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# Adaptive and maladaptive microstructural remodelling of the maternal brain revealed by diffusion kurtosis imaging

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**Article**

**Keywords:** Postpartum depression, diffusion kurtosis imaging, maternal brain, microstructure, Edinburgh Postnatal Depression Scale

**Posted Date:** November 1st, 2026

**DOI:** https://doi.org/10.21203/rs.3.rs-9977087/v1

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**Additional Declarations:** No competing interests reported.

# Abstract

Postpartum depression (PPD) is a major maternal mental health concern that may arise during neurobiological and emotional adaptation. Alterations in these adaptive processes may contribute to depressive symptom vulnerability; however, the neurobiological basis of postpartum brain adaptation remains unclear. We investigated microstructural brain remodelling in postpartum women using diffusion kurtosis imaging (DKI) and evaluated its association with Edinburgh Postnatal Depression Scale (EPDS) scores. We compared brain magnetic resonance imaging findings between 15 women one month postpartum and 10 nulliparous women without psychiatric disorders. Tract-based spatial statistics and regions of interest were analysed using diffusion tensor and kurtosis metrics. Compared with nulliparous women, postpartum women showed significantly lower mean and axial diffusivity values in white matter regions, including the frontal lobe, basal ganglia, and corticospinal tract. The posterior insular cortex showed increased mean and radial kurtosis, whereas the putamen demonstrated decreased diffusivity. EPDS scores showed positive correlations with kurtosis metrics in the amygdala and negative correlations with diffusivity metrics in the hypothalamus. These findings suggest that the postpartum brain undergoes coordinated microstructural remodelling involving emotional regulation, stress response, and maternal behavioural adaptations. Thus, DKI may provide an objective neuroimaging biomarker for identifying maladaptive postpartum brain changes associated with depressive symptoms.


# Introduction

Postpartum depression (PPD), defined as the onset of depressive episodes after childbirth, develops at a critical juncture in a woman's life and can persist for extended periods[1, 2]. Maternal mental health has become an increasingly important public health concern in Japan, where suicide has emerged as the leading cause of maternal death since 2020[3], necessitating a paradigm shift toward more robust mental health support. Reflecting this urgency, the Japan Association of Obstetricians and Gynaecologists released a 2023 safety recommendation advocating comprehensive biopsychosocial (BPS) assessment for expectant mothers[3]. Moreover, the year-on-year rise in child abuse consultations[4] also underscores the need to address maternal mental health, as it directly influences parental nurturing capacity, infant attachment, and broader family outcomes[5].

Globally, PPD affects a substantial proportion of postpartum women. Wang et al. reported a pooled prevalence of 17.22% (95% CI 16.00–18.51) based on 565 studies across 80 countries[6]. While the prevalence is reported to be between 10% and 15% in developed countries[7], studies in Japan indicate that it affects approximately 15% of postpartum women[8]. Because PPD may contribute to maternal outcomes, including suicide, early detection and appropriate interventions through comprehensive BPS assessment are critical.

The Edinburgh Postnatal Depression Scale (EPDS) is widely used for PPD screening and has improved detection rates in clinical practice[9]. However, despite its advantages of simplicity, non-invasiveness, and cost-effectiveness, the EPDS remains a subjective self-reported assessment tool with limited positive predictive value (sensitivity, 75%; specificity, 93%; positive predictive value, 50%).

To address this issue, brain magnetic resonance imaging (MRI) has emerged as a promising objective and sensitive approach for investigating the neural basis of psychiatric disorders. Major depressive disorder (MDD) has been extensively studied using diffusion tensor imaging (DTI); however, research employing diffusion kurtosis imaging (DKI) remains limited[10, 11]. Unlike conventional DTI, DKI provides enhanced sensitivity to non-Gaussian diffusion, enabling the detection of subtle microstructural tissue changes through voxel-based metrics such as kurtosis and skewness. Therefore, DKI may provide a valuable tool for investigating maternal brain remodelling during the postpartum period.

