Supplementary Material: Women's neuroplasticity during gestation, childbirth, and postpartum

Table SM 1 Demographics of the main and replication datasets.

	Main Dataset		Replication Dataset	
Characteristic	**Controls**, N = 34	**Mothers**, N = 110	**Controls**, N = 24	**Mothers**, N = 29
Age at pregnancy session [years]				
Mean (SD)	33.32 (4.56)	33.12 (3.98)	31.49 (3.35)	32.74 (3.76)
Minimum-Maximum	25.41–45.98	24.10–43.79	25.04–39.38	26.12–38.50
Gestational weeks at pregnancy session [weeks]				
Mean (SD)		36.23 (0.96)		34.32 (0.84)
Minimum-Maximum		33.14–38.71		33.57–36.43
Gestational weeks at childbirth [weeks]				
Mean (SD)		39.67 (1.06)		39.76 (1.51)
Minimum-Maximum		37.10–41.50		36.29–42.43
Type of parturition [nos. of participants (%)]				
Vaginal		87 (79%)		22 (76%)
Emergency C-section		12 (11%)		5 (17%)
Scheduled C-section		11 (10%)		2 (6.9%)
Postpartum time [days]				
Mean (SD)		21.68 (8.05)		33.07 (5.84)
Median (IQR)		20 (16, 25.75)		31.00 (30, 34)
Minimum-Maximum		7–53		26–55
Time between sessions [days]				
Mean (SD)	43.97 (10.11)	47.15 (11.67)	73.54 (11.74)	71.16 (10.71)
Minimum-Maximum	31–70	27–90	57–98	51–87
Percentage of postpartum time between sessions				
Mean (SD)		46.43 (13.79)		47.61 (11.19)
Minimum-Maximum		12.73–82.14		33.33–73.68
Education [nos. of participants (%)]				
Primary	0 (0%)	4 (3.6%)		
Secondary	6 (18%)	15 (14%)	2 (8.3%)	1 (3.4%)
Higher	28 (82%)	91 (83%)	22 (92%)	28 (97%)
WAIS-IV Digits				
Mean (SD)	28.67 (5.39)	27.71 (4.76)	29.41 (4.45)	27.45 (4.85)
Minimum-Maximum	18–44	16–44	23–40	18–42

Datasets did not differ neither in age ($t(195)=1.55$; $P=0.12$), WAIS-IV digits ($t(192)=-0.46$; $P=0.65$) nor educational level ($\chi^2(2,197)=4.62$; $P=0.10$), but differed in intersession days ($t(195)=-14.22$; $P<0.0001$). In mothers, no differences were found in gestational weeks at delivery ($t(35.52)=-0.33$; $P=0.75$), percentage of postpartum time between sessions ($t(137)=-0.42$; $P=0.67$), or type of parturition ($\chi^2(2,139)=1.02$; $P=0.60$). However, mothers' differed in gestational weeks at pregnancy session ($t(137)=9.80$; $P<0.0001$) and postpartum time ($W=381.5$; $P<0.0001$).

There were no differences between mothers and nulliparous women ("Controls") in terms of age, time between sessions, or education in any of the datasets. Details of the within-dataset comparisons can be found in "Methods" - Data acquisition protocol.

The main sample size was 144 (110 mothers and 34 controls) in all variables except for the WAIS-IV, which had missing data from one control. The replication sample size was 53 (29 mothers and 24 controls) in all variables except for the WAIS-IV, which had missing data from two controls.

Normality distributions within datasets were ensured through skewness and kurtosis, and equal variances within and between datasets were ensured through F-tests. All variables were normally distributed except for the mothers' postpartum time of the replication dataset. For this variable, the median and interquartile ranges were also reported. All variables had equal variances between datasets except for the mothers' gestational weeks at childbirth. Therefore, two-tailed two-sample student T-tests were employed across variables except for between-dataset comparisons of mothers' postpartum time (two-tailed Wilcoxon non-parametric test) and mothers' gestational weeks at childbirth (two-tailed Welch's T-test). Abbreviations: SD= standard deviation. IQR=interquartile range, and WAIS-IV= Wechsler Adult Intelligence Scale.

Table SM 2 Descriptives and comparison statistics of the global differences in cortical metrics at Pregnancy session ("Prg"), Postpartum session ("Post"), and "Prg-to-Post" in mothers and nulliparous women ("Controls").

