

Research paper

Stressed-out parenting brain: Effects of parenting stress, depression and anxiety on caregivers' brain structure and function

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ABSTRACT

Background: Parenting stress (PS) arises when child-rearing becomes a stressor. Since the brain directs adaptation to stressors, we explored how the parenting brain adapts to PS in relation to depression and anxiety.

Method: This study involved 167 primary caregivers (all mothers; mean [SD] age = 40.76 [3.09] years old) who completed the Parenting Stress Index (PSI) and Beck Depression/Anxiety Inventory (BDI/BAI) and underwent 3 T MR scanning. Structural and resting-state functional data were preprocessed using FreeSurfer and CONN. We conducted 1) partial correlation and multivariate linear regression analyses between psychological and brain structural measurements, and 2) seed-to-voxel analysis using left entorhinal cortex (L.ERC) as the seed. Lastly, structural equation modeling analyses were conducted to assess the statistical relationships between psychological and brain measurements.

Results: L.ERC surface area was negatively correlated with BDI ($r = -0.255$, p -adjusted = 0.035). Mediation analyses indicated that PSI subscales indirectly associated with L.ERC via parent characteristic domain and BDI, while BDI was directly negatively associated with L.ERC ($\beta = -0.32$, $p = 0.001$). Resting-state functional connectivity (RSFC) between L.ERC and a right occipital/precuneus cluster was negatively associated with BDI and PSI subscales. In the function-based model (fit: CFI = 0.993, RMSEA = 0.038), RSFCs loaded onto a latent brain function construct, and higher PS was associated with increased BDI, which in turn was associated with reduced RSFC ($b = -0.36$, $p < 0.001$).

Conclusion: Structural and functional aspects of the parenting brain were associated with PS, in conjunction with depression, rather than anxiety, reflecting the cumulative and enduring neurobiological effects of depression over transient effects of anxiety.

1. Introduction

Parenting stress (PS) is the distress perceived by caregivers, where child-rearing becomes a stressor (Deater-Deckard, 1998). Maladaptation to PS can hinder adjustment to parenthood and compromise mental health (Kim, 2021). Considering that the brain directs adaptation to stressors (McEwen, 2016) and mental illness involves changes in brain structure and function (National Institutes of Health (US), 2007), it is of great interest to explore how PS relates to caregivers' brain adaptation along with depression and anxiety.

Humans, as alloparenting animals with long-term child-rearing, may experience chronic stress from parenting (Glasper et al., 2019). However, research on structural adaptation to PS has mainly focused on childbirth maternal brains (McCormack et al., 2023), and functional adaptation studies have primarily involved mothers of infants or

preschoolers (Noriuchi et al., 2019; Azhari et al., 2019; Barrett et al., 2012). The maternal brain undergoes dynamic changes during childbirth, known as the "mommy brain" (McCormack et al., 2023). Magnetic resonance imaging (MRI) scans before and after childbirth showed that pregnancy-related reductions in brain volume and increases in ventricles typically reverse six months postpartum (Oatridge et al., 2002). Although Oatridge et al. (2002) provided a unified trajectory, subsequent studies have revealed inconsistent findings on structural changes in the child-birthing brain varying by brain region, morphological features, participants (e.g., being a first-time mother), and the timing of scans (Martínez-García et al., 2021; Hoekzema et al., 2017). During the postpartum period, fathers exhibited region-specific structural changes similar to those of mothers (Kim et al., 2014), including increased volumes in the limbic structures of the reward network (e.g., striatum) and cortical structures of mentalization (e.g., prefrontal cortex) (Kim et al.,

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2010). Notably, depression is related to the changes in these cortical regions (Zhang et al., 2018). The stress-reward-mentalizing model by Luyten and Fonagy (2018) suggests that depression results from the impaired interactions among stress, reward, and mentalizing systems. Thus, the dynamic structural adaptations of the parenting brain to PS could be intricately connected with depression through interactions with other systems.

Regarding the functional adaptation of the parenting brain, PS also involves reward, cognitive, and emotional processing. PS plays a role in the neural activation of the orbitofrontal cortex, a part of the reward system, indicating the parenting brain's adaptive response (Noriuchi et al., 2019). Particularly, increased PS is linked to reduced orbitofrontal cortex activation in first-time mothers watching videos of their own child feeding compared to other children. A functional near-infrared spectroscopy hyperscanning study found that high PS levels reduced neural synchrony between mother and child in the inferior frontal gyrus, frontal eye field, and dorsolateral prefrontal cortex (Azhari et al., 2019). Another neuroimaging study examined how PS, anxiety, and depression are associated with the emotional aspects of the parenting brain. The activation level of the amygdala was measured when mothers, three months postpartum, rated positive facial expressions of their own child compared to other children (Barrett et al., 2012). This study found notable decreases in amygdala activation associated with PS and anxiety.

Current literature suggests that PS is associated with negative impacts on the caregivers' mental health, in conjunction with depression and anxiety, by altering the structure and function of the parenting brain. In specific, the parenting brain undergoes structural and functional adaptations to PS, and these adaptations may involve brain regions of shared networks (e.g., the reward network, mentalizing component, and emotion network). Thus, we posited the following research hypotheses: 1) PS would correlate with depression and anxiety at the behavioral level; 2) PS, depression, and anxiety would correlate with structural alterations in the cortical regions of the parenting brain at the structural level; and 3) the structurally modified brain regions would display aberrant functional connectivity, reflecting the effects of PS, depression, and anxiety at the functional level.