To our knowledge, our previous report was the first study to evaluate postpartum depression using DKI[12]. Building upon this work, the present study investigated the clinical significance of EPDS in PPD screening by analysing neuroimaging changes in DKI/DTI parameters, including fractional anisotropy (FA), mean kurtosis (MK), and mean diffusivity (MD) in postpartum and nulliparous women.

## Results

# Participant characteristics

From June 2020 to March 2025, this study enrolled 17 postpartum patients. Two participants were excluded due to incomplete MRI or psychiatric evaluations. During the same period, 11 nulliparous women were enrolled, one of whom was excluded because MRI was not performed (Fig. 1).

The median ages did not differ significantly between the postpartum and nulliparous groups (33.0 years vs. 29.0 years; p = 0.133). Participant characteristics of the postpartum group are summarised in Table 1. Subgroup analyses stratified by EPDS score ≥ 9 revealed significant differences for all parameters except age and birth history (Table 2).

## TBSS

Figure 2 shows the results of the voxel-wise TBSS analysis comparing postpartum and nulliparous groups. MD was significantly lower in the postpartum group than in the nulliparous group in the corticospinal tract and pontine cerebellar fibres. We also observed significant differences in axial diffusivity (AD) in widespread regions involving the frontal lobe, basal ganglia, and occipital lobe.

The proportions of voxels showing significant MD and AD changes relative to the mean FA skeleton were 0.5% and 14.2%, respectively. Furthermore, the mean AD value in the white matter fibre bundle ROI was significantly lower in the postpartum group (median [range]: 1.41 [1.38–1.43]) than in the nulliparous

group (1.43 [1.40–1.44]; p < 0.01). We observed no significant differences in other DKI and DTI indices of the white matter between the groups.

## Region-specific changes and functional significance

Figure 3 shows the ROI analysis. The MK and RK values of the posterior insular cortex (pIC) in the postpartum group were significantly higher (median [range]: 0.59 [0.57–0.62] and 0.78 [0.73–0.87]) than those of the nulliparous group (0.57 [0.55–0.59] and 0.74 [0.71–0.78] ($p < 0.05$)).

In contrast, the MD and AD values of the putamen in the postpartum group (0.72 [0.69–0.79] and 0.98 [0.93–1.05]) were significantly lower than those in the nulliparous group (0.76 [0.71–0.82] and 1.02 [0.97–1.12]) ($p < 0.05$).

The correlations between EPDS scores and DKI/DTI indices in the postpartum group are shown in Table 3 and Fig. 4. In the amygdala, MK and radial kurtosis (RK) values showed significant moderate positive correlations with EPDS score ($\rho = 0.58$ and 0.57; $p < 0.05$). Conversely, MD, AD, and radial diffusivity (RD) values in the hypothalamus showed significant moderate negative correlations with EPDS scores ($\rho$ = -0.57, -0.53, and − 0.62, $p < 0.05$).

## Discussion

The results of this study demonstrated significant postpartum microstructural changes identified using DKI and DTI. Compared with nulliparous women, postpartum women showed widespread alterations in diffusivity and kurtosis metrics, particularly in the white matter, putamen, amygdala, and posterior insula. Collectively, these findings support a conceptual framework of adaptive maternal brain remodelling, in which the postpartum brain undergoes coordinated microstructural changes to optimise maternal responsiveness and internal state regulation.

AD alterations involved approximately 14.2% of the white matter skeleton, indicating that the postpartum neural remodelling effects extend across distributed brain networks rather than isolated regions. The reduced diffusivity observed in the postpartum group may reflect microstructural reorganisation related to myelin remodelling, synaptic refinement, or altered cellular density occurring during the transition to motherhood. In particular, the frontal lobe integrates limbic emotional inputs into higher-order cognitive processing, a coordination that appears to be stably maintained in nulliparous individuals. However, the reductions in MD in the postpartum group suggest a divergence from these baseline processing patterns. Such microstructural shifts likely reflect a period of heightened neuroplasticity, representing specialised maternal adaptation to profound hormonal fluctuations and the behavioural demands of early caregiving.

