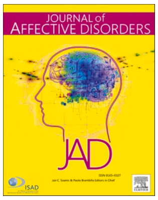
Journal of Affective Disorders 356 (2024) 177–189

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad



Research paper

Maternal prenatal depressive symptoms and child brain responses to affective touch at two years of age

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ARTICLE INFO

Keywords:
Affective touch
Child
Diffuse optical tomography
Prenatal depression

ABSTRACT

Background: Touch is an essential form of mother-child interaction, instigating better social bonding and emotional stability.
Methods: We used diffuse optical tomography to explore the relationship between total haemoglobin (HbT) responses to affective touch in the child's brain at two years of age and maternal self-reported prenatal depressive symptoms (EPDS). Affective touch was implemented via slow brushing of the child's right forearm at 3 cm/s and non-affective touch via fast brushing at 30 cm/s and HbT responses were recorded on the left hemisphere.
Results: We discovered a cluster in the postcentral gyrus exhibiting a negative correlation (Pearson's $r = -0.84$, $p = 0.015$ corrected for multiple comparisons) between child HbT response to affective touch and EPDS at gestational week 34. Based on region of interest (ROI) analysis, we found negative correlations between child responses to affective touch and maternal prenatal EPDS at gestational week 14 in the precentral gyrus, Rolandic operculum and secondary somatosensory cortex. The responses to non-affective touch did not correlate with EPDS in these regions.
Limitations: The number of mother-child dyads was 16. However, by utilising high-density optode arrangements, individualised anatomical models, and video and accelerometry to monitor movement, we were able to minimize methodological sources of variability in the data.
Conclusions: The results show that maternal depressive symptoms during pregnancy may be associated with reduced child responses to affective touch in the temporoparietal cortex. Responses to affective touch may be considered as potential biomarkers for psychosocial development in children. Early identification of and intervention in maternal depression may be important already during early pregnancy.

1. Introduction

Child development is influenced by a combination of prenatal and postnatal factors, including prenatal maternal depression (PMD) and post-partum depression (PPD) (Bernard-Bonnin et al., 2004; Liu et al., 2017; Park et al., 2018; Rifkin-Graboi et al., 2015). PMD is associated with an increased risk of preterm birth and low birth weight (Accortt et al., 2015) and may have a significant impact on child development, affecting the processing of negative emotions, cognition, executive function, and structural brain development (Prado et al., 2021; Hutchison et al., 2019; Oh et al., 2020; Zou et al., 2019).

Mother-child interaction, especially through touch and caressing, is a

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Abbreviations: DOT, diffuse optical tomography; EPDS, Edinburgh Perinatal/Postnatal Depression Scale; gwk, gestational week; HbT, total haemoglobin concentration; ROI, region of interest.

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https://doi.org/10.1016/j.jad.2024.03.092
Received 4 April 2023; Received in revised form 13 March 2024; Accepted 16 March 2024

critical factor in social bonding and threat perception (Dunbar, 2010; Harlow and Zimmermann, 1958). Social touch has positive developmental effects on primates and humans, and its deprivation leads to aggression or dejection (Harlow and Zimmermann, 1958; Jablonski, 2021). Maternal affective touch reduces the physiological stress response in babies and helps them to develop neurobehavioural, cognitive, and social-emotional skills (Feldman and Eidelman, 2003; Feldman et al., 2010), which may be associated with decreased cortisol levels (Morelius et al., 2015). Paternal skin-to-skin contact has also been shown to improve biophysiological indices in newborns, such as respiration and glucose levels, and to have psychological calming effects (Bauer et al., 1996; Christensson, 1996; Erlandsson et al., 2007; Shorey et al., 2016; Velandia et al., 2012).

Mother-child interaction can be influenced by prenatal as well as postnatal factors. Postpartum factors such as PPD can directly influence mother-child interaction, e.g., mothers with PPD touch their infants less frequently and likely in a less gentle manner than non-depressed mothers (Field, 2010), and as a compensatory mechanism, these infants spend more time caressing their own skin (Hentel et al., 2000; Herrera et al., 2004). PMD can modulate mother-child interaction through fetal programming or a postnatal continuity effect. "Fetal programming" is a model that explains the long-lasting effects of prenatal depression on child development (Godfrey and Barker, 2001). According to this model, the fetal environment may have a permanent influence on the structure, physiology and metabolism of the child brain. For example, infants born to mothers with higher levels of prenatal depression were reported to have greater functional connectivity between the amygdala and the anterior cingulate and prefrontal cortices in a magnetic resonance imaging (fMRI) functional connectivity study (Qiu et al., 2015). Animal studies have shown that the effects of fetal programming can survive a test by cross-fostering, i.e., where the offspring of prenatally stressed mothers are fostered by non-stressed mothers (Holloway et al., 2013). Prenatally depressed mothers were reported to have a higher tendency to avoid looking at images of distressed infant faces (Macrae et al., 2015). PMD may interfere with the mother's psychological preparation for motherhood (Flykt et al., 2010). Maternal depression may continue in the postnatal period, potentially influencing the mother-child interaction and child development. Adverse fetal physiological effects in the uterus may alter the infant's self-regulatory capacity (Flykt et al., 2010) and introduce behavioural difficulties (Bind, 2022). Thus, dyadic interaction may be altered by contributing factors from both sides. Taken together, prenatal maternal depression and postnatal mother-child interaction, especially through touch, have significant impacts on the brain development and behavior of the offspring. Understanding the interplay between these is crucial in understanding the pathobiological mechanism.

The human brain can easily differentiate between affective and non-affective touch. While affective or emotional touch is primarily relayed by thin, unmyelinated, slow-conducting C-tactile afferent fibres, non-affective or discriminative touch is relayed by fast-conducting, large, myelinated Aβ-afferent fibres (Björnsdotter et al., 2014; McGlone et al., 2014; Morrison, 2016; Olausson et al., 2010). Research using a robotic tactile stimulator and microneurographic recordings in adult human participants showed that CT afferents respond most strongly to slow stroking at a velocity of 1–10 cm/s and brushing at these velocities was also considered the most pleasant by the participants (Ackerley et al., 2014; Löken et al., 2009). By contrast, brushing at 30 cm/s preferentially stimulates myelinated afferents whose responses do not correlate with pleasantness ratings (Löken et al., 2009). Affective touch responses in newborns have been found as early as 11–36 days after birth in an fMRI study indicating that these reactions begin quite early (Tuulari et al., 2019). Björnsdotter et al. (2014) used fMRI to examine emotional touch responses in adult-defined regions of interest in the primary somatosensory cortex (SI), secondary somatosensory cortex (SII), insular cortex and right posterior superior temporal sulcus (pSTS) in healthy children (5–13 years of age), adolescents (14–17 years of age), and adults (25–35 years of age), and observed similar activation responses in all age groups (Björnsdotter et al., 2014).

Touch responses have also been studied with near-infrared spectroscopy (NIRS), a non-invasive technique typically used to measure changes in the concentrations of oxygenated (HbO_2), deoxygenated (HbR), and total haemoglobin (HbT) based on differential absorption of visible red and near-infrared light by these chromophores (Jöbsis, 1977; Maria et al., 2018; Villringer and Chance, 1997). Diffuse optical tomography (DOT) is a three-dimensional imaging method based on the absorption and scatter of NIR light. In DOT, model-based image reconstruction is used to create images of hemodynamic changes related to brain activity (Arridge, 1999; Gibson et al., 2006; Heiskala et al., 2009; Maria et al., 2020; Schweiger et al., 2003; Shekhar et al., 2019). The method permits some degree of subject movement and offers a relatively convenient setup. Jönsson et al. investigated affective and non-affective touch processing in two-month-old infants with DOT, confirming greater activation to affective touch than non-affective touch in the insula (Jönsson et al., 2018). Maria et al. showed a similar result in the insula of two-year-olds whereas an area of the postcentral gyrus, Rolandic operculum and superior temporal gyrus showed greater activation to non-affective than affective touch (Maria et al., 2022).

There are no reported studies on whether PMD symptoms are associated with altered hemodynamic responses to affective touch in the offspring. Therefore, we explored the relationship between maternal self-reported depressive symptoms (Edinburgh Perinatal/Postnatal Depression Scale, EPDS) during the prenatal period and the two-year-old child's HbT responses to affective and non-affective touch by combining the experimental data recorded for the Maria et al. (2022) study with self-reported EPDS data at gestational weeks (gwk) 14, 24, and 34. We hypothesized that prenatal maternal depressive symptoms may alter neural responses to affective touch in areas of the child brain which process affective touch and emotion.

2. Materials and methods

The experiment, subjects, DOT data collection, signal processing and image reconstruction are described in detail in Maria et al. (2022). In this section, we summarise the essential steps and focus on the analysis specific to the present study.