	Controls, N=34			Mothers, N=110			Two-Sample Comparisons		
Measure/Statistic	**Prg**	**Post**	**Prg-to-Post**	**Prg**	**Post**	**Prg-to-Post**	**Prg**	**Post**	**Prg-to-Post**
Cortical Volume [cm^3]									
Mean (SD)	469.19 (33.7)	468 (33.59)	−0.25 (1.14)	447.87 (29.51)	450.86 (29.7)	0.68 (1.38)			
t-statistic			−1.26			5.15	3.56	2.85	−3.54
Unc. P			0.218			<0.0001*	0.0005*	0.005*	0.0005*
Cohen's d			−0.22			0.49	0.7	0.56	−0.69
Cortical Thickness [mm]									
Mean (SD)	2.47 (0.08)	2.47 (0.09)	−0.08 (1.03)	2.41 (0.07)	2.42 (0.06)	0.64 (1.07)			
t-statistic			−0.46			6.26	4.42	3.29	−3.46
Unc. P			0.6464			<0.0001*	<0.0001*	0.0013*	0.0007*
Cohen's d			−0.08			0.6	0.87	0.65	−0.68
Surface Area [cm^2]									
Mean (SD)	1683.31 (114.77)	1681.19 (113.95)	−0.12 (0.47)	1655.9 (110.03)	1658.36 (110.2)	0.15 (0.55)			
t-statistic			−1.52			2.86	1.26	1.05	−2.6
Unc. P			0.1391			0.0051*	0.2108	0.2967	0.0102
Cohen's d			−0.26			0.27	0.25	0.21	−0.51

Statistics were calculated using two-tailed one-sample T-tests, except for the columns "Two-sample Comparison," which report two-tailed two-sample T-tests statistics. The degrees of freedom for the two-tailed one-sample T-tests are 33 (controls) and 109 (mothers). The degrees of freedom for the two-tailed two-sample T-tests are 142. Asterisks indicate those comparisons surviving an FDR-corrected P<0.05. Abbreviations: SD=standard deviation, Prg=Pregnancy session, Post=Postpartum session, Unc.: uncorrected, and Prg-to-Post=percentage of change from late pregnancy to early postpartum.

Table SM 3 Mothers' neuropsychological levels at late pregnancy ("Prg") and early postpartum ("Post") sessions.

Questionnaire	**Postpartum** Mean (SD)	**Pregnancy** Mean (SD)	**Difference: Post - Prg** Mean (SD)	**t(109)**
Perceived Stress (PSS)	20.48 (9.72)	15.88 (8.08)	4.6 (7.37)	6.55*
Sleep Quality (PSQI)	10.36 (3.22)	8.18 (3.84)	2.18 (3.95)	5.8*
Depression Symptoms (EDS)	6.05 (4.99)	4.2 (3.75)	1.85 (4.36)	4.44*
Maternal Attachment (MAS)	80.08 (7.08)	71.76 (5.92)	8.32 (6.53)	13.36*
Pregnancy anxiety (PRAS)		62.96 (12.1)		
Maternal Stress (MSS)	26.55 (6.95)			
Birth Experience (BEQ)	3.27 (0.92)			

The sample size was 110 for all the questionnaires. Normality distributions were ensured through skewness and kurtosis, and equal variances were ensured through F-tests. Therefore, paired sample T-tests were employed. Asterisks indicate a False Discovery Rate-corrected P<0.05. Abbreviations: SD=Standard Deviation, Prg=Pregnancy session, Post=Postpartum session, PSS=Perceived Stress Scale, PSQI=Pittsbugh Sleep Quality Index, MAS=Maternal Attachment Scales, EDS=Edinburgh Depression Scales, PRAS=Pregnancy-related Anxiety Scale, MSS=Maternal Stress Scale, and BEQ=Birth Experience Questionnaire.

Table SM 4 Neuropsychological comparisons between mothers and nulliparous women.

	Controls, N=34 Mean (SD)		**Mothers, N=110** Mean (SD)		**ANOVA Repeated Measures**		
Questionnaire	**Prg**	**Post**	**Prg**	**Post**	**Group** F(1,142)	**Session** F(1,142)	**Group:Session** F(1,142)
Sleep Quality (PSQI)	5.79 (3.08)	6 (3.08)	8.18 (3.84)	10.36 (3.22)	34.61*	11.2*	7.67*
Perceived Stress (PSS)	19.94 (7.08)	21.53 (10.12)	15.88 (8.08)	20.48 (9.72)	2.54	19.87*	4.71*

Mothers and nulliparous women differed in PSS at "Prg" and PSQI at both sessions. Mothers differed in PSQI and PSS between "Prg" and "Post" sessions. Normality distributions were ensured through skewness and kurtosis, and equal variances were ensured through F-tests. Therefore, paired sample T-tests were employed. The sample size was 144 (110 mothers and 34 nulliparous women). Asterisks indicate a False Discovery Rate-corrected P<0.05. Abbreviations: SD=Standard Deviation, Prg=Pregnancy session, Post=Postpartum session, PSQI=Pittsburgh Sleep Quality Index, and PSS=Perceived Stress Scale.