ROI analyses further demonstrated significantly increased MK and RK values in the pIC of the postpartum group. The pIC, also known as the "visceral" insula, provides evidence for changes in tissue

complexity and microstructural alterations in this region. The pIC is a major cortical convergence site for signals within and outside the body[13, 14]. Anatomical tracing studies in non-human primates have described extensive connectivity between the insula and the frontal, temporal, and parietal lobes, as well as with the thalamus, hippocampus, amygdala, and putamen[15, 16]. The putamen is also thought to be involved in instrumental learning and somatosensory processing, particularly pain[17]. These findings suggest that microstructural changes associated with increased neuronal and dendritic density in these regions may enhance sensory information processing in the pIC. The insula integrates both emotional and interoceptive signals[18] and is involved in the parental brain network. It contributes to maternal sensitivity and responsiveness to infant cues[19]. We speculate that this enhancement likely facilitates the processing of somatosensory information from the infant and the mother's physiological changes, which may in turn be reflected in maternal caregiving behaviours[20, 21].

The significant correlations observed between the EPDS scores and diffusion metrics in specific brain regions are particularly noteworthy. Positive correlations with MK and RK values in the amygdala and negative correlations with MD, AD, and RD values in the hypothalamus suggest that the neural substrates for postpartum psychological states and uncomfortable emotional regulation are reflected in maternal caregiving behaviours.

The amygdala plays a central role in emotional response processing and short-term memory and is crucial for processing emotions and feelings, intuition, fear, memory formation, pain, and stress responses, particularly anxiety, tension, and fear reactions. In the postpartum period, the amygdala may respond strongly to emotional stimuli such as infant cries or facial expressions, thereby enhancing the sensitivity and attentiveness required for childcare[22, 23]. Previous structural MRI studies have reported decreased volumes of the amygdala and hippocampus in the limbic system relative to pregnancy levels[24–26], a change that has been interpreted as a synaptic pruning–like process potentially supporting maternal behaviour[27].

During the postpartum period and in caregiving, the hypothalamus produces oxytocin (the "love hormone") and releases it from the pituitary gland. This contributes to the milk-ejection reflex during breastfeeding and the formation of attachments to the child[21]. Excessive stress or sleep deprivation during childcare can burden the hypothalamus, leading to autonomic dysfunction, thermoregulation instability, or eating disorders[28–30]. The amygdala provides a major excitatory drive to the hypothalamic–pituitary–adrenal (HPA) axis. When this is combined with impaired glucocorticoid feedback, it can result in sustained overactivity of HPA axis[31]. The structural changes observed in the hypothalamus during the postpartum period are likely associated with this dysregulation[29,30,32].

The present findings, therefore, suggest a dual-axis model of postpartum brain regulation, in which dysregulation of emotional salience (amygdala) and homeostatic control (hypothalamus) jointly contribute to vulnerability to depressive symptoms.

Our findings extend previous neuroimaging studies of the maternal brain. Structural MRI investigations have primarily reported volumetric amygdala and hippocampus in the limbic system, and grey matter changes during pregnancy and the early postpartum period, which are interpreted as synaptic pruning that enhances neural efficiency for maternal behaviours [33]. In contrast, our study highlights microstructural alterations in both white and grey matter, suggesting that postpartum brain adaptation involves not only volumetric changes, but also reorganisation at a finer microstructural level. Furthermore, the directionality of the diffusion changes observed in this study differs from those typically reported in MDD, where increased diffusivity is often associated with white matter disruption[34]. These white matter alterations complemented the grey matter changes observed in the ROI analyses in the present study, suggesting a coordinated network-level reorganisation rather than isolated regional effects.

The decreased diffusivity observed in postpartum women suggests a distinct neurobiological profile, reinforcing the notion that PPD is not simply a subtype of MDD, but is rather rooted in unique physiological and neuroendocrine processes[35].

This approach may be particularly valuable in clinical settings where early identification is required, but psychiatric assessment resources are limited. Therefore, integrating neuroimaging findings with biopsychosocial assessment frameworks may enable a more comprehensive and personalised approach to maternal mental healthcare.

In the future, this perspective is expected to support a unified pathophysiological theory of hormonal changes, environmental stressors[36], and neuroplastic changes observed using DKI neuroimaging, which will help inform prevention and intervention strategies.