2. Materials and methods

2.1. Participants

This study included 167 healthy mothers who recognized themselves as primary caregivers (mean [SD] age = 40.76 [3.09]) of school children (95 boys; mean [SD] age = 9.20 [1.65] years) (Table 1). Exclusion criteria included the following: 1) major physical illness and brain injury history and 2) psychiatric disorder diagnosis or psychiatric drug intake for participants and their children at the time of participation. All participants, who were remunerated with KRW 50,000, provided informed consent. The Ethics Committee of the Institutional Board of the Korea Brain Research Institute approved this study, which was conducted in accordance with the Declaration of Helsinki (23-BR-05-01).

2.2. Behavioral assessment of PS

We assessed the PS levels using the 4th edition of the Parenting Stress Index (PSI-IV) (Abidin, 2012), a self-report questionnaire. Based on a 5-point Likert scale, the 120 items measure PS from child and parent characteristic domains in addition to life stress. The 47 items in the child characteristic domain measure how children's characteristics contribute to PS. The child characteristic domain is the sum of six subscales: 1) adaptability (11 items), 2) distractibility/hyperactivity (nine items), 3) demandingness (nine items), 4) mood (five items), 5) acceptability (seven items), and 6) reinforce parent (six items). Subsequently, 54 items in the parent characteristic domain examine how caregivers' characteristics are devoted to PS. The parent characteristic domain is the

Table 1

Demographic characteristics and summary of BDI, BAI and PSI scores.

Demographics		Participants (N = 167 mothers)	
		Mean	SD
Age		40.76	3.09
Handedness		N	%
	Right	161	96.41
	Left	1	0.6
Ambidextrous		5	2.99
Number of children at household		N	%
	1	31	18.56
	2	103	61.68
	3	29	16.17
	4	4	2.4
Behavioral assessment tools		Mean	SD
BDI		9.89	7.11
BAI		4.53	4.97
PSI	Distractibility/hyperactivity	44.11	9.78
	Adaptability	42.60	9.24
	Reinforces parent	43.11	9.39
	Demandingness	45.31	9.34
	Mood	47.35	10.77
	Acceptability	46.85	9.21
	Child characteristic domain	43.40	9.43
	Competence	47.50	10.62
	Isolation	45.86	9.67
	Attachment	47.52	10.16
	Health	46.63	10.19
	Role restriction	47.97	9.94
	Depression	49.29	9.93
	Spouse	47.98	10.35
	Parent characteristic domain	46.95	10.13
	Parenting stress total	44.95	9.77
	Life Stress	52.28	13.22

Note. Percentages may not sum to 100 due to rounding.

sum of seven subscales: 1) competence (13 items), 2) isolation (six items), 3) attachment (seven items), 4) health (five items), 5) role restriction (seven items), 6) depression (nine items), and 7) spouse (seven items). Finally, the 19 items allow us to estimate the level of life stress in addition to PS.

2.3. Behavioral assessment of depression and anxiety

We used the second version of the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) to determine the depression and anxiety levels in the participants. The BDI and the BAI are self-reported measurements based on a 4-point Likert scale. Each inventory consists of 21 items.

2.4. Brain image acquisition

Structural and resting-state functional MRI data were acquired using a 3 T MR scanner (Siemens MAGNETOM Skyra, Erlangen, Germany) with a 20-channel head coil at K-MEDI Hub. We collected high-resolution T1-weighted image (repetition time (TR) = 2400 ms, inversion time (TI) = 1140 ms, echo time (TE) = 2.3 ms, flip angle (FA) = 8°, field of view (FOV) = 230 mm, 256 slices, voxel size = 0.7 × 0.7 × 0.7 mm³) and T2*-weighted image (slice-thickness = 3.0 mm, TR = 2000 ms, TE = 28 ms, FA = 64°, FOV = 192 mm, 180 measurements, 36 slices with full brain coverage; voxel size = 3.0 × 3.0 × 3.0 mm³).

2.5. Imaging preprocessing

Structural MRI data were preprocessed for cortical parcellation using

FreeSurfer v.7.2.0 to extract reliable information on the 68 parcellated brain surface areas. The preprocessing steps were as follows: (1) bias field correction; (2) motion and heterogeneity correction; (3) Talairach transformation; (4) intensity normalization; (5) skull stripping and subcortical white and gray matter segmentation; and (6) parcellation (Fischl, 2012).

Resting-state functional MRI data were pre-processed for functional connectivity (FC) analysis using SPM12 (Penny et al., 2011) with the CONN ver.22 toolbox implemented in MATLAB ver.2022 (Whitfield-Gabrieli and Nieto-Castanon, 2012). The preprocessing steps include 1) discarding the first five volumes to reduce the effects of magnetic field inhomogeneity during the initial scan, 2) realignment to the mean image, 3) slice-timing correction, 4) ART-based volume removal based on a mean intensity >5 SD of the mean global signal or 0.9 mm/repetition rate framewise displacement to reduce head movement effects, 5) anatomical component-based noise correction to reduce physiological and other noise artifacts, 6) normalization, 7) smoothing with a 6-mm full-width at half-maximum Gaussian, and 8) band-pass filtering of functional images (0.008–0.09 Hz).

