidence but was not feasible given the difficulty of recruiting women prior to conception, the ten-month gestational period, and limited MRI access. Second, selection bias may have influenced results, as participants in both groups may have joined the study for reasons unrelated to pregnancy and childbirth; however, we found no group differences in response to control faces for our three seed regions (Additional file 10), suggesting any such effect was minimal. Third, fMRI captures BOLD signal—an indirect haemodynamic proxy for neural activity—rather than neuronal activity or neuroplastic change directly, and no noninvasive method currently allows direct measurement of these processes in humans. Fourth, the three seed regions used for functional connectivity analyses were themselves selected based on their activation differences and oxytocin correlations within this dataset; because functional connectivity was then

assessed at these same regions, this seed-selection procedure is not fully statistically independent of the connectivity findings that followed, a form of non-independence common to seed-based connectivity studies. In contrast, the four regions of interest used for connectivity comparisons (OFC, amygdala, TPJ, VTA) were selected a priori from the existing theory of mind, reward and oxytocin literature, independently of the present data. Fifth, saliva was collected within a relatively narrow afternoon window (12:35–15:40) for practical reasons, as standardising collection time across participants or scheduling a separate visit was not feasible; collection time did not differ significantly between groups (never-pregnant: 14:14 ± 0.91 h; postpartum: 14:05 ± 0.97 h; $t = 0.57$, $p = 0.57$), suggesting that any diurnal variation in oxytocin is unlikely to have systematically biased the between-group comparisons. Sixth, cluster-based correction relied on parametric Gaussian random field theory rather than non-parametric permutation testing; while this is standard practice in FSL-based analyses, parametric cluster correction with a stringent cluster-forming threshold has been reported to yield somewhat liberal family-wise error rates in some contexts, and future work using permutation-based methods would help confirm the robustness of the present findings.

Few studies have examined neuroplastic changes induced by pregnancy and childbirth in humans, despite their likely importance for successful reproduction and child-rearing. Advancing this understanding may help inform more effective support for the maternal reproductive process.

Conclusions

We compared brain activity in response to unfamiliar infant faces between postpartum and never-pregnant women. In the postpartum group, viewing an unfamiliar infant's face elicited stronger FC between face perception regions and the theory of mind network, and between affective and cognitive theory of mind components via the anterior insular cortex; salivary oxytocin correlated positively with dorsomedial prefrontal and anterior insular activity. Viewing their own nurtured infant's face further increased connectivity—again via the anterior insula—among face perception, episodic memory and affective theory of mind regions, including components of the dopamine reward system, while connectivity with the TPJ was weaker; activation in theory of mind- and reward-related regions was also greater relative to unfamiliar infant faces. These findings suggest that pregnancy, childbirth and nurturing enhance the motivational and emotional influence of infant faces on maternal behaviour via neuroplastic changes in networks dedicated to face perception, episodic memory, affective theory of mind and dopamine reward.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the National Centre of Neurology and Psychiatry (approval number: B2021-075) and performed in accordance with the 1964 Declaration of Helsinki and

its later amendments. Written informed consent was obtained from all individual participants included in the study, and from the parents of all infants photographed or whose data were used.

Consent for publication

The authors affirm that written informed consent for publication of facial images in Fig. 1 and Additional file 4 was obtained from the adult individuals depicted and, for the infant models, from their parents.

Availability of data and materials

All relevant data supporting the conclusions of this study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare no competing interests.

Funding

This study was supported by an Intramural Research Grant (3-Y2) for Neurological and Psychiatric Disorders of NCNP, and JSPS KAKENHI Grant Number 24K20365.

Authors' contributions

K.H. was responsible for designing the study, collecting, analysing and interpreting the data and writing the manuscript. Y.N. played a key role in the recruitment of participants. Both authors participated in the revision of the manuscript and approved the final version for publication.

Acknowledgements

This work was made possible through the contributions of many individuals and organizations, to whom we extend our deepest gratitude. Our ethics application was supported by the efforts of R. Okubo and M. Inoue. The application for research funding was adeptly helped by I. Funayama and K. Takahashi, while A. Kobayashi, R. Fukuzawa, M. Tokudome, and Y. Inoue played crucial roles in the management of these funds. M. Sasaki, R. Yagishita, and A. Tsuchiya helped recruit participants. We are grateful for data collection by A. Inoue, M. Inoue, Y. Wakayama, and H. Fukuoka. T. Hanakawa, D. Togo, and K. Takeda provided insightful advice. Y. Ota offered invaluable advice on the collection of saliva samples and measurement of oxytocin. K. Yoshinaga provided expert guidance on image analysis. The preservation

of saliva samples was helped by H. Kaneko and K. Hattori. We also extend our thanks to K. Takeyama and the team at Airplants-Bio Corporation for their precise measurement of salivary oxytocin levels. We would also like to thank Enago (www.enago.jp) for English language editing of this manuscript. Each of these contributions was integral to the success of our study, and we are profoundly thankful for the support and expertise provided by all involved.

Ethical considerations regarding interpretation

The group differences in brain activity and functional connectivity observed in this study are not interpreted as indications of superiority or inferiority in ability, but rather as functional adaptations shaped by specific experiential contexts. The findings are not intended to establish any normative standards for suitability as a caregiver. Importantly, this study does not negate the diversity of emotional expression or the variability of mother–infant relationships. Furthermore, the study is not based on the assumption that women's roles are biologically determined, nor do the findings imply any biological essentialism or serve to justify normative claims regarding gender roles or the sexual division of labour. The results should not be construed as suggesting that the never-pregnant group possesses deficient brain function or lacks caregiving capacity. Likewise, the study does not imply that pregnancy or childbirth leads to the "completion" or "maturation" of women's traits or abilities. Finally, the findings do not diminish the importance of caregiving capacities in non-parous individuals, including fathers and non-biological caregivers.