## Study limitations

The relatively small sample size limits the generalisability of the findings, while the cross-sectional design precludes causal inferences regarding the temporal dynamics of brain changes. Additionally, the analysis did not fully control for potential confounding factors such as sleep deprivation, hormonal fluctuations, and psychosocial variables. Future longitudinal studies incorporating larger cohorts and multimodal assessments are required to validate and extend these findings.

## Conclusion

The results of the present study provide evidence that postpartum brain microstructural remodelling represents a continuum from physiological adaptation to potential dysregulation. These findings offer a neurobiological framework for understanding postpartum mental health.

## Methods

# Study Participants

This study was conducted in accordance with the principles of the Declaration of Helsinki and the Ethical Guidelines for Medical and Health Research Involving Human Subjects established by the Ministry of Health, Labor, and Welfare of Japan. The study protocol was approved by Iwate Medical University Hospital Independent Ethics Committee (approval no. MH2020-016). Written informed consent was obtained from all participants, including both patients and healthy controls.

# Study population and eligibility criteria

Participants were categorised into nulliparous and postpartum groups. Postpartum women were recruited from patients who delivered at Iwate Medical University Hospital between June 2020 and March 2025. The nulliparous group comprised women of reproductive age who had not given birth within the year preceding study participation during the same recruitment period.

Participants in both groups were excluded if they met any of the following criteria: (1) contraindications to MRI, such as metal implants or claustrophobia; (2) history of psychiatric disorders, including depression; (3) intracranial organic abnormalities; (4) age < 20 years; or (5) potential for excessive mental, physical, or social burden through their participation in the study. Additionally, postpartum mothers with stillbirths were excluded from the study.

# MRI acquisition and clinical assessments

Postpartum participants underwent MRI approximately one month after delivery and were evaluated by a psychiatrist within two months of delivery (and within one month of MRI acquisition). PPD was defined according to the American Psychiatric Association (APA) as a MDD with onset during pregnancy or within four weeks postpartum[37]. Psychiatric diagnoses were established using the *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition* (DSM-5). In the nulliparous group, psychiatric evaluations were performed by a psychiatrist within one month of the MRI scan to confirm the absence of overt psychiatric illness.

# MRI protocol

All participants underwent MRI using a 3T scanner with a gradient slew rate of 120mT $m^{-1}$ $ms^{-1}$ and a 48-channel head coil (SIGNA Architect, GE Healthcare, Milwaukee, WI, USA). DKI and DTI source images were obtained using a single-shot spin-echo echo-planar imaging sequence. Detailed acquisition parameters are provided in Table 4.

# Image analyses

We performed voxel-wise statistical analysis of DKI and DTI maps using tract-based spatial statistics (TBSS) implemented in the Functional Magnetic Resonance Imaging of the Brain (FMRIB) Software Library (FSL) 6.0.7, as described previously[12].

Region of interest (ROI) analyses of grey matter structures were performed using Advanced Normalisation Tools[38]. ROIs within the limbic system and basal ganglia were defined using the Johns Hopkins University Eve[39] and Neuromorphometrics atlases implemented in SPM12.

## Statistical analyses

We performed voxel-wise comparison of DKI and DTI values in postpartum and nulliparous women using TBSS. Statistical significance was defined as $p < 0.05$ using threshold-free cluster enhancement (TFCE) with family-wise error (FWE) correction for multiple comparisons (corrected $p < 0.05$, 5000 permutations).

ROI-based DKI and DTI values in the white matter fibre bundle and grey matter were compared between the postpartum and nulliparous groups using the Mann–Whitney *U* test. Associations between ROI diffusion metrics and EPDS scores were evaluated using Spearman's correlation coefficient ($\rho$). Clinical characteristics between the postpartum and nulliparous groups were also compared using the Mann–Whitney *U* test. Statistical analyses were performed using IBM SPSS Statistics, 29.0. For all tests, the significance level was set at $\alpha = 0.05$.

## Declarations

## Competing interests

The authors declare no competing interests.

## Funding

This work was supported by the Japan Society for the Promotion of Science (JSPS) KAKENHI (Grant Number JP20K16630).

