Supplementary material

Supplementary Text I: Assessing the cortical gray matter volume using generalized additive modelling.

Global gray matter volume changes were also analyzed under a generalized additive model (GAM) models using the *mgcv* package in R (version 1.8.42). We selected GAM as it is well-suited statistical method to assess non-linear trajectories. The model incorporated Group as a fixed effect and a smooth function for Session that allowed to model different trajectories for each group with a maximum spline of 3. To account for confounding factors, we also included z-standardized covariates of age at session 1, eTIV, mean Euler number of each session, and time interval between sessions 1 and 2. Additionally, we incorporated a random intercept to control for subject-specific difference (see Formula A).

(A) Cortical gray matter volume ~ Group + s(Session, by = Group, k=3) + eTIV + Age + Euler + Inter-session Interval + (1 | participant ID)

The fitting of the GAM model in Formula B was compared to the equivalent LMER model (Formula 1) using Bayesian Information Criteria (BIC). The model with a lower BIC was selected as the better-fitted model.

Supplementary Text II: Effect of eTIV on the gray matter volume changes during pregnancy and postpartum

As a sensitivity analysis, we tested the effect of eTIV on the gray matter volume changes observed during pregnancy and postpartum as a function of group. We fitted an LME model using total cortical volume as the dependent variable. We used group (gestational mother, non-gestational mother, and nulliparous women), a linear and quadratic term for session, and 7 interactions (i.e., group*linear term for session, group*quadratic term for session, group*eTIV, linear term for session*eTIV, quadratic term for session*eTIV, group*eTIV* linear term for session, and group*eTIV*, quadratic term for session) as fixed effects. To account for confounding factors, we also included z-standardized covariates of age at session 1, mean Euler number of each session, and time interval between sessions 1 and 2. Moreover, we incorporated a random intercept to control for subject-specific differences (see Formula B).

(B) Cortical Metric ~ Group + Session + Session^2 + Group*Session + Group*Session^2 + Group*eTIV + Session*eTIV + Session*eTIV + Group*Session*eTIV + Group*Session^2*eTIV + Age + Euler + Inter-session Interval + (1 | participant ID)

The fitting of model B was compared with the model in Formula 1 (see Methods section) by means of an analysis of variance using the anova function on the R stats library.

Supplementary Text III: Effect of BMI on the gray matter volume changes during pregnancy and postpartum

Following a reviewer's suggestion, we tested the effect weight fluctuation on the GM volume trajectory adding the BMI of each session as an extra covariable on Formula 1 (see Methods section).

Supplementary Text IV: Urinary phase II steroid profile

Reagents and chemicals

Aqueous ammonia solution (25%), methanol, acetonitrile and formic acid (FA) (LC–MS grade) were from Merck (Darmstadt, Germany). Phosphoric acid and ammonium formate were provided by Sigma-Aldrich (Louis, MO, USA) and VWR Prolabs Chemicals (Leuven, Belgium), respectively. Ultrapure water was obtained using a Milli-Q purification system (Millipore Ibérica, Barcelona, Spain).

Standards

References to phase II steroid compounds´ standards suppliers are given along with MS characteristics of metabolites in the table S28.

Quantitative synthesis on customer demand of androst-5-ene-3β17β-diol bisulfate, pregn-5-ene-3β20α-diol and 3β20β-diol bisulfates, 5α-pregnane-3β20α-diol bisulfate was performed according to previously described procedure (60), whereas pregn-5-ene-3β20α-diol 3β-sulfate, 20α-glucuronide and estradiol 3-sulfate, 17β-glucuronide were quantitatively synthesized using another published methodology (61).

Stably labeled 17-S{^{18}O}$_3$-5α-androstane-3α,17β-diol bisulfate and 17-S{^{18}O}$_3$-5α-androstane-3β,17β-diol bisulfate, 3-S{^{18}O}$_3$-epiandrosterone-sulfate and 3-S{^{18}O}$_3$-5α-androstane-3β,17β-diol 3β-sulfate, 17β-

glucuronide were synthetized by the same means and used as internal standards: ISTD-biSulf_1, ISTD-biSulf_2, ISTD-Sulf_2 and ISTD-SulfGluc, respectively (table S28).

Compounds 11-dehydrocorticosterone sulfate, pregn-5-enediol 3b,20a 3-sulfate, pregn-5-enediol 3b,20a 20-sulfate, pregn-5-enetriol 3b,17,20a 3,20-bisulfate, 5b-pregnanediol 3a,20a 20-sulfate, 5a-pregnanediol 3a,20a 20-sulfate, 5a-pregnanediol 3a,20b 20-sulfate, 5b-pregnanediol 3b,20a 20-sulfate and 16b-hydroxydehydroepiandrosterone 3-sulfate were qualitatively synthetized *in-house* on small scale for identification purposes applying earlier mentioned methodology (60).

All standards were diluted in 100% methanol and stored at -20ºC prior to use.

Sample preparation

On the day of analysis, an aliquot of urine samples was thawed at room temperature and processed for steroid phase II metabolites extraction and concentration using solid-phase extraction (SPE) method. First, 15 µL of internal standards (ISTD) mix was added to each urine sample (1 mL) and then the mixture was acidified with 1 mL of 4% aqueous phosphoric acid. The SPE was performed using Oasis HLB 3 cc cartridges (Waters Associates, Milford, MA, USA) previously activated with 2 mL of methanol, and equilibrated with 2 mL of water and 2 mL of 2% FA in water. After washing with 2 mL of 2% FA in water, steroids were eluted in two stages: the first elution was performed with 1 mL of 2% FA in methanol followed with 1 mL of methanol; the second one was performed with 1 mL of 5% ammonia in methanol followed with 1 mL of methanol. Both elutes from the same sample were dried separately under N_2 at 40 ºC and reconstituted each in 1 mL of methanol. After combination of both reconstituted extracts, the mix was evaporated under N_2 at 40 ºC. The residue was reconstituted with 100 µL of 10% acetonitrile in water, and 5 µL were injected on the UHPLC-MS/MS system. Due to the logistics of the volunteers' recruitment and specificity of both, samples processing and instrumental analysis, urine samples were processed in several batches along with corresponding calibration curves and a set of quality control (QC) samples. Calibration curves in SPE-stripped urine and set of QCs were prepared for each batch along with urine samples.

Preparation of stripped urine for calibration curves

Urine pool from different subjects was passed in through Oasis HLB 6 cc cartridge (Waters) previously conditioned with 3 mL of methanol and equilibrated with 3 mL of water. The unretained portion of urine was collected after load, checked for absence of residual steroid metabolites and labelled as SPE-stripped urine.

UHPLC-MS/MS instrumentation

The chromatographic separation of urine extracts was performed at flow rate of 400 uL/min at 30ºC on an Acquity UPLC Class I chromatographic system (all from Waters Associates) using an Acquity UPLC CSH C18 column (2.1 × 100 mm i.d., 1.7 μm) fixed to Acquity UPLC CSH C18 VanGuard Pre-Column (2.1 × 5 mm i.d., 1.7 μm) (all from Waters Associates).

For direct determination of phase II steroid metabolites, acetonitrile:water (9:1, v/v) and water, both with ammonium formate (25 mM), were used as organic and aqueous mobile phase solvents, respectively. The gradient elution program was applied, where the percentage of organic solvent was linearly changed as follows: 0 min, 10%; 0.5 min, 10%; 15 min, 47%; 15.5 min, 100%; 18,5 min, 100%; 19 min, 10%; 20 min, 10%. In total, the chromatographic method lasted 20 min.

MS/MS analysis was carried out on a triple quadrupole (XEVO TQ-S micro) mass spectrometer equipped with an orthogonal Z-spray-electrospray ionization source (ESI) form Waters Associates. Nitrogen was used as drying and nebulizing gas. The desolvation gas flow was 1200 L/h, and the cone gas flow was 50 L/h. A cone voltage of 20 V and a capillary voltage of 2 kV were used in negative ionization mode. The nitrogen desolvation temperature was 600 °C, and the source temperature was 150 °C. The monitoring and quantification of all analytes was performed using selective reaction monitoring (SRM) mode. The specific transitions and optimum collision energy are summarized in table S28 for each detected steroid metabolite.

Data analysis

MassLynx V4.1 and TargetLynx XS software (Waters) were used for data management, instrument manipulation and quantification of urinary steroid metabolites by UHPLC-MS/MS analysis.

The response of compounds was calculated as ratio between analyte´s and internal standard´s areas. Concentrations of endogenous steroid metabolites were calculated using slopes of compound specific

calibration curves built in steroid stripped urine. Endogenous metabolites for which quantitative standards were not available were identified by qualitative standards and relatively quantified using calibration curves of available quantitative standards of their isomers or structurally resemble steroid metabolites, assuming equal response for representative mass spectrometric transitions.

Non-detectable values for a given metabolite were converted to the half of its lowest concentration detected in over-all samples of the study (62). Normalized concentrations were log10-transformed for statistical analysis.

Samples normalization

Creatinine urinary concentrations were measured by method published earlier (63). Concentration of urinary endogenous steroid metabolites were normalized to concentrations of excreted creatinine and expressed in ng/mg of creatinine.

Fig S1.