References

1. Luo LZ, Li H, Lee K. Are faces really more appealing than those of adults? Testing the baby schema hypothesis beyond infancy. J Exp Child Psychol. 2011;110:115-124. doi:10.1016/j.jecp.2011.04.002
2. Brosch T, Sander D, Scherer KR. That baby caught my eye... attention capture by infant faces. Emotion. 2007;7:685-689. doi:10.1037/1528-3542.7.3.685
3. Lorenz K. The innate forms of potential experience. Z Tierpsychol. 1943;5:235-409. doi:10.1111/j.1439-0310.1943.tb00655.x
4. Grieb ZA, Lonstein JS. Oxytocin interactions with central dopamine and serotonin systems regulate different components of motherhood. Philos Trans R Soc Lond B Biol Sci. 2022;377:20210062. doi:10.1098/rstb.2021.0062
5. Strathearn L. Maternal neglect: oxytocin, dopamine and the neurobiology of attachment. J Neuroendocrinol. 2011;23:1054-1065. doi:10.1111/j.1365-2826.2011.02228.x
6. Swain JE, Kim P, Spicer J, Ho SS, Dayton CJ, Elmadih A, Abel KM. Approaching the biology of human parental attachment: brain imaging, oxytocin and coordinated assessments of mothers and fathers. Brain Res. 2014;1580:78-101. doi:10.1016/j.brainres.2014.03.007
7. van 't Hof SR, Straathof M, Spalek K, Hoekzema E. Theory of mind during pregnancy and postpartum: a systematic review. J Neuroendocrinol. 2023;35:e13266. doi:10.1111/jne.13266

8. Bak Y, Nah Y, Han S, Lee SK, Kim J, Shin NY. Neural correlates of empathy for babies in postpartum women: a longitudinal study. Hum Brain Mapp. 2021;42:3295-3304. doi:10.1002/hbm.25435
9. Zhang K, Rigo P, Su X, Wang M, Chen Z, Esposito G, Putnick DL, Bornstein MH, Du X. Brain responses to emotional infant faces in new mothers and nulliparous women. Sci Rep. 2020;10:9560. doi:10.1038/s41598-020-66511-x
10. Hodges SD, Kiel KJ, Kramer ADI, Veach D, Villanueva BR. Giving birth to empathy: the effects of similar experience on empathic accuracy, empathic concern, and perceived empathy. Pers Soc Psychol Bull. 2010;36:398-409. doi:10.1177/0146167209350326
11. Ferrey AE, Santascoy N, McCrory EJ, Thompson-Booth C, Mayes LC, Rutherford HJ. Motivated attention and reward in parenting. Parenting. 2016;16:284-301. doi:10.1080/15295192.2016.1184928
12. Wigton R, Radua J, Allen P, Averbeck B, Meyer-Lindenberg A, McGuire P, Shergill SS, Fusar-Poli P. Neurophysiological effects of acute oxytocin administration: systematic review and meta-analysis of placebo-controlled imaging studies. J Psychiatry Neurosci. 2015;40:E1-E22. doi:10.1503/jpn.130289
13. Scheele D, Kendrick KM, Khouri C, Kretzer E, Schläpfer TE, Stoffel-Wagner B, Güntürkün O, Maier W, Hurlemann R. An oxytocin-induced facilitation of neural and emotional responses to social touch correlates inversely with autism traits. Neuropsychopharmacol. 2014;39:2078-2085. doi:10.1038/npp.2014.78
14. Weisman O, Zagoory-Sharon O, Feldman R. Intranasal oxytocin administration is reflected in human saliva. Psychoneuroendocrinology. 2012a;37:1582-1586. doi:10.1016/j.psyneuen.2012.02.014
15. Weisman O, Zagoory-Sharon O, Feldman R. Oxytocin administration to parent enhances infant physiological and behavioral readiness for social engagement. Biol Psychiatry. 2012b;72:982-989. doi:10.1016/j.biopsych.2012.06.011
16. Striepens N, Kendrick KM, Maier W, Hurlemann R. Prosocial effects of oxytocin and clinical evidence for its therapeutic potential. Front Neuroendocrinol. 2011;32:426-450. doi:10.1016/j.yfrne.2011.07.001
17. Kemp A, Guastella AJ. The role of oxytocin in human affect. Curr Dir Psychol Sci. 2011;20:222-231. doi:10.1177/0963721411417547
18. Bartz JA, Zaki J, Bolger N, Ochsner KN. Social effects of oxytocin in humans: context and person matter. Trends Cogn Sci. 2011;15:301-309. doi:10.1016/j.tics.2011.05.002
19. Veinante P, Freund-Mercier M. Distribution of oxytocin- and vasopressin-binding sites in the rat extended amygdala: a histoautoradiographic study. J Comp Neurol. 1997;383:305-325. doi:10.1002/(sici)1096-9861(19970707)383:3<305::aid-cne3>3.3.co;2-2
20. Insel TR, Gelhard R, Shapiro LE. The comparative distribution of forebrain receptors for neurohypophyseal peptides in monogamous and polygamous mice. Neuroscience. 1991;43:623-630. doi:10.1016/0306-4522(91)90321-e