## Author Contribution

H.Ka. and F.M. conceived and designed the study. H.Ka., F.M., K.F., and M.S. performed the experiments. H.Ka., F.M., and R.O. analyzed and interpreted the data. K.F., E.H., T.S., H.Ko., and M.Y. curated the data. C.I., G.H., and E.K. provided resources for the study. H.Ka. and F.M. wrote the original manuscript. R.O. reviewed and edited the manuscript. H.Ka. acquired funding for the study. T.B. supervised the study. All authors reviewed and approved the final manuscript.

## Acknowledgement

The authors thank Zora Kikinis, PhD (Assistant Professor, Department of Psychiatry, Brigham and Women's Hospital, Harvard Medical School), and Yuri Sasaki, M.D., PhD for valuable advice. The authors

also sincerely thank all healthcare professionals who contributed to this study for their support and cooperation. The authors would also like to thank Editage for English language editing.

# Data Availability

The datasets generated during and/or analysed the current study are available from the corresponding author on reasonable request.

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## Tables

Tables 1 to 4 are available in the Supplementary Files section.

## Figures

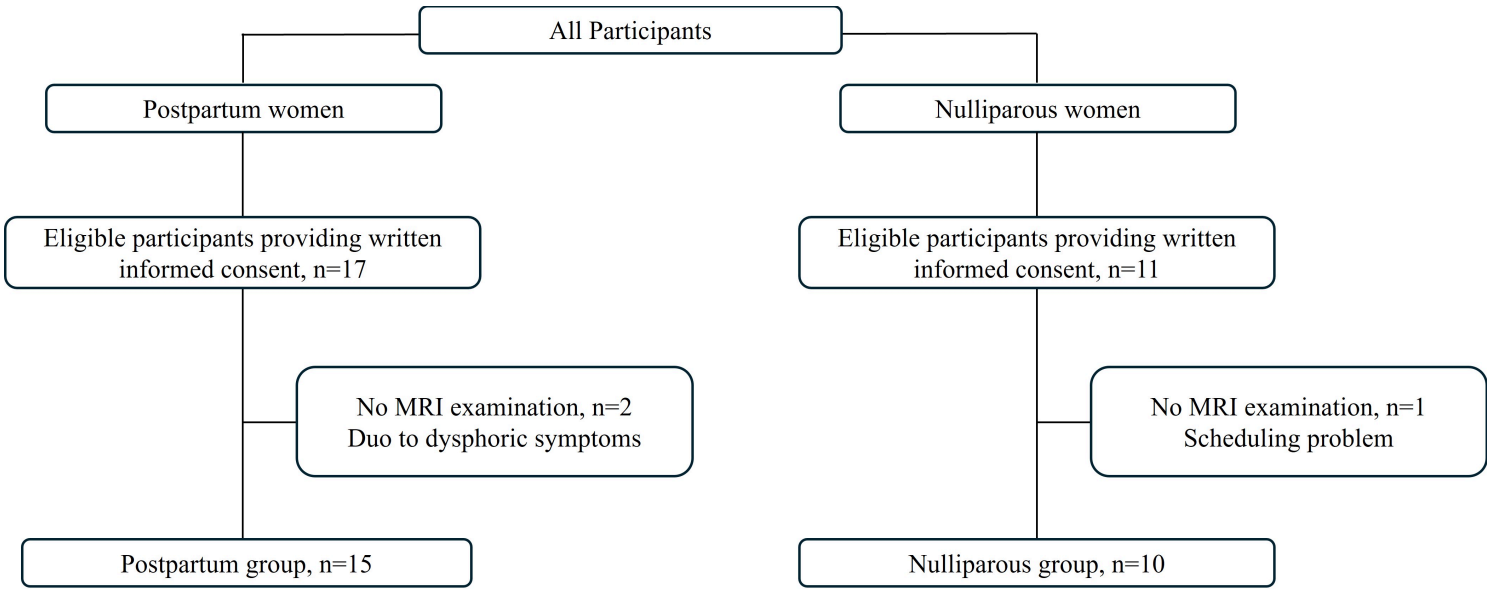



**Figure 1**

Participants flow.

Flow chart showing participant enrollment and exclusion in postpartum and nulliparous groups.