We performed a voxel-wise seed-based correlation analysis for FC calculation using a predefined seed of interest, the left entorhinal cortex (L.ERC), which was chosen based on FreeSurfer parcellation and subsequently imported into CONN. Functional correlation values were computed between the region and every voxel in the whole brain. We extracted the average time course of the blood-oxygen-level-dependent (BOLD) signals of the seed region and correlated them with the BOLD signal time series of other voxels in the whole brain to create individual FC maps for all participants. The resulting Pearson's correlation coefficients were converted into Fisher's z-scores. In the second-level general linear model analysis, the main effects of PSI, BDI, and BAI scores were regressed while controlling for mothers' age, handedness, number of children, and children's sex. Voxel-wise thresholds of $p < 0.001$ were uncorrected and a cluster-level correction was subsequently applied at FDR-corrected $p < 0.05$.

2.6. Statistical analysis

Partial correlation analyses were conducted 1) among PSI, BDI, and BAI scores; 2) between the psychological questionnaire scores and 34 surface area measures for each brain hemisphere; and 3) between the scores and RSFC values. The p -values were adjusted using a Bonferroni correction with a significance threshold of $\alpha = 0.05/34$ (i.e., 34 surface-area parcels per hemisphere were treated as the family of tests for each psychological score; the full uncorrected correlation matrix across all PSI subscales, BDI, and BAI is presented in Supplementary Fig. 2). Subsequently, we conducted multivariate linear regression analyses for each brain metric that survived the correlation analyses. Each regression model included all psychological measurements and covariates as predictors, applying backward selection to identify significant variables. For correlation and regression analyses, covariates included mothers' age, handedness, intracranial volume, number of children, and children's sex.

We established two separate models using structural equation modeling analysis with variables survived from correlation and regression analyses to explore statistically significant paths between psychological and brain measurements. First, the brain structure-based mediation model included three psychological measurements (BDI, adaptability, and parenting characteristic domain) and L.ERC surface area to test whether BDI was statistically associated with the associations between PS and brain structure. Indirect effects were tested using bias-corrected bootstrap confidence intervals ($B = 10,000$). Second, the brain function-based model included three psychological measures (BDI, depression, role restriction) and the four resting-state functional connectivity (RSFC) indices. Each RSFC represents connectivity between the L.ERC and clusters encompassing both the right superior lateral occipital cortex (R.sLOC) and right precuneus (R.PCUN), identified separately for

BDI, adaptability, competence, and isolation.

We conducted one-way analysis of covariance to investigate whether depression severity is linked to structural change in L.ERC by creating three groups based on the BDI scores: (1) highly depressed (score ≥ 16 ; $N = 36$, ca. 21.56%), (2) mildly depressed ($16 > \text{score} \geq 4$; $N = 96$, ca. 57.49%), and (3) barely depressed (score < 3 ; $N = 35$, ca. 20.96%). All statistical analyses were performed using R 4.2.3.

3. Results

3.1. Associations across the BDI, BAI, and PSI scores

Significant associations were found across most psychological measurements at p -adjusted = 0.05. No significant associations were found (1) between BDI and distractibility/hyperactivity, adaptability, reinforces parent, and life stress; and (2) between BAI and distractibility/hyperactivity, adaptability, reinforces parent, mood, and life stress.

Significant associations were found across most PSI subscales. However, distractibility/hyperactivity was not significantly associated with isolation or spouse. Reinforce parent was not significantly associated either isolation or role restriction. Life stress did not show significant associations with other subscales except for depression ($r = 0.259$, p -adjusted = 0.030, $R^2 = 0.025$) (Supplementary Fig. 1).

3.2. Associations between brain structure and psychological measurements

The L.ERC's surface area was negatively associated with BDI ($r = -0.255$, p -adjusted = 0.035, $R^2 = 0.065$; Fig. 1). Multivariate linear regression analysis revealed that BDI ($\beta = -0.31$, 95% CI $[-0.50, -0.12]$, $p = 0.002$, $\eta_p^2 = 0.08$) and adaptability ($\beta = -0.28$, $[-0.51, -0.06]$, $p = 0.015$, $\eta_p^2 = 0.03$) were significantly associated with L.ERC area. No other variables showed significant associations ($ps > 0.05$), although parenting characteristic domain was marginally significant ($\beta = 0.29$, $[-0.04, 0.61]$, $p = 0.083$, $\eta_p^2 = 0.02$) (Supplementary Table 1). The overall model was significant ($F(7, 159) = 3.68$, $p = 0.001$, R^2 -adjusted = 0.10) (Supplementary Fig. 2 for associations across all psychological and brain measurements).

3.3. Effects of depression severity on the L.ERC

A significant effect of caregiver's depression severity on the L.ERC surface area was observed ($F(2, 158) = 5.93$, $p = 0.003$, $\eta_p^2 = 0.07$; Fig. 2). Post hoc Tukey adjusted comparisons revealed that the highly depressed group exhibited significantly smaller L.ERC area compared to both the barely depressed ($T = 3.39$, $p = 0.003$, $d = 0.82$) and mildly depressed groups ($T = 2.51$, $p = 0.034$, $d = 0.50$), whereas the difference between the mildly and barely depressed groups was not significant ($p = 0.242$).