21. Knobloch HS, Charlet A, Hoffmann LC, Eliava M, Khrulev S, Cetin AH, Osten P, Schwarz MK, Seeburg PH, Stoop R, Grinevich V. Evoked axonal oxytocin release in the central amygdala attenuates fear response. Neuron. 2012;73:553-566. doi:10.1016/j.neuron.2011.11.030
22. Kohl J, Babayan BM, Rubinstein ND, Autry AE, Marin-Rodriguez B, Kapoor V, Miyamishi K, Zweifel LS, Luo L, Uchida N, Dulac C. Functional circuit architecture underlying parental behaviour. Nature. 2018;556:326-331. doi:10.1038/s41586-018-0027-0
23. Rappeneau V, Castillo Díaz F. Convergence of oxytocin and dopamine signalling in neuronal circuits: Insights into the neurobiology of social interactions across species. Neurosci Biobehav Rev. 2024;161:105675. doi:10.1016/j.neubiorev.2024.105675
24. Abu-Akel A, Shamay-Tsoory S. Neuroanatomical and neurochemical bases of theory of mind. Neuropsychologia. 2011;49:2971-2984. doi:10.1016/j.neuropsychologia.2011.07.012
25. Shamay-Tsoory SG, Aharon-Peretz J. Dissociable prefrontal networks for cognitive and affective theory of mind: a lesion study. Neuropsychologia. 2007;45:3054-3067. doi:10.1016/j.neuropsychologia.2007.05.021
26. Caillaud M, Bejanin A, Laisney M, Gagnepain P, Gaubert M, Viard A, Clochon P, de La Sayette V, Allain P, Eustache F, Desgranges B. Influence of emotional complexity on the neural substrates of affective theory of mind. Hum Brain Mapp. 2020;41:139-149. doi:10.1002/hbm.24794
27. Bartels A, Zeki S. The neural correlates of maternal and romantic love. Neuroimage. 2004;21:1155-1166. doi:10.1016/j.neuroimage.2003.11.003
28. Pritschet L, Taylor CM, Cossio D, Santander T, Grotzinger H, Faskowitz J, Handwerker DA, Layher E, Chrastil ER, Jacobs EG. Neuroanatomical changes observed over the course of a human pregnancy. Nat Neurosci. 2024;27:2253-2260. doi:10.1038/s41593-024-01741-0
29. Hoekzema E, Barba-Müller E, Pozzobon C, Picado M, Lucco F, García-García D, Soliva JC, Tobeña A, Desco M, Crone EA, Ballesteros A, Carmona S, Vilarroya O. Pregnancy leads to long-lasting changes in human brain structure. Nat Neurosci. 2017;20:287-296. doi:10.1038/nn.4458
30. Rigo P, Kim P, Esposito G, Putnick DL, Venuti P, Bornstein MH. Specific maternal brain responses to their own child's face: an fMRI meta-analysis. Dev Rev. 2019;51:58-69. doi:10.1016/j.dr.2018.12.001
31. Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia. 1971;9:97-113. doi:10.1016/0028-3932(71)90067-4
32. Okano T, Murata M, Masuji F, Tamaki R, Nomura J, Miyaoka H. Validation and reliability of Japanese version of the EPDS. Arch Psychiatr Diagn Clin Evaluat. 1996;7:525-533.
33. Oshio A, Abe S, Cutrone P. Development, reliability, and validity of the Japanese version of ten item personality inventory (TIPI-J). Jpn J Personal. 2012;21:40-52. doi:10.2132/personality.21.40
34. Gosling SD, Rentfrow PJ, Swann WB. A very brief measure of the big-five personality domains. J Res Pers. 2003;37:504-528. doi:10.1016/s0092-6566(03)00046-1
35. Hofer MK, Buckels EE, White CJM, Beall AT, Schaller M. Individual differences in activation of the parental care motivational system: an empirical distinction between protection and nurturance. Soc Psychol Personal Sci. 2018;9:907-916. doi:10.1177/1948550617728994

36. Woolrich MW, Ripley BD, Brady M, Smith SM. Temporal autocorrelation in univariate linear modeling of FMRI data. Neuroimage. 2001;14:1370-1386. doi:10.1006/nimg.2001.0931
37. Behzadi Y, Restom K, Liau J, Liu TT. A component based noise correction method (CompCor) for BOLD and perfusion based fMRI. Neuroimage. 2007;37:90-101. doi:10.1016/j.neuroimage.2007.04.042
38. Shishido E, Shuo T, Takahata K, Horiuchi S. Changes in salivary oxytocin levels and bonding disorder in women from late pregnancy to early postpartum: a pilot study. PLoS One. 2019;14:e0221821. doi:10.1371/journal.pone.0221821
39. O'Reilly JX, Woolrich MW, Behrens TEJ, Smith SM, Johansen-Berg H. Tools of the trade: psychophysiological interactions and functional connectivity. Soc Cogn Affect Neurosci. 2012;7:604-609. doi:10.1093/scan/nss055
40. Friston KJ, Buechel C, Fink GR, Morris J, Rolls E, Dolan RJ. Psychophysiological and modulatory interactions in neuroimaging. Neuroimage. 1997;6:218-229. doi:10.1006/nimg.1997.0291
41. Golec-Staśkiewicz K, Wojciechowski J, Haman M, Wolak T, Wysocka J, Pluta A. Unveiling the neural dynamics of the theory of mind: a fMRI study on belief processing phases. Soc Cogn Affect Neurosci. 2024;19:nsae095. doi:10.1093/scan/nsae095
42. Schurz M, Radua J, Aichhorn M, Richlan F, Perner J. Fractionating theory of mind: a meta-analysis of functional brain imaging studies. Neurosci Biobehav Rev. 2014;42:9-34. doi:10.1016/j.neubiorev.2014.01.009
43. Pauli WM, Nili AN, Tyszka JM. A high-resolution probabilistic in vivo atlas of human subcortical brain nuclei. Sci Data. 2018;5:180063. doi:10.1038/sdata.2018.63
44. Lehmann V, Huis in't Veld EMJ, Vingerhoets AJ. The human and animal baby schema effect: correlates of individual differences. Behav Processes. 2013;94:99-108. doi:10.1016/j.beproc.2013.01.001
45. Beuriat PA, Cohen-Zimerman S, Smith GNL, Krueger F, Gordon B, Grafman J. Evidence of the role of the cerebellum in cognitive theory of mind using voxel-based lesion mapping. Sci Rep. 2022;12:4999. doi:10.1038/s41598-022-09104-0
46. Van Overwalle F, Ma Q, Heleven E. The posterior crus II cerebellum is specialized for social mentalizing and emotional self-experiences: a meta-analysis. Soc Cogn Affect Neurosci. 2020;15:905-928. doi:10.1093/scan/nsaa124
47. Kanwisher N, Yovel G. The fusiform face area: a cortical region specialized for the perception of faces. Philos Trans R Soc Lond B Biol Sci. 2006;361:2109-2128. doi:10.1098/rstb.2006.1934
48. Kanwisher N, McDermott J, Chun MM. The fusiform face area: a module in human extrastriate cortex specialized for face perception. J Neurosci. 1997;17:4302-4311. doi:10.1523/jneurosci.17-11-04302.1997
49. Grill-Spector K, Knouf N, Kanwisher N. The fusiform face area subserves face perception, not generic within-category identification. Nat Neurosci. 2004;7:555-562. doi:10.1038/nn1224