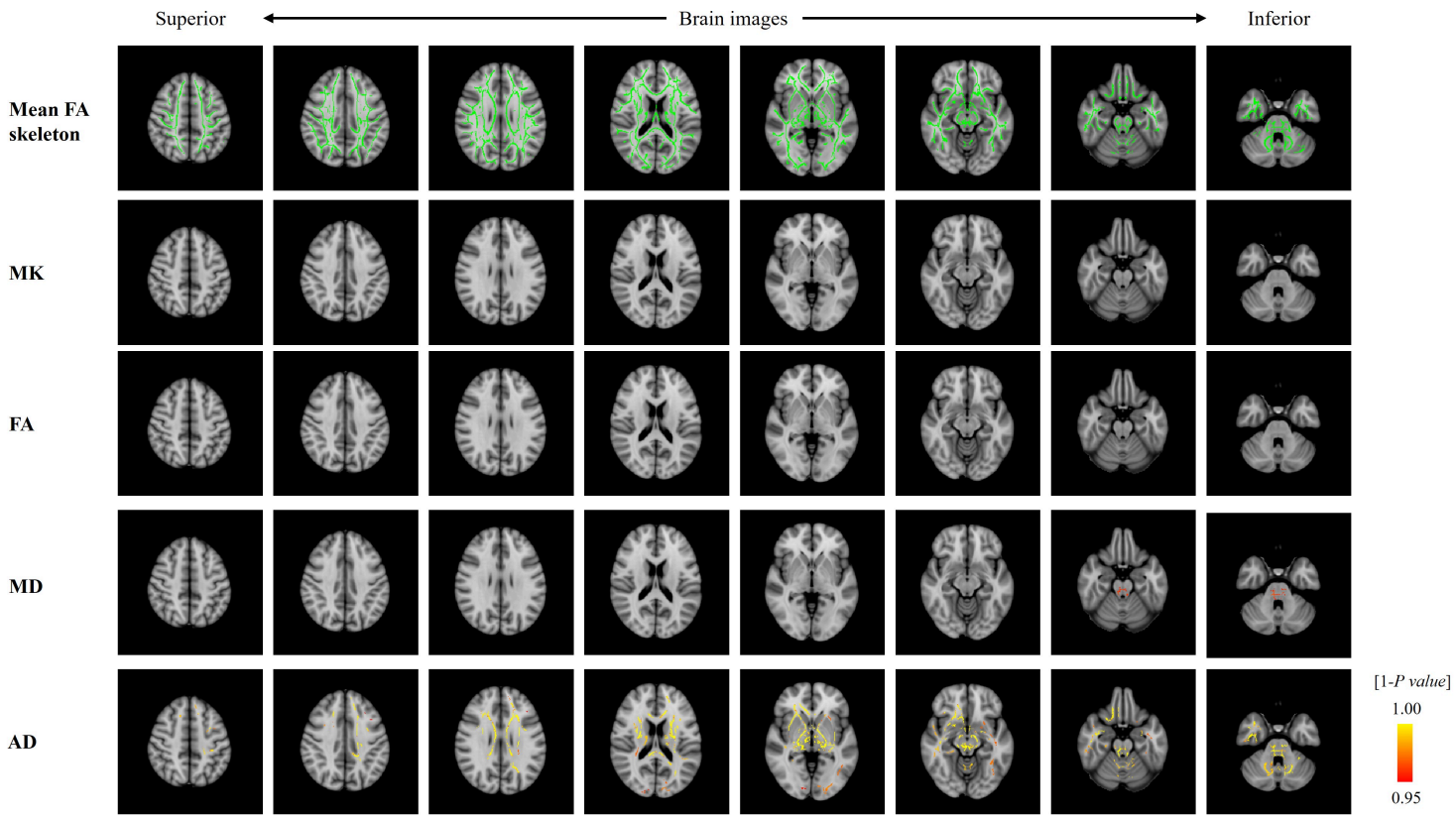