3.4. The brain structure-based model

A mediation analysis examined whether the association between adaptability and L.ERC is influenced by parent characteristic domain and BDI (Fig. 3). Adaptability was positively associated with parent characteristic domain (path a^1 : $b = 0.513$, 95% CI $[0.380, 0.651]$, $p < 0.001$). Subsequently, parent characteristic domain was positively associated with BDI (path d : $b = 0.504$, $[0.413, 0.594]$, $p < 0.001$). Adaptability showed a significant negative association with BDI (path a^2 : $b = -0.155$, $[-0.267, -0.039]$, $p = 0.007$). Higher BDI scores were significantly associated with reduced L.ERC (path b : $b = -3.122$, $[-4.858, -1.383]$, $p < 0.001$).

Regarding direct effects, adaptability demonstrated a significant negative association with L.ERC (path c' : $b = -1.604$, $[-2.780, -0.379]$, $p = 0.009$), whereas the direct association between parent characteristic domain and L.ERC was not significant ($b = 1.068$, $[-0.246, 2.347]$, $p =$

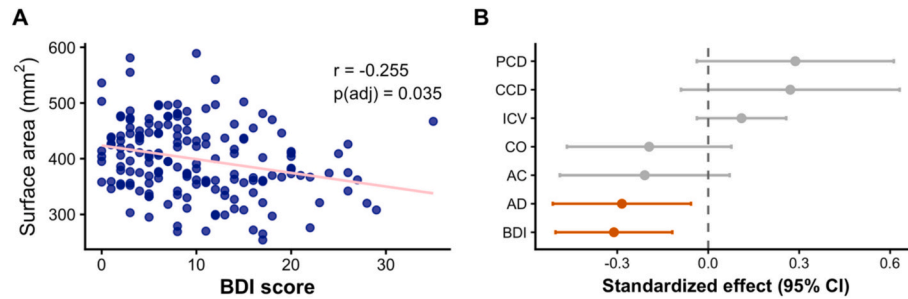


Fig. 1. Associations between psychological measurements and L.ERC surface area (A) Partial correlation plot between BDI and L.ERC controlling for covariates; (B) forest plot of multivariate linear regression predicting L.ERC. Orange indicates significant predictors ($p < 0.05$) and gray indicates non-significant ones; BDI = Beck Depression Inventory, AC = acceptability, AD = adaptability, CCD = child characteristic domain, CO = competence, ICV = intracranial volume, PCD = parent characteristic domain; L.ERC = surface area of the left entorhinal cortex.

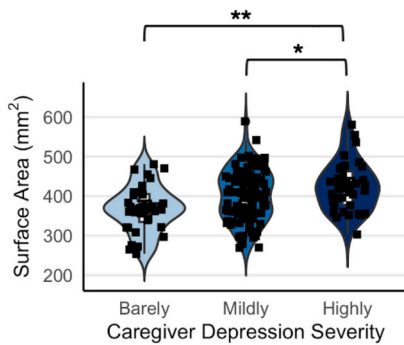


Fig. 2. Effects of severity of depression on surface area of left entorhinal cortex (L.ERC). Significant difference in L.ERC between highly depressed and mildly depressed as well as between highly depressed and barely depressed group. * $p < 0.05$, ** $p < 0.005$.

0.107). In terms of indirect effects, adaptability was significantly associated with L.ERC through parent characteristic domain and BDI ($b = -0.808$, $[-1.350, -0.345]$, $p = 0.002$). The specific indirect effect via BDI was also significant ($b = 0.484$, $[0.096, 0.976]$, $p = 0.030$), whereas the path via parent characteristic domain alone was not significant ($b = 0.548$, $[-0.132, 1.248]$, $p = 0.115$). The total indirect effect was not significant ($b = 0.224$, $[-0.466, 0.878]$, $p = 0.509$). The total effect of adaptability on L.ERC remained significant ($b = -1.380$, $[-2.500, -0.318]$, $p = 0.013$).

3.5. Identification of four RSFCs between L.ERC and R.sLOC/R.PCUN cluster

The BDI scores were negatively associated with the RSFC (BDI-RSFC;

$K = 79$, FDR-corrected $p = 0.026$; $T(161) = -4.38$, p -uncorrected < 0.001). Among PSI subscales, adaptability, competence and isolation showed significant associations with RSFC. Specifically, higher adaptability scores were associated with decreased RSFC (AD-RSFC; $K = 105$, FDR-corrected $p = 0.011$; $T(161) = -4.66$, p -uncorrected < 0.0001). RSFC was also negatively associated with competence (CO-RSFC; $K = 75$, FDR-corrected $p = 0.040$; $T(161) = -5.14$, p -uncorrected < 0.0001) and isolation (IS-RSFC; $K = 130$, FDR-corrected $p = 0.002$; $T(161) = -4.61$, p -uncorrected < 0.0001) (Fig. 4).

3.6. Associations between brain function and psychological factors

Regarding the associations between psychological factors and the four identified RSFCs, each RSFC showed significant negative correlation for its corresponding psychological scores: (1) BDI score and BDI-RSFC ($r = -0.329$, p -adjusted < 0.001 , $R^2 = 0.108$); (2) competence and CO-RSFC ($r = -0.375$, p -adjusted < 0.001 , $R^2 = 0.141$); (3) adaptability and AD-RSFC ($r = -0.344$, p -adjusted < 0.001 , $R^2 = 0.119$); and (4) isolation and IS-RSFC ($r = -0.340$, p -adjusted < 0.001 , $R^2 = 0.116$).