2.1. Study participants and symptom scores

25 healthy children from the FinnBrain Birth Cohort (Karlsson et al., 2018) participated in the study. All the participating children were born full-term (36–42 weeks of gestation) between January and April 2014 to Finnish non-smoking, middle-class mothers with no relevant past or present neurological, medical or psychiatric disorders. More information on the subjects is given in Table 1 in Maria et al. (2022). 16 of the children were successfully imaged (8 girls and 8 boys); nine subjects were rejected due to the subject movement affecting the quality and quantity of data. The mean age of the successfully imaged children at the time of measurement was 2.1 years and the mean age of the mothers when they gave birth was 34 years. The mothers filled in maternal prenatal depression symptom questionnaires (EPDS) at weeks 14, 24 and 34 of the pregnancy, as well as at six months post-partum. EPDS was developed in the 1980s and is a 10-item self-report questionnaire relating to depressive symptoms experienced since giving birth. The EPDS is often used as a standard measure to estimate the severity of depression among pregnant women. Items on the EPDS are scored on a 0–3 scale, where "0" means "not at all" and "3" means "very much so." Statistics for the EPDS values are given in Table 1. The mothers were recruited from a healthy population and most of the EPDS values were below what would be considered indicative of depression in clinical practice.

Table 1
Edinburgh Perinatal/Postnatal Depression Scale (EPDS) values for the mothers of the subjects used in the analysis of this study (gwk = gestational week).

	Mean	Median	Range
EPDS gwk 14 (N = 16)	4.6	5	0–11
EPDS gwk 24 (N = 15)	4.4	3.5	1–11
EPDS gwk 34 (N = 16)	3.8	5	0–7
EPDS 6 months post-partum (N = 16)	4.3	4	0–10

2.2. *Experimental setup*

The Ethics Committee of the Hospital District of Southwest Finland approved the study which was conducted in accordance with the Declaration of Helsinki (decision ETMK 31/180/2011 § 534 Nov 17, 2015). The parents signed a written informed consent form on behalf of their child, and the measurements were conducted on the child's terms. We used the frequency-domain (FD) DOT device built at Aalto University (formerly Helsinki University of Technology; Nissilä et al., 2002 & 2005) with a single near-infrared wavelength of 798 nm.

The device injects radiofrequency (100 MHz) intensity-modulated light into the tissue and measures both the modulation amplitude and phase shift of the detected photon density wave. 15 source fibres and 15 detector fibre bundles connect the instrument to the high-density measurement probe made of black silicone. The detectors are photomultiplier tubes (PMT), and the fibre end with 4-mm glass prism terminals to guide the insertion of the light into the tissue and the detection of light exiting the tissue. The sources are time-multiplexed with a microelectromechanical system (MEMS) technology switch with a 50-ms pulse duration per source and an image frame acquisition time of 1.4 s. An accelerometer is embedded into the probe to provide data on subject movement.

The probe was wrapped over the left frontotemporal cortex of each child with self-adhesive bandage (Fig. 1b). The accelerometer data and video recording of the whole session were used to detect excessive child movement and other sources of artefact or missed touch stimuli. We measured in total 25 two-year-olds (12 female, 13 male), but got insufficient data from nine subjects due to practical or technical reasons. The threshold for inclusion was 10 artefact-free stimuli responses. The EPDS-scores for gwk 24 were also missing for one subject, which lowered N to 15 for this specific time point.

Prior to the measurement, the child wore a mesh cap with colourful glass pearls, which was photographed with a two-camera system from 5 to 7 angles to reconstruct the head shape of the subject with photogrammetry. Additional marker stickers were attached to the anatomical landmarks (nasion and preauricular points) and other facial points to register the probe location to the head with photographs taken after the probe had been attached.

During the experiment, the child sat on the parent's lap in a dimmed room and watched cartoons to help them sit still for most of the 1–1.5 h measurement session (Fig. 1a). The touch stimuli were provided by author AM, who manually stroke the child's right dorsal forearm skin with a soft paintbrush. Affective touch was administered with a single 6-cm stroke at 3 cm/s in a proximal-to-distal direction, and non-affective touch with multiple 6-cm strokes at 30 cm/s. The Presentation © software by Neurobehavioural Systems provided the stimulus onset trigger signals to guide the experimenter with "slow" (= affective touch) and "fast" clues on a laptop screen, and to mark the stimulus onset timings in the measured data. On average, 37 slow and 36 fast two-second stimuli were presented with an average inter-stimulus interval (ISI) of 31 s. From these, 27 slow and 28 fast stimuli, on average, were accepted to the analysis. The responses were measured contralaterally from the left hemisphere, with reportedly shorter brain–scalp distances (Beauchamp et al., 2011). The image, or the corresponding HbT changes in the brain, can be reconstructed from multiple overlapping measurements.

2.3. *Raw signal processing and image reconstruction*

Image reconstruction was based on the amplitude data. The measured raw amplitude time course was first linearly interpolated to a 2-Hz time grid for each source–detector pair and the logarithm was taken. The baseline signal drift was estimated by fitting a piecewise linear function to the mean of log amplitude in the pre-stimulus intervals [−2 s, 0 s] relative to blocks of stimuli with ISI ≤ 20 s. The baseline drift was subtracted from the signal and stimulus triggers corresponding to epochs with motion or other artefacts indicated by the accelerometer data or the video recording were removed. The data was low-pass filtered at a cut-off frequency of $f_{-3\ dB} = 0.2$ Hz. To obtain the average response magnitudes for both affective and non-affective touch, a hemodynamic response function (HRF) kernel, modified from the canonical HRF from the SPM software, was convolved with the triggers for the remaining stimuli for each stimulus type and fitted simultaneously to the time course of the filtered log amplitude signal. The response magnitudes obtained in this way reflect the hemodynamic responses in the expected time window relative to baseline while minimising errors arising from partial temporal overlap between responses to consecutive stimuli.

The corresponding cortical hemodynamic changes were reconstructed from a linear finite difference approximation to the relationship between the measured and the modelled logarithm of amplitude responses:

$$\Delta log(\boldsymbol{A}) = \boldsymbol{J}_{log(\boldsymbol{A})}\left(\vec{\mu}_a\right)\Delta\vec{\mu}_a$$

The left side of the equation has the vector with the measured changes for each source and detector, $\boldsymbol{J}_{log(\boldsymbol{A})}$ gives the sensitivities of the measurements to absorption coefficient changes in each $1 \times 1 \times 1$ mm^3-voxel, and $\Delta\vec{\mu}_a$ contains the unknown absorption coefficient changes, which are solved and converted to HbT changes by using the extinction

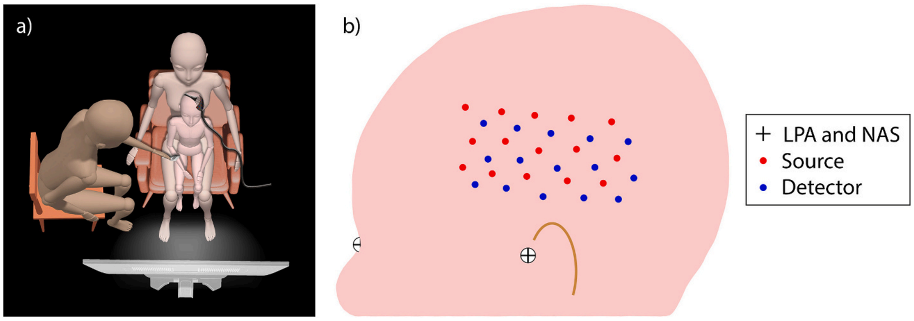

Fig. 1. a) Experimental session with parent, child, display, experimenter with brush, probe and video screen. b) Optode array placement on one subject on the atlas model of the head with left preauricular point (LPA) and nasion (NAS) marked with a '+' symbol, red dots indicating the approximate positions of source and blue dots of detector optodes. (Figure should be printed in colour.)

coefficients from Cope (1991). HbO_2 and HbR cannot be distinguished with one wavelength. HbT describes the increased arteriolar blood volume following increased neuronal activity and is less sensitive to the venous compartment than HbO_2 and HbR (Hillman et al., 2007). We only included the source–detector pairs with separation (SDS) <50 mm, since the signal-to-noise-ratio (SNR) decreases, and the risk of light leakage increases with larger SDSs. The mean SDS of the source-detector pairs used in the analysis was 30 mm and the range was 7–50 mm, providing varying depth sensitivity profiles.