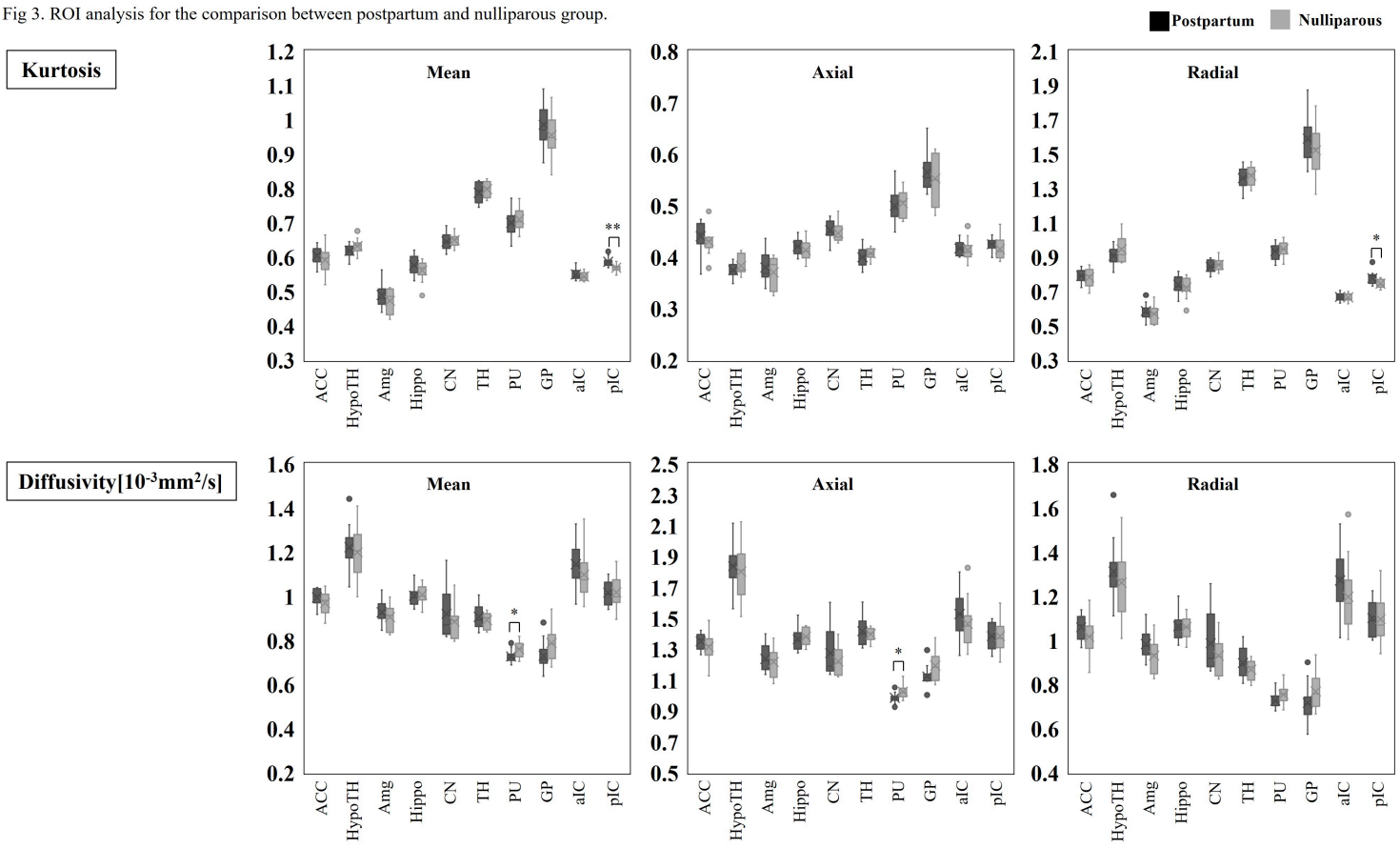



