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RESEARCH ARTICLE

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Significant increases of the amygdala between immediate and late postpartum: Pronounced effects within the superficial subregion

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Abstract

Research exploring the underlying neuroanatomical correlates of early motherhood seems to suggest that the period after giving birth is marked by tissue increases in the mother's brain. While some studies point to the amygdala as one of the areas undergoing postpartum changes, existing analyses did not discriminate between the different subregions of this functionally heterogeneous structure. Thus, to further extend this understudied field of research and to better understand the potential role of the amygdala when transitioning to motherhood, we applied an advanced region-of-interest technique that enabled us to analyze the amygdala as a whole as well as its different subareas, specifically the left and right centromedian (CM), laterobasal (LB), and superficial (SF) regions. Comparing the brains of 14 healthy women between immediate postpartum (within 1–2 days of childbirth) and late postpartum (at 4–6 weeks after childbirth), we revealed increases of the amygdala. However, effects manifested differentially across subareas, with particularly strong effects for the SF region, moderate effects for the CM region, and no effects for the LB region. These findings might reflect region-specific adaptations of the mother's brain tuning into the distinct and ever-changing needs of a newborn, either as a cause for it or as a consequence thereof.

KEYWORDS

amygdala, anxiety, gray matter, MRI, postpartum, pregnancy

1 | INTRODUCTION

Postpartum research in humans points to significant structural changes in the mother's brain after giving birth (Barba-Muller et al., 2019; Carmona et al., 2019; Hoekzema et al., 2017; Kim et al., 2010; Lisofsky et al., 2019; Luders et al., 2018, 2020; Martinez-Garcia et al., 2021; Oatridge et al., 2002; Sacher et al., 2020). The current study seeks to extend this field of study by conducting a region-of-interest analysis with a particular focus on the amygdala, which has been demonstrated to play a significant role in the circuit for maternal behavior and responses as well as for early infant–parent interactions and attachments (Numan et al., 2010; Paul et al., 2019; Swain et al., 2007).

While the animal literature points to an important role of the amygdala in the framework of pregnancy and motherhood, there is a lack of neuroimaging research targeting the structure of the postpartum

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amygdala in humans. However, significant changes of the amygdala—in addition to other brain regions—were observed when conducting nontargeted analyses. Kim et al. (2010) compared voxel-wise gray matter in 19 women between 2–4 weeks and 3–4 months after giving birth, and reported significant increases in a cluster that included the left and right amygdala. They also observed that the increased gray matter within the amygdala (among other regions) was associated with the mother's positive perception of her baby. The findings of the postpartum tissue increase were confirmed by Luders et al. (2020) when comparing voxel-wise gray matter in 14 women between 1–2 days and 4–6 weeks after giving birth. Note, although the amygdala was not explicitly mentioned in the latter article, significant effects within the amygdala were evident within both hemispheres, as shown Figure 1.

Altogether, these findings suggest that the amygdala is a relevant structure when exploring the underlying neuroanatomical correlates of early motherhood. However, it is important to remember that the amygdala contains different subregions, each with their own cytoarchitectonic properties, functional specialization, and development (Amunts et al., 2005; Bzdok et al., 2013; Kedo et al., 2018; Yilmazer-Hanke, 2015). Thus, the main goal of our study was to investigate changes in amygdala volume between immediate and late postpartum while discriminating between centromedian (CM), laterobasal (LB), and superficial (SF) areas (Amunts et al., 2005; Kedo et al., 2018), in addition to examining the amygdala as a whole. We expected to find increases in amygdala volume, but possibly with different effects in its subregions.

In addition to these main analyses, we conducted a set of supplemental analyses examining links between the amygdala, anxiety, and hormone levels based on the following premises: The amygdala is known to be involved in the processing of emotions in general and also constitutes a key element of the anxiety circuitry (Amano et al., 2011; Babaev et al., 2018; Bzdok et al., 2013; Costafreda et al., 2008; LeDoux, 2000; Yilmazer-Hanke, 2015). Given that postpartum anxiety is not uncommon (Pawluski et al., 2017), the question arises whether possible changes in the anatomy of the amygdala as a whole (or any of its subregions) are associated with changes in state anxiety. In addition, given that the amygdala has been reported to undergo changes in steroid hormone receptor expression during transition to motherhood (Pereira & Ferreira, 2016), it remains to be explored whether amygdala changes are correlated with hormonal changes, with a particular focus on progesterone and estrogen. Last but not least, given that postpartum anxiety itself has been linked to altered steroid hormone levels (Lonstein, 2007), it also seems worth investigating whether anxiety changes are correlated with hormone changes.