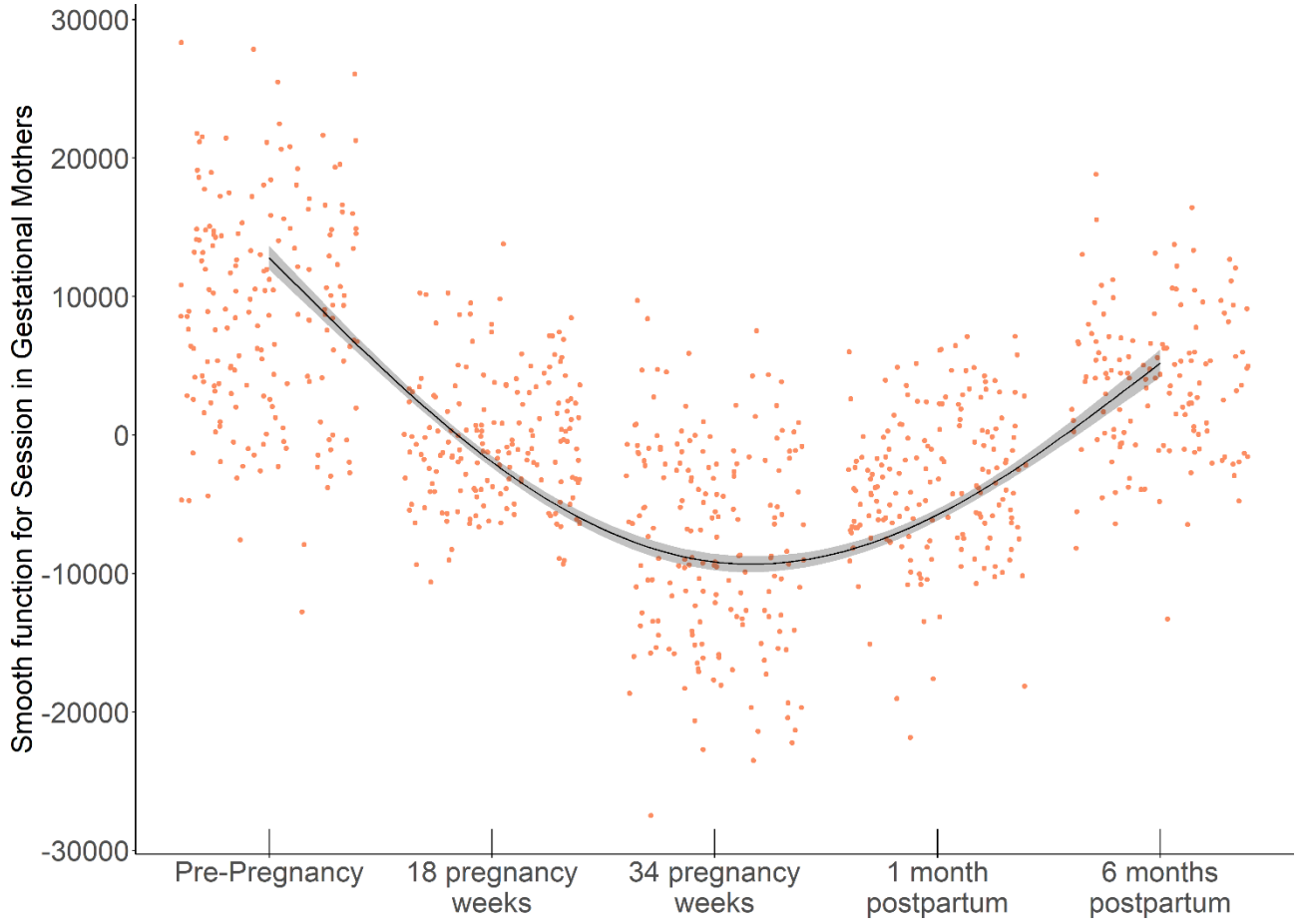

Fig S1. Gray matter volume trajectory in gestational mothers using a generalized added model (N = 127). Gray matter volume changes over pregnancy and postpartum period. The partial effect plot for the session smooth was derived from the following generalized added model*: Cortical gray matter volume ~ Group + s(Session, by = Group, k=3) + eTIV + Age + Euler + Inter-session Interval + (1 | participant ID).* Shaded areas represent a 95% confidence interval derived from the model.

Fig S2.

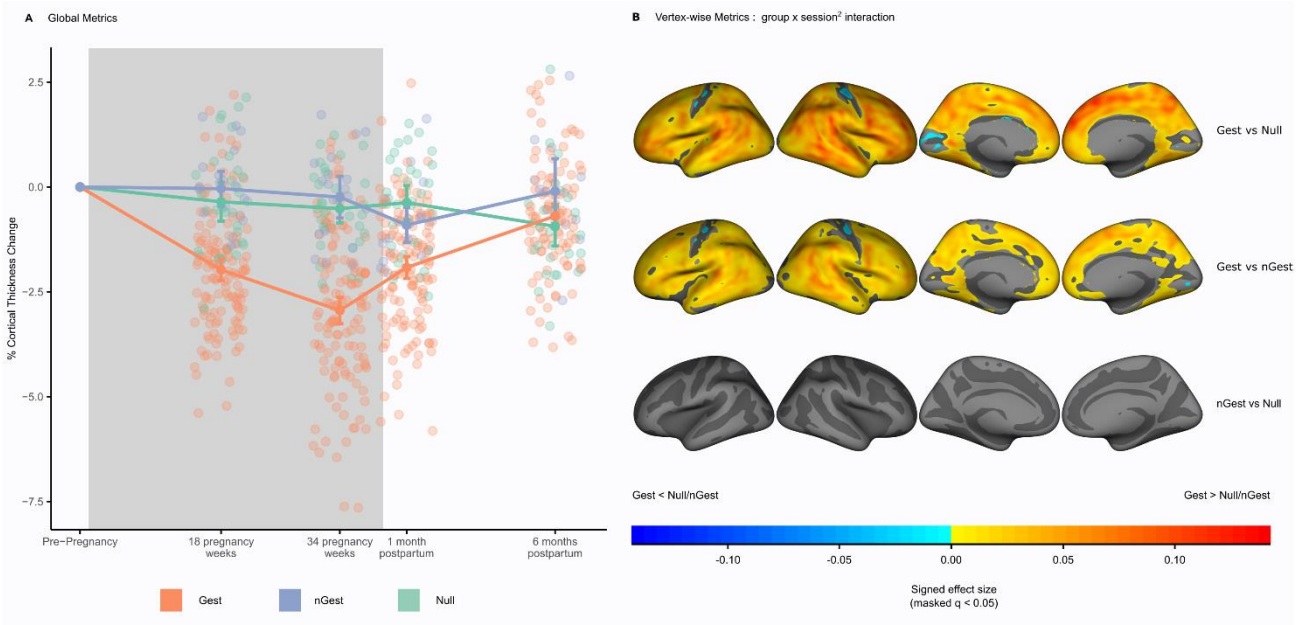

Fig S2. Longitudinal cortical thickness trajectory across pregnancy and postpartum (N = 179). Longitudinal changes were derived from the group x session^2 fixed effect term of the adjusted linear mixed effect model: Cortical Thickness ~ Group + Session + Session^2 + Group*Session + Group*Session^2 + eTIV + Age + Euler + Inter-session Interval + (1 | participant ID). A. Mean percentage of cortical GM volume change per group and session in relation to the baseline (i.e., Session 1 - Pre-pregnancy Session). Error bars correspond to 95% confidence intervals around the sample's mean at each experimental group and session. The gray shading corresponds to the pregnancy period. B. Vertex-wise signed effect size maps (η_p^2) of the group x session^2 interaction (q-value < 0.05). Indicating larger quadratic effects (red) and smaller quadratic effects (blue) in gestational mothers than in nulliparous or non-gestational mothers. Signed effect size maps were projected to the inflated fsaverage template provided by the FreeSurfer software. Colors were collapsed to ±0.14, which indicated a large effect size. Gest, gestational mothers; nGest, non-gestational mothers; Null, nulliparous women.

Fig S3.

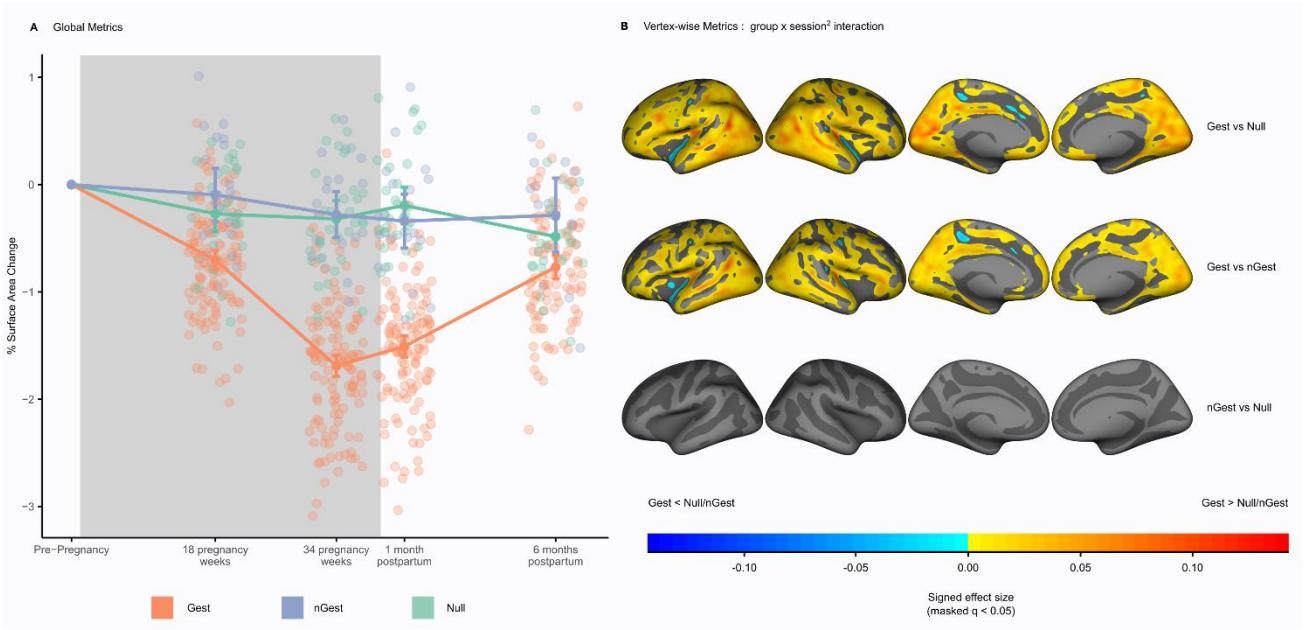

Fig S3. Longitudinal surface area trajectory across pregnancy and postpartum (N = 179). Longitudinal changes were derived from the group x session^2 fixed effect term of the adjusted linear mixed effect model: Surface Area ~ Group + Session + Session^2 + Group*Session + Group*Session^2 + eTIV + Age + Euler + Inter-session Interval + (1 | participant ID). A. Mean percentage of cortical GM volume change per group and session in relation to the baseline (i.e., Session 1 - Pre-pregnancy Session). Error bars correspond to 95% confidence intervals around the sample's mean at each experimental group and session. The gray shading corresponds to the pregnancy period. B. Vertex-wise signed effect size maps (η_p^2) of the group x session^2 interaction (q-value < 0.05). Indicating larger quadratic effects (red) and smaller quadratic effects (blue) in gestational mothers than in nulliparous or non-gestational mothers. Signed effect size maps were projected to the inflated fsaverage template provided by the FreeSurfer software. Colors were collapsed to ±0.14, which indicated a large effect size. Gest, gestational mothers; nGest, non-gestational mothers; Null, nulliparous women.