**Figure 2**

TBSS for the comparison between postpartum and nulliparous group.

Tract-based spatial statistics (TBSS) showing areas that differ significantly between the postpartum and nulliparous groups on eight brain images arranged from superior to inferior axial slices of diffusion kurtosis image (DKI) and tensor image (DTI) maps. The mean fractional anisotropy (FA) skeleton generated by TBSS for all participants is shown in green. Mean kurtosis (MK) and FA values do not differ significantly between the groups. Mean diffusivity (MD) values are significantly lower in the postpartum than the nulliparous group in the corticospinal tract and pontine cerebellar fibres. Axial diffusivity (AD) values are significantly lower in the postpartum than the nulliparous group in extensive areas of the frontal lobe, basal ganglia, and occipital lobe. Areas with significantly decreased MD and AD values in the postpartum group are shown in yellow to red ($p$ <0.05)




## Figure 3

ROI analysis for the comparison between postpartum and nulliparous group. Comparisons of regions-of-interest (ROIs) between the postpartum and nulliparous groups. The mean kurtosis (MK) and radial kurtosis (RK) values of the posterior insular cortex (pIC) are significantly higher in the postpartum group than in the nulliparous group. The mean and axial diffusivity values of the putamen (PU) are significantly lower in the postpartum group than in the nulliparous group. ($p$ <0.05, Mann–Whitney $U$ test).

Acc, Anterior cingulate cortex; HypoTH, hypothalamus; Amg, amygdala; Hippo, hippocampus; CN, caudate nucleus; TH, thalamus; PU, putamen; GP, globus pallidus; aIC, anterior insular cortex; pIC, posterior insular cortex.

Fig 4 DKI and DTI indices based on different EPDS scores

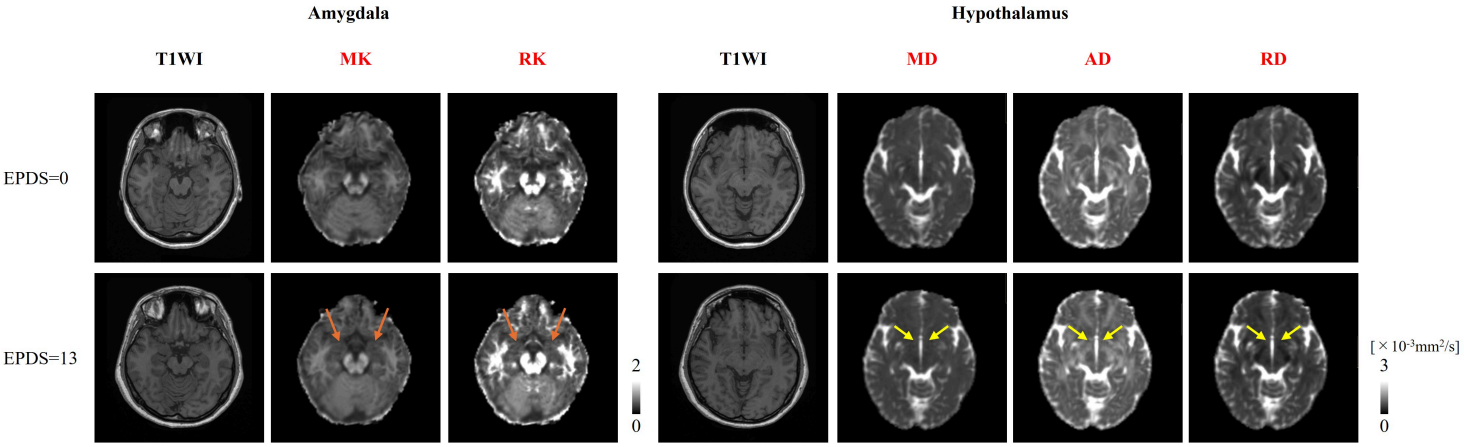



**Figure 4**

DKI and DTI indices based on different EPDS scores.

In the amygdala of MK and RK, the EPDS score of 13 showed higher values compared to the EPDS score of 0. In the hypothalamus of MD, AD, and RD, the EPDS score of 13 showed lower values compared to the EPDS score of 0. Orange arrows indicate areas of significant change in the amygdala, and yellow arrows indicate areas of significant change in the hypothalamus. MK, mean kurtosis, RK, radial kurtosis, MD, mean diffusivity, AD axial diffusivity, RD, radial diffusivity, EPDS, Edinburgh Postnatal Depression Scale

# Supplementary Files

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

- Tables.docx