Significance

Analyzing the brains of 14 healthy women in a longitudinal study, we revealed increases of the amygdala at late postpartum compared to immediate postpartum. Interestingly, effects manifested differentially across the different subareas of the amygdala, with strong increases of the superficial region, moderate increases of the centromedian region, and no changes of the laterobasal region. These findings might reflect region-specific adaptations of the mother's brain.

2 | METHODS

2.1 | Study sample and data collections

Our study included 14 healthy postpartum women between 25 and 38 years of age (mean ± *SD*: 32.8 ± 4.0 years), recruited from the maternity ward of the Department of Obstetrics and Gynecology at Uppsala University Hospital (Sweden). For half of the women ($n = 7$), it was a first-time delivery. For all of the women ($n = 14$), it was a singleton pregnancy, with uncomplicated delivery ($n = 9$ vaginal; $n = 5$ caesarean). All women had at least one night of sleep following delivery and were breastfeeding at the time of the late postpartum brain scan. Exclusion criteria were newborn admission to the intensive care unit, any postpregnancy complications, depression or anxiety disorders according to the Swedish version of the Mini International Neuropsychiatric Interview (Sheehan et al., 1998), contraindications to magnetic resonance imaging, and treatment with hormonal compounds and/or psychotropic drugs within 3 months prior to brain scanning. For additional sample characteristics, see Table 1.

Hormonal measures, structural brain images, as well as state and trait anxiety measures were collected at immediate and late postpartum, as detailed below. All procedures were approved by the Regional Ethical Review Board, Uppsala (Sweden), and all participants provided written informed consent.

2.2 | Hormonal data

Blood was drawn approximately 20 minutes prior to each brain scanning session. As previously described (Gingnell et al., 2015; Luders et al., 2018), serum progesterone and estradiol levels were analyzed by competitive immunometric electrochemical luminescence using a Cobas e601 analyzer and Cobas Elecsys estradiol and progesterone reagent kits (Roche Diagnostics, Bromma, Sweden). The measurement intervals for progesterone and estradiol were 0.1–191 nmol/l and 18.4–15,781 pmol/l, respectively. The intra-assay coefficients of variation for progesterone were 2.2% at 2.4 nmol/l and 2.8% at 31.6 nmol/l; for estradiol they were 6.8% at 85.5 pmol/l and 2.8% at 1,640 pmol/l.

2.3 | Brain data

The original aim of the data collection was to conduct a study on postpartum emotion reactivity using functional magnetic resonance imaging (Gingnell et al., 2015). However, in addition to the functional brain images of interest, structural brain images were acquired by default, both at immediate and late postpartum. These structural brain images

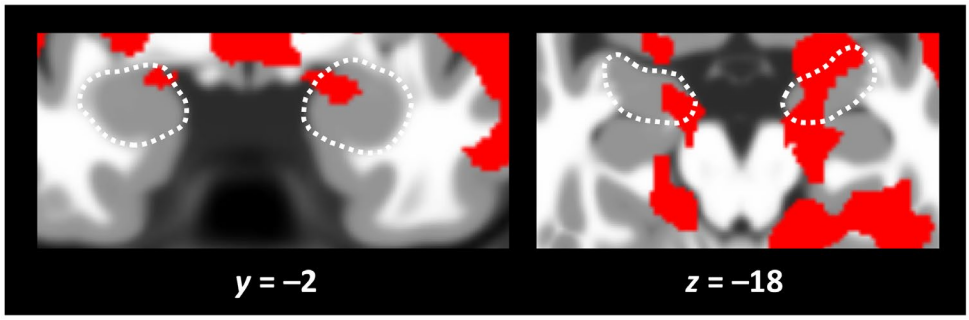

FIGURE 1 Voxel-based findings in the amygdala. A prior study investigating the current sample of 14 women using voxel-based morphometry (VBM) revealed a significant increase in voxel-wise gray matter at late postpartum (4–6 weeks after giving birth) compared to immediate postpartum (1–2 days after giving birth). The red significance cluster—displayed on coronal and axial sections of the MNI single-subject template at $y = -2$ and $z = -18$, respectively—emerged at a threshold of $p \leq 0.05$, family-wise error corrected. The dotted white contour outlines the amygdala. The findings of this VBM study (Luders et al., 2020) were reported at stricter thresholds of $p \leq 0.01$ as well as $p \leq 0.001$, family-wise error corrected. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 1 Sample characteristics ($n = 14$)

Caucasian	$n = 14$ (100%)
Nordic origin	$n = 13$ (92.9%)
Married or cohabiting	$n = 13$ (92.9%)
University education	$n = 11$ (78.6%)

are the basis of the current study. They were acquired on a Philips Achieva 3T-X MRI system (R2.1.3) using a phase-sensitive inversion recovery (PSIR) T1-weighted sequence and the following parameters: 5,700 ms repetition time, 15 ms echo time, 400 ms inversion time, 90° flip angle, 23 cm field of view, and $0.45 \times 0.45 \times 2.0$ mm^3 voxel size.