50. Palejwala AH, O'Connor KP, Milton CK, Anderson C, Pelargos P, Briggs RG, Conner AK, O'Donoghue DL, Glenn CA, Sughrue ME. Anatomy and white matter connections of the fusiform gyrus. Sci Rep. 2020;10:13489. doi:10.1038/s41598-020-70410-6
51. Haxby JV, Hoffman EA, Gobbini MI. The distributed human neural system for face perception. Trends Cogn Sci. 2000;4:223-233. doi:10.1016/s1364-6613(00)01482-0
52. Phillips ML, Young AW, Scott SK, Calder AJ, Andrew C, Giampietro V, Williams SC, Bullmore ET, Brammer M, Gray JA. Neural responses to facial and vocal expressions of fear and disgust. Proc R Soc Lond B. 1998;265:1809-1817. doi:10.1098/rspb.1998.0506
53. Schurz M, Tholen MG, Perner J, Mars RB, Sallet J. Specifying the brain anatomy underlying temporo-parietal junction activations for theory of mind: a review using probabilistic atlases from different imaging modalities. Hum Brain Mapp. 2017;38:4788-4805. doi:10.1002/hbm.23675
54. Feldman R, Weller A, Zagoory-Sharon O, Levine A. Evidence for a neuroendocrinological foundation of human affiliation: plasma oxytocin levels across pregnancy and the postpartum period predict mother-infant bonding. Psychol Sci. 2007;18:965-970. doi:10.1111/j.1467-9280.2007.02010.x
55. Sabihi S, Dong SM, Maurer SD, Post C, Leuner B. Oxytocin in the medial prefrontal cortex attenuates anxiety: anatomical and receptor specificity and mechanism of action. Neuropharmacology. 2017;125:1-12. doi:10.1016/j.neuropharm.2017.06.024
56. Liao PY, Chiu YM, Yu JH, Chen SK. Mapping central projection of oxytocin neurons in unmated mice using cre and alkaline phosphatase reporter. Front Neuroanat. 2020;14:559402. doi:10.3389/fnana.2020.559402
57. Rogers-Carter MM, Varela JA, Gribbons KB, Pierce AF, McGoey MT, Ritchey M, Christianson JP. Insular cortex mediates approach and avoidance responses to social affective stimuli. Nat Neurosci. 2018;21:404-414. doi:10.1038/s41593-018-0071-y
58. Riem MME, Bakermans-Kranenburg MJ, Pieper S, Tops M, Boksem MAS, Vermeiren RRJM, van IJzendoorn MH, Rombouts SARB. Oxytocin modulates amygdala, insula, and inferior frontal gyrus responses to infant crying: a randomized controlled trial. Biol Psychiatry. 2011;70:291-297. doi:10.1016/j.biopsych.2011.02.006
59. Schmahmann JD, Guell X, Stoodley CJ, Halko MA. The theory and neuroscience of cerebellar cognition. Annu Rev Neurosci. 2019;42:337-364. doi:10.1146/annurev-neuro-070918-050258
60. Quintana DS, Rokicki J, van der Meer D, Alnæs D, Kaufmann T, Córdova-Palomera A, Dieset I, Andreassen OA, Westlye LT. Oxytocin pathway gene networks in the human brain. Nat Commun. 2019;10:668. doi:10.1038/s41467-019-08503-8
61. Chau BKH, Jarvis H, Law CK, Chong TTJ. Dopamine and reward: a view from the prefrontal cortex. Behav Pharmacol. 2018;29:569-583. doi:10.1097/fbp.0000000000000424
62. Sun F, Yang T, Liu N, Wan X. The causal role of temporoparietal junction in mediating self-other mergence during mentalizing. J Neurosci. 2023;43:8442-8455. doi:10.1523/JNEUROSCI.1026-23.2023

63. Grasso DJ, Moser JS, Dozier M, Simons R. ERP correlates of attention allocation in mothers processing faces of their children. Biol Psychol. 2009;81:95-102. doi:10.1016/j.biopsycho.2009.03.001
64. de Waal N, Boekhorst MGBM, Nyklíček I, Pop VJM. Maternal-infant bonding and partner support during pregnancy and postpartum: associations with early child social-emotional development. Infant Behav Dev. 2023;72:101871. doi:10.1016/j.infbeh.2023.101871

Figures

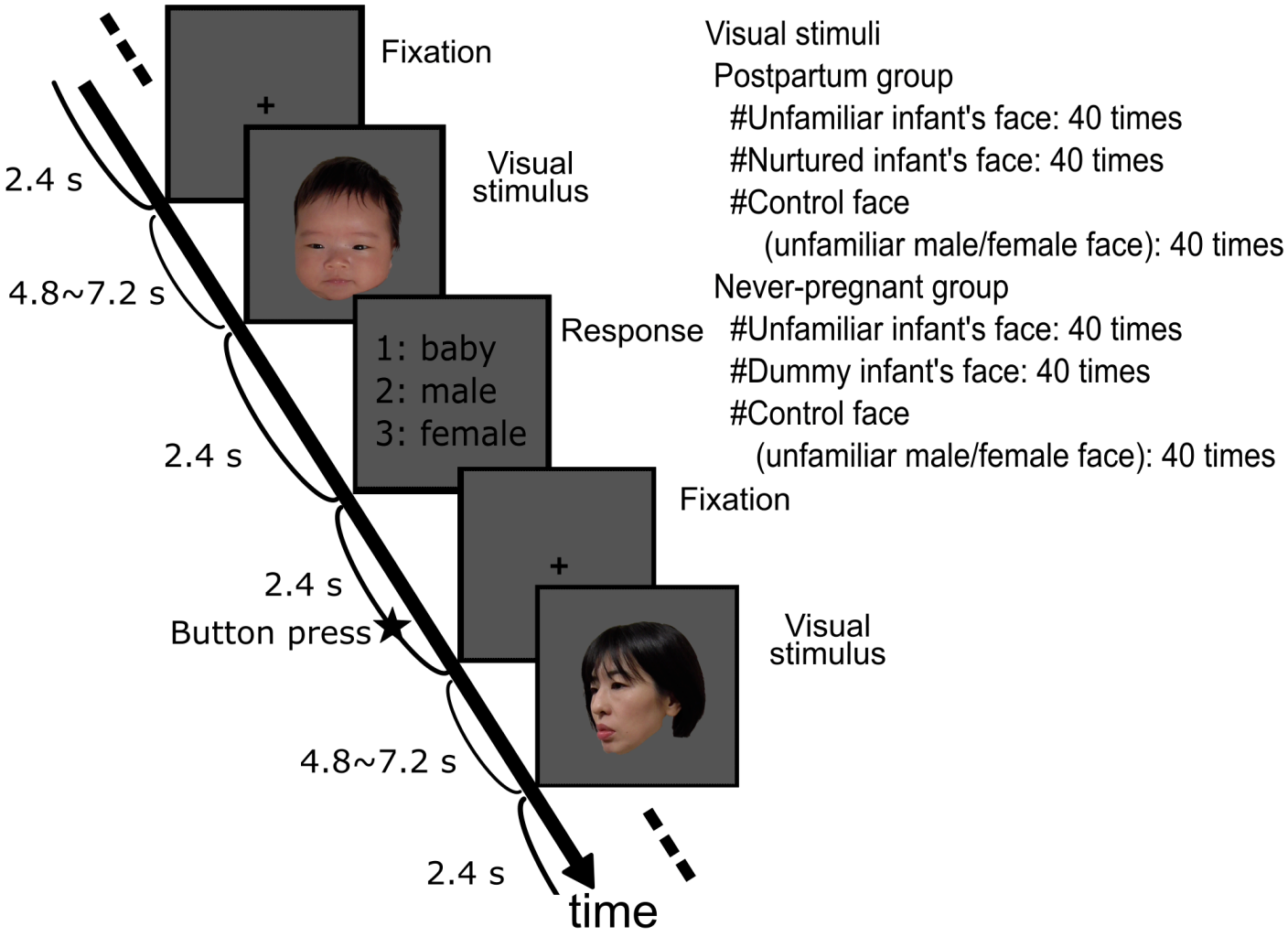


Figure 1

Task paradigm presented during MRI scanning.