Fig S4.

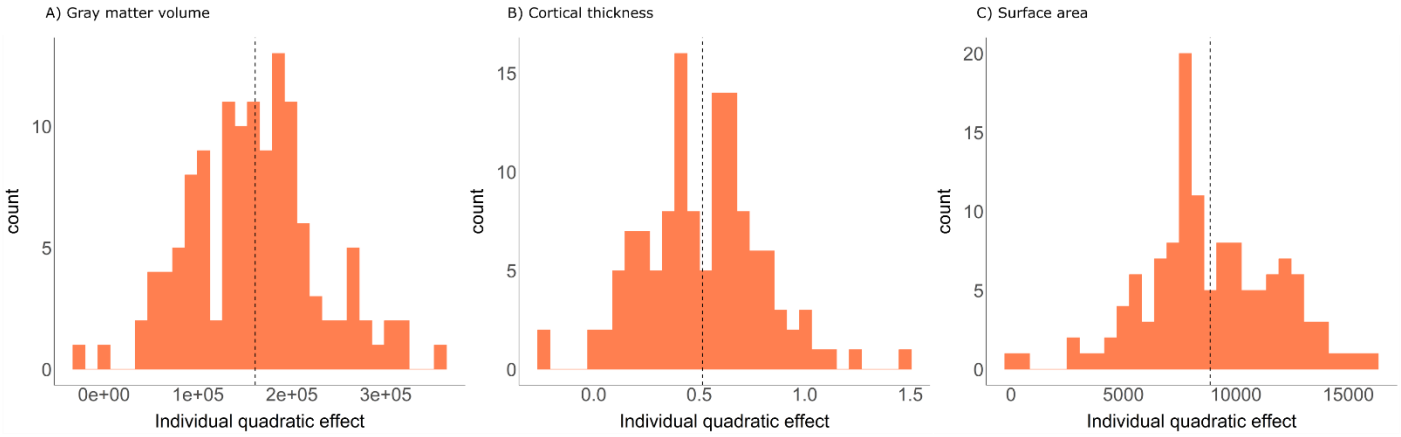

Fig S4. Interindividual variation on the quadratic trajectory for brain structure metrics in gestational mothers (N=127). Each participant's conditional means of the quadratic random effects were derived from the following models: Cortical Metric ~ 1 + (Session + Session^2 | participant ID). A, B, and C, represent the frequency distribution of the quadratic effect on cortical gray matter volume, cortical thickness and surface area. The black dashed line is set on the mean for each cortical metric.

Fig S5.

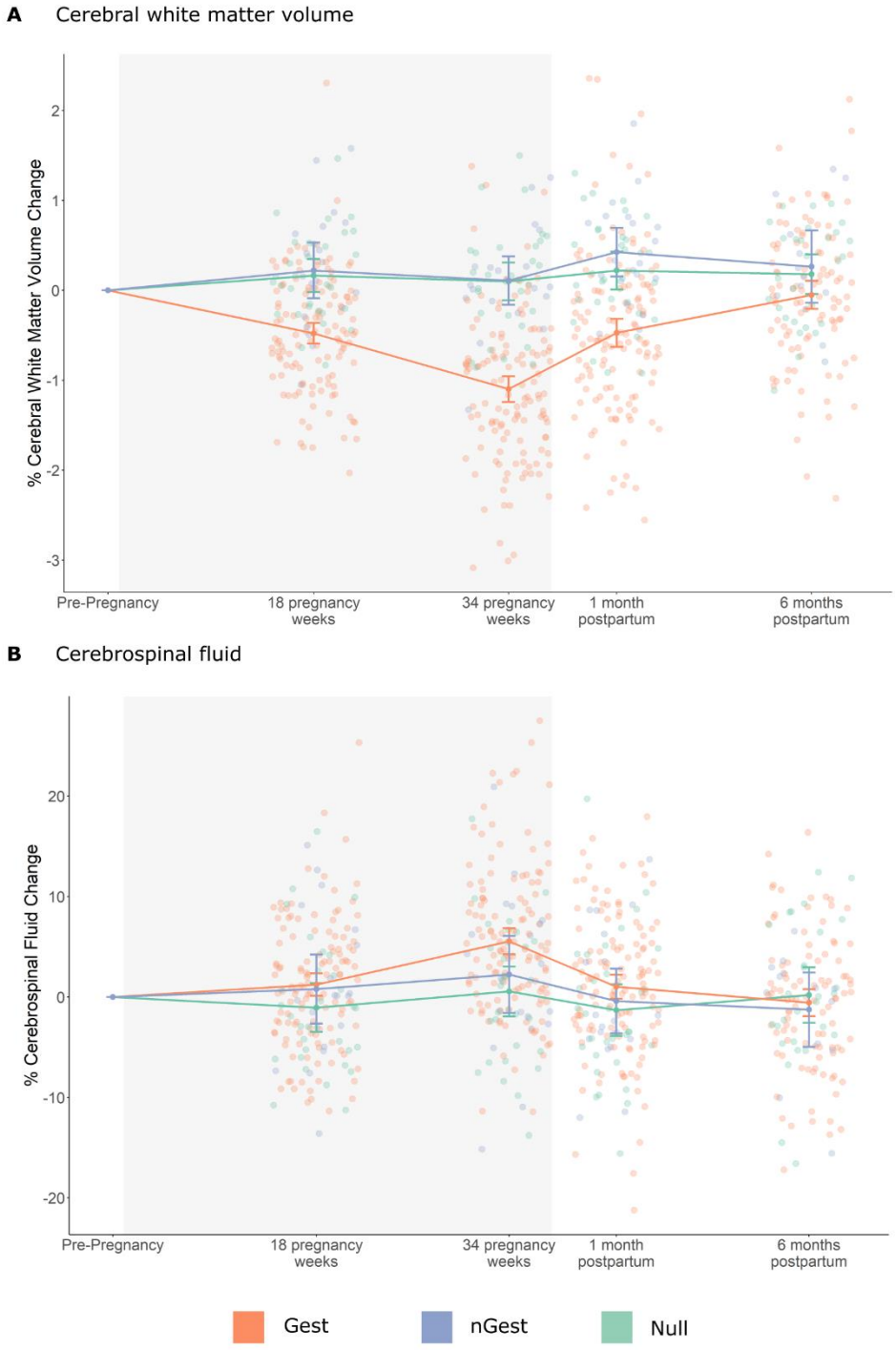
A
Cerebral white matter volume
% Cerebral White Matter Volume Change
2
1
0
-1
-2
-3
Pre-Pregnancy
18 pregnancy weeks
34 pregnancy weeks
1 month postpartum
6 months postpartum
B
Cerebrospinal fluid
% Cerebrospinal Fluid Change
20
10
0
-10
-20
Pre-Pregnancy
18 pregnancy weeks
34 pregnancy weeks
1 month postpartum
6 months postpartum
Gest
nGest
Null

Fig S5. Longitudinal cerebral white matter volume and cerebrospinal fluid trajectory across pregnancy and postpartum (N = 179). A. Mean percentage of cortical white matter (WM) volume change per group and session in relation to the baseline (i.e., Session 1 - Pre-pregnancy Session). B. Mean percentage of cerebrospinal fluid (CSF) change per group and session in relation to the baseline (i.e., Session 1 - Pre-pregnancy Session). In both panels, longitudinal changes were derived from the group x session^2 fixed effect term of the adjusted linear mixed effect models: WM volume or CSF ~ Group + Session + Session^2 + Group*Session + Group*Session^2 + eTIV + Age + Euler + Inter-session Interval + (1 | participant ID). Error bars correspond to 95% confidence intervals around the sample's mean at each experimental group and session. The gray shading corresponds to the pregnancy period. Gest, gestational mothers; nGest, non-gestational mothers; Null, nulliparous women.

Fig. S6.