Additionally, BDI-RSFC was significantly associated with parenting characteristic domain ($r = -0.288$, p -adjusted = 0.007, $R^2 = 0.083$), competence ($r = -0.283$, p -adjusted = 0.009, $R^2 = 0.08$), and total PS ($r = -0.264$, p -adjusted = 0.023, $R^2 = 0.07$). CO-RSFC showed significant correlations with parent characteristic domain ($r = -0.325$, p -adjusted < 0.001 , $R^2 = 0.105$), total PS ($r = -0.317$, p -adjusted = 0.013, $R^2 = 0.101$), attachment ($r = -0.296$, p -adjusted = 0.044, $R^2 = 0.088$), isolation ($r = -0.267$, p -adjusted = 0.020, $R^2 = 0.071$), PSI depression ($r = -0.258$, p -adjusted = 0.031, $R^2 = 0.066$), BDI ($r = -0.253$, p -adjusted = 0.038, $R^2 = 0.064$), and acceptability ($r = -0.248$, p -adjusted = 0.049, $R^2 = 0.061$). AD-RSFC was significantly associated with child characteristic domain ($r = -0.304$, p -adjusted = 0.003, $R^2 =$

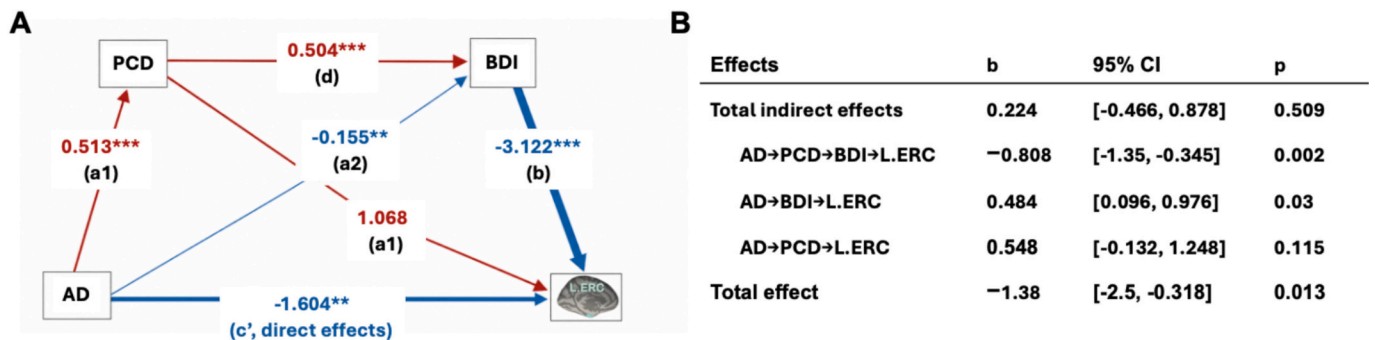


Fig. 3. Estimated brain structure-based mediation model. (A) diagram of the model; (B) summary of the model: AD = adaptability of parenting stress index, BDI = Beck depression index score, PCD = parent characteristic domain of parenting stress index, L.ERC = left entorhinal cortex area; red = positive effect, blue = negative effect; ** $p < 0.01$, *** $p < 0.001$.

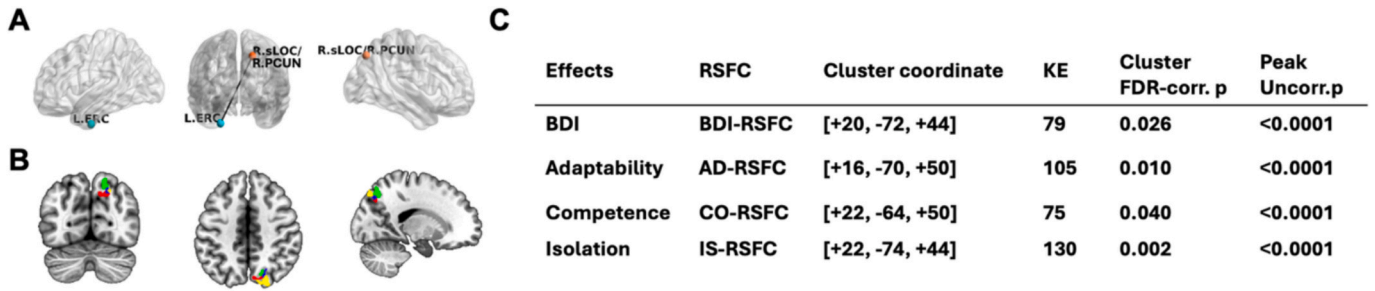


Fig. 4. Resting state functional connectivity (RSFC) showing significant psychological effects. (A) RSFCs between L.ERC seed (cyan) and R.sLOC/R.PCUN cluster (orange); (B) R.sLOC/R.PCUN cluster overlay of 4 RSFCs; red = cluster showing BDI effect (BDI-RSFC), green = cluster showing adaptability (AD-RSFC), blue = cluster showing competence effect (CO-RSFC); yellow = cluster showing isolation effect (IS-RSFC); (C) summary of 4 RSFCs (cluster FDR-corrected $p < 0.05$; voxel p -uncorrected < 0.0001). BDI = Beck Depression Inventory, AD = adaptability, CO = competence, IS = isolation; L.ERC = left entorhinal cortex, R.PCUN = right precuneus gyrus, R.sLOC = right superior lateral occipital cortex.