Table SM 5 Descriptives and comparison statistics of the global differences in cortical metrics at the late pregnancy session ("Prg"), early postpartum session ("Post"), and "Prg-to-Post" in "Labor" and "Pre-labor" mothers.

	Labor mothers, N=99			**Pre-Labor mothers**, N=11			**Two-Sample Comparisons**		
Measure/Statistic	**Prg**	**Post**	**Prg-to-Post**	**Prg**	**Post**	**Prg-to-Post**	**Prg**	**Post**	**Prg-to-Post**
Cortical Volume [cm^3]									
Mean (SD)	448.44 (29.29)	450.64 (29.23)	0.5 (1.22)	442.71 (32.4)	452.83 (35.23)	2.27 (1.74)			
t-statistic			4.08			4.33	0.61	−0.23	−4.36
Unc. P			0.0001*			0.0015*	0.5437	0.8172	<0.0001*
Cohen's d			0.41			1.31	0.19	−0.07	−1.39
Cortical Thickness [mm]									
Mean (SD)	2.41 (0.07)	2.42 (0.06)	0.51 (0.96)	2.39 (0.08)	2.43 (0.07)	1.77 (1.36)			
t-statistic			5.3			4.32	1	−0.41	−3.94
Unc. P			<0.0001*			0.0015*	0.3209	0.6849	0.0001*
Cohen's d			0.53			1.3	0.32	−0.13	−1.25
Surface Area [cm^2]									
Mean (SD)	1656.61 (108.79)	1658.22 (108.19)	0.1 (0.53)	1649.49 (126.15)	1659.63 (132.84)	0.59 (0.59)			
t-statistic			1.91			3.34	0.2	−0.04	−2.89
Unc. P			0.0595			0.0075*	0.8398	0.9681	0.0046*
Cohen's d			0.19			1.01	0.06	−0.01	−0.92

Statistics were calculated using two-tailed one-sample T-tests, except for the columns "Two-sample Comparisons," which report two-tailed two-sample T-tests statistics. The degrees of freedom for the two-tailed one-sample T-tests are 98 (labor mothers) and 10 (pre-labor mothers). The degrees of freedom for the two-tailed two-sample T-tests are 108. Asterisks indicate those comparisons surviving a False Discovery Rate-corrected P<0.05. Abbreviations: SD=standard deviation, Prg=Pregnancy session, Post=Postpartum session, Unc.=uncorrected, and Prg-to-Post=percentage of change from late pregnancy to early postpartum.

Table SM 6 Descriptives and comparison statistics of the global percentages of changes in cortical metrics in "Labor" and "Pre-labor" mothers after excluding the effects of gestational weeks at childbirth and time between childbirth and postpartum session.

Measure	**Labor, N=99** Mean (SD)	**Pre-Labor, N=11** Mean (SD)	**t(108)**	**Unc. P**	**Cohen's d**
Cortical Volume [cm^3]	−0.08 (1.13)	0.76 (1.82)	−2.19	0.0308*	−0.70
Cortical Thickness [mm]	−0.07 (0.94)	0.65 (1.41)	−2.30	0.0233*	−0.73
Surface Area [cm^2]	−0.01 (0.46)	0.08 (0.61)	−0.62	0.5393	−0.20

Statistics were calculated using two-tailed two-sample T-tests. Asterisks indicate those comparisons surviving a False Discovery Rate-corrected P<0.05. Abbreviations: SD=standard deviation and Unc. P=uncorrected P-value.

Table SM 7 Descriptives and comparison statistics of the global percentages of change in cortical metrics as a function of the delivery method.

	One-Sample Comparisons			Omnibus Test	Two-Sample Comparisons		
Measure/Statistic	**Vaginal N=87**	**Emergency C-section N=12**	**Scheduled C-section N=11**	**F(2,109)**	**Vaginal vs. Emergency C-section**	**Vaginal vs. Scheduled C-section**	**Emergency C-section vs. Scheduled C-section**
Cortical Volume							
Mean (SD)	0.53 (1.25)	0.3 (1.05)	2.27 (1.74)				
Statistic	3.95	0.99	4.33	9.616	0.61	−4.17	−3.33
Unc. P	0.0002*	0.3442	0.0015*	0.0001*	0.5460	<0.0001*	0.0030*
Cortical Thickness							
Mean (SD)	0.56 (0.98)	0.18 (0.79)	1.77 (1.36)				
Statistic	5.33	0.77	4.32	8.576	1.3	−3.7	−3.49
Unc. P	<0.0001*	0.4551	0.0015*	0.0004*	0.1970	0.0004*	0.0020*
Surface Area							
Mean (SD)	0.09 (0.53)	0.15 (0.57)	0.59 (0.59)				
Statistic	1.68	0.91	3.34	4.204	−0.34	−2.92	−1.83
Unc. P	0.0967	0.3837	0.0075*	0.0170*	0.7370	0.0040*	0.0810