The structural brain images were processed in Matlab (http://www.mathworks.com/products/matlab) using the VBM8 toolbox (http://dbm.neuro.uni-jena.de/vbm) and a workflow optimized for longitudinal processing. More specifically, for each woman, the images from immediate postpartum (time point 1) and late postpartum (time point 2) were first bias-field corrected and halfway-registered using rigid body transformations. In addition, a subject-specific mean image was calculated from both time points. Subsequently, the registered images from time points 1 and 2 as well as the mean image were tissue-classified into gray matter, white matter, and cerebrospinal fluid, while accounting for partial volume effects (Tohka et al., 2004). The remainder of the processing stream was then conducted using the gray matter segments from both time points and the mean thereof.

First, the gray matter segments of the mean images were spatially normalized to the DARTEL template using linear transformations and nonlinear warping (Ashburner, 2007). Then, the resulting normalization parameters were applied to the gray matter segments of time points 1 and 2, followed by modulating the normalized gray matter segments of time points 1 and 2 (Ashburner & Friston, 2000; Good et al., 2001; Kurth et al., 2017, 2018). Finally, a difference image was created by subtracting the subject-specific modulated, normalized gray matter segments at time point 1 from time point 2. This image reflects the difference in voxel-wise gray matter between immediate and late postpartum, with positive values indicating an increase and negative values indicating a decrease.

The difference images were multiplied with cytoarchitectonic probabilities (Amunts et al., 2005; Eickhoff et al., 2005; Kedo et al., 2018) of the CM, LB, and SF regions in each hemisphere (see Figure 2), as detailed elsewhere (Kurth et al., 2018, 2019). Volume changes in these probability-weighted subregions as well as the amygdala (AMY) as a whole (AMY = CM + LB + SF) were then calculated in cubic millimeters and entered as the dependent variables in the statistical model.

2.4 | Statistical analyses

One-sample *t*-tests were applied to detect possible changes in amygdala volumes and subvolumes. Significance levels were corrected for multiple comparisons by controlling the false discovery rate (FDR; Hochberg & Benjamini, 1990). In addition to this main analysis, we conducted three supplemental analyses calculating Pearson correlations between (I) changes in amygdala (sub)volumes and changes in state anxiety, (II) changes in amygdala (sub)volumes and changes in hormonal levels, and (III) changes in state anxiety and changes in hormonal levels. Given the exploratory nature of these supplemental analyses, we abstained from applying corrections for multiple comparisons.

State and trait anxiety measures were collected using the State-Trait Anxiety Inventory (Spielberger et al., 1983). Given that interindividual differences in trait anxiety might affect the magnitude of potential changes in state anxiety, the anxiety-related correlation analyses I and III were conducted with and without covarying for trait anxiety. For the hormone-related correlation analyses II and III, the hormonal serum measures were converted into log10-scaled values in order to account for the large differences in values over time and variance across individuals. Since serum levels at immediate postpartum were not available for four women (Luders et al., 2018), all hormonal analyses were based on 10 women.

3 | RESULTS

3.1 | Main analysis

Regardless of whether corrections for multiple comparisons were applied or not, there were no significant amygdala *decreases* between immediate and late postpartum. In contrast, at uncorrected

levels, there were significant *increases* for the left SF, right SF, and right CM regions with large effect sizes. In addition, there was a trend toward significant increases for the left CM and right AMY regions, again with large effect sizes. However, only the effects within the left and right SF regions survived corrections for multiple comparisons. Cohen's *d* as well as statistical *T* and *p* values are provided in Table 2. The individual changes with respect to all volumes and subvolumes of the amygdala are visualized in Figures 3 and 4.

3.2 | Supplemental analysis I

There were no significant *positive* correlations between changes in volumes and subvolumes of the amygdala and changes in state anxiety. In contrast, there was a significant *negative* correlation for the right SF region, indicating that subvolume increases are accompanied by state anxiety decreases (see Figure 5). The effect was significant and large, regardless of whether we accounted for the variance explained by trait anxiety ($p = 0.024$; $r = -0.620$) or did not ($p = 0.031$; $r = -0.576$). With respect to state anxiety *per se*, there were no significant postpartum changes (Cohen's $d = -0.500$, $T = -0.901$, $p = 0.384$), with comparable measures (mean ± *SD*) at late postpartum (29.9 ± 7.0) and immediate postpartum (32.1 ± 7.3).