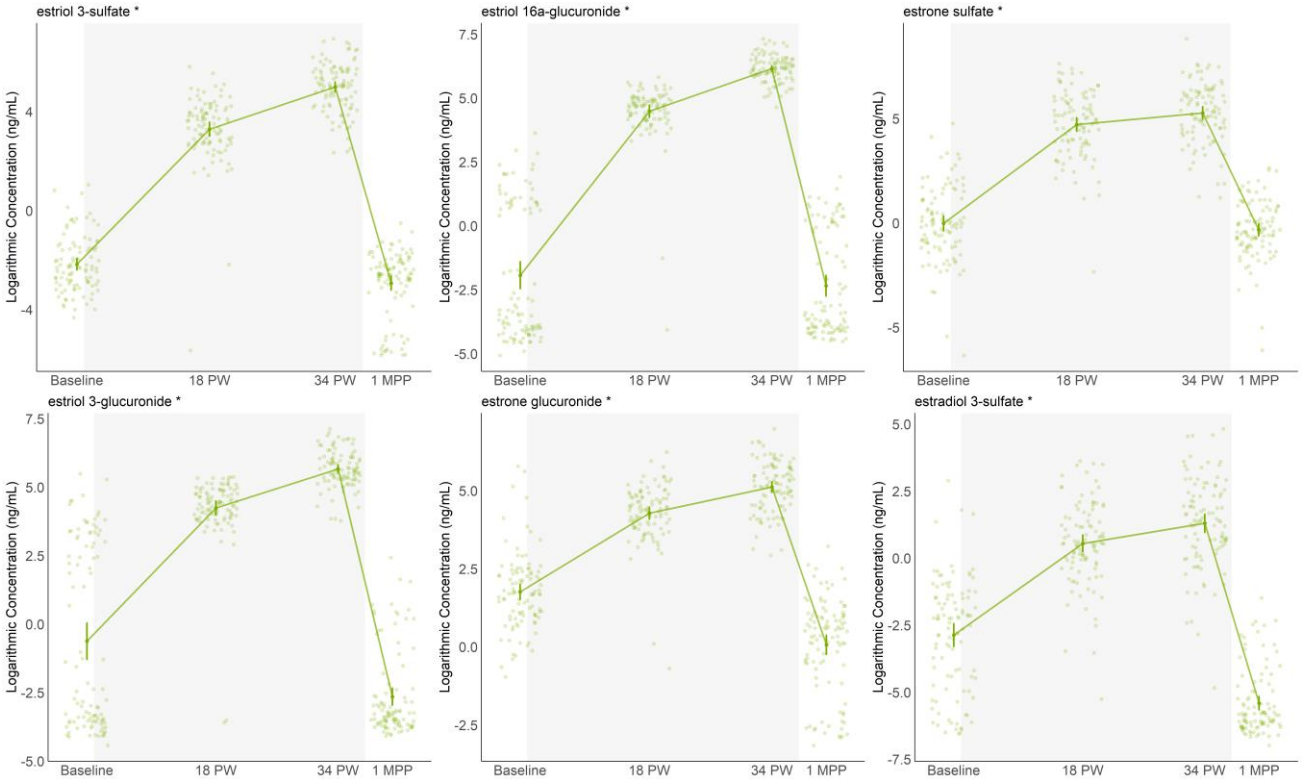

Fig S6. Longitudinal estrogenic trajectories across pregnancy and postpartum in gestational mothers (N = 100). Longitudinal changes derive from the group x session^2 fixed effect term of the following linear mixed effect model: Steroid concentration ~ Group + Session + Session^2 + Group*Session + Group*Session^2 + Age + BMI + Inter-session Interval + (1 | participant ID). Here, we plot the mean concentration per session for each of the six estrogens analyzed in the study. Error bars correspond to 95% confidence intervals around the sample's mean at each experimental session. The gray shading corresponds to the pregnancy period. Concentrations are plotted in their logarithmic form and with a creatinine correction. An asterisk to the right of each estrogen name marks whether it follows a significant quadratic trajectory over sessions (see table S24). Baseline, Pre-pregnancy session; 18 PW, 18-pregnancy weeks session; 34 PW; 34 pregnancy weeks session; 1MPP, one-month postpartum session.

Fig. S7

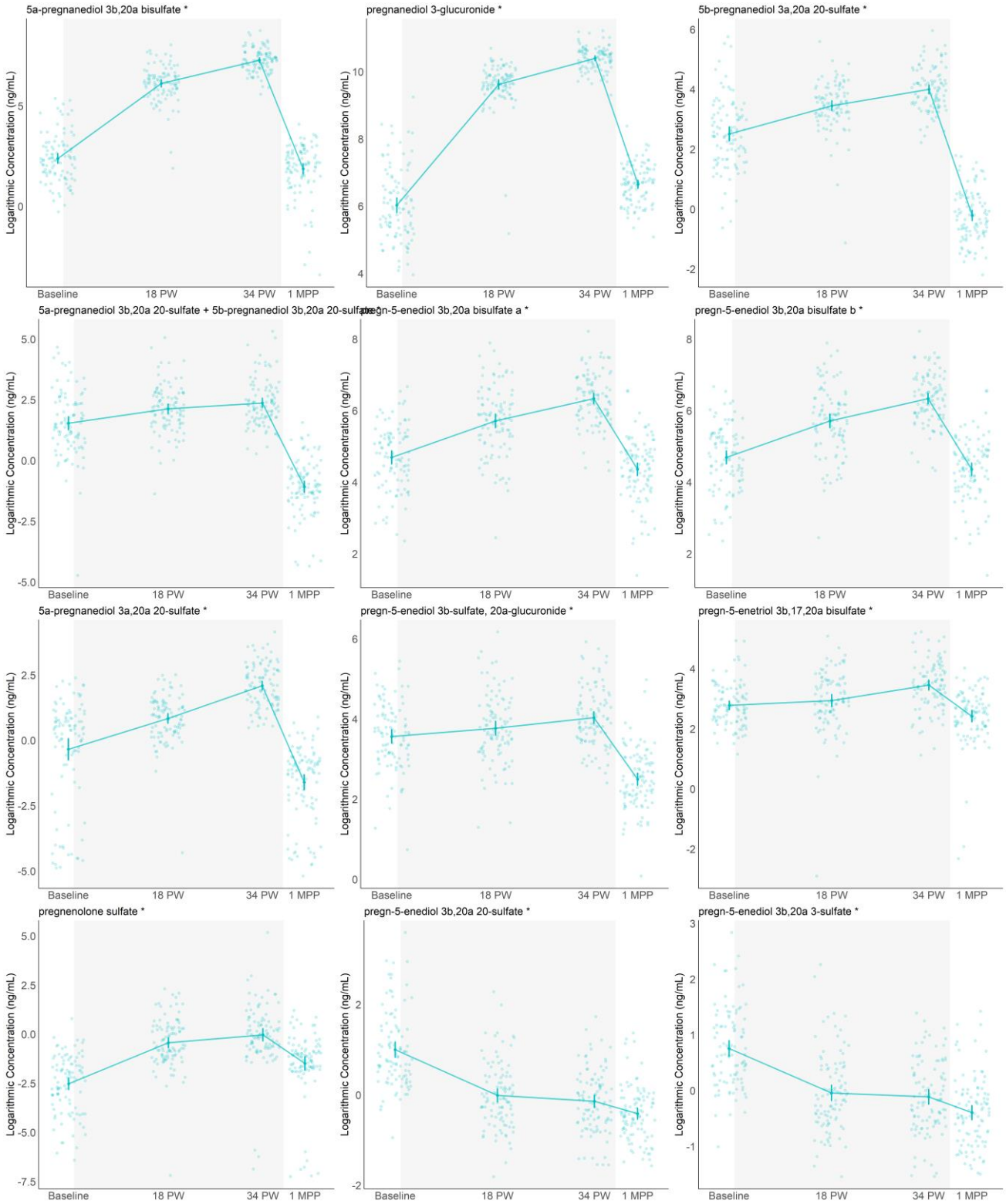
5a-pregnanediol 3b,20a bisulfate *
pregnanediol 3-glucuronide *
5b-pregnanediol 3a,20a 20-sulfate *
5a-pregnanediol 3b,20a 20-sulfate + 5b-pregnanediol 3b,20a 20-sulfate *
pregn-5-enediol 3b,20a bisulfate a *
pregn-5-enediol 3b,20a bisulfate b *
5a-pregnanediol 3a,20a 20-sulfate *
pregn-5-enediol 3b-sulfate, 20a-glucuronide *
pregn-5-enetriol 3b,17,20a bisulfate *
pregnenolone sulfate *
pregn-5-enediol 3b,20a 20-sulfate *
pregn-5-enediol 3b,20a 3-sulfate *
Logarithmic Concentration (ng/mL)
Baseline
18 PW
34 PW
1 MPP

Fig S7. Longitudinal trajectories for progestogens across pregnancy and postpartum in gestational mothers (N = 100). Longitudinal changes derive from the group x session^2 fixed effect term of the following linear mixed effect model: Steroid concentration ~ Group + Session + Session^2 + Group*Session + Group*Session^2 + Age + BMI + Inter-session Interval + (1 | participant ID). Here, we plot the mean concentration per session for each of the twelve progestogens analyzed in the study. Error bars correspond to 95% confidence intervals around the sample's mean at each experimental session. The gray shading corresponds to the pregnancy period. Concentrations are plotted in their logarithmic form and with a creatinine correction. An asterisk to the right of each progestogen name marks whether it follows a significant quadratic trajectory over sessions (see table S24). Baseline, Pre-pregnancy session; 18 PW, 18-pregnancy weeks session; 34 PW; 34 pregnancy weeks session; 1MPP, one-month postpartum session.

Fig. S8

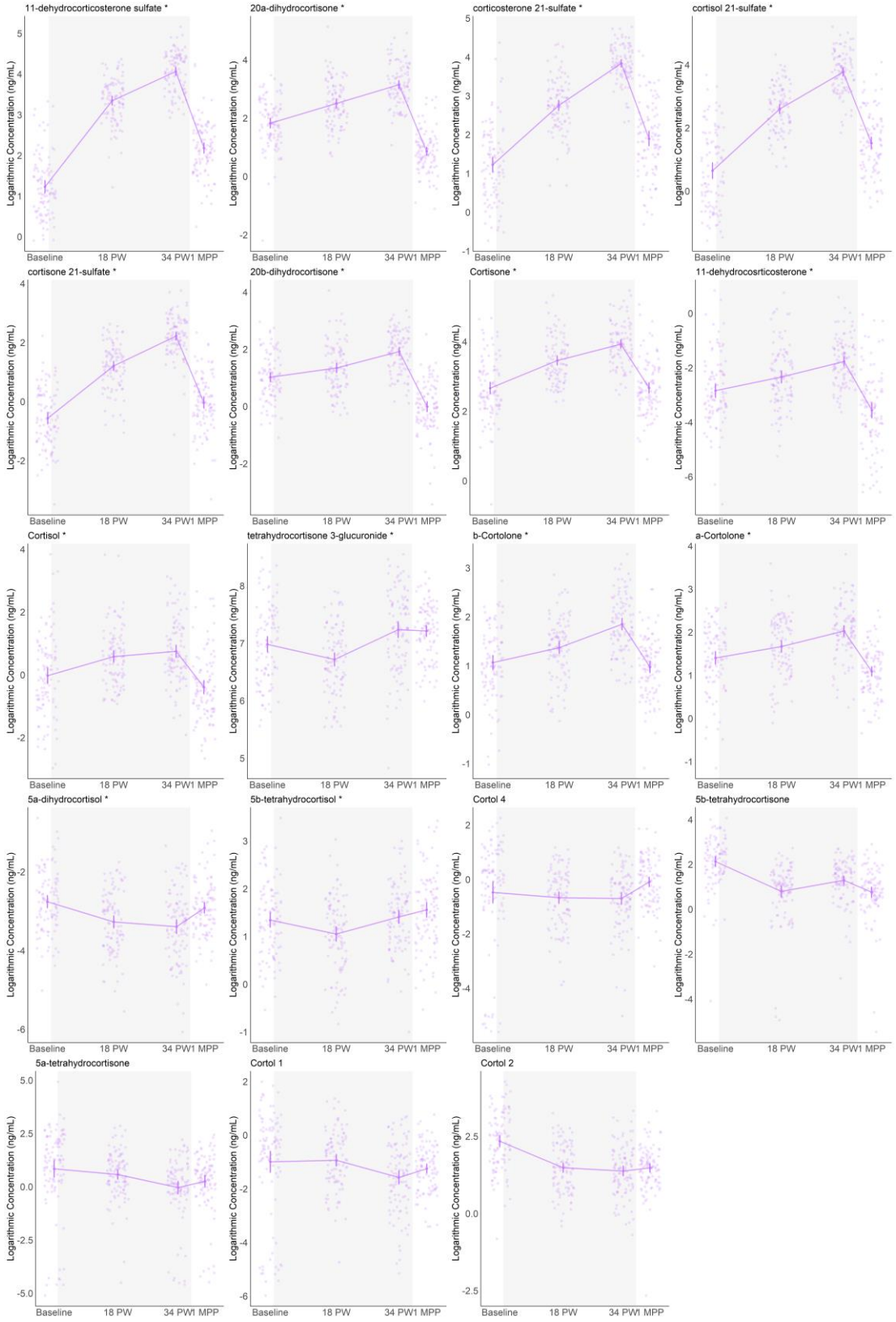
11-dehydrocorticosterone sulfate *
20a-dihydrocortisone *
corticosterone 21-sulfate *
cortisol 21-sulfate *
cortisone 21-sulfate *
20b-dihydrocortisone *
Cortisone *
11-dehydrocosrticosterone *
Cortisol *
tetrahydrocortisone 3-glucuronide *
b-Cortolone *
a-Cortolone *
5a-dihydrocortisol *
5b-tetrahydrocortisol *
Cortol 4
5b-tetrahydrocortisone
5a-tetrahydrocortisone
Cortol 1
Cortol 2
Logarithmic Concentration (ng/mL)
Baseline
18 PW
34 PW1 MPP