Asterisks indicate those comparisons surviving a False Discovery Rate-corrected $P<0.05$. The degrees of freedom for the two-tailed one-sample T-test are 86 (Vaginal), 11 (Emergency C-section), and 10 (Scheduled C-section). The degrees of freedom for the independent two-tailed two-sample T-tests are 97 (Vaginal vs. Emergency C-section), 96 (Vaginal vs. Scheduled C-section), and 21 (Emergency C-section vs. Scheduled C-section). Abbreviations: SD=standard deviation and Unc. P=uncorrected P-value.

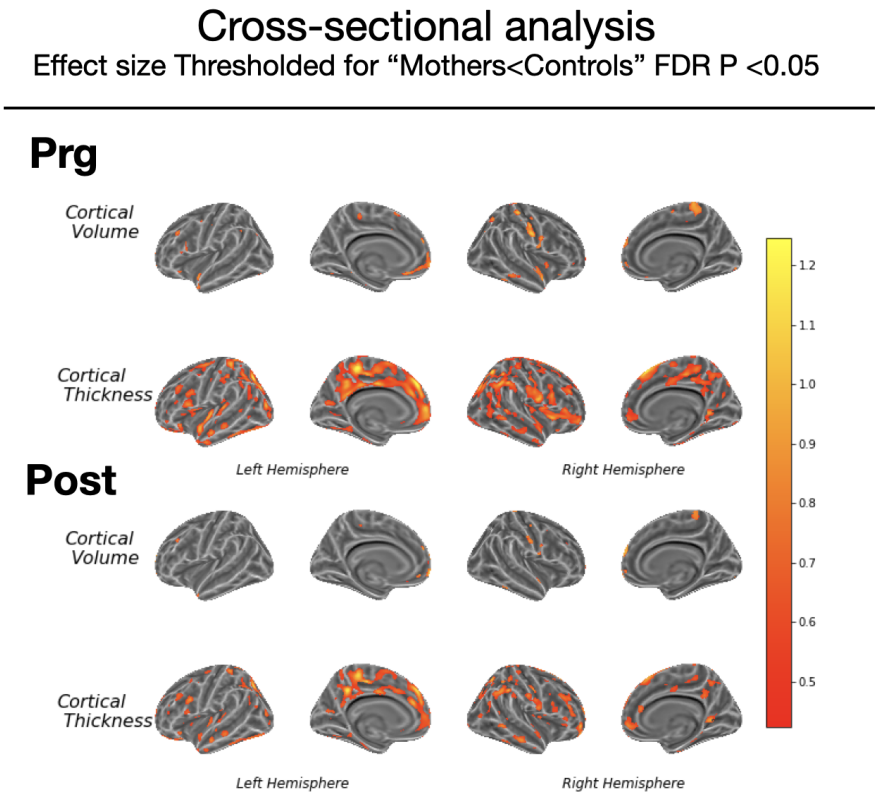

Fig. SM 1 Vertex-wise *Cohen*'s d maps of the cortical decreases in mothers (N=110) compared to nulliparous women ("Controls", N=34) at late pregnancy ("Prg") and early postpartum ("Post") sessions (P<0.05, False Discovery Rate-corrected). *Cohen*'s d maps were projected to the inflated *fsaverage* template provided by the FreeSurfer software.

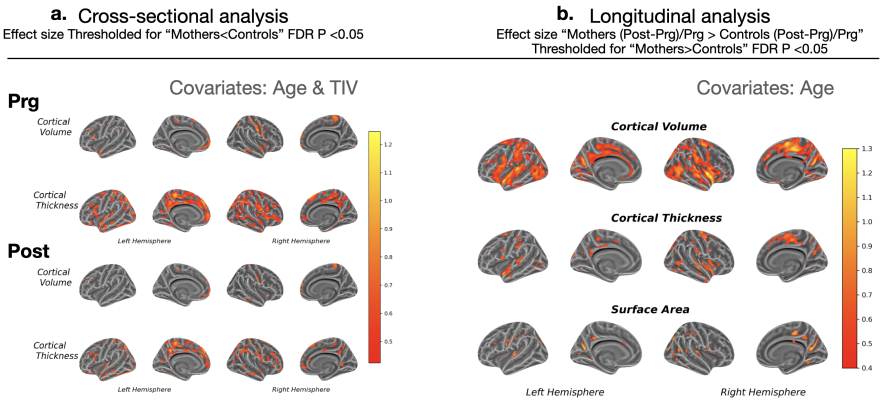

Fig. SM 2 (a) Vertex-wise *Cohen*'s d maps of the cortical decreases in mothers (N=110) compared to nulliparous women ("Controls", N=34) at late pregnancy ("Prg") and early postpartum ("Post") sessions excluding the potential effects of age and total intracranial volume (TIV) (P<0.05, False Discovery Rate (FDR)-corrected). (b) Vertex-wise *Cohen*'s d maps of the "Prg-to-Post" cortical increases in mothers compared to controls excluding the potential effects of age (P<0.05, FDR-corrected). *Cohen*'s d maps were projected to the inflated *fsaverage* template provided by the FreeSurfer software.