3.3 | Supplemental analyses II and III

There were no significant positive or negative correlations between changes in volumes and subvolumes of the amygdala and changes in hormonal measures. Similarly, there were no significant positive or negative correlations between changes in state anxiety and changes in hormonal measures, regardless of whether trait anxiety was included as a covariate or not. With respect to hormonal measures *per se*, there were significant postpartum changes, as reported elsewhere (Luders et al., 2018), with significantly lower serum concentrations of estradiol and progesterone at late compared to immediate postpartum.

4 | DISCUSSION

During the postpartum period, specifically within 4–6 weeks after giving birth, we observed an increase of the amygdala, which is in

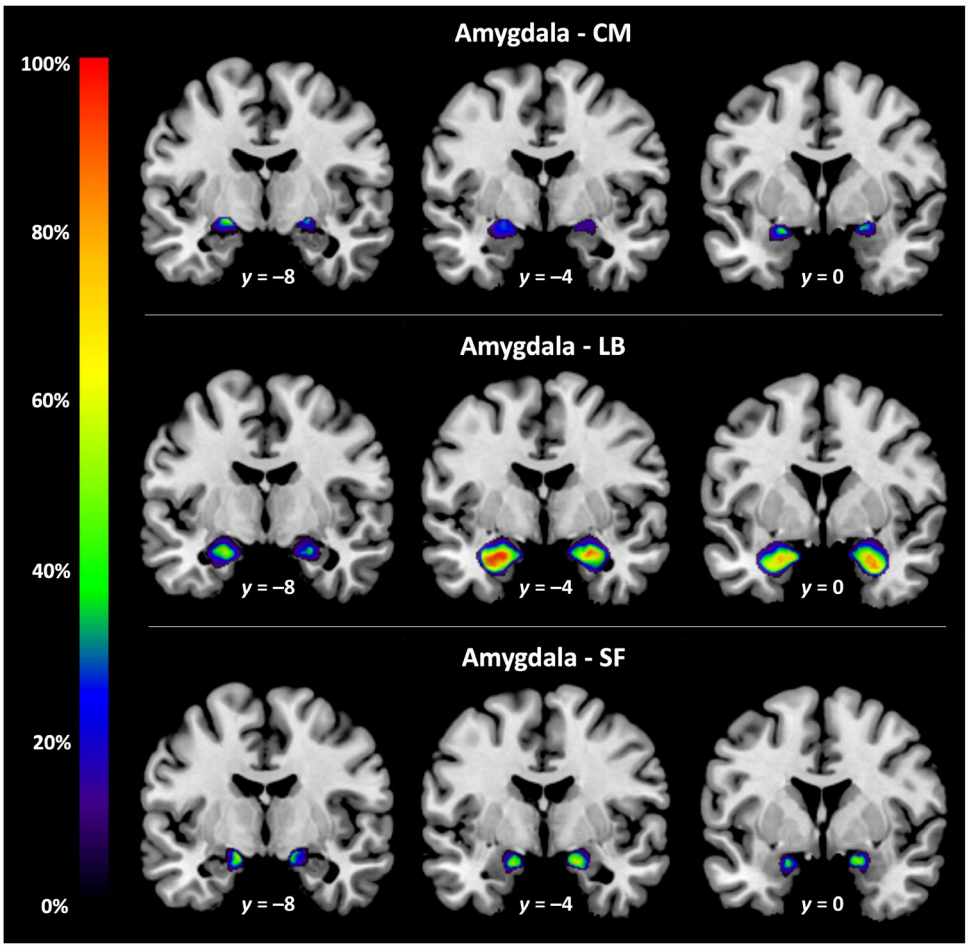

FIGURE 2 Cytoarchitectonic probabilities. Maps of the centromedian (CM), laterobasal (LB), and superficial (SF) subarea, displayed on coronal sections of the MNI single-subject template at $y = -8$, $y = -4$, and $y = 0$. The color bar encodes the regional probability as derived from cytoarchitectonic mapping in 10 *post mortem* brains (Amunts et al., 2005; Kedo et al., 2018). Figure reproduced with permission (Kurth et al., 2019). [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 2 Postpartum increases in volumes and subvolumes of the amygdala

	Left Hemisphere			Right Hemisphere		
Region	Cohen's *d*	*T*	*p*	Cohen's *d*	*T*	*p*
CM	0.898	1.618	0.065	1.053	1.898	0.040*
LB	−0.024	−0.043	0.517	0.432	0.778	0.225
SF	1.541	2.777	0.008**	1.496	2.696	0.009**
AMY	0.465	0.839	0.208	0.956	1.723	0.054