0.093), acceptability ($r = -0.294$, p -adjusted = 0.005, $R^2 = 0.087$), and total PS ($r = -0.259$, p -adjusted = 0.029, $R^2 = 0.067$). IS-RSFC showed significant negative associations with parent characteristic domain ($r = -0.282$, p -adjusted < 0.01 , $R^2 = 0.079$), competence ($r = -0.248$, p -adjusted = 0.047, $R^2 = 0.062$), role restriction ($r = -0.249$, p -adjusted = 0.048, $R^2 = 0.062$), and BDI ($r = -0.248$, p -adjusted = 0.050, $R^2 = 0.061$) (Supplementary Fig. 2).

Multivariate linear regression analysis demonstrated that BDI-RSFC is significantly associated with BDI ($\beta = -0.26$, $[-0.46, -0.06]$, $p = 0.010$, $\eta_p^2 = 0.12$), distractibility/hyperactivity ($\beta = 0.29$, $[0.06, 0.52]$, $p = 0.014$, $\eta_p^2 = 0.01$), and child characteristic domain ($\beta = -0.43$, $[-0.83, -0.02]$, $p = 0.038$, $\eta_p^2 = 0.04$). The BDI-RSFC regression model was significant ($F(12, 154) = 3.166$, $p < 0.001$, R^2 -adjusted = 0.135) (Supplementary Table 2).

For AD-RSFC regression model ($F(10, 156) = 2.777$, $p < 0.005$, R^2 -adjusted = 0.097), only the child characteristic domain showed a significant negative association ($\beta = -0.48$, $[-0.75, -0.21]$, $p < 0.001$, $\eta_p^2 = 0.10$) (Supplementary Table 3). The CO-RSFC was significantly associated with parent characteristic domain ($\beta = -0.59$, $[-0.86, -0.32]$, $p < 0.001$, $\eta_p^2 = 0.09$) and maternal age ($\beta = -0.16$, $[-0.30, -0.01]$, $p = 0.036$, $\eta_p^2 = 0.03$). The CO-RSFC model was significant ($F(4, 162) = 6.916$, $p < 0.001$, R^2 -adjusted = 0.125 (Supplementary Table 4). The IS-RSFC regression model ($F(7, 157) = 3.677$, $p < 0.005$, R^2 -adjusted = 0.102) had four significant predictors: distractibility/hyperactivity ($\beta = 0.26$, $[0.06, 0.46]$, $p = 0.001$, $\eta_p^2 < 0.001$), demandiness ($\beta = 0.29$, $[0.02, 0.55]$, $p = 0.032$, $\eta_p^2 < 0.01$), spouse ($\beta = 0.27$, $[0.05, 0.49]$, $p = 0.015$, $\eta_p^2 < 0.001$), and total PS ($\beta = -1.20$, $[-1.76, -0.64]$, $p < 0.001$, $\eta_p^2 = 0.10$) (Supplementary Table 5). For each of four

models, no other predictors showed significant associations ($ps > 0.05$).

3.7. The brain function-based model

A structural equation model examined associations across PS, BDI, and RSFC. A good fit was observed for the estimated function-based model ($\chi^2(12) = 14.951$, $p = 0.244$, CFI = 0.993, TLI = 0.989, RMSEA = 0.038, SRMR = 0.039, NFI = 0.968, GFI = 0.968) (Fig. 5). The latent brain function latent factor was significantly defined by all four RSFCs: (1) BDI-RSFC ($B = 0.893$, $SE = 0.063$, $T = -12.224$, $p < 0.001$, $R^2 = 0.906$), (2) AD-RSFC ($B = 0.606$, $SE = 0.068$, $T = 8.889$, $p < 0.001$, $R^2 = 0.418$), (3) CO-RSFC ($B = 0.649$, $SE = 0.067$, $T = 9.674$, $p < 0.001$, $R^2 = 0.478$), and (4) IS-RSFC ($B = 0.713$, $SE = 0.065$, $T = 10.891$, $p < 0.001$, $R^2 = 0.577$). A significant residual covariance was observed between AD-RSFC and CO-RSFC ($B = 0.281$, $SE = 0.056$, $T = 4.992$, $p < 0.001$).

PSI depression ($B = 0.413$, $SE = 0.070$, $T = 5.941$, $p < 0.001$) and role restriction ($B = 0.283$, $SE = 0.070$, $T = 3.930$, $p < 0.001$) showed significant positive associations with BDI. BDI demonstrated a significant negative association with the latent brain function ($B = -0.361$, $SE = 0.083$, $T = -4.277$, $p < 0.001$, $R^2 = 0.342$). The structural model explained 11.5% of the variance in the brain function factor.