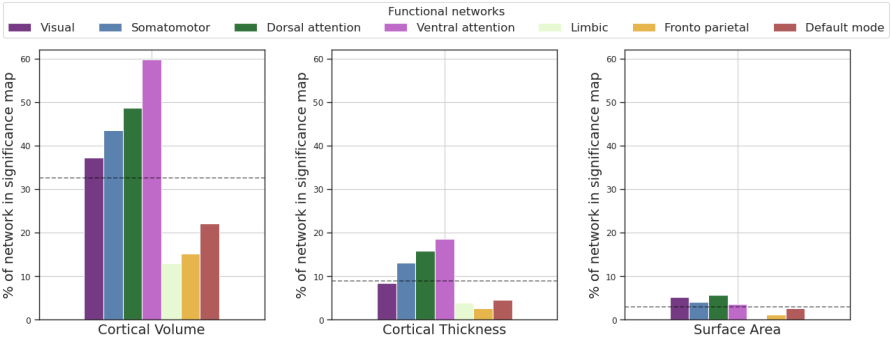

Fig. SM 3 Percentage of vertices in the seven large-scale functional brain networks [18] with significant "Prg-to-Post" increases in cortical volume, thickness, and surface area in mothers (N= 110) compared to nulliparous women ("Controls", N= 34) from Figure 2. The dashed black line indicates the percentage of significant vertices at a whole-brain level. Abbreviations: Prg=pregnancy session, Post=postpartum session, and Prg-to-Post=from late pregnancy to early postpartum sessions.

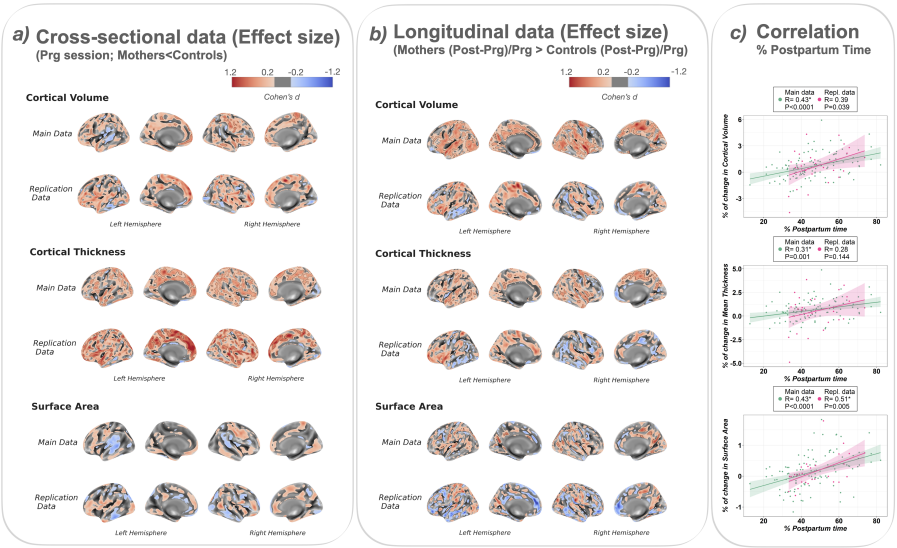

Fig. SM 4 Vertex-wise *Cohen*'s d maps of the cortical changes in the main (110 mothers and 34 nulliparous women ("Controls")) and replication (29 mothers and 24 controls) datasets. a) Cross-sectional vertex-wise cortical decreases (red) and increases (blue) in mothers compared to controls at the "Prg" session. Black outlines enclose results surviving a False Discovery Rate (FDR)-corrected P<0.05. b) Longitudinal vertex-wise "Prg-to-Post" cortical increases (red) and reductions (blue) in mothers compared to controls. Black outlines enclose results surviving an FDR-corrected P<0.05. c) Correlations between the global percentages of change in cortical metrics and the percentage of postpartum time between sessions. The shading on the least squares regression line represents the 95% confidence interval. Asterisks indicate *Pearson* coefficients (R) surviving an FDR-corrected P<0.05. *Cohen*'s d maps were projected to the inflated *fsaverage* template provided by the FreeSurfer software. Effect sizes were collapsed to ±1.2. Abbreviations: Prg=Pregnancy session and Post=postpartum session.