Photographic images of human faces were presented during MRI scanning. After the presentation of the face stimulus (2.4 s), never-pregnant and postpartum women were required to identify the face by pressing the appropriate button during the response period (2.4 s). The same sets of face stimuli were presented to the postpartum and never-pregnant groups except that postpartum women also viewed

images of their own nurtured infant while the never-pregnant women viewed a different unfamiliar infant (dummy infant) to balance the total number of stimuli presented to both groups. Detailed information on each type of facial photograph is found in Additional file 4.

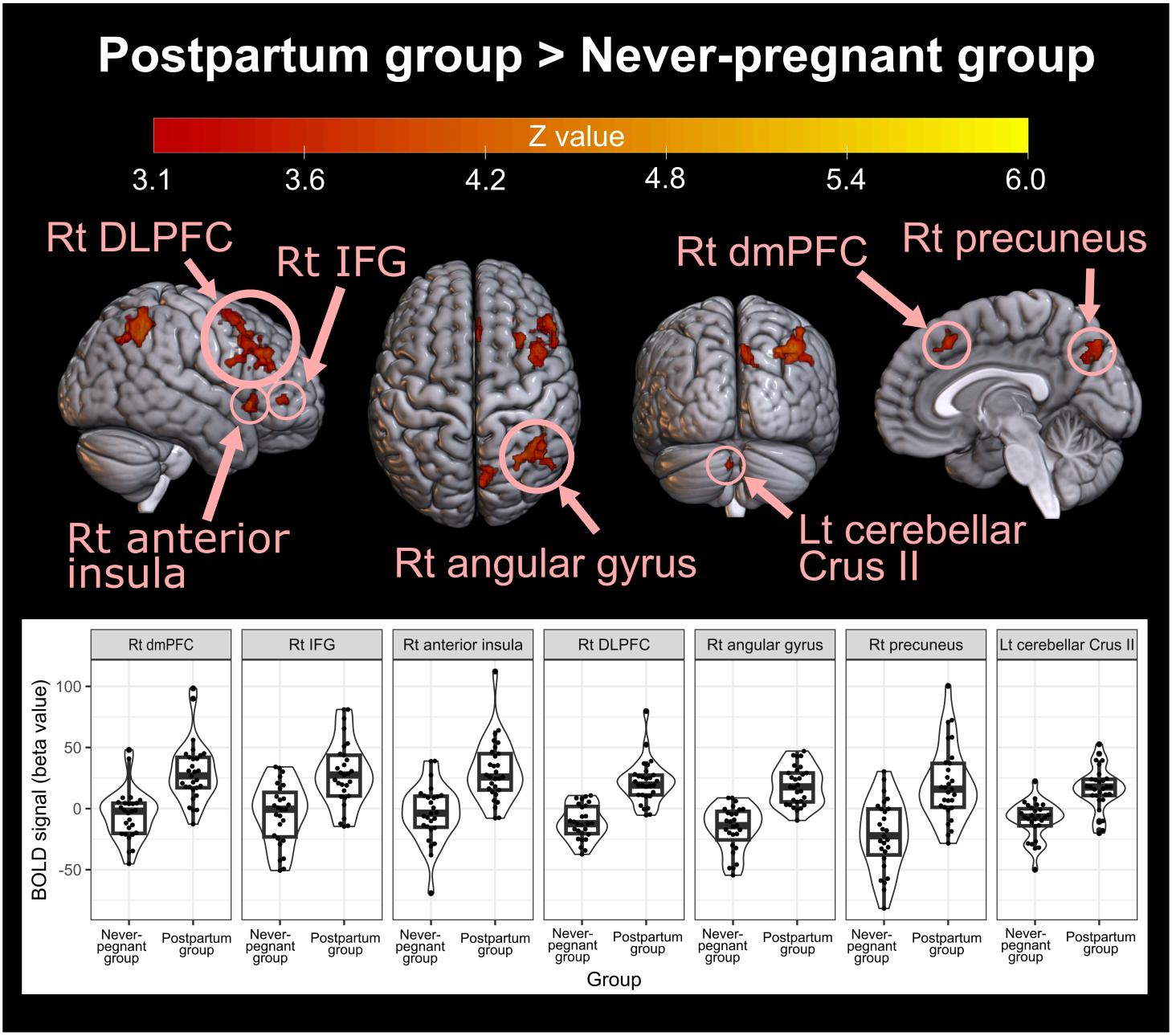


Figure 2

Unfamiliar infant's face viewing induced stronger regional brain activity in postpartum than never-pregnant women.

The red to yellow areas show brain regions where significant activation was observed, representing the interaction effect between group (never-pregnant vs. postpartum) and stimulus type (control face vs. unfamiliar infant's face). The voxel-level threshold was set at $p < 0.001$ and cluster-level threshold at $p <$

0.05, corrected for multiple comparisons. Peak coordinates are shown in Additional file 6. Violin plots show BOLD signal strengths (beta value differences between unfamiliar infant and control face conditions) of each region in the never-pregnant and postpartum groups; bars indicate the 25th, 50th and 75th percentiles. Abbreviations: BOLD, blood oxygen level-dependent; DLPFC, dorsolateral prefrontal cortex; dmPFC, dorsomedial prefrontal cortex; IFG, inferior frontal gyrus; Lt, left; Rt, right.