Abbreviations: AMY, amygdala as a whole; CM, centromedian region; LB, laterobasal region; SF, superficial region
*Significant, uncorrected ($p \leq 0.05$) **Significant, corrected ($p \leq 0.0125$)

line with previous observations (Kim et al., 2010; Luders et al., 2020). Interestingly, this effect was not evenly distributed across the entire amygdala but manifested differently in its subareas (strong effects for the SF region, moderate effects for the CM region, and no effects for the LB region). In addition, exploring possible links between amygdala changes and anxiety changes, we detected significant negative correlations for the right SF region (increases in volume are accompanied by decreases in state anxiety).

4.1 | Strong effects within the SF region

We observed significant increases of the left and right SF regions as well as significant negative links between right SF changes and anxiety changes. These findings are not surprising as the SF region is known to be a major moderator of social behavior (Aggleton, 2000; Goossens et al., 2009; Haruno & Frith, 2010; Hurlemann et al., 2008). The observed volume increase occurring postpartum may therefore be a consequence of (or cause for) the special attachment that forms between a mother and her newborn. This interpretation may also be supported by the reports of increased activation within the amygdala and uncus (which is located directly above the amygdala in close proximity to the SF region) when mothers were presented with photographs of their own infant versus other infants (Paul et al., 2019).

The SF region is also known to serve as a major sensory input station for the amygdala, receiving, for example, direct olfactory input unlike any of the other amygdala subareas (Yilmazer-Hanke, 2015). Olfactory input has been related to intraspecies communication and social functioning, not only in different mammals and primates, but also in humans (Bzdok et al., 2013; Moreno & Gonzalez, 2007; Scalia & Winans, 1975). Olfactory information may therefore play an important role postpartum (i.e., when the mother starts communicating and bonding with her newborn). In support of this assumption, it was demonstrated that experimental anosmia significantly reduces maternal behavior (Ehret & Buckenmaier, 1994). Although this latter study was conducted in mice, its outcomes may also be applicable to humans and, as such, corroborate our current findings of increasing SF regions after giving birth.

Finally, the SF region has been reported to process the widest range of emotions of all amygdala subregions (Bzdok et al., 2013). The observed volume increase of the SF region may thus also reflect heightened emotions during the postpartum period. While no data on positive emotions (e.g., happiness) have been collected in the current study, this interpretation seems to be in line with reported links between changes in amygdala volume and a mother's perception of her child (Kim et al., 2010); the more positively the infant was perceived, the larger the increase of the amygdala. As far as negative emotions (e.g., anxiety) are concerned, there were no significant changes of state anxiety during the postpartum period, but we detected negative correlations with the change in SF volume; volume increases are accompanied by anxiety decreases. This may come as a surprise as some studies have suggested that the amygdala processes valence in a bipolar manner, with positive stimuli leading to a decrease in amygdala activity, and negative stimuli to an increase in amygdala activity (Alexander et al., 2021; Burgdorf & Panksepp, 2006; Koepp et al., 2009). Thus, one might expect that an increase of anxiety (negative valence) is linked to an increase in amygdala volume. However, not all studies have confirmed the bipolar response model (e.g., Garavan et al., 2001). Moreover, those that confirmed the bipolar response model usually do not mention the SF, but rather the whole amygdala or other subregions, such as LB (e.g., Styliadis et al., 2014).

4.2 | Moderate effects within the CM region

We observed significant increases of the right CM region (and a trend toward significance for the left CM region), although effects did not survive corrections for multiple comparisons. Unlike the SF region, which serves as an input station, the CM region has been characterized as an output station, receiving and integrating information from the LB and SF regions and transmitting information to other brain regions, such as the cholinergic nuclei of the basal forebrain or the thalamus (Bzdok et al., 2013). Functionally, the CM region is involved in mediating autonomic and behavioral responses, as well as processing emotions (Bzdok et al., 2013; LeDoux, 2000; Pessoa, 2010; Yilmazer-Hanke, 2015). In addition, the CM region has been deemed important for the reallocation of attentional processes and for emotional learning (Yilmazer-Hanke, 2015), as well as for toning up (or down) levels of sensory stimuli and shaping environmental perception and attention (Hunter et al., 2010). Thus, increasing CM regions after giving birth (i.e., a period requiring drastic adaptations in terms