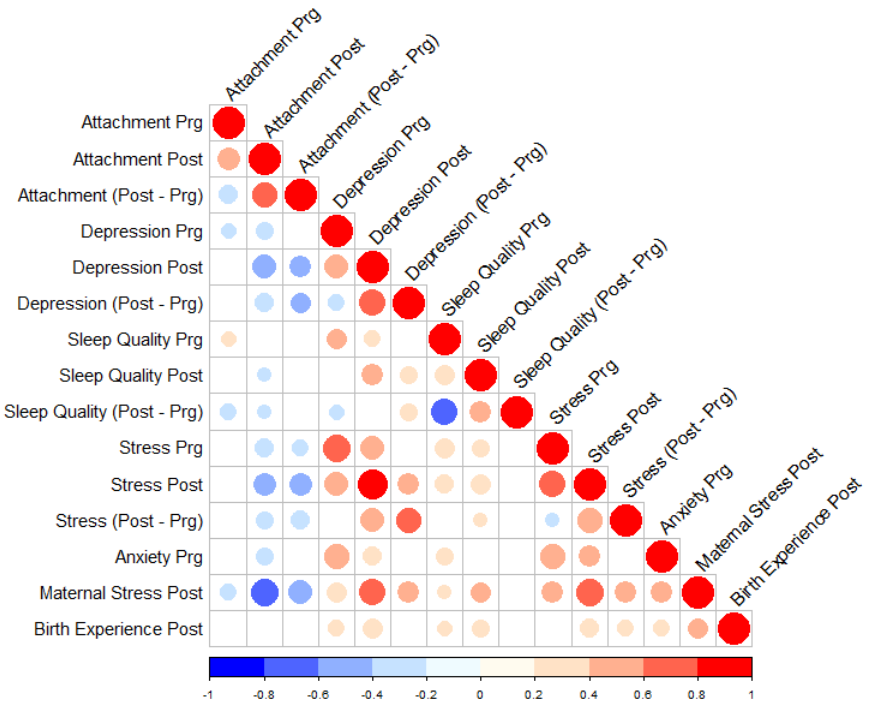

Fig. SM 5 Complete correlation matrix of the neuropsychological variables in the mothers (N=110), including the scales at the late pregnancy ("Prg") and early postpartum ("Post") sessions. Circles represent the two-tailed *Pearson* coefficients of those correlations surviving a False Discovery Rate-corrected P<0.05. Blue and red circles indicate negative and positive correlations, respectively. From top to bottom, the neuropsychological variables correspond to the following questionnaires: Maternal Attachment Scale, Edinburgh Depression Scale, Pittsburgh Sleep Quality Index, Perceived Stress Scale, Pregnancy Anxiety Scale, Maternal Stress Scale, and Birth Experience Questionnaire. Abbreviations: Prg=Pregnancy session and Post=Postpartum session.

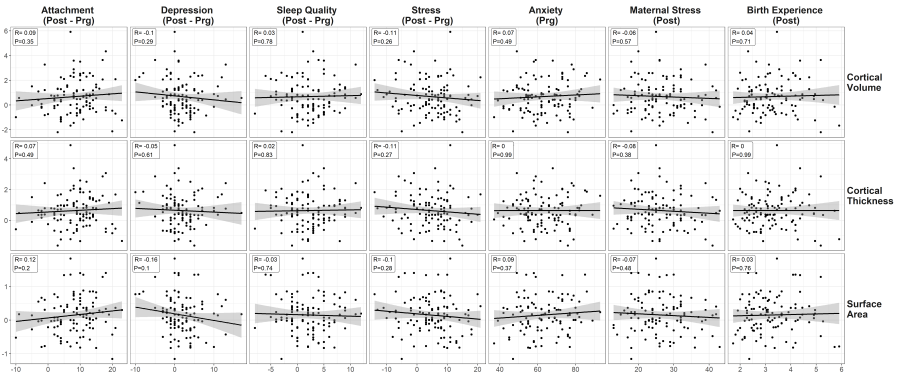

Fig. SM 6 Correlation matrix between the mothers' global percentages of change in cortical metrics and the neuropsychological variables. None of the correlations survived the False Discovery Rate-corrected P<0.05. From left to right, the neuropsychological variables correspond to the following questionnaires: Maternal Attachment Scale, Edinburgh Depression Scale, Pittsburgh Sleep Quality Index, Perceived Stress Scale, Pregnancy Anxiety Scale, Maternal Stress Scale, and Birth Experience Questionnaire. Abbreviations: Prg=Pregnancy session, Post=Postpartum session, R=two-tailed *Pearson* correlation coefficient, and P=uncorrected P-value