The sensitivities, or Jacobian matrices, for FD amplitude data and absorption coefficient were computed in atlas-based voxel head models using the FD "replay" mode of the Monte Carlo eXtreme (MCX) photon simulation software (MCX/MCXLAB; https://mcx.space/nightly accessed 15 February, 2024; Fang and Boas, 2009; Yao et al., 2018; Hirvi et al., 2023). We simulated 10^{10} photon packets per source for 10 ns. Atlas-based models were obtained by registering the two-year-old's population-level atlas by Shi et al. (2011) to each individual's head shape as measured with photogrammetry (Shi et al., 2011). The models were deformed with an iteratively-optimized, nine-parameter linear affine transformation. The optode locations were interpolated to the head surface by using the photogrammetry data and the known probe layout. The original atlas by Shi et al. – with probabilities for cerebrospinal fluid (CSF), gray (GM) and white matter (WM) – was segmented into five tissue types by adding the combined scalp and skull layer, and by separating the semidiffusive subarachnoid CSF from the clearer CSF deeper in the sulci and ventricles. The optical properties for the tissue types used in the models of the present study can be found in Table 2 of Maria et al. (2022).

The Tikhonov-regularized solution for the voxel-wise HbT changes was computed in the least-squares sense in MATLAB (see Sec. 2.10 in Maria et al., 2022). The solutions were obtained in the individual registered atlas-models, and inverse-transformed back to the common atlas-frame for group level correlation analysis over all 16 subjects. The field-of-view (FOV) for the analysis was defined based on the relative sensitivity of each amplitude measurement to absorption changes in the following way: The relative sensitivity was defined as the inverse-transformed absorption Jacobian divided by its maximum value within the brain tissue. The FOV was defined as consisting of GM voxels where the largest value of the relative sensitivity calculated over all source–detector pairs included in the measurement averages at least 0.01 over all subjects.

2.4. *Correlation analysis*

2.4.1. *Clustering*

We used Pearson's linear correlation to find voxels and contiguous regions (clusters) within the measurement FOV which exhibited a statistically significant correlation between the maternal prenatal EPDS score and the child HbT response to slow brushing (affective touch) and fast brushing (non-affective touch, for comparison) over the mother-child dyads included. For clusters found based on correlation of maternal EPDS with child response to slow brushing, correlation with response to fast brushing in the same region was also calculated for comparison. Linear correlation analysis was selected because it made it easier to study the effects of secondary regressors in the analysis, although arguments can be made in favour of the use of monotonic rank correlation (Spearman). The voxel-wise correlation coefficients and corresponding *p*-values were calculated using MATLAB's `corrcoef` function. Cluster-wise correlation coefficients and p-values were calculated by first averaging the HbT response amplitudes over the voxels within the cluster for each subject and forming a vector which is correlated with the prenatal EPDS vector. Details on the clustering algorithm are given in Maria et al. (2020) and Maria et al. (2022). The cluster-wise *p*-values were further verified using permutation testing where the elements in the HbT cluster average vector were randomly permuted and correlated with the EPDS vector without permutation. The fraction of random permutations which gives a higher absolute value of the correlation coefficient than the original permutation is the p-value. Multiple comparison correction was performed using the Bonferroni method with $N_{MC} = 163$ which is the average number of source-detector pairs used for image reconstruction; thus, the corrected p-values were calculated from the uncorrected p-values by multiplying with 163. The minimum cluster size was set to 50 mm^3 according to the validation procedure (False Detection Rate (FDR) = 0.05; Maria et al., 2022). The EPDS scores tested included gwk 14 ($N = 16$), gwk 24 ($N = 15$), and gwk 34 (N = 16) which were used as regressors separately as well as an average over the three time points (N = 15). Since the prenatal EPDS values are correlated across time points (Table 2) and the number of questionnaires returned differed across time points, we did not use them together in a multiple regression analysis.

In addition to Pearson's correlation coefficient, we calculated the coefficient of determination (R^2) that describes which fraction of the variance of the test variable (HbT response magnitude) is explained by variation in the explanatory variable (prenatal EPDS score). Permutation testing was used to calculate the p-values for the difference between R^2 and zero to observe whether R^2 for affective touch was statistically significantly greater than the R^2 for non-affective touch. Finally, the role of postnatal depressive symptoms at six months post-partum was investigated as a confound. MATLAB's `fitlm` function was used with two explanatory variables (prenatal and postnatal EPDS) and the statistical significance of the primary explanatory variable (prenatal EPDS) in the presence of the secondary variable (postnatal EPDS) was tested and the p-values for both regressors reported. The multiple regression model for the affective touch responses can be written as

$$HbT_{si} = \beta_0 + \beta_{prenatal} EPDS_{si,tp} + \beta_{postnatal} EPDS_{si,6mo\ pp} + e_{si}.$$

where si = subject index, tp = time point, and e_{si} is the residual. 95 % confidence intervals for Pearson's correlation coefficients were calculated using the Fisher transformation.

2.4.2. *Region-of-interest analysis*

HbT responses over regions which are labelled in the Automated Anatomical Labelling (AAL) atlas (Shi et al., 2011) and are known to be involved in the processing of affective touch or in emotional/sensory integration were tested for Pearson's correlation with prenatal EPDS scores. We selected the following regions of interest (ROI): insula (INS-L 29) (Pirazzoli et al., 2019; Maria et al., 2022; Morrison et al., 2011; Jönsson et al., 2018), opercular inferior frontal gyrus (IFGoperc-L 11) (Davidovic et al., 2016; Pirazzoli et al., 2019), secondary somatosensory cortex (SII-L) (Björnsdotter et al., 2014), Rolandic operculum (ROL-L 17) (Maria et al., 2022), precentral gyrus (PreCG-L 1) (Maria et al., 2022; Davidovic et al., 2016), supramarginal gyrus (SMG-L 63) (Gordon et al., 2013), superior temporal gyrus (STG-L 81) (Maria et al., 2022), postcentral gyrus (PoCG-L 57) (Maria et al., 2022; Davidovic et al., 2016; Morrison et al., 2011), middle temporal gyrus (MTG-L 85) (Jönsson et al., 2018; Cascio et al., 2012), middle frontal gyrus (MFG-L 7) (Cascio et al., 2012), inferior parietal lobule (IPL-L 61) (Björnsdotter

Table 2
Pearson's correlation coefficients (r) between EPDS scores at different time points and the corresponding *p*-values. pp = post-partum. * = statistically significant correlation with $p < 0.05$.

	EPDS gwk 14	EPDS gwk 24	EPDS gwk 34
EPDS gwk 24	r = 0.51 p = 0.052		
EPDS gwk 34	r = 0.51* p = 0.045*	*r* = 0.45 *p* = 0.089	
EPDS 6 months pp	*r* = 0.05 *p* = 0.85	*r* = 0.37 *p* = 0.17	*r* = 0.31 *p* = 0.24

et al., 2014), and middle occipital gyrus (MOG-L 51) (Björnsdotter et al., 2014). SII ROI voxels were segmented manually, but the other ROIs were segmented using the AAL values in the atlas (Shi et al., 2011). Only voxels in the FOV were included in the ROIs. The HbT response values for slow and fast brushing for all the voxels within each ROI were averaged prior to statistical testing. Statistical tests for the ROIs were similar to those made for the clusters described in Section 2.4.1. The Bonferroni correction for the ROI analysis used a correction factor $N_{ROI} = 12$ according to the number of regions tested.

3. Results

3.1. Symptom scores

No statistically significant differences were found between the mean EPDS values across the four time points. The range of EDPS values in the present study is typical of that of healthy mothers (Matijasevich et al., 2014; Luciano et al., 2022). The study did not include any mothers with major depression disorder (MDD). The EPDS values corresponding to gwk 14 and gwk 34 had a statistically significant positive correlation (*r*