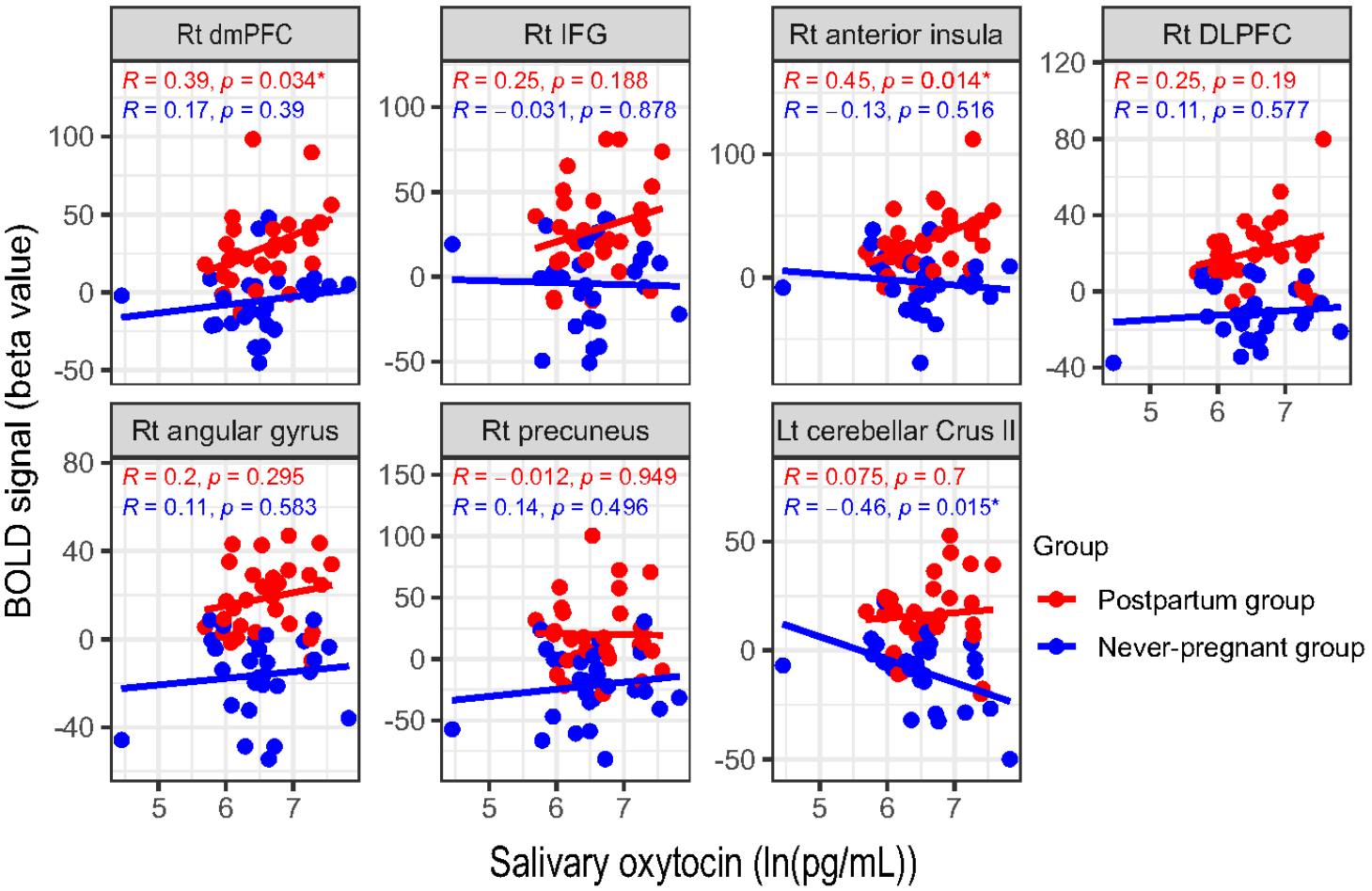


Figure 3

Associations between regional brain activity and salivary oxytocin while viewing unfamiliar infant faces.

Plots are shown separately for the never-pregnant and postpartum groups. The x-axis of each plot represents the concentration of salivary oxytocin for each individual and the y-axis represents the average BOLD signal (beta value) of each brain region in response to the unfamiliar infant's face versus a control face. Associations were tested using Pearson's correlation analysis with $P < 0.05$ considered significant. Abbreviations: BOLD, blood oxygen level-dependent; DLPFC, dorsolateral prefrontal cortex; dmPFC, dorsomedial prefrontal cortex; IFG, inferior frontal gyrus; Lt, left; Rt, right.