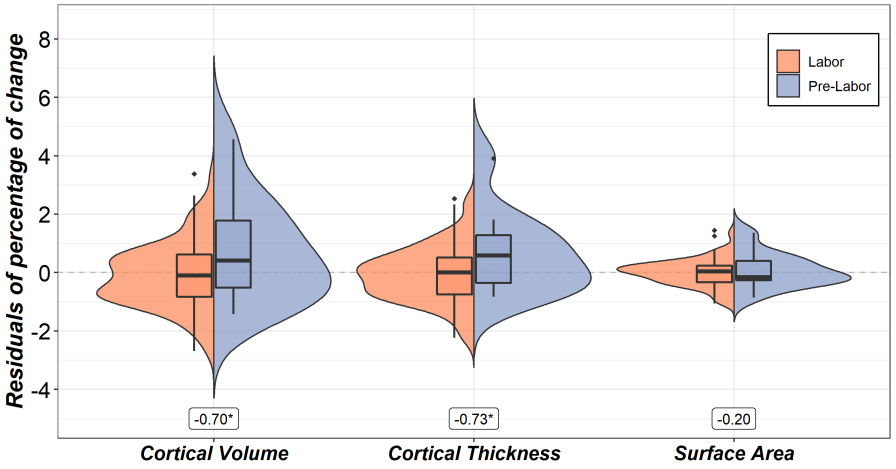

Fig. SM 7 Global percentages of change in cortical metrics in mothers who initiated labor ("Labor", N=99) and mothers who underwent a scheduled cesarean section ("Prelabor", N=11) excluding the potential effects of gestational weeks at childbirth and time between childbirth and postpartum session. Effect sizes of the between-mothers comparisons were calculated as Cohen's d. Asterisks indicate results surviving a two-tailed P<0.05 False Discovery Rate correction.

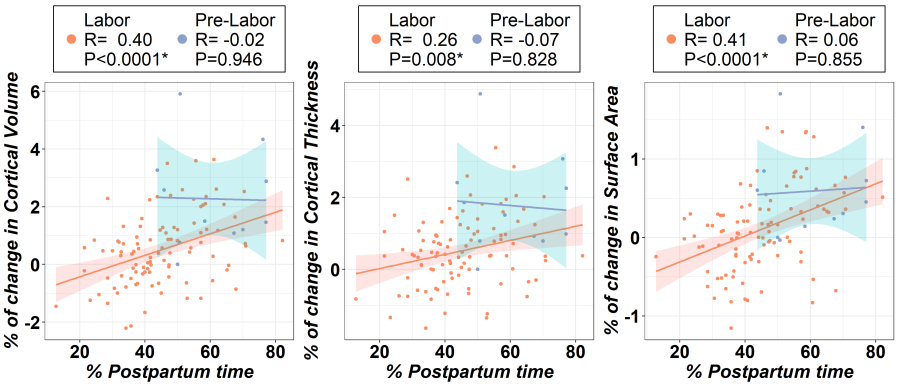

Fig. SM 8 Correlations between the global percentages of change in cortical metrics and the percentage of postpartum time between sessions in "Labor" (orange, N=99) and "Pre-labor" (purple, N=11) mothers. The shading on the least squares regression line represents the 95% confidence interval. Asterisks indicate two-tailed *Pearson* coefficients (R) surviving the False Discovery Rate-corrected P<0.05. Abbreviations: R=two-tailed *Pearson* correlation coefficients and P=uncorrected P-value.

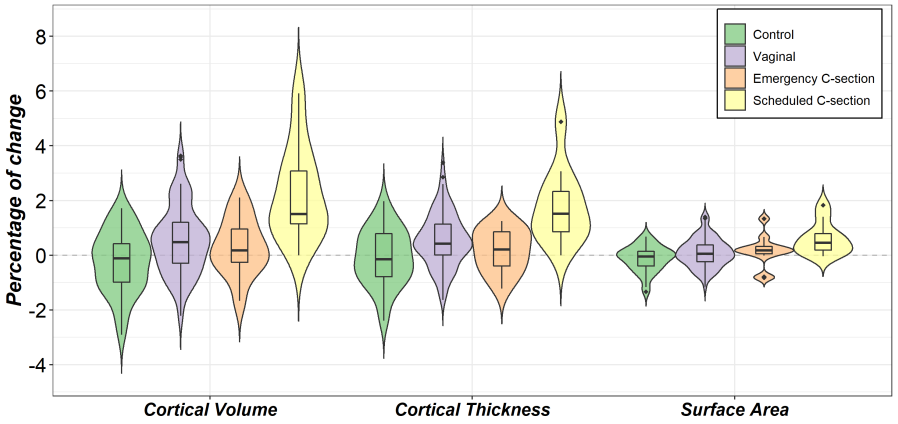

Fig. SM 9 Global percentages of change in cortical metrics in mothers who underwent a vaginal (N=87), emergency cesarean section (C-section, N=12), or scheduled C-section (N=11). Nulliparous women ("Control", N=34) are displayed as a reference.