Fig S8. Longitudinal trajectories for corticoids across pregnancy and postpartum in gestational mothers (N = 100). Longitudinal changes derive from the group x session^2 fixed effect term of the following linear mixed effect model: Steroid concentration ~ Group + Session + Session^2 + Group*Session + Group*Session^2 + Age + BMI + Inter-session Interval + (1 | participant ID). Here, we plot the mean concentration per session for each of the nineteen progestogens analyzed in the study. Error bars correspond to 95% confidence intervals around the sample's mean at each experimental session. The gray shading corresponds to the pregnancy period. Concentrations are plotted in their logarithmic form and with a creatinine correction. An asterisk to the right of each corticoid name marks whether it follows a significant quadratic trajectory over sessions (see table S24). Baseline, Pre-pregnancy session; 18 PW, 18-pregnancy weeks session; 34 PW; 34 pregnancy weeks session; 1MPP, one-month postpartum session.

Fig. S9

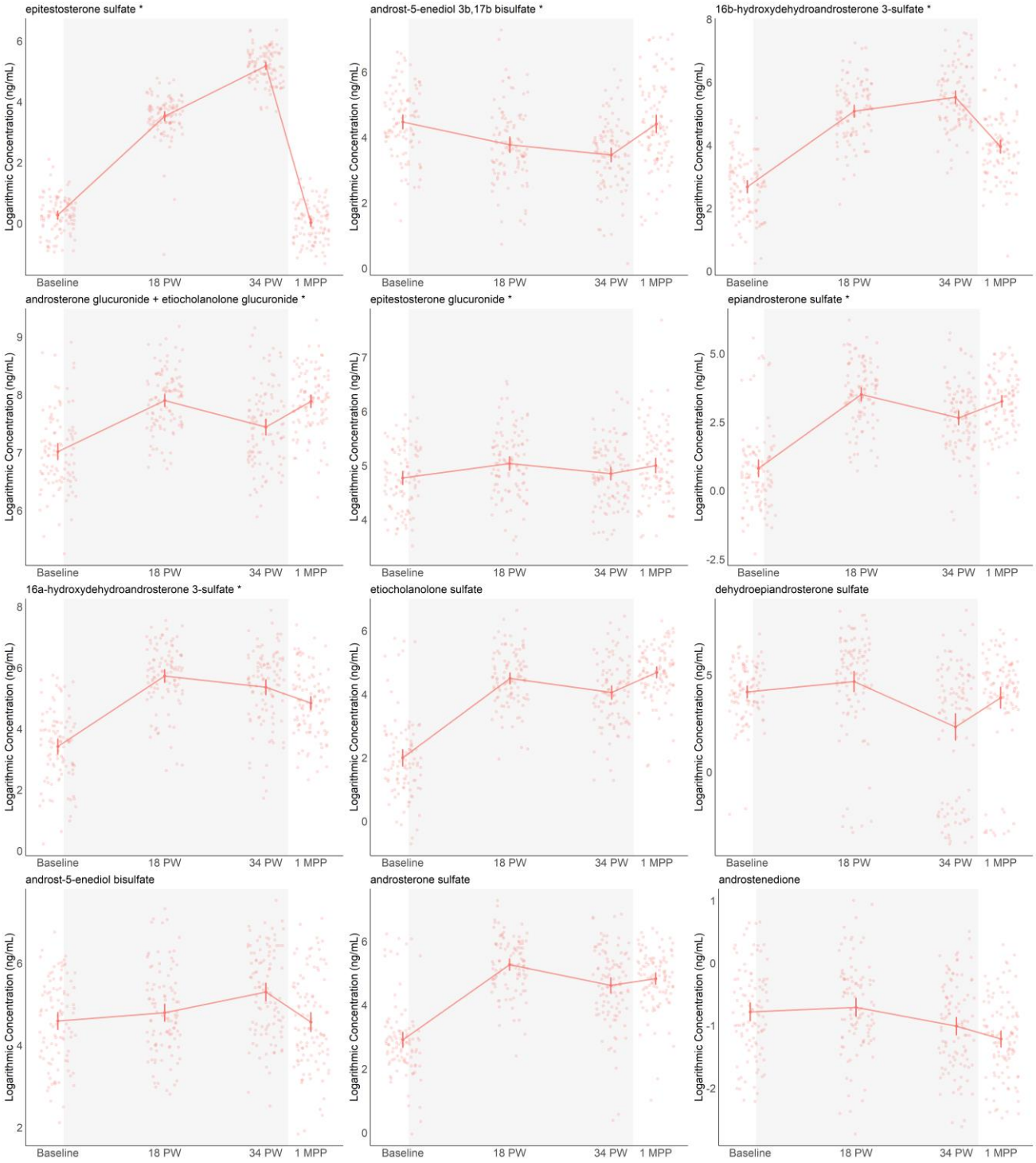
epitestosterone sulfate *
androst-5-enediol 3b,17b bisulfate *
16b-hydroxydehydroandrosterone 3-sulfate *
androsterone glucuronide + etiocholanolone glucuronide *
epitestosterone glucuronide *
epiandrosterone sulfate *
16a-hydroxydehydroandrosterone 3-sulfate *
etiocholanolone sulfate
dehydroepiandrosterone sulfate
androst-5-enediol bisulfate
androsterone sulfate
androstenedione
Logarithmic Concentration (ng/mL)
Baseline
18 PW
34 PW
1 MPP

Fig S9. Longitudinal trajectories for androgens across pregnancy and postpartum in gestational mothers (N = 100). Longitudinal changes derive from the group x session^2 fixed effect term of the following linear mixed effect model: Steroid concentration ~ Group + Session + Session^2 + Group*Session + Group*Session^2 + Age + BMI + Inter-session Interval + (1 | participant ID). Here, we plot the mean concentration per session for each of the twelve androgens analyzed in the study. Error bars correspond to 95% confidence intervals around the sample's mean at each experimental session. The gray shading corresponds to the pregnancy period. Concentrations are plotted in their logarithmic form and with a creatinine correction. An asterisk to the right of each androgen name marks whether it follows a significant quadratic trajectory over sessions (see table S24). Baseline, Pre-pregnancy session; 18 PW, 18-pregnancy weeks session; 34 PW; 34 pregnancy weeks session; 1MPP, one-month postpartum session.