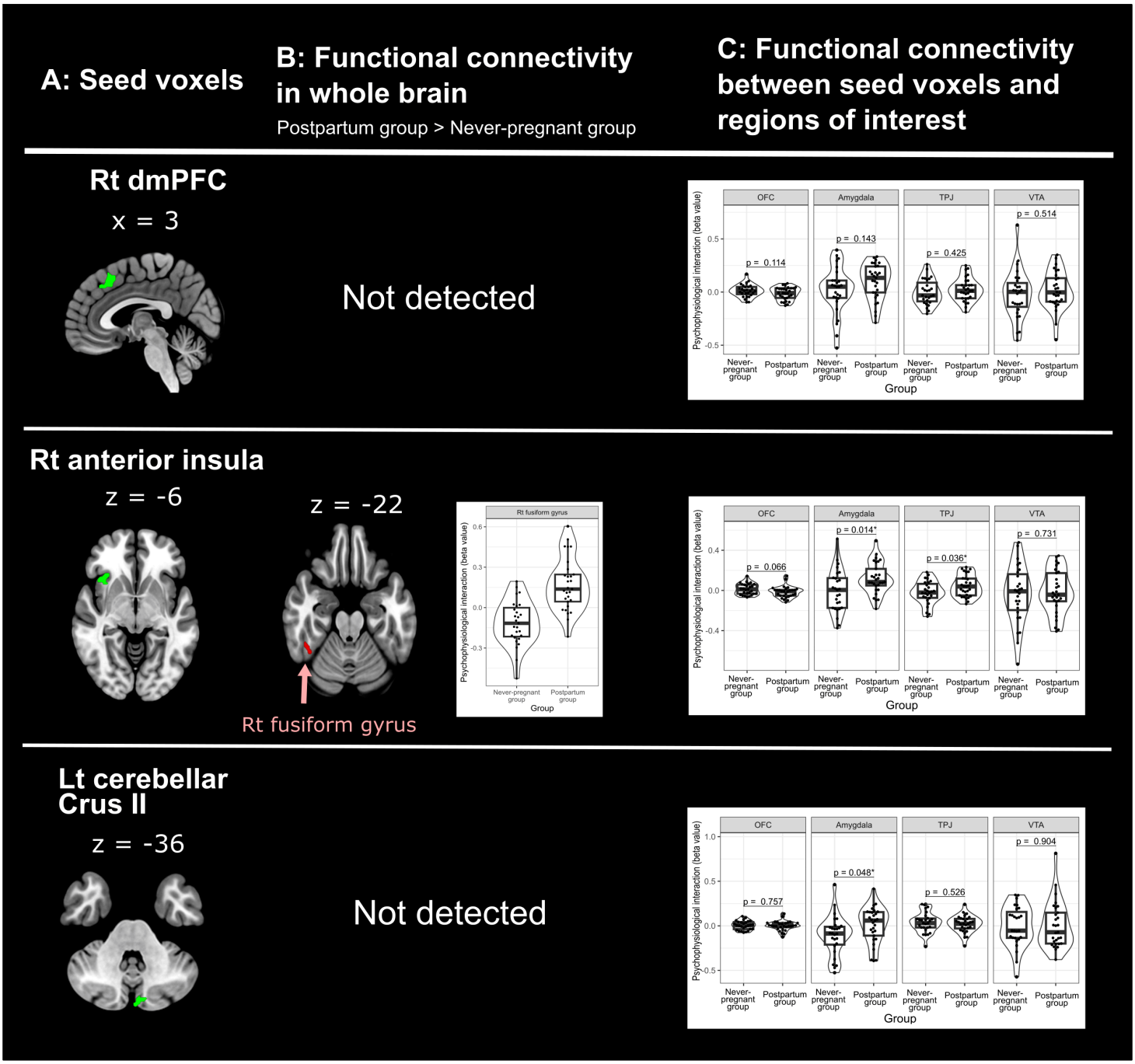


Figure 4

Differences in FC between never-pregnant and postpartum women while viewing the faces of unfamiliar infants.

A: PPI analysis used the right dorsomedial prefrontal cortex, right anterior insula and left cerebellar Crus II as seed regions (green areas), based on significantly greater activation in response to unfamiliar infant's face stimuli in the postpartum group and correlations with salivary oxytocin levels (see Figs. 2, 3). B: FC to seed regions across the whole brain. The red area indicates significantly stronger FC during unfamiliar infant's face presentation in the postpartum group versus never-pregnant group (voxel-level $p < 0.001$, cluster-level $p < 0.05$, corrected). Peak coordinates are in Additional file 11. Violin plots show PPI

values for connectivity between seed voxels and the detected region (right fusiform gyrus). C: PPI values for connectivity between seed voxels and the four ROIs (OFC, amygdala, TPJ, VTA). Dots represent mean beta values (arbitrary units) of PPI; bars indicate the 25th, 50th and 75th percentiles. Statistics: Student's t-test (*P < 0.05). Abbreviations: dmPFC, dorsomedial prefrontal cortex; OFC, orbitofrontal cortex; Rt, right; TPJ, temporoparietal junction; VTA, ventral tegmental area.

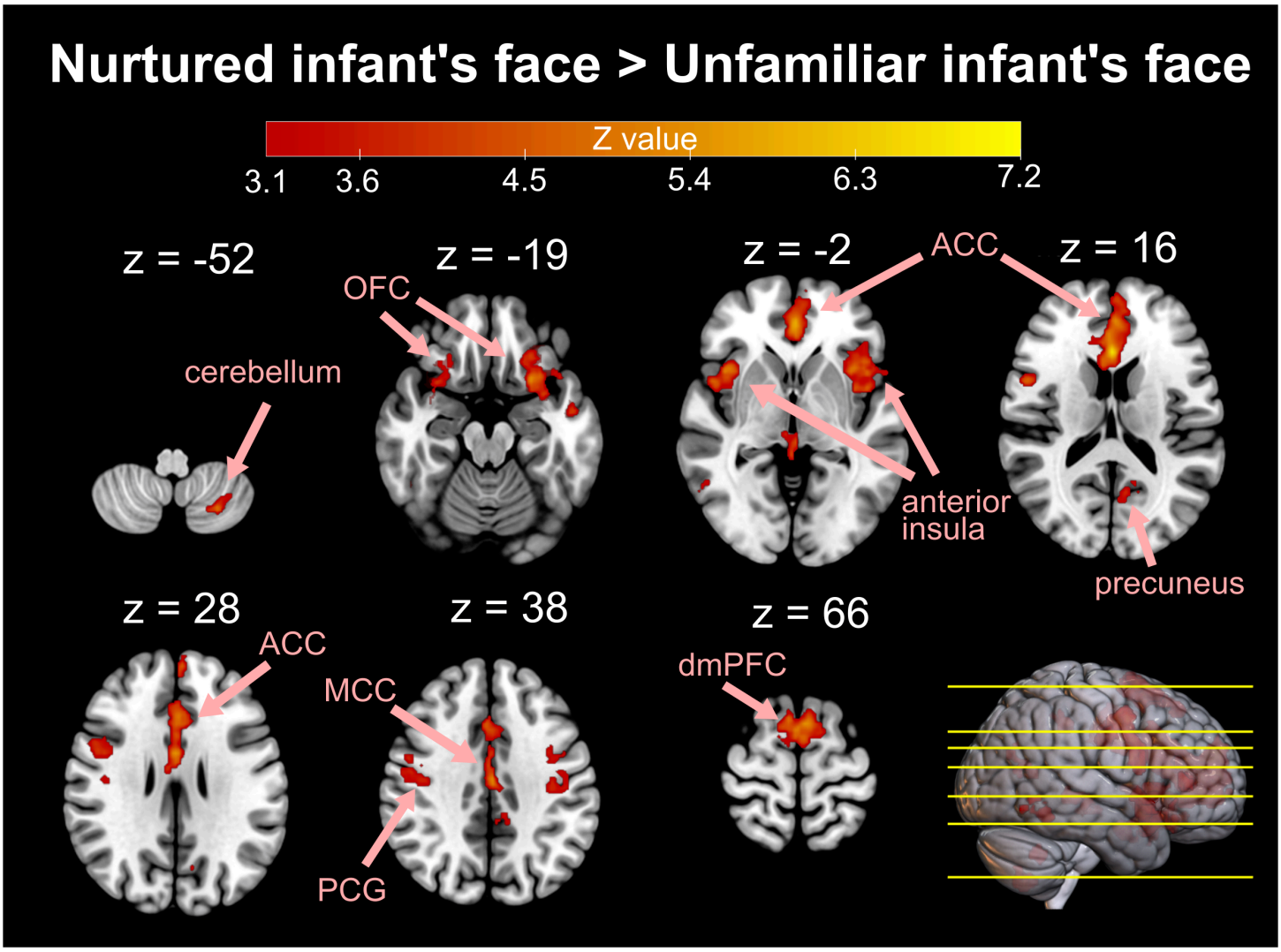


Figure 5

Activation map of the postpartum group viewing the nurtured versus unfamiliar infant's face.