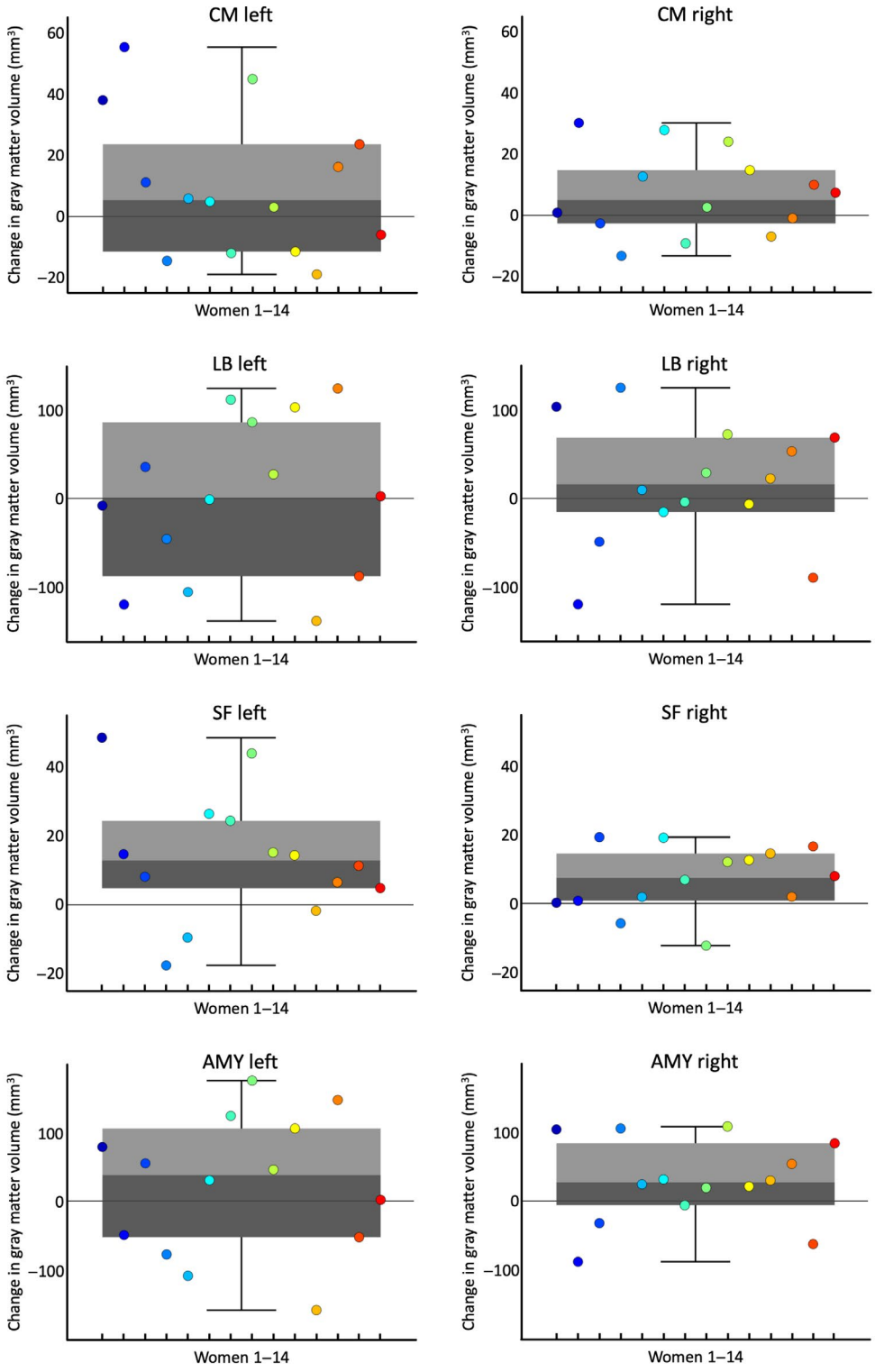

FIGURE 3 Changes in amygdala (sub)volumes between immediate and late postpartum. The left panel refers to the left hemisphere and the right panel refers to the right hemisphere. Positive numbers indicate volume increases (in mm^3) and negative numbers indicate decreases. Data are displayed as boxplots; the border in the middle demarcates the median. The gray-shaded areas contain the values between the 25th and 75th percentiles of the sample; the whiskers indicate the 1.5 interquartile range. The 14 color-coded markers correspond to the 14 women. AMY, amygdala as a whole; CM, centromedian; LB, laterobasal; SF, superficial subregions of the amygdala [Color figure can be viewed at wileyonlinelibrary.com]