Fig. S10

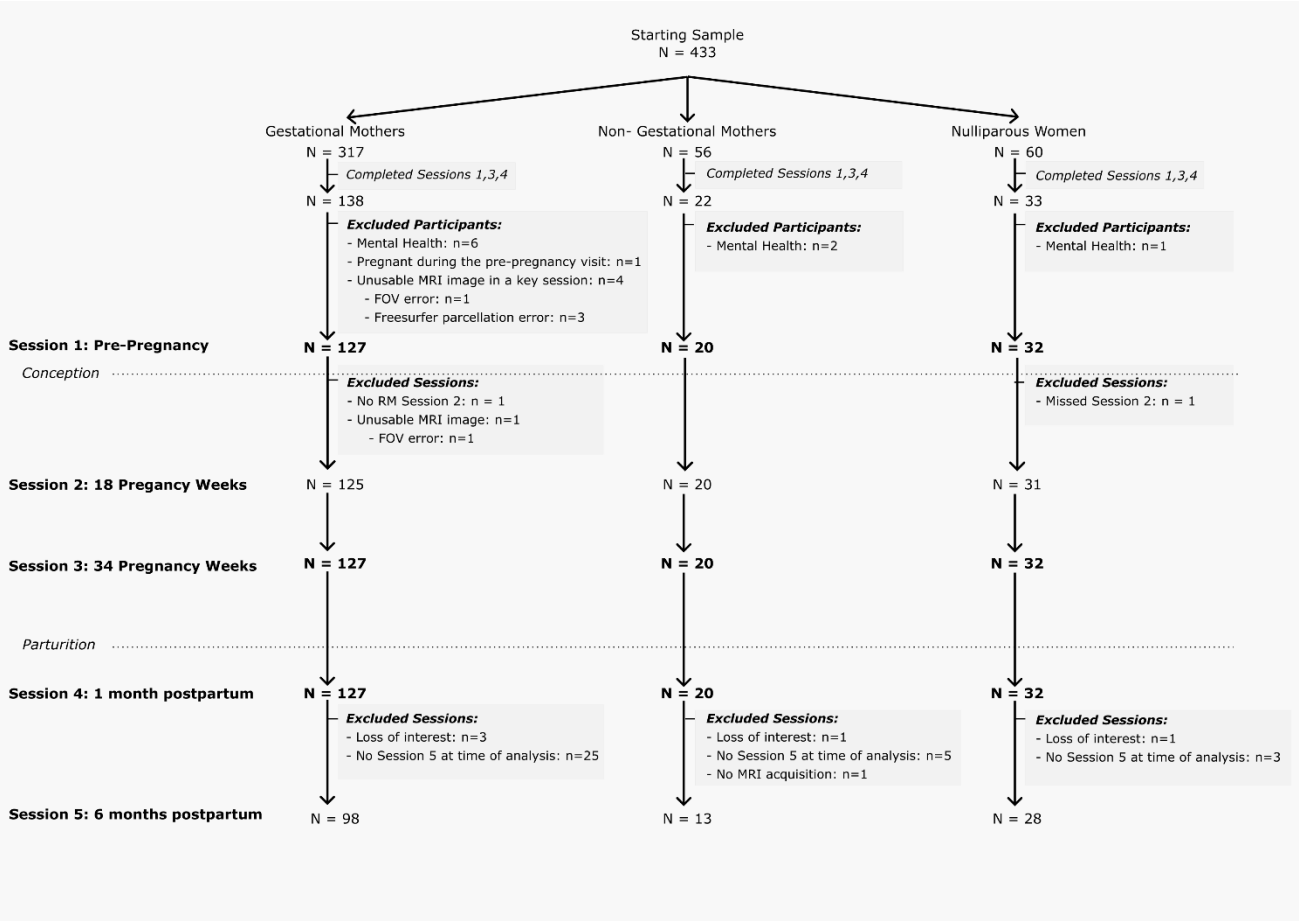

Fig. S10. Schematic overview of group allocation and dropout for the neuroanatomical sample. Number of gestational mothers, non-gestational mothers in the first session and subject dropout for each of the five sessions. Only participants who completed the Session 1, 3 and 4, were included in the study (key sessions).

Fig. S11

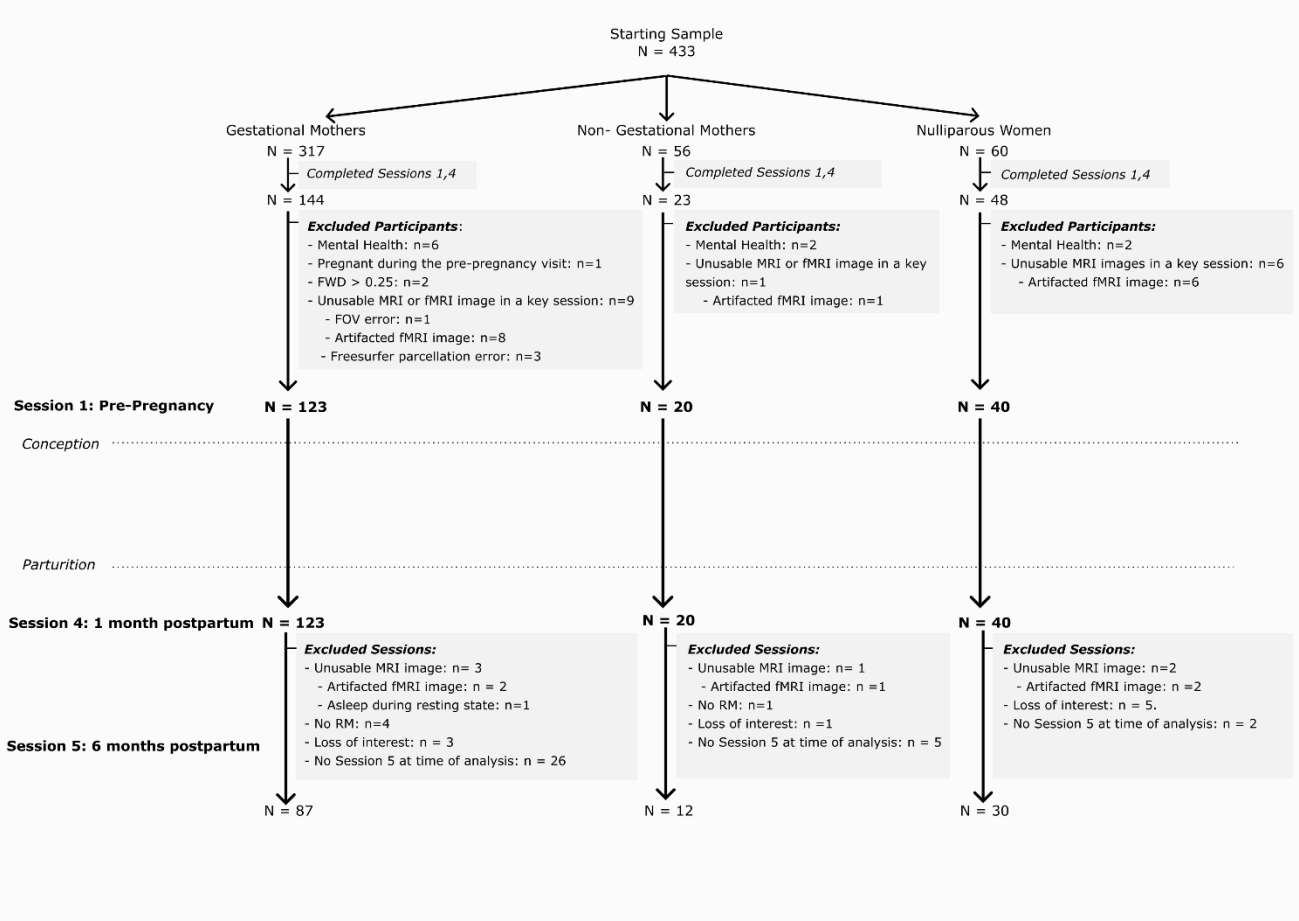

Fig. S11. Schematic overview of group allocation and dropout for the functional sample. Number of gestational mothers, non-gestational mothers in the first session and subject dropout for each of the three sessions. Only participants who completed the Session 1, and 4, were included in the study (key sessions).

Fig. S12

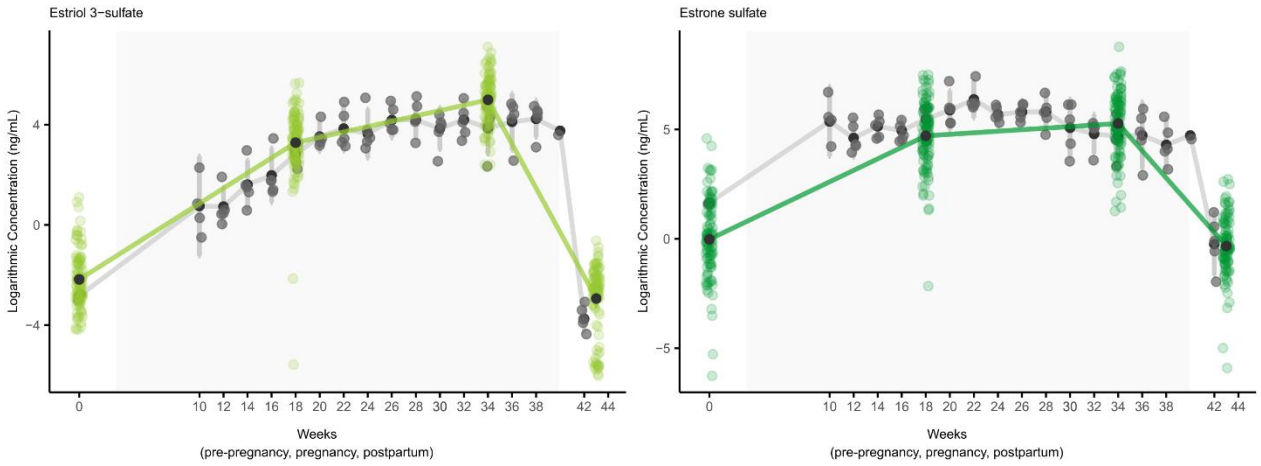

Fig S12. Longitudinal trajectories for estriol 3-sulfate and estrone sulfate across pregnancy across pregnancy and postpartum in gestational mothers. Mean concentration per session for estriol 3-sulfate (left) and estrone sulfate (right) in the gestational mother's group. Concentrations are plotted in their logarithmic form and corrected for the creatinine levels. In both plots we depict the correspondence between the longitudinal trajectories assessed at four sessions (pre-pregnancy, 18-weeks of pregnancy, 34 weeks of pregnancy, and one-month postpartum) (N=100), and the trajectories assessed with a hormonal dense sampling (N=5). For the dense sampling, urine samples were collected at the pre-pregnancy session, every two weeks during pregnancy (pregnancy weeks, 10,12,14,18,20,22,24,26,28,30,32,34,36,38,40), and at two weeks postpartum. Error bars correspond to 95% confidence intervals around the sample's mean at each experimental session. The gray shading corresponds to the pregnancy period.

Table S1.

Sample characteristics

Experimental Groups	**Gestational Mothers**	**non-Gestational Mothers**	**Nulliparous Women**
Sample Size			
Session 1	127	20	32
Session 2	125	20	31
Session 3	127	20	32
Session 4	127	20	32
Session 5	98	13	28
Age at baseline [years]	33.67 (4.04)	32.15 (3.53)	30.38 (3.23)
Conception method			
Assisted	69.00 (54.33%)		
Natural	58.00 (45.67%)		
Assisted reproduction method			
Artificial insemination	16.00 (23.19%)		
In-vitro fertilization	28.00 (40.58%)		
Intracytoplasmic sperm injection	25.00 (36.23%)		
Weeks of Pregnancy [weeks]			
Session 2	18.25 (0.94)		
Session 3	34.20 (0.90)		
Childbirth	39.46 (1.56)		
Parturition type			
Vaginal delivery	78.00 (61.90%)		
Scheduled c-section	14.00 (11.11%)		
Unplanned c-section	34.00 (26.98%)		
(Missing)	1		
Number of babies delivered			
Single baby	124.00 (98.41%)		
Monozygotic twins	1.00 (0.79%)		
Dizygotic twins	1.00 (0.79%)		
(Missing)	1		
Baby's biological sex			
Male	71.00 (56.80%)		
Female	54.00 (43.20%)		
(Missing)	2		
Breastfeeding			
Exclusive breastfeeding	105.00 (84.68%)		
Mixed Breastfeeding	9.00 (7.26%)		
No breastfeeding	10.00 (8.06%)		
(Missing)	3		
Education level			

Table S1.