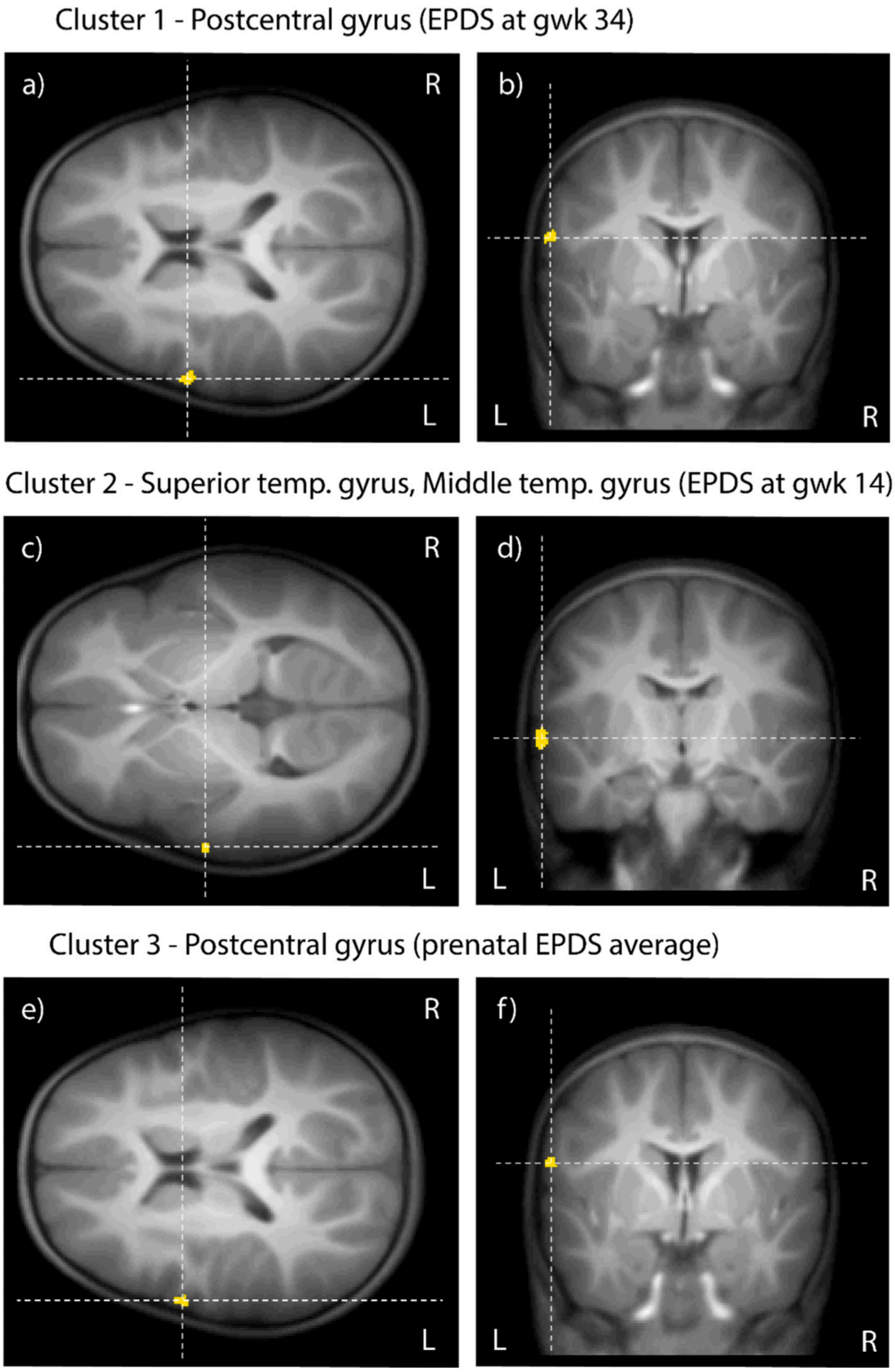

Fig. 2. Axial (a, c, and e) and coronal (b, d, and f) slices through the centers of gravity of Cluster 1 (a–b), Cluster 2 (c–d), and Cluster 3 (e–f). (See Tables 3 and 4). The voxels belonging to each cluster are marked in yellow in their respective images. (Figure should be printed in colour.)

= 0.51*, p = 0.045*). Pearson's correlation coefficients across time points and corresponding p-values indicating statistical significance of the correlation are given in Table 2.

3.2. Results from clustering

We first searched for statistically significant correlations between child HbT responses to affective touch and maternal EPDS scores for individual time points (gwk 14, 24, 34) and their average. One cluster was found in the Postcentral gyrus (PoCG-L) where the affective touch response exhibited a statistically significant negative correlation with EPDS at gwk 34 (Cluster 1; Pearson's $r = -0.84$**; $p_{MC} = 0.015$**; $R^2 =$ 0.70**; $p_{MC} = 0.033$**; Fig. 2a–b; Fig. 3a–b; Fig. 4; Tables 3 and 4). A second cluster in the Superior temporal gyrus (STG-L) and Middle temporal gyrus (MTG-L) exhibited nearly statistically significant negative correlation between EPDS at gwk 14 and the child response to affective touch (Cluster 2; $r = -0.76$*; $p_{MC} = 0.17$*; $R^2 = 0.58$*; $p_{MC} =$ 0.22*; Fig. 2c–d; Fig. 4; Tables 3 and 4). Finally, based on maternal prenatal average EPDS over the three time points, we found a third cluster in the Postcentral gyrus (PoCG-L; Cluster 3; $r = -0.81$*; $p_{MC} =$ 0.068*; $R^2 = 0.66$**; $p_{MC} = 0.033$**; Fig. 2e–f; Fig. 4; Tables 3 and 4). No clusters were found based on a search for a correlation between child brain responses to non-affective touch and maternal prenatal EPDS.

Statistics for the clusters are given in Tables 3 and 4, the locations are shown in Figs. 2 and 4. The scatter plots of the individual subject cluster-average responses and maternal scores for Cluster 1 are shown in Fig. 3. A 3D rendering of the locations of the clusters on the cortical surface of the atlas model is shown in Fig. 4.

Clusters 1 and 3 reside in the primary somatosensory area in the parietal cortex and are near the secondary somatosensory cortex (SII). Cluster 2 resides inferiorly to Clusters 1 and 3 on the side of the temporal cortex (see Figs. 2 and 4). None of the clusters 1–3 exhibit a statistically significant correlation between the prenatal EPDS and child brain response to non-affective touch (third column, Table 3). In Clusters 1 and 3, the coefficient of determination (R^2) for affective touch and prenatal EPDS is statistically significantly greater than for non-affective touch (Table 3, fourth column).

Clusters 1, 2, and 3 were tested also by using postnatal EPDS value for 6 months post-partum as an additional regressor to test if the result could have been due to post-partum depression instead. The p-value for the primary explanatory variable (EPDS gwk 34, 14 and prenatal average, respectively) remained statistically significant when the postnatal regressor was included (Table 3, fifth column).

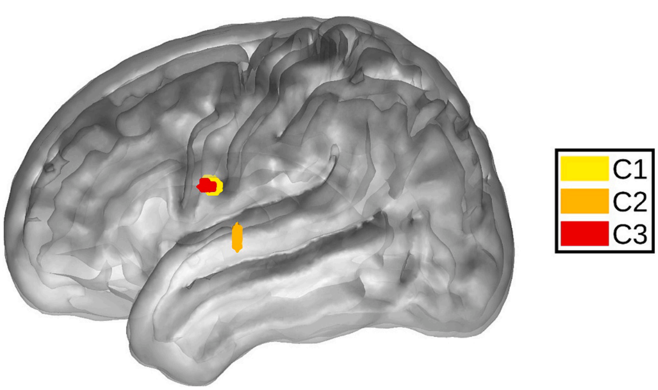

Fig. 4. Locations of Cluster 1 in the Postcentral gyrus (PoCG-L) with statistically significant correlation between maternal EPDS at gestational week 34 and child total haemoglobin (HbT) responses to affective touch (yellow); Cluster 3 in PoCG-L based on correlation between prenatal average EPDS and affective touch (red), and Cluster 2 in the Superior temporal gyrus (STG-L) and Middle temporal gyrus (MTG-L) with almost statistically significant correlation between EPDS at gwk 14 and affective touch responses (orange). Cluster 1 = C1, Cluster 2 = C2, Cluster 3 = C3. (Figure should be printed in colour.)

Table 4 shows the correlation coefficients (r) and R^2 values computed using the EPDS values acquired at different time points and the HbT responses to affective touch for Clusters 1–3. The Pearson's correlation coefficient (r) is negative for all prenatal EPDS collection time points. Additional permutation tests revealed that there is statistically significantly greater R^2 for prenatal EPDS average than for gwk 24 in Cluster 1 ($p = 0.017$*), while no statistically significant differences were found between the R^2 values for the other individual time points. In Cluster 1, the R^2 for affective touch and prenatal EPDS at gwk 34 was almost statistically significantly greater than R^2 for affective touch and postnatal EPDS at six months post-partum ($p = 0.052$). In Cluster 2, the R^2 values for affective touch responses and EPDS at gwk 14 ($p = 0.047$*) and prenatal average ($p = 0.036$*) were greater than for gwk 24. In Cluster 3, the R^2 values for affective touch vs. prenatal EPDS average ($p = 0.0089$*) and EPDS at gwk 34 ($p = 0.020$*) were greater than for EPDS at six months post-partum, and the R^2 value for prenatal EPDS average was greater than the corresponding value for EPDS at gwk 24 ($p =$ 0.0067*).