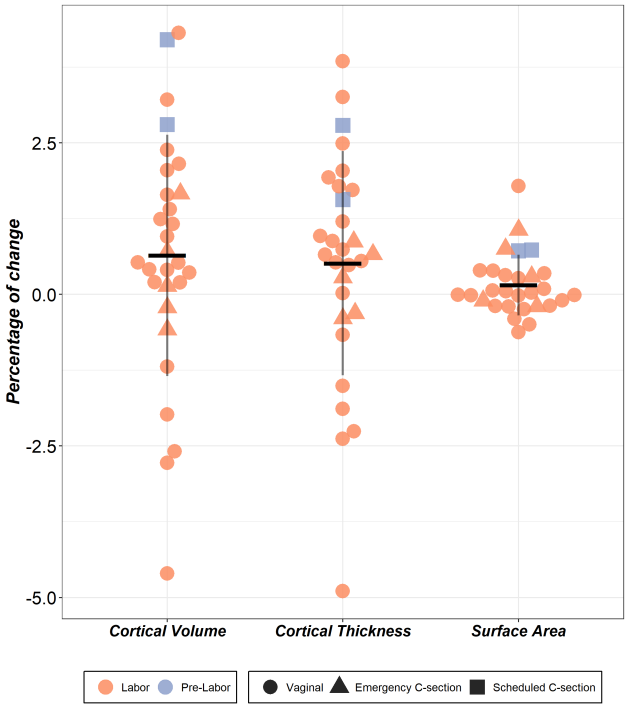

Fig. SM 10 Global percentages of change in cortical volume, thickness, and surface area in mothers (N=29) of the replication sample. Orange circles represent mothers who underwent a vaginal delivery (N=22), orange triangles show those who experienced emergency cesarean section (C-section, N=5), and purple squares represent those mothers with scheduled C-sections (N=2). Black horizontal lines represent the mean percentages of change values for the whole mothers' sample and vertical lines their standard deviation.

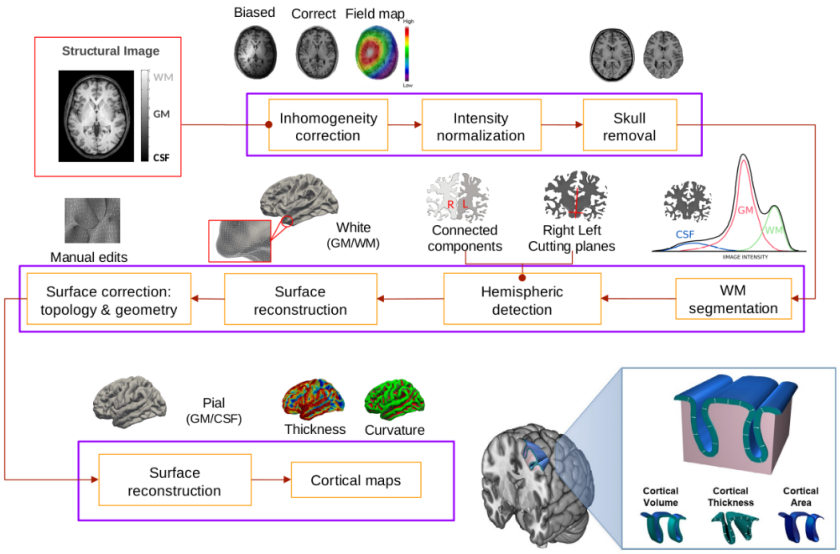

Fig. SM 11 Schematic representation of the FreeSurfer's cross-sectional pipeline.

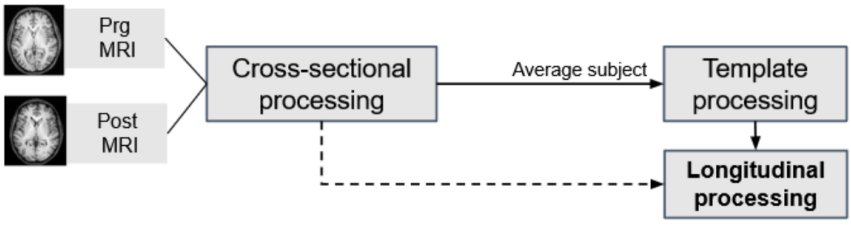

Fig. SM 12 Schematic representation of the FreeSurfer's longitudinal pipeline.