Sample characteristics

Experimental Groups	**Gestational Mothers**	**non-Gestational Mothers**	**Nulliparous Women**
Primary education	2.00 (1.57%)	0.00 (0.00%)	0.00 (0.00%)
Secondary education	10.00 (7.87%)	0.00 (0.00%)	3.00 (9.38%)
Higher education	115.00 (90.55%)	20.00 (100.00%)	29.00 (90.63%)
Time between sessions [weeks]			
Session 1 & 2	39.46 (21.14)	38.90 (20.64)	27.95 (15.73)
Session 2 & 3	16.09 (1.03)	16.28 (1.20)	16.17 (1.29)
Session 3 & 4	10.13 (1.75)	9.76 (1.82)	10.96 (3.25)
Session 4 & 5	21.74 (1.80)	21.85 (0.96)	21.35 (3.32)
Mean euler number			
Session 1	-12.21 (5.40)	-11.15 (8.57)	-12.63 (6.90)
Session 2	-11.55 (5.47)	-11.15 (6.89)	-12.52 (5.50)
Session 3	-10.26 (5.65)	-10.60 (6.44)	-11.66 (5.82)
Session 4	-10.81 (5.35)	-11.85 (6.06)	-11.38 (5.03)
Session 5	-11.76 (5.77)	-12.15 (4.28)	-11.00 (6.72)

For numeric variables, values are expressed as *Mean (sd).* For categorical variables, values are expressed as *n (% percentual frequency)*. Details of the between groups comparisons can be found in “Methods” (See Study design and participants). Session 1, Pre-pregnancy; Session 2, 18 pregnancy weeks; Session 3, 34 pregnancy weeks; Session 4, one month postpartum; Session 5, six months postpartum.

Table S2.

Statistical summary of the linear mixed effects model assessing quadratic cortical gray matter volume changes between groups (Gestational Mothers, non-Gestational mothers, and Nulliparous Women) along the five experimental sessions (Session 1 to 5).

	Est.	CI 2.5%	CI 97.5%	SE	df	t value	p-value	q-value	Sig.
(Intercept)	467838.32	459165.71	476510.93	4477.13	172.95	104.50	3.30e-158	4.96e-158	***
Group [Gestational Mother]	-6751.50	-16607.32	3104.30	5087.95	172.95	-1.33	0.186	0.279	ns
Group [non-Gestational Mother]	862.13	-12755.65	14479.90	7030.01	173.07	0.12	0.903	0.981	ns
Session [Linear Term]	-54837.61	-81633.53	-28024.14	13727.97	666.47	-3.99	7.20e-05	2.16e-04	***
Session [Quadratic Term]	4729.19	-22052.81	31520.41	13718.71	666.27	0.34	0.730	0.839	ns
eTIV	21675.86	18066.60	25285.14	1863.24	172.95	11.63	1.78e-23	5.33e-23	***
Age	-6924.33	-10643.89	-3204.75	1920.18	173.20	-3.61	4.06e-04	6.09e-04	***
Euler Number	-366.87	-1019.31	283.18	333.60	694.12	-1.10	0.272	0.345	ns
Inter-Session Time	2305.01	-1322.37	5932.38	1872.59	173.09	1.23	0.220	0.330	ns
Group [Gestational Mother] x Session [Linear Term]	-40173.11	-70276.07	-10089.45	15412.21	666.39	-2.61	0.009	0.014	*
Group [non-Gestational Mother] x Session [Linear Term]	7779.27	-37305.44	52846.61	23085.74	666.83	0.34	0.736	0.736	ns
Group [Gestational Mother] x Session [Quadratic Term]	207552.67	177360.29	237723.63	15457.46	666.43	13.43	1.49e-36	4.47e-36	***
Group [non-Gestational Mother] x Session [Quadratic Term]	12068.55	-32703.24	56831.77	22927.68	666.55	0.53	0.599	0.629	ns

The adjusted linear mixed effect model corresponded to *Cortical Gray Matter Volume ~ Group + Session + Session^2 + Group*Session + Group*Session^2 + eTIV + Age + Euler + Inter-session Interval + (1 | participant ID)*. Statistics are shown for the fixed effects of the model. P-values were corrected for multiple testing across cortical metrics (cortical gray matter volume, cortical thickness, and surface area). P-values below the threshold of 0.001 are reported in exponential notation. Asterisks indicate significance under False Discovery Rate correction (ns, q-value > 0.05; *, q-value < 0.05; **, q-value < 0.01; ***, q-value < 0.001). Est, Estimate; CI, Confidence Interval; SE, Standard Error; df, degrees of freedom, Sig, Significance; eTIV, estimated Total Intracranial Volume; ns, non-significant.

Table S3.

Statistical summary of the linear mixed effects model assessing quadratic cortical gray matter volume changes between groups (Gestational Mothers, non-Gestational mothers, and Nulliparous Women) along the five experimental sessions (Session 1 to 5) with BMI as an added covariable.

	Est.	CI 2.5%	CI 97.5%	SE	df	t value	p-value	Sig.
(Intercept)	467563.24	458844.62	476282.16	4501.88	173.26	103.86	5.69e-158	***
Group [Gestational Mother]	-6414.11	-16323.82	3495.25	5116.72	173.34	-1.25	0.212	ns
Group [non-Gestational Mother]	1273.89	-12414.53	14961.87	7067.81	173.29	0.18	0.857	ns
Session [Linear Term]	-50279.74	-77462.60	-23127.72	13923.90	661.19	-3.61	3.28e-04	***
Session [Quadratic Term]	8149.14	-19094.62	35363.98	13955.54	660.69	0.58	0.559	ns
eTIV	21670.04	18046.31	25293.79	1871.11	172.42	11.58	2.60e-23	***
Age	-6841.10	-10577.14	-3105.12	1929.07	172.93	-3.55	5.03e-04	***
Euler Number	-323.81	-977.91	327.65	334.62	687.72	-0.97	0.334	ns
Inter-Session Time	2183.81	-1461.11	5828.82	1882.06	173.10	1.16	0.248	ns
BMI	-812.92	-1844.19	232.84	531.74	742.40	-1.53	0.127	ns
Group [Gestational Mother] x Session [Linear Term]	-43781.42	-74097.30	-13459.82	15539.02	660.27	-2.82	0.005	**
Group [non-Gestational Mother] x Session [Linear Term]	4620.74	-40811.31	50046.80	23283.48	660.62	0.20	0.843	ns
Group [Gestational Mother] x Session [Quadratic Term]	199226.76	167546.47	231019.10	16264.96	666.72	12.25	2.95e-31	***
Group [non-Gestational Mother] x Session [Quadratic Term]	9521.13	-35448.68	54506.65	23052.03	660.31	0.41	0.680	ns

The adjusted linear mixed effect model corresponded to *Cortical Gray Matter Volume ~ Group + Session + Session^2 + Group*Session + Group*Session^2 + eTIV + Age + Euler + Inter-session Interval + BMI + (1 / participant ID)*. Statistics are shown for the fixed effects of the model. Multiple comparison corrections were applied across cortical metrics (cortical gray matter volume, cortical thickness, and surface area). P-values below the threshold of 0.001 are reported in exponential notation. Asterisks indicate significance under False Discovery Rate correction (ns, q-value > 0.05; *, q-value < 0.05; **, q-value < 0.01; ***, q-value < 0.001). Est, Estimate; CI, Confidence Interval; SE, Standard Error; df, degrees of freedom, Sig, Significance; eTIV, estimated Total Intracranial Volume; BMI, Body Mass Index; ns, non-significant.

Table S4.

Analysis of variance between two nested models analyzing gray matter volume changes through time (Linear Model vs. Quadratic Model)

	npar	AIC	BIC	logLik	deviance	Chisq	Df	Pr(>Chisq)
Model A. Linear Model	12	18,570.51	18,627.48	-9,273.25	18,546.51			
Model B. Quadratic Model	15	18,006.29	18,077.51	-8,988.15	17,976.29	570.21	3	2.89e-123

Model A corresponds to the following linear mixed effect model: *Gray Matter Volume ~ 1 + Group + Session + Group*Session + eTIV + Age + Euler + Inter-session Interval + (1 / participant ID)*. Model B corresponds to the following linear mixed effect model: *Gray Matter Volume ~ 1 + Group + Session + Session^2 + Group*Session + Group*Session^2 + eTIV + Age + Euler + Inter-session Interval + (1 / participant ID).* Both models were fitted with a maximum likelihood estimation. P-values below the threshold of 0.001 are reported in exponential notation. npar, number of parameters in the model; AIC, Akaike Information Criterion; BIC; Bayesian Information Criterion; logLik, Log-likelihood of the model; deviance, measure of goodness of fit for each model; Chisq, Chi-squared statistic; Df, degrees of freedom, Pr(>Chisq), p-value associated with the chi-square test.

Table S5.