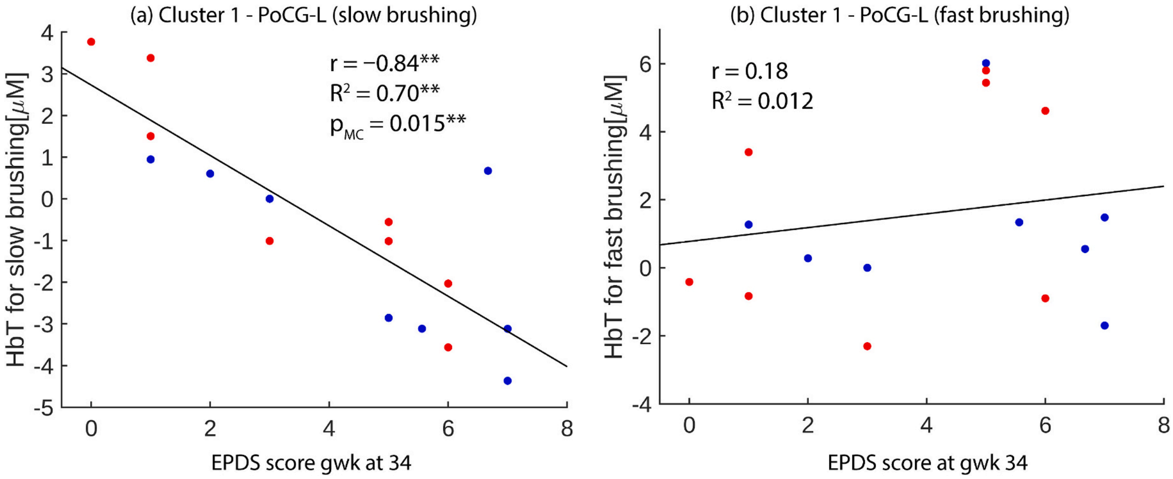

Fig. 3. Scatter plots for EPDS on the x axis and average HbT response in Cluster 1 on the y axis to (a) slow and (b) to fast brushing. Cluster 1 resides in the Postcentral gyrus (PoCG-L). (See Tables 3 and 4). r = Pearson's correlation coefficient; R^2 = coefficient of determination; p_{MC} = p-value from `corrcoef` multiplied with N_{MC} = 163 (based on the Bonferroni method for multiple comparison correction). Red dots = female, blue dots = male. (Figure should be printed in colour).

Table 3

Cluster analysis results for individual EPDS collection time points. The first column shows the cluster location and volume, along with the lead statistical test. Superior temporal gyrus left = STG-L; Middle temporal gyrus left = MTG-L; Postcentral gyrus left = PoCG-L. The second and third columns show Pearson's correlation coefficient (r), 95 % confidence interval (CI), and *p*-value between EPDS and HbT responses to affective and non-affective touch, followed by the coefficient of determination (R^2) and its p-value. Statistical significance of the difference between R^2 values for affective and non-affective touch (vs. the tested prenatal EPDS value) is given in the fourth column. The overall R^2 for the multiple regression model, regressor-specific coefficients (β) and corresponding *p*-values for the multiple regression analysis with prenatal EPDS (lead test variable) and postnatal EPDS at six months post-partum as a second regressor are given in the fifth column (see Sec. 2.4.1). Statistically significant correlations are marked with * when $p < 0.05$ and with ** and in **bold** when $p < 0.05/N_{MC}$ based on the Bonferroni principle with $N_{MC} = 163$. PA = prenatal average (over gwks 14, 24, and 34), pp = post-partum, gwk = gestational week.

Region	Affective vs. prenatal EPDS	Non-affective vs. prenatal EPDS	R^2(affective) = R^2(non-affective)?	Overall model R^2; β and p-values for individual regressors in multiple regression analysis
Cluster 1 PoCG-L Vol 113 mm^3 L1 Lead test: Affective touch vs. EPDS gwk 34 (N = 16) (Figs. 2a–b, 3a–b, 4)	**$r = -0.84**$** CI = [−0.94, −0.57] $p = 9.4 \times 10^{-5}**$ $p_{MC} = 0.015**$ **$R^2 = 0.70**$** $p = 2 \times 10^{-4}**$	r = 0.18 CI = [−0.37,0.63] p = 0.52 $R^2 = 0.012$ p = 0.51	$p < 10^{-4}**$	**$R^2 = 0.71**$** $\beta_{gwk\ 34} = -0.80*$, $p = 5.8 \times 10^{-4}*$ $\beta_{6\ mo\ pp} = -0.11$, p = 0.52
Cluster 2 STG-L, MTG-L Vol 82 mm^3 L3 Lead test: Affective touch vs. EPDS gwk 14 (N = 16)	$r = -0.76*$ CI = [−0.92, −0.40] $p = 0.0010*$ $p_{MC} = 0.17*$ $R^2 = 0.58*$ $p = 0.0014*$	r = −0.31 CI = [−0.71,0.24] p = 0.27 $R^2 = 0.094$ p = 0.27	p = 0.40	$R^2 = 0.66*$ $\beta_{gwk\ 14} = -0.58*$, $p = 0.0017*$ $\beta_{6\ mo\ pp} = -0.27$, p = 0.12
Cluster 3 PoCG-L Vol 64 mm^3 L1 Lead test: Affective touch vs. Prenatal EPDS average (N = 15)	$r = -0.81*$ CI = [−0.94, −0.49] $p = 4.2 \times 10^{-4}*$ $p_{MC} = 0.068*$ **$R^2 = 0.66**$** $p = 2 \times 10^{-4}**$	r = 0.13 CI = [−0.43, 0.62] p = 0.65 $R^2 = 0.018$ p = 0.64	$p < 10^{-4}**$	$R^2 = 0.66*$ $\beta_{PA} = -0.89*$, $p = 0.0013*$ $\beta_{6\ mo\ pp} = -0.021$, p = 0.91

Table 4

Pearson's correlation coefficients (r) and coefficients of determination (R^2) for HbT responses to affective touch in Clusters 1–3 in the two-year-old children and maternal EPDS values at different time points. CI = 95 % confidence interval for Pearson's correlation coefficient. * = statistically significant correlation with $p < 0.05$ without multiple comparison correction. ** and **bolded** = statistically significant correlation with ($p \times N_{MC}$) < 0.05 after correction for multiple comparisons using the Bonferroni method ($N_{MC} = 163$). Gwk = gestational week.

Region	Gwk 14 (N = 16)	Gwk 24 (N = 15)	Gwk 34 (N = 16)	Prenatal average (gwks 14, 24 & 34) (N = 15)	Postnatal (N = 16)
Cluster 1 (Figs. 2, 3 and 4)	$r = -0.66*$ CI = [−0.87, −0.22] $p = 0.0080*$ $R^2 = 0.43*$ $p = 0.0062*$	r = −0.51 CI = [−0.82,0.027] p = 0.062 $R^2 = 0.26$ p = 0.064	**$r = -0.84**$** CI = [−0.94, −0.57] $p = 9.4 \times 10^{-5}**$ **$R^2 = 0.70**$** $p = 2 \times 10^{-4}**$	$r = -0.79*$ CI = [−0.93, −0.45] $p = 7.3 \times 10^{-4}*$ $R^2 = 0.63*$ $p = 0.0018*$	r = −0.45 CI = [−0.78, 0.082] p = 0.093 $R^2 = 0.20$ p = 0.092
Cluster 2	$r = -0.76*$ CI = [−0.92, −0.40] $p = 0.0010*$ $R^2 = 0.58*$ $p = 0.0014*$	r = −0.50 CI = [−0.81, 0.045] p = 0.070 $R^2 = 0.25$ p = 0.075	$r = -0.57*$ CI = [−0.84, −0.087] $p = 0.025*$ $R^2 = 0.33*$ $p = 0.024*$	$r = -0.74*$ CI = [−0.91, −0.35] $p = 0.0023*$ $R^2 = 0.55*$ $p = 0.0028*$	r = −0.44 CI = [−0.78,0.094] p = 0.10 $R^2 = 0.19$ p = 0.10
Cluster 3	$r = -0.72*$ CI = [−0.90, −0.31] $p = 0.0037*$ $R^2 = 0.52*$ $p = 0.003*$	r = −0.52 CI = [−0.82,0.016] p = 0.057 $R^2 = 0.27$ p = 0.057	$r = -0.82*$ CI = [−0.94, −0.51] $p = 3.4 \times 10^{-4}*$ $R^2 = 0.67*$ $p = 6.0 \times 10^{-4}*$	$r = -0.81*$ CI = [−0.94, −0.49] $p = 4.2 \times 10^{-4}*$ **$R^2 = 0.66**$** $p = 2 \times 10^{-4}**$	r = −0.37 CI = [−0.72, 0.27] p = 0.28 $R^2 = 0.095$ p = 0.29

3.3. Results from ROI analysis

Table 5 shows the statistically significant findings from ROI analysis. The Precentral gyrus (PreCG-L) showed statistically significant negative correlations between child HbT responses to affective touch and prenatal maternal EPDS at gwk 14. In the Rolandic operculum (ROL-L) and secondary somatosensory cortex (SII-L) ROIs, a negative correlation was exhibited between child HbT responses to affective touch and maternal EPDS at gwk 14 as well as the mean prenatal EPDS. No statistically significant correlations were found between child HbT responses to non-affective touch and maternal prenatal EPDS scores. The R^2 values for affective touch (vs. maternal prenatal EPDS scores) were statistically significantly greater than for non-affective touch in all cases reported in Table 5. The reported results remain statistically significant ($p < 0.05$) when postnatal EPDS at 6 months post-partum is used as a second regressor (5th column of Table 5).