4. Discussion

This study examined how the parenting brain in mothers adapts to parenting stress, with a focus on its links with depression and anxiety. The present study revealed various aspects of this adaptation. Notably,

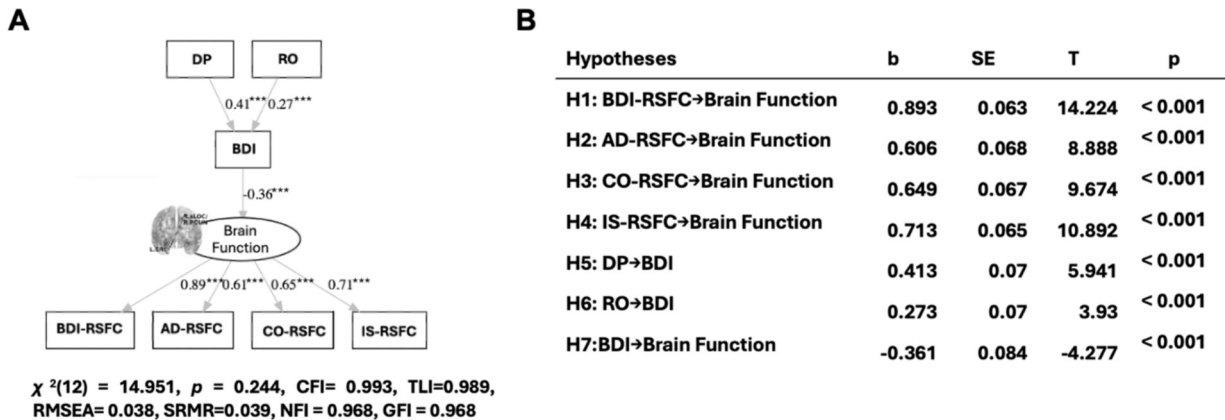


Fig. 5. Estimated brain function-based model. (A) Diagram of the model; (B) summary of the model; BDI = Beck depression index score; DP = parenting stress index depression; RSFC = resting state functional connectivity between L.ERC and R.sLOC/R.PCUN cluster, L.ERC = left entorhinal cortex seed, R.PCUN = right precuneus, R.sLOC = right superior lateral occipital cortex; AD-RSFC = RSFC showing adaptability effect, BDI-RSFC = RSFC showing BDI effect, CO-RSFC = RSFC showing competence effect, IS-RSFC = RSFC showing isolation effect.

depression—rather than anxiety—showed significant associations with this adaptation. Our hypothesis regarding the associations among PS, depression, anxiety, and parenting brain is partially supported. Although PS was associated with depression and anxiety at the behavioral level, only depression demonstrated significant associations with structural and functional modification in the parenting brain. This suggests that, in the context of parenting stress, depression may be more strongly embedded in neurobiological processes, whereas anxiety may reflect a more transient or state-like response that is less readily captured by the parenting brain. Considering that depression is past-oriented while anxiety is future-oriented (Eysenck et al., 2006), neural processes underlying depression may accumulate over time, and thus more likely to manifest in measurable brain changes. Additionally, given our sample consisted of psychologically healthy individuals, anxiety may reflect a normative response to stressor rather than a stable neurobiological alteration.

We observed that a structural alteration in the parenting brain, characterized by reduction in L.ERC surface area, was associated with depression and parenting stress. Additionally, RSFC analyses showed significant connectivity between the L.ERC seed and the R.sLOC/R. PCUN cluster, suggesting that the structurally altered brain regions may contribute to functional reorganization. Therefore, our hypothesis that structurally altered brain regions are associated with functional abnormalities is partially supported. Regions identified via the structural measurements were used as seed for seed-based functional connectivity, allowing a direct test of structure–function correspondence. However, functional connectivity extended beyond structurally altered areas, indicating that functional networks are not fully constrained by local structural variation. This partial correspondence may reflect differences in measurement: structural alterations may indicate long-term structural changes involving multiple processes (e.g., cell growth and neurogenesis), whereas functional connectivity reflects transient, state-dependent processes (May, 2011).

4.1. Structural adaptation of the parenting brain

A structure-based model indicated that depression was statistically associated with the relationship between parenting stress and the structural change in the parenting brain, with a significant difference in the L.ERC surface area depending on the level of depression. It is important to note that the mediation model revealed a nuanced pattern linking parenting stress, depression, and L.ERC. Specifically, the pathway from adaptability to L.ERC via parent characteristic domain and depression suggests that stress related to a child's low adaptability is associated with increased parent-related stress, which in turn relates to elevated level of depression and reduced L.ERC surface area (Fig. 3). In contrast, adaptability was also directly associated with lower depressive symptoms, which were linked to greater L.ERC. This pattern can be interpreted within a framework distinguishing external and internal stressors: a child's low adaptability could be considered as an external stressor that becomes internalized as parent-related stress, with downstream depression and L.ERC. It is also known that the locus of the stressor is related not only to perceived control over stress but also to cortisol regulation (Zhan et al., 2023). Supporting this, experimental animal studies have demonstrated not only that chronic stress leads to a longitudinal volumetric reduction in rat ERC (Magalhães et al., 2018) but also that psychosocial stress could modulate the activity of stress-responsive proteins in the ERC and that manipulation of this ERC circuitry altered depression-like behaviors (Yun et al., 2018). As a gateway to the hippocampus, the ERC projects to the CA3 area and dentate gyrus, suggesting structural changes in this circuit may be potential structural markers of stress and depression (McEwen, 2016; Yun et al., 2018).