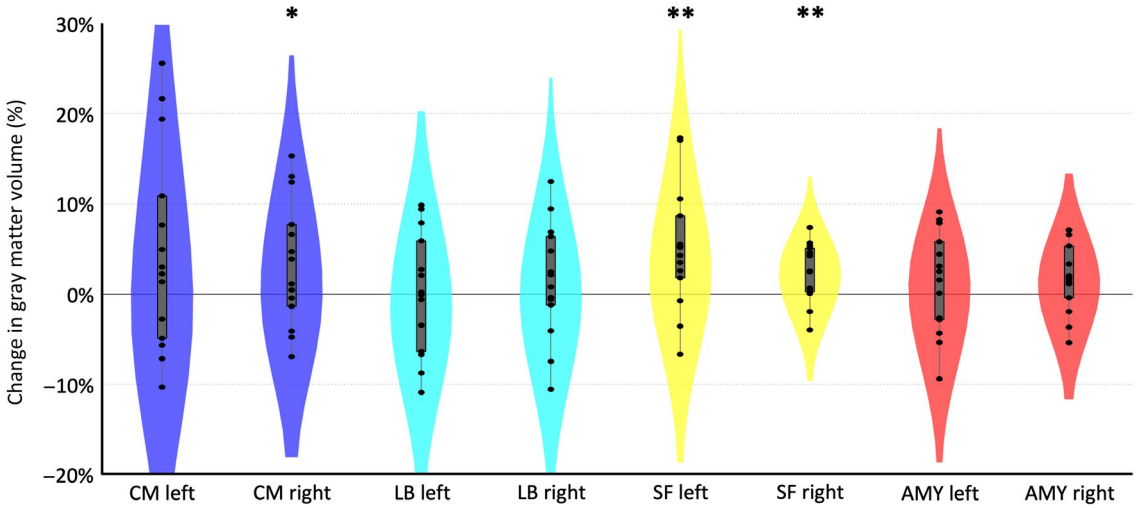

FIGURE 4 Percent change in amygdala (sub)volumes between immediate and late postpartum. Positive numbers indicate volume increases (in %) and negative numbers indicate decreases (in %). Data are displayed as violin plots. The gray center of each violin contains the values between the 25th and 75th percentiles of the sample. The 14 black oval markers correspond to the 14 women. The asterisks indicate significant increases between immediate and late postpartum (*uncorrected; **corrected). AMY, amygdala as a whole; CM, centromedian; LB, laterobasal; SF, superficial subregions of the amygdala [Color figure can be viewed at wileyonlinelibrary.com]

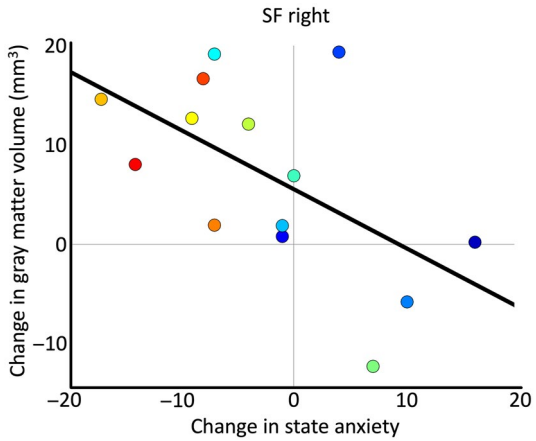

FIGURE 5 Correlations between changes in right SF subvolume and changes in state anxiety. The 14 color-coded markers correspond to the 14 women. The slope of the regression line indicates a negative correlation ($p = 0.031$; $r = -0.576$). Outcomes were comparable when including trait anxiety as a covariate in the statistical model ($p = 0.024$; $r = -0.620$); graph not shown. [Color figure can be viewed at wileyonlinelibrary.com]

of behavioral, autonomic, perceptual, attentional, and emotional patterns) seem plausible. While comparable data with respect to postpartum changes of the CM region do not exist, a resting-state study observed increased postpartum connectivity between the amygdala and the basal ganglia (Dufford et al., 2019), to which the CM region also projects (Bzdok et al., 2013). These findings seem to support our currently observed trends (albeit not significance) for increasing CM regions after giving birth. On this note, it is very likely that, with a sample size of 14, our study was simply underpowered, and that significance could have been established at corrected thresholds in a larger sample. More specifically, given the current effect sizes of $d = 0.898$ (left CM) and $d = 1.053$ (right CM), a sample of 22 women (of 19 women, respectively) would be required to achieve a p value of 0.0125 (which corresponds to an FDR-corrected p value of 0.05).