In Table 6, we show how Pearson's correlation coefficient (r) and coefficient of determination (R^2) vary for the different EPDS collection time points in ROIs with statistically significant correlations for at least one time point and HbT response to affective touch. We also performed additional permutation tests to compare the R^2 values across the different EPDS collection time points. In the Rolandic operculum (ROL-

Table 5

Results corresponding to regions of interest (ROI). Each region is designated a shorthand name (Rolandic operculum left = ROL-L; precentral gyrus left = PreCG-L; secondary somatosensory cortex left = SII-L) and indicated in the first column along with the volume of the region within the field-of-view (FOV) in mm^3, the time point giving statistically significant correlation between the child average total haemoglobin (HbT) response within the ROI and Edinburgh Postnatal Depression Scale (EPDS) data collected at the designated time point (or average over gwks 14, 24, and 34), and the number of mother-child dyads (N). The second and third columns give the values of Pearson's correlation coefficient (r) and coefficient of determination (R^2) for affective and non-affective touch, and the *p*-values indicating statistical significance of the correlation. The fourth column gives p-values for the difference between R^2 values between affective and non-affective touch. The overall R^2 for the multiple regression model, regressor-specific coefficients (β) and corresponding p-values for the multiple regression analysis with prenatal EPDS (lead test variable) and postnatal EPDS at six months post-partum as a second regressor are given in the fifth column (See Sec. 2.4.1). Underlining and * = statistically significant at $p < 0.05$ level (uncorrected). ** = statistically significant at $p < 0.05$ using Bonferroni correction with $N_{ROI} = 12$ regions. CI = 95 % confidence interval for Pearson's correlation coefficient, PA = prenatal average (over gwks 14, 24, and 34).

Region	Affective touch vs. prenatal EPDS	Non-affective touch vs. prenatal EPDS	R^2(affective) = R^2(non-affective)?	Overall model R^2; β and *p*-values for individual regressors in multiple regression analysis
PreCG-L Vol 3659 mm^3 Lead test: EPDS gwk 14 ($N = 16$)	$r = -0.53$* CI = [−0.81, −0.04] $p = 0.036$* $R^2 = 0.28$* $p = 0.038$*	$r = 0.11$ CI = [−0.41,0.57] $p = 0.69$ $R^2 = 0.012$ $p = 0.68$	p = 0.012*	$R^2 = 0.28$* $\beta_{gwk\ 14} = -0.17$*, $p = 0.042$* $\beta_{6\ mo\ pp} = 0.024$, $p = 0.76$
ROL-L Vol = 1427 mm^3 Lead test: EPDS gwk 14 ($N = 16$) (Fig. 5)	$r = -0.68$* CI = [−0.87, −0.24] $p = 0.0056$* $R^2 = 0.43$* $p = 0.0049$*	$r = -0.0057$ CI = [−0.50,0.49] $p = 0.98$ $R^2 = 3.3 \times 10^{-5}$ p = 0.98	$p = 0.0092$*	$R^2 = 0.43$* $\beta_{gwk\ 14} = -0.27$*, $p = 0.0076$* $\beta_{6\ mo\ pp} = 0.016$, $p = 0.86$
Lead test: Prenatal EPDS average ($N = 15$)	$r = -0.62$* CI = [−0.86, −0.16] $p = 0.013$* $R^2 = 0.39$* $p = 0.014$*	$r = 0.10$ CI = [−0.43,0.58] $p = 0.72$ $R^2 = 0.010$ p = 0.72	$p = 0.012$*	$R^2 = 0.43$* $\beta_{PA} = -0.38$*, $p = 0.011$* $\beta_{6\ mo\ pp} = 0.089$, $p = 0.39$
SII-L Vol = 598 mm^3 Lead test: EPDS at gwk 14 ($N = 16$)	r = −0.68** CI = [−0.88, −0.27] $p = 0.0040$** $R^2 = 0.46$* p = 0.0052*	$r = 0.085$ CI = [−0.43,0.56] $p = 0.75$ $R^2 = 0.0073$ p = 0.75	$p = 0.006$*	$R^2 = 0.48$* $\beta_{gwk\ 14} = -0.38$, $p = 0.054$ $\beta_{6\ mo\ pp} = -0.083$, $p = 0.49$
Lead test: EPDS prenatal average ($N = 15$)	$r = -0.65$* CI = [−0.87, −0.20] $p = 0.0094$* $R^2 = 0.42$* $p = 0.0091$*	r = 0.085 CI = [−0.45,0.57] $p = 0.76$ $R^2 = 0.0076$ $p = 0.77$	$p = 0.0032$**	$R^2 = 0.42$* $\beta_{PA} = -0.48$*, $p = 0.016$* $\beta_{6\ mo\ pp} = -0.0016$, $p = 0.99$

Table 6

Pearson's correlation coefficients (r) and coefficients of determination (R^2) for HbT responses to affective touch in regions of interest (ROIs) in the two-year-old children and maternal EPDS values at different time points. CI = 95 % confidence interval for Pearson's correlation coefficient. Underlining and * = statistically significant correlation with $p < 0.05$ without multiple comparison correction. ** = statistically significant correlation with ($p \times N_{ROI}$) < 0.05 after correction for multiple comparisons using the Bonferroni method ($N_{ROI} = 12$). Gwk = gestational week.

Region	Gwk 14 (N = 16)	Gwk 24 ($N = 15$)	Gwk 34 ($N = 16$)	Prenatal average (gwks 14, 24 and 34) (N = 15)	Postnatal (N = 16)
PreCG-L	r = −0.53* CI = [−0.81, −0.04] $p = 0.036$* $R^2 = 0.28$* $p = 0.038$*	$r = 0.15$ CI = [−0.40, 0.60] $p = 0.60$ $R^2 = 0.021$ p = 0.60	$r = -0.33$ CI = [−0.71,0.20] $p = 0.22$ $R^2 = 0.11$ p = 0.22	$r = -0.28$ CI = [−0.69,0.27] $p = 0.32$ $R^2 = 0.077$ $p = 0.31$	$r = 0.048$ CI = [−0.46, 0.53] $p = 0.86$ $R^2 = 0.0023$ p = 0.86
ROL-L	r = −0.68* CI = [−0.87, −0.24] $p = 0.0056$* $R^2 = 0.43$* $p = 0.0049$*	$r = -0.49$ CI = [−0.80,0.025] $p = 0.062$ $R^2 = 0.24$ $p = 0.064$	$r = -0.32$ CI = [−0.71,0.21] p = 0.22 $R^2 = 0.10$ p = 0.22	r = −0.62* CI = [−0.86, −0.16] $p = 0.013$* $R^2 = 0.39$* $p = 0.014$*	$r = 0.0040$ CI = [−0.49,0.50] $p = 0.99$ $R^2 = 1.6 \times 10^{-5}$ p = 0.99
SII-L	r = −0.68** CI = [−0.88, −0.27] $p = 0.0040$** $R^2 = 0.46$* $p = 0.0052$*	$r = -0.36$ CI = [−0.74,0.19] $p = 0.19$ $R^2 = 0.13$ p = 0.19	$r = -0.46$ CI = [−0.78,0.048] $p = 0.074$ $R^2 = 0.21$ $p = 0.075$	r = −0.65* CI = [−0.87, −0.20] $p = 0.0094$* $R^2 = 0.42$* $p = 0.0091$*	$r = -0.18$ CI = [−0.62,0.35] $p = 0.52$ $R^2 = 0.031$ p = 0.52