Regions with significantly greater activation (voxel-level p < 0.001, cluster-level p < 0.05, corrected) in response to the nurtured infant's face are indicated by red to yellow. Peak coordinates are shown in Additional file 12. Abbreviations: ACC, anterior cingulate cortex; dmPFC, dorsomedial prefrontal cortex; MCC, middle cingulate cortex; OFC, orbitofrontal cortex; PCG, postcentral gyrus.

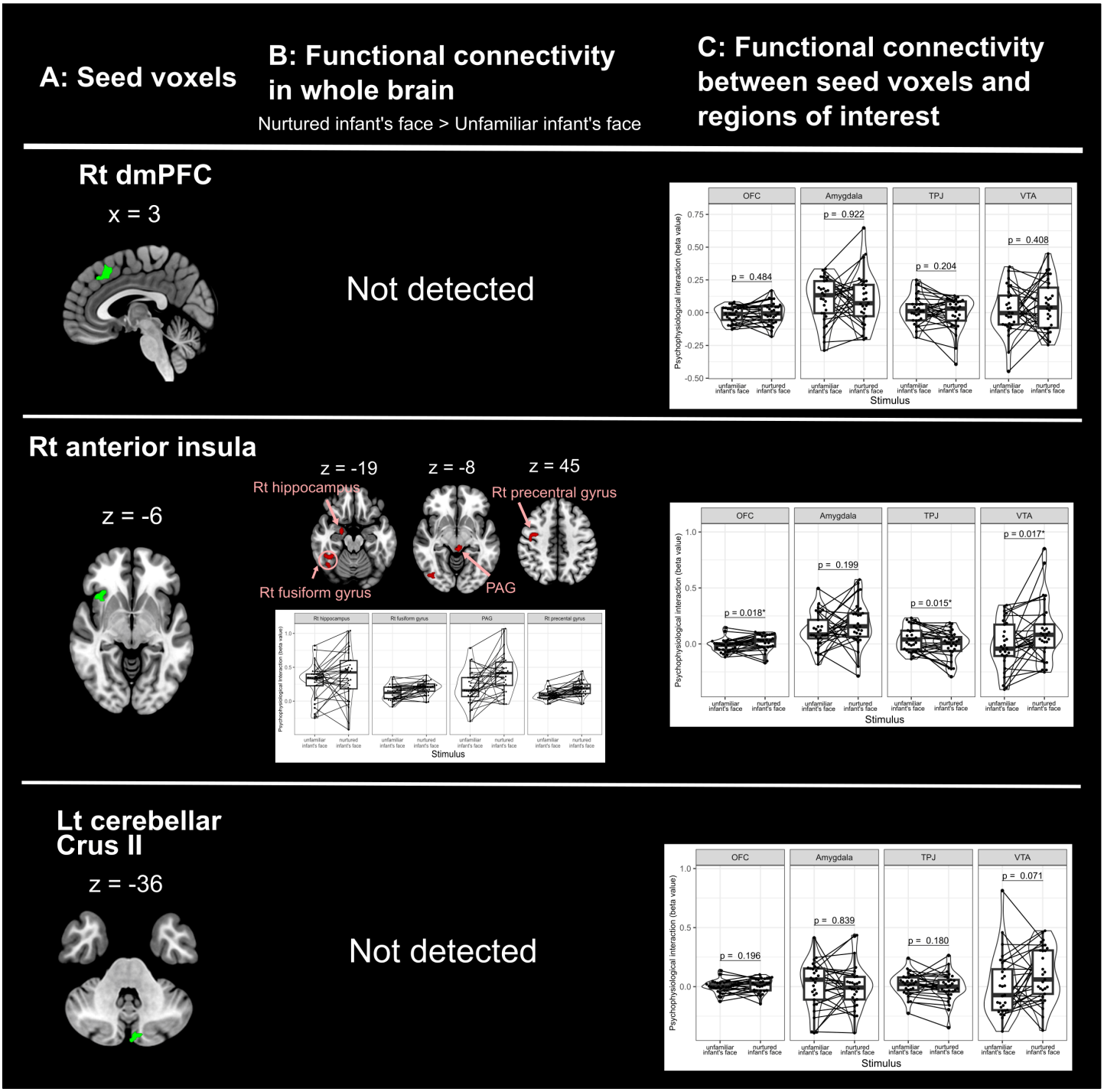


Figure 6

Differences in FC while viewing the nurtured infant's face compared to an unfamiliar infant's face.

A: PPI analysis used the same three seed regions as the unfamiliar-infant analysis (right dorsomedial prefrontal cortex, right anterior insula, left cerebellar Crus II; green areas; see Fig. 4A). B: FC to seed regions across the whole brain. The red area indicates significantly stronger FC from the right anterior insula during nurtured infant's face presentation versus unfamiliar infant's face (voxel-level $p < 0.001$, cluster-level $p < 0.05$, corrected), including the right fusiform gyrus, hippocampus, precentral gyrus and

periaqueductal grey. Peak coordinates are in Additional file 14. Violin plots show PPI values for connectivity between seed voxels and each of these four regions. C: PPI values for connectivity between the right anterior insula and the four ROIs (OFC, amygdala, TPJ, VTA). Connectivity with the OFC and VTA was significantly stronger, and connectivity with the TPJ significantly weaker, during nurtured infant's face viewing. Dots represent mean beta values (arbitrary units) of PPI; bars indicate the 25th, 50th and 75th percentiles. Statistics: paired Student's t-test (*P < 0.05). Abbreviations: FC, functional connectivity; OFC, orbitofrontal cortex; PPI, psychophysiological interaction; Rt, right; TPJ, temporoparietal junction; VTA, ventral tegmental area.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Additionalfile1.xlsx
- Additionalfile8.xlsx
- Additionalfile14.xlsx
- Additionalfile12.xlsx
- Additionalfile9.xlsx
- Additionalfile11.xlsx
- Additionalfile6.xlsx
- Additionalfile2.xlsx
- Additionalfileslegends.docx
- Additionalfile4.tiff
- Additionalfile7.tiff