4.3 | No effects within the LB region

After giving birth, there were no significant changes of the LB region (and no significant links with state anxiety). Similar to the SF region, the LB region is known as a sensory input station (Yilmazer-Hanke, 2015), receiving signals from various cortical and subcortical regions (Bzdok et al., 2013; Yilmazer-Hanke, 2015), and integrating a wide range of perceptual information (Bzdok et al., 2013). LB has been demonstrated to play an important role in encoding valence (Brockett et al., 2021; Namburi et al., 2015, 2016), with distinct populations of neurons encoding negative valence (projecting predominantly to CM) and positive valence (projecting to the nucleus accumbens). The latter circuit in particular was shown to be critical for the expression of goal-directed maternal responses in postpartum rats (Numan et al., 2010). Thus, the null effect for LB might be surprising, but findings from animal research may not always directly translate to findings in humans. A similar explanation might exist for the missing link to state anxiety, especially since the LB region has been proposed to play an important role in fear processing and classic fear conditioning (Amano et al., 2011; Bzdok et al., 2013; Davis et al., 2010; LeDoux, 2000; Yilmazer-Hanke, 2015). An alternative explanation for this missing link might be that women in the current study were not characterized by excessive postpartum anxiety. It is certainly possible that the LB region would show significant changes and/or significant links to anxiety changes in women suffering from pathological levels of postpartum anxiety.

4.4 | No significant links to hormonal measures

Finally, we also examined if there were any links between hormonal changes and anxiety changes amygdala changes, respectively), but there were none. This might be a consequence of the massive plunge in hormone levels postpartum which stands in no relation to the minute changes in state anxiety (Gingnell et al., 2015), or perhaps only negligible relation to the amygdala changes, as currently observed. Nevertheless, given the small sample size in our study, it would be premature to draw a definite conclusion.

4.5 | Summary and implications for future studies

The present findings confirm and extend existing knowledge on postpartum effects within the amygdala by revealing tissue increases (rather than decreases) and differential effects within the CM, LB, and SF regions (rather than homogenous effects across the entire amygdala). These findings might reflect region-specific adaptations of the mother's brain tuning into the distinct and ever-changing needs of a newborn, either as a cause for it or as a consequence thereof.

However, given that the findings of the current study are based on 14 women, they require replication in larger samples. The current study compared data between two time points obtained relatively shortly after giving birth. Ideally, future studies will add additional data points several months (or even years) into motherhood as well as before pregnancy. Moreover, the current study acquired data with a voxel size of $0.45 \times 0.45 \times 2.0$ mm^3, which may compromise anatomic accuracies (Mulder et al., 2019). Thus, future studies may want to consider imaging protocols with small and isotropic voxel dimensions. It also seems worth emphasizing that the amygdala has been implicated in various functions, ranging from regulating emotions, to assigning value to states and stimuli, to making decisions, to selecting actions (Brockett et al., 2021), so future neuroimaging studies might want to obtain measures beyond anxiety to grasp the behavioral consequences (or correlates) of changing amygdala volumes when transitioning to motherhood. Finally, future region-of-interest studies may expand their focus from the amygdala to other brain regions (e.g., prefrontal cortex, hippocampus, thalamus, nucleus accumbens, bed nucleus of the stria terminalis) as implicated in prior research on maternal care (Paul et al., 2019) or reported in the framework of postpartum research using whole-brain voxel-based analyses (Hoekzema et al., 2017; Kim et al., 2010; Lisofsky et al., 2019; Luders et al., 2020).

DECLARATION OF TRANSPARENCY

The authors, reviewers and editors affirm that in accordance to the policies set by the *Journal of Neuroscience Research*, this manuscript presents an accurate and transparent account of the study being reported and that all critical details describing the methods and results are present.

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COMPLIANCE WITH ETHICAL STANDARDS

All procedures were approved by the Regional Ethical Review Board, Uppsala (Sweden), and all participants provided written informed consent.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

All authors listed contributed to this work: Conceptualization, E.L., F.K. and I.S.P.; Data Collection, M.G., J.E. and I.S.P.; Formal Analysis, F.K. and C.G.; Writing - Original Draft, E.L., F.K. and I.S.P.; Writing - Review & Editing (all authors); Visualization, F.K. and E.L.; Project Administration, I.S.P. and E.L.; Funding Acquisition, I.S.P.

DATA AVAILABILITY STATEMENT

The conditions of our ethical approval do not permit public archiving of anonymized study data. Readers seeking access to the data should contact the corresponding author. Access will be granted to named individuals after completion of a formal data sharing agreement, in accordance with ethical procedures governing the reuse of sensitive data.

PEER REVIEW

The peer review history for this article is available at https://publons.com/publon/10.1002/jnr.24855.

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