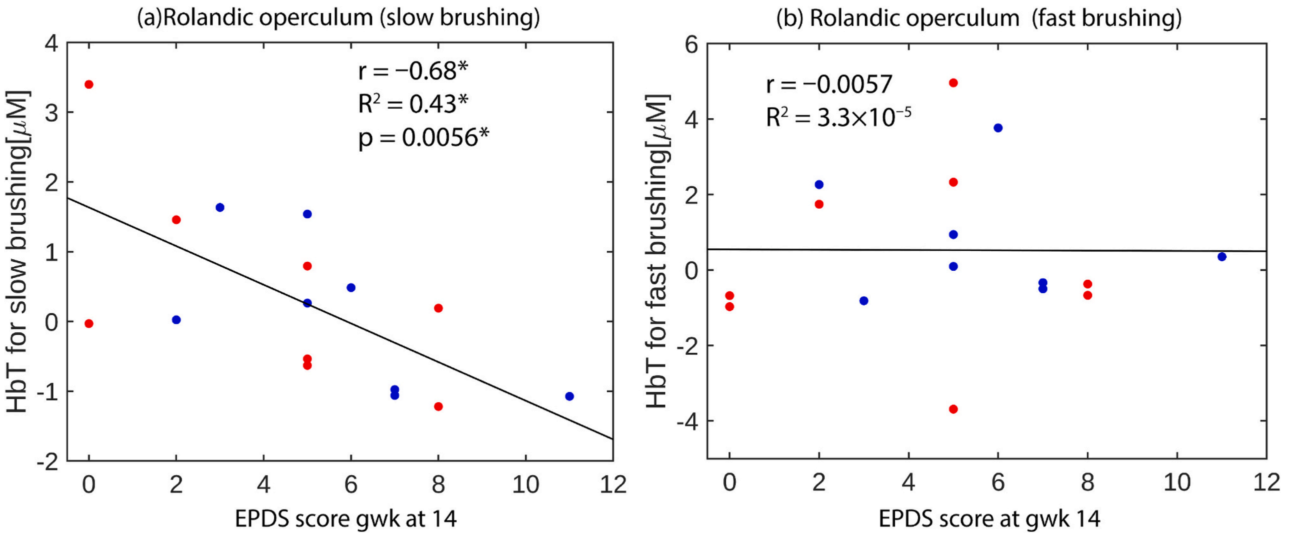

Fig. 5. Scatter plots for EPDS at gestational week 14 on the x axis and average HbT response to (a) slow brushing and (b) fast brushing in Rolandic operculum (ROL-L) on the y axis. Red dots = female, blue dots = male. (Tables 5 and 6.) (Figure should be printed in colour). r = Pearson's correlation coefficient; R^2 = coefficient of determination; p = p-value from `corrcoef`. (Figure should be printed in colour.)

L) ROI, the affective touch response has a significantly higher R^2 for EPDS at gwk 14 (p = 0.027*), gwk 24 (p = 0.0029**), prenatal average EPDS (p = 0.0063*) than EPDS at six months post-partum. In the Precentral gyrus (PreCG-L) ROI, the affective touch response was modelled by the EPDS at gwk 14 with a significantly higher R^2 than EPDS at gwk 24 (p = 0.0011**), gwk 34 (p = 0.012*), or prenatal average EPDS (p = 0.031*), and the R^2 was greater for EPDS at gwk 34 than gwk 24 (p = 0.025*) and greater for prenatal EPDS average than gwk 24 ($p = 1 \times 10^{-4}$). In the secondary somatosensory cortex (SII) ROI, the affective touch response was modelled significantly better (higher R^2) by prenatal EPDS average than at gwk 24 (p = 0.019*).

Finally, we show the correlation between EPDS at gestational week 14 and affective touch response in Rolandic operculum (ROL-L) as a scatter plot in Fig. 5.

4. Discussion

This study investigated the correlation between neural responses to affective and non-affective touch recorded from the left hemisphere using diffuse optical tomography (DOT) in two-year-old children and maternal self-reported depressive symptom (EPDS) scores at three different gestational time points. Affective touch was represented by slow brushing (3 cm/s) of the right forearm and non-affective touch by fast brushing (30 cm/s) of the same area. We hypothesized that prenatal depressive symptoms would be associated with altered activation/inactivation in response to affective touch. The depressive symptoms were within the range 0–11 with means 3.8–4.6 (on a scale 0–30) and most of the mothers would probably not be considered depressed in clinical practice. The results of the study should not be extrapolated to clinically depressed mothers and their children without further study.

We found a cluster with voxels residing in the left postcentral gyrus (primary somatosensory cortex or SI) which exhibited a negative correlation between child total haemoglobin responses to affective touch at two years of age and maternal EPDS scores at gestational week 34 and a corresponding partially overlapping cluster based on correlation with prenatal EPDS average over the requested questionnaire time points (14, 24, and 34 weeks). No corresponding statistically significant correlation with non-affective touch was found in these regions. The correlation between child response to slow brushing and prenatal depressive symptoms could not be explained by postnatal depressive symptoms of the mother. Additionally, we found a cluster with almost statistically significant correlation between affective touch responses and maternal prenatal symptoms at gestational week 14 close to the postcentral gyrus clusters but on the side of the temporal cortex, however, in that area, the variability of the affective touch responses across subjects explained by EPDS at gestational week 14 was not greater than for the non-affective touch response, thus we see qualitatively different behavior in the temporal cortex.

Using ROI analysis based on the automated anatomical labeling (AAL) regions and prior literature information regarding areas of the brain that process emotion, touch and affective touch, we found maternal EPDS at gestational week 14 to correlate negatively with child responses to affective touch in the precentral gyrus, Rolandic operculum and secondary somatosensory cortex (SII). Additionally, in the Rolandic operculum and SII, we found a negative correlation between prenatal average depressive symptoms and child brain responses to affective touch. The responses to non-affective touch did not correlate with prenatal depressive symptoms, and the R^2 values for affective touch were significantly greater than for non-affective touch. Including a postnatal EPDS as a second regressor did not appreciably alter the significance of the primary regressor (prenatal EPDS).

The primary somatosensory cortex (SI) is located in a ridge of the cerebral cortex known as the postcentral gyrus. While previous research indicates that the SI is primarily involved in the processing of non-affective touch in adults and young children (Cohen et al., 1991; Knecht et al., 2003; Lundblad et al., 2011; Maria et al., 2022; Tegenthoff et al., 2005), some studies find S1 also to be involved in the processing of affective touch (Gazzola et al., 2012; McCabe et al., 2008; Björnsdotter et al., 2014; Tuulari et al., 2019). Our findings suggest that exposure to prenatal maternal depressive symptoms may suppress the postcentral gyrus activation for emotional touch in an area near the SII but no similar effect was found for non-affective touch. In line with this thinking, individuals with autism spectrum disorder (ASD), who have challenges in emotional perception and processing, show an enhanced response to non-CT-targeted versus CT-targeted touch in S1 and reduced activation in response to CT-targeted touch in areas related to social emotional processing, when compared to typically developing children (Kaiser et al., 2016). This suggests an important role of the postcentral gyrus in affective touch processing and responses may vary based on overall functional connectivity with other networks. Furthermore, exposure to maternal perinatal anxiety at 19 weeks of gestation has been associated with gray matter volume reductions in the postcentral gyrus in addition to the prefrontal cortex, premotor cortex, medial temporal lobe, lateral temporal cortex, and cerebellum whereas in later pregnancy, anxiety at 24 and 31 weeks did not reveal such an association (Buss et al., 2010). This suggests early exposure may have a greater impact on fetal brain development.

The postcentral gyrus is normally expected to process both affective and non-affective touch, however, the affective touch processing in this area appears to be suppressed in the children of mothers who scored higher in the EPDS during pregnancy. Our findings follow the Developmental Origin of Health and Disease (DOHAD) hypothesis, where the intrauterine environment and maternal factors during pregnancy may affect the neurodevelopment of the fetus (Gluckman et al., 2010; Räikkönen et al., 2011; Van den Bergh, 2011) and these changes may continue to influence the child later in life. Sawyer et al., 2019 discussed the role of various epigenetic and molecular mechanisms such as glucocorticoid receptors and related genes, oxytocin, estrogen and immune pathways and their role in neuroplasticity that can carry forward the changes later in life (Sawyer et al., 2019). These molecular mechanisms ultimately are suggested to have effects on key brain functions and may manifest as structural and functional brain changes (Godfrey and Barker, 2001; Buss et al., 2012; Donnici et al., 2021). As reported in a large birth cohort, prenatal maternal depression is associated with increased functional connectivity of the amygdala with the left temporal cortex and insula in addition to medial orbitofrontal, bilateral anterior cingulate and ventromedial prefrontal cortices in the 6-month-old, an observation similar to findings on adolescent and adult subjects with major depressive disorder (MDD) (Qiu et al., 2015), whereas at four years of age, researchers of the same cohort noted decreased amygdala functional connectivity in girls (Soe et al., 2018). In another cohort, high level of anxiety during pregnancy was associated with gray matter density reduction in various regions of the brain and exposure to maternal depression in utero led to cortical thinning in 6–9-year-old children (Sandman et al., 2015). Taken together, these findings emphasize the importance of considering maternal mental health during pregnancy and the potential long-lasting effects it may have on the developing fetus, highlighting the need for early intervention and support for mothers-to-be.