Analysis of variance between two nested models analyzing gray matter volume changes through time (Linear Model vs. Quadratic Model)

	npar	AIC	BIC	logLik	deviance	Chisq	Df	Pr(>Chisq)
Model A. Quadratic Model	15	18,006.29	18,077.51	-8,988.15	17,976.29			
Model B. Triple interaction eTIV Model	23	18,012.53	18,121.73	-8,983.27	17,966.53	9.76	8	0.282

Model A corresponds to the following linear mixed effect model: *Gray Matter Volume ~ 1 + Group + Session + Session^2 + Group*Session + Group*Session^2 + eTIV + Age + Euler + Inter-session Interval + (1 / participant ID)*. Model B corresponds to the following linear mixed effect model: *Cortical Metric ~ Group + Session + Session^2 + Group*Session + Group*Session^2 + Group*eTIV + Session*eTIV + Session*eTIV + Group*Session*eTIV + Group*Session*eTIV + Age + Euler + Inter-session Interval + (1 / participant ID).* Both models were fitted with a maximum likelihood estimation. P-values below the threshold of 0.001 are reported in exponential notation. npar, number of parameters in the model; AIC, Akaike Information Criterion; BIC; Bayesian Information Criterion; logLik, Log-likelihood of the model; deviance, measure of goodness of fit for each model; Chisq, Chi-squared statistic; Df, degrees of freedom, Pr(>Chisq), p-value associated with the chi-square test.

Table S6.

Percentage of cortical gray matter volume change at each session relative to baseline in gestational mothers.

Time Interval	% GM Volume Change	CI 2.5%	CI 97.5%
Baseline to 18 pregnancy weeks	-2.7	-3.0	-2.5
Baseline to 32 pregnancy weeks	-4.9	-5.2	-4.6
Baseline to 1 month postpartum	-3.7	-4.0	-3.4
Baseline to 6 months postpartum	-1.6	-1.9	-1.3

The percentage of Gray Matter Volume change at each session compared to baseline was calculated as *((Gray Matter Volume at session X – Gray Matter Volume at Session 1)/ Gray Matter Volume at Session 1) * 100.* CI, Confidence Interval.

Table S7.

Statistical summary of the linear mixed effects model assessing cortical gray matter volume changes between Session 1 and 5 in gestational mothers

	Est.	CI 2.5%	CI 97.5%	SE	df	t value	p-value	Sig.
(Intercept)	473,709.80	469,076.16	478,345.45	2,386.30	128.66	198.51	6.62e-162	***
Session	-7,693.05	-9,371.04	-6,010.90	857.18	97.82	-8.97	2.06e-14	***
eTIV	21,175.03	16,602.54	25,747.17	2,353.82	122.84	9.00	3.56e-15	***
Age	-8,187.96	-12,729.74	-3,648.68	2,337.49	123.87	-3.50	6.41e-04	***
Euler Number	190.19	-1,691.48	2,033.67	949.44	123.44	0.20	0.842	ns
Inter-Session Time	2,316.72	-2,121.56	6,757.13	2,285.43	124.10	1.01	0.313	ns

The adjusted linear mixed effect model corresponded to cortical *Gray Matter Volume ~ 1 + Session (1 and 5) + eTIV + Age + Euler + Inter-session Interval + (1 / participant ID)*. Statistics are shown for the fixed effects of the model. No multiple correction applied for this model. P-values below the threshold of 0.001 are reported in exponential notation. Asterisks indicate significance (ns, p-value > 0.05; *, p-value < 0.05; **, p-value < 0.01; ***, p-value < 0.001). Est, Estimate; CI, Confidence Interval; SE, Standard Error; df, degrees of freedom, Sig, Significance; eTIV, estimated Total Intracranial Volume; ns, non-significant.

Table S8.

Statistical summary of the linear mixed effects model assessing group differences (gestational mothers, non-gestational mothers, nulliparous women) between Session 1 and 5.

	Est.	CI 2.5%	CI 97.5%	SE	df	t value	p value	Sig.
(Intercept)	473,635.02	469,247.48	478,023.88	2,266.54	180.85	208.97	1.40e-217	***
Session [5]	-7,684.11	-9,303.29	-6,063.13	832.59	137.34	-9.23	4.41e-16	***
Group [non-gestational mothers]	-3,202.58	-15,051.37	8,644.53	6,119.52	180.42	-0.52	0.601	ns
Group [nulliparous women]	-2,753.45	-12,993.83	7,486.85	5,289.10	179.48	-0.52	0.603	ns
eTIV	21,871.12	18,157.24	25,584.28	1,917.75	172.54	11.40	8.21e-23	***
Age	-8,106.94	-11,938.32	-4,276.64	1,978.37	173.44	-4.10	6.39e-05	***
Euler Number	110.22	-1,261.84	1,464.78	700.18	176.16	0.16	0.875	ns
Inter-Session Time	2,911.18	-825.40	6,648.18	1,929.81	173.52	1.51	0.133	ns
Session [5] x Group [non-gestational mothers]	5,661.89	909.52	10,408.82	2,441.14	138.71	2.32	0.022	*
Session [5] x Group [nulliparous women]	72.22	-3,362.64	3,520.97	1,768.46	136.79	0.04	0.967	ns

The adjusted linear mixed effect model corresponded to cortical *Gray Matter Volume ~ 1 + Group + Session (1 and 5) + Group*Session + eTIV + Age + Euler + Inter-session Interval + (1 | participant ID)*. Statistics are shown for the fixed effects of the model. No multiple correction applied for this model. P-values below the threshold of 0.001 are reported in exponential notation. Asterisks indicate significance (ns, p-value > 0.05; *, p-value < 0.05; **, p-value < 0.01; ***, p-value < 0.001). Est, Estimate; CI, Confidence Interval; SE, Standard Error; df, degrees of freedom, Sig, Significance; eTIV, estimated Total Intracranial Volume; ns, non-significant.

Table S9.

Cortical allocation of quadratic changes in cortical gray matter volume with a medium to large effect size for gestational mothers compared to nulliparous women.

Region (Desikan-Killiany)	% GM volume change (LH)	% GM volume change (RH)	% GM volume change (Global)
Inferior parietal	10.3	10.4	20.7
Superior frontal	8.9	10.1	19.0
Supramarginal	10.1	8.5	18.6
Precuneus	7.8	7.5	15.3
Superior temporal	8.0	6.5	14.6
Rostral middle frontal	3.8	7.5	11.2
Middle temporal	4.7	5.1	9.8
Precentral	3.0	4.6	7.7
Inferior temporal	4.0	2.8	6.8
Lateral occipital	3.8	2.6	6.5
postcentral	2.5	3.9	6.3
Fusiform	4.0	2.3	6.3
Bankssts	3.1	2.8	5.8
Pars triangularis	2.8	2.9	5.7
Pars opercularis	2.6	2.8	5.4
Superior parietal	2.2	2.7	5.0
Lingual	2.6	2.0	4.6
Insula	3.0	1.3	4.4
Paracentral	1.7	2.1	3.8
Lateral orbitofrontal	2.1	1.5	3.7
Posterior cingulate	2.3	1.4	3.7
Caudal middle frontal	0.2	2.7	2.9
Transverse temporal	1.4	1.0	2.4
Pars orbitalis	1.0	1.2	2.2
Isthmus cingulate	1.2	1.0	2.2

Table S9.

Cortical allocation of quadratic changes in cortical gray matter volume with a medium to large effect size for gestational mothers compared to nulliparous women.

Region (Desikan-Killiany)	% GM volume change (LH)	% GM volume change (RH)	% GM volume change (Global)
Cuneus	0.8	0.5	1.3
Medial orbitofrontal	0.3	0.9	1.2
Caudal anterior cingulate	0.5	0.7	1.2
Rostral anterior cingulate	0.8	0.2	1.0
Frontal pole	0.3	0.4	0.7
Para hippocampal	0.2	0.1	0.3

Vertex-wise statistical analyses of significant group differences for the quadratic effect of session in left and right gray matter volume using the linear mixed effect model: *gray matter volume ~ 1 + Group + Session + Session^2 + Group*Session + Group*Session^2 + eTIV + Age + Euler + Inter-session Interval + (1 / participant ID)*. The results mask was obtained by thresholding the FDR-corrected partial eta squared maps to maintain all vertices with an effect size bigger than 0.06 (i.e., medium effect size). *Region* corresponds to the labels of the Desikan-Killiany atlas, and *Percentage of allocation by region (LH, RH and global)* corresponds to the percentage of significant vertices located in each region to the total number of significant vertices. We only display those regions in which there were significant changes in at least one hemisphere.

Table S10.

Statistical summary of the linear mixed effects model assessing quadratic cortical thickness changes between groups (Gestational Mothers, non-Gestational mothers, and Nulliparous Women) along the five experimental sessions (Session 1 to 5).

	Est.	CI 2.5%	CI 97.5%	SE	df	t value	p-value	q-value	Sig.
(Intercept)	2.47	2.45	2.49	0.01	172.80	253.57	3.83e-224	1.15e-223	***
Group [Gestational Mother]	-0.02	-0.04	-0.001	0.01	172.80	-2.05	0.042	0.126	ns
Group [non-Gestational Mother]	-0.004	-0.03	0.03	0.02	173.26	-0.28	0.783	0.981	ns
Session [Linear Term]	-0.18	-0.29	-0.06	0.06	667.72	-2.99	0.003	0.003	**
Session [Quadratic Term]	0.01	-0.10	0.13	0.06	667.00	0.20	0.839	0.839	ns
eTIV	-0.001	-0.01	0.01	0.004	172.80	-0.36	0.722	0.722	ns
Age	-0.02	-0.03	-0.01	0.004	173.70	-4.16	4.91e-05	1.47e-04	***
Euler Number	0.001	-0.001	0.004	0.001	761.56	0.95	0.345	0.345	ns
Inter-Session Time	0.01	-0.002	0.01	0.004	173.33	1.40	0.162	0.330	ns
Group [Gestational Mother] x Session [Linear Term]	-0.01	-0.14	0.12	0.07	667.44	-0.16	0.869	0.869	ns
Group [non-Gestational Mother] x Session [Linear Term]	0.04	-0.15	0.23	0.10	669.05	0.43	0.665	0.736	ns
Group [Gestational Mother] x Session [Quadratic Term]	0.73	0.60	0.86	0.07	667.58	11.02	4.68e-26	4.68e-26	***
Group [non-Gestational Mother] x Session [Quadratic Term]	0.08	-0.11	0.27	0.10	668.06	0.79	0.427	0.629	ns

The adjusted linear mixed effect model corresponded to Cortical thickness ~ *1 + Group + Session + Session^2 + Group*Session + Group*Session^2 + eTIV + Age + Euler + Inter-session Interval + (1 | participant ID)*. Statistics are shown for the fixed effects of the model