In line, human neuroimaging studies have reported that structural alterations in ERC were associated with depression and stress. Specifically, individuals with the depressive spectrum have demonstrated reduced volumes (Lener et al., 2016). Perceived stress levels have been

linked to volumetric increase (Li et al., 2014) and stress has been suggested to induce structural brain changes through hormonal regulation (Kim, 2021; McEwen, 2016). Lener et al. (2016) used the term depressive spectrum to suggest an association between specific cortical changes and specific depressive behaviors. Our findings indicate that structural changes in the ERC are particularly linked to depression (Lener et al., 2016). Consistent with the proposed ERC–HPC circuit as a potential marker of stress- and depression-related processes in animal model, an intracortical recording study demonstrated that human ERC neurons exhibit flexible, environment-adaptive responses in coordination with hippocampal neurons (Nadasdy et al., 2017).

4.2. Functional adaptation of the parenting brain

Our findings revealed that the four L.ERC-based RSFCs converged onto the R.sLOC/R. PCUN cluster regardless of psychological measurements (Fig. 4). However, each RSFC exhibited partially overlapping yet distinctive spatial pattern depending on specific measurements. The convergence on a single cluster suggests not only that depression and parenting stress—particularly domains related to adaptability, competence, and isolation—engage a common neural circuitry linking affective processing in the entorhinal cortex (ERC) (Wang et al., 2022) with higher-order integrative regions (sLOC/PCUN) (Wang et al., 2026), but also that distinct psychological factors modulate this shared circuit in partially overlapping yet specific ways. Although this warrants a further investigation with human subjects, animal research has provided evidence that distinct neural circuits underlie specific stress behaviors (Ausderau et al., 2023). Notably, Lu et al. (2022) showed that chronic stress-induced depression-like behaviors in mice are regulated by projections from entorhinal cortex layer Va to layers II/III of the medial secondary visual cortex. This entorhinal–visual pathway aligns with our findings of RSFC between L.ERC and the sLOC/PCUN cluster, suggesting a potential circuit-level mechanism underlying the association between parenting stress and depression. In addition, distinctive spatial pattern observed in the RSFC may reflect contributions from different ERC subregions. In various species, including humans, the medial and lateral ERC are known for their unique cytoarchitecture, distinct structural connectivity, and functional specialization (e.g., dorsal versus ventral stream) (Witter et al., 2017). Notably, long-term stress exposure deteriorates the navigation function of the grid cells in the medial ERC, exhibiting a high corticosteroid receptor density (Hartner and Schrader, 2018). In humans, perceived chronic stress has also been associated with altered spatial navigation, an effect that has been proposed to be affected by elevated cortisol levels (Akan et al., 2023). Together, these findings suggest that the medial ERC may be involved in stress-related neural networks; however, this requires further investigation.

The present study showed a significant role of depression between parenting stress and the parenting brain in the function-based model in consistent with the structure model. Structural model showed both child- and parent-related component of parenting stress were linked to depression whereas the functional model comprised only parent-related ones (i.e., parenting stress associated with depression and role restriction; Fig. 5). This discrepancy may reflect differences in structural and functional measurements as well as in external and internal stressor as discussed above. Structural alterations may reflect cumulative and integrative effects of both external (child-related) and internal (parent-related) stressors, whereas RSFC may be more sensitive to proximal, parent-centered emotional states. Especially, role restriction reflects the caregiver's perceived confinement of personal freedom and loss of the self because of the parenting role. This distinction suggests that external caregiving demands may influence brain structure through longer-term internalization, whereas functional dynamics are more closely aligned with current subjective stress.

This study has some limitations. One of the assumptions of the current study is structure–function coupling; accordingly, we used structurally defined regions as seeds for functional connectivity analyses.

This approach may not fully characterize network-level structure–function coupling (Suo et al., 2025; Suo et al., 2026). Future studies incorporating measures such as structural covariance networks and functional one may provide a more comprehensive understanding of coupled structure–function changes associated with parenting stress. Although we explored statistical causal associations in structure- and function-based models using statistical equation modeling analysis, establishing relationships across parenting stress, depression, structures, and functional changes in the parenting brain in real human life requires longitudinal investigation. Additionally, our use of a self-report questionnaire to measure PS levels may differ from physiological measurements (e.g., cortisol concentrations in hair or salivary samples). This study did not include contextual factors (e.g., caregiver educational level, socioeconomic status, and social support), due to a general reluctance to disclose sensitive socioeconomic information and administrative constraints in the Republic of Korea. Considering that these factors may influence both brain and psychological outcomes, the findings should be interpreted with caution given the possibility of unmeasured confounding. Furthermore, due to the nature of child-rearing, our data may exhibit a sex bias toward mothers.

CRediT authorship contribution statement

Yong Jeon Cheong: Writing – original draft, Visualization, Validation, Supervision, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Seonkyoung Lee:** Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Ji Hyeon Ro:** Writing – original draft, Software, Methodology, Formal analysis, Data curation. **Jihyun Bae:** Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Minyoung Jung:** Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Consent for publication

Not applicable.

Ethics approval and consent to participate

The Ethics Committee of the Institutional Board of the Korea Brain Research Institute approved this study (approval number: 23-BR-05-01), which was conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent prior to participation.

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Declaration of competing interest

The authors declare that they have no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jad.2026.122001>.

Data availability

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

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