Social touch is necessary for normal primate development; primates who are deprived of it have higher levels of anxiety and lower fertility than those who receive social touch on a regular basis (Jablonski, 2021). In a retrospective study of human adults who lacked early nurturing during childhood, tactile stimulation showed reduced sensitivity to affective touch (Devine et al., 2020). In a prospective cohort, exposure to postpartum maternal depression markedly increased the propensity of the child to develop Axis-I disorder at six and ten years, attenuated the level of oxytocin in the child, and there was decreased mother-child synchrony at six but not at ten years (Priel et al., 2019). At baseline, young kids 7–16 years with anxiety disorder had a lower level of oxytocin in comparison to healthy kids and showed increased oxytocin responses when exposed to increased affective touch (Lebowitz et al., 2017). Cortisol and oxytocin levels are altered in anxiety disorder, but affective touch may modulate the release of these hormones which may kindle the subjects for better social interaction (Li et al., 2019; Van Puyvelde et al., 2021).

We would like to encourage caution and avoid making strong conclusions about differences in sensitivity of the fetus to maternal depression in different phases of the pregnancy as more evidence is needed to make firm conclusions about this topic. Our results show areas where the neuronal responses to affective touch are sensitive to exposure to maternal depressive symptoms at gestational weeks 14 or 34, and in several clusters and ROIs the sensitivity to symptoms at gestational week 24 appears lower than at 14, 34, or the prenatal average. However, a larger data set would be needed to establish such differences with confidence. In Maria et al. (2020), maternal prenatal pregnancy-related anxiety (PRAQ) was found to affect infant responses to sad speech in the temporoparietal junction (TPJ) at gestational week 24 and less so at gestational week 34 (PRAQ data for gestational week 14 was not available) (Maria et al., 2020).

If those mothers who experience depressive symptoms, in general, have lower neural sensitivity to affective touch, the observed neural responses to affective touch in the children of those mothers could simply be an inherited trait rather than a result of an altered intrauterine environment. However, the reported symptoms changed over time during the period investigated and we could not get statistically significant correlations by using maternal depression scores averaged over all pre- and postnatal time points and child affective touch responses. Thus, the effects appear to be at least somewhat specific to the prenatal period and not likely a result of inherited lower sensitivity to affective touch from mother to child. A larger data set would be needed to investigate the effects of postnatal depression.

The precentral gyrus is predominantly involved in motor activation in the contralateral side of the body. Positive or reward stimuli have been shown to motivate people to take action (Roesch and Olson, 2003). The observation of negative stimuli also stimulates cortical regions related to motor function (Grezes et al., 2007; Kveraga et al., 2015; Portugal et al., 2020). These activations in motor response may arise due to body expression of negative emotional reactions (Grezes et al., 2013). In general, adults with MDD had lower brain surface area and gray matter volume in the precentral gyrus (Schmaal et al., 2017). Furthermore, percental gyrus shows increased regional homogeneity in depression in adolescents vs. controls (Mao et al., 2020) and increased spontaneous neural activity in peripartum depression (Che et al., 2020).

Rolandic operculum located in Brodmann area 43 is involved in various higher-level cognitive processing, including emotional and music processing (Koelsch et al., 2006) and social touch (Rizzolatti et al., 2021). Lesions in the right Rolandic operculum are associated with high apathy, depression, anxiety, and perceived stress (Sutoko et al., 2020), whereas the right Rolandic operculum shows increased connectivity in children with obsessive-compulsive disorder (Weber et al., 2014). Patients with post-traumatic depression displayed increased connectivity between the insula and a region encompassing the Rolandic operculum and the superior temporal cortex and reduced connectivity between the thalamus and the dorsolateral prefrontal cortex (Moreno-Lopez et al., 2016). Patients carrying the high-risk allele of the FK506 binding protein 51 (FKBP5) gene (linked to MDD) demonstrated decreased activity in the Rolandic operculum, in addition to Heschl gyrus, insula, parahippocampal gyrus, posterior cingulate cortex, and inferior frontal gyrus during an emotional attention task (Tozzi et al., 2016).

Prenatal EPDS scores showed a correlation with infants' affective brain responses. This may suggest that maternal depressive symptoms not only affect the mother but could have negative consequences on emotional fetal development, including potential impacts on key developmental regions of the brain. Thus, our findings further underline the importance for screening pregnant women and providing appropriate treatment. Furthermore, exposure to maternal depressive symptoms during pregnancy is one vulnerability factor to be identified and specifically it may be relevant for the development of emotion regulation systems.

If the suppressed affective touch responses in the children are associated with reduced emotional reward from the mother's affective touch in the prenatally depressed mothers' offspring, this could lead to increased stress in the child and potentially contribute to the adverse developmental outcomes reported in the literature (Lautarescu et al., 2020).

Future studies could benefit from using time- or frequency-domain data types for the dynamic imaging problem and a larger number of sources and detectors, which could potentially improve image quality and depth resolution. Additionally, conducting larger studies with older children could shed light on whether these early brain responses persist over time or if there are additional changes not found in the present study. Finally, studies which include both larger sample sizes in functional neuroimaging and follow-up behavioural studies could allow linking the functional changes in the brain with psychosocial development.

4.1. Limitations

One limitation of our study was the moderate sample size which affects our ability to detect smaller effects and makes it difficult to make firm conclusions about the possible specificity of the effect to particular time points. DOT is more sensitive to superficial cortical regions than deeper areas and our knowledge of the optical structure of the probed tissue is imperfect. Despite these limitations, we observed robust negative correlations between maternal prenatal depressive symptoms and affective touch responses in the parietal cortex of two-year-olds.

5. Conclusions

Affective touch is a primal form of mother-child interaction. In this work, we studied the relationship between cortical hemodynamic responses to affective touch at two years of age and maternal self-reported prenatal depression scores at gestational weeks 14, 24 and 34. The total haemoglobin concentration responses were imaged with diffuse optical tomography over the left hemisphere, contralaterally to the simulated right dorsal forearm. Areas in the parietal cortex including postcentral gyrus, Rolandic operculum, secondary somatosensory cortex, and precentral gyrus exhibited negative correlations between prenatal depressive symptom scores and child neural responses to affective touch. The relationship between early prenatal depressive symptoms (reported at gestational week 14) and affective touch was evident in the lower lip of the parietal cortex (Rolandic operculum and secondary somatosensory cortex) while in clusters in the primary somatosensory cortex in the Postcentral gyrus, the depressive symptoms averaged over the prenatal period and at gestational week 34 correlated negatively with affective touch responses in the children. The statistical significance of the correlations between affective touch responses and prenatal EPDS remained when EPDS scores from six months postpartum were added as a postnatal regressor. None of the aforementioned clusters or ROIs showed a significant correlation with non-affective touch responses. These results suggest that maternal prenatal depressive symptoms could be associated with altered responses to affective touch in young children and that these effects can be imaged successfully with diffuse optical tomography in toddlers. Although we lack complete behavioural follow-up data on the children whose affective touch responses were investigated in the present study, suppressed affective touch responses in the offspring could be part of the mechanism which links maternal prenatal stress with increased stress in the children and subsequent risk of anxiety and depression.

CRediT authorship contribution statement

Shashank Shekhar: Writing – review & editing, Writing – original draft, Investigation, Funding acquisition, Data curation. **Pauliina Hirvi:** Writing – review & editing, Writing – original draft, Visualization, Software, Methodology, Funding acquisition, Formal analysis. **Ambika Maria:** Writing – review & editing, Investigation, Funding acquisition, Data curation. **Kalle Kotilahti:** Writing – review & editing, Software, Resources, Methodology, Investigation, Formal analysis. **Jetro J. Tuulari:** Writing – review & editing. **Linnea Karlsson:** Writing – review & editing, Supervision, Resources, Funding acquisition, Conceptualization. **Hasse Karlsson:** Writing – review & editing, Supervision, Resources, Project administration, Funding acquisition, Conceptualization. **Ilkka Nissilä:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

None.

Acknowledgements

We would like to thank the participating families for their patience and time, and Eija Jossandt and Jussi Kasurinen for their help during the experiments. The Monte Carlo simulations were carried out using computer resources of the Aalto University School of Science "Science-IT" project.

Role of the funding source

This work was supported by the Academy of Finland (projects 269282, 273451, and 303937 (to IN); 134950 (to HK); 253270 (to HK); 325292 (Profi5/LK); 336788 and 336789 (to PH)), Päivikki and Sakari Sohlberg Foundation (to IN), Jane and Aatos Erkko Foundation (to HK), Signe and Ane Gyllenberg Foundation (to HK, LK), State Research Grant (EVO) (to HK, LK), Vilho, Yrjö and Kalle Väisälä Foundation of the Finnish Academy of Science and Letters (to PH), Alfred Kordelin foundation (to PH), the Finnish Society of Sciences and Letters 2012 (to SS), The National Graduate School of Clinical Investigation (VKTK) 2012 (to SS), and the Research Council of Finland (Flagship of Advanced Mathematics for Sensing, Imaging, and Modeling grant 359181). The funding sources had no involvement in the study design, collection, analysis or interpretation of data, in the writing of the report or the decision to submit the article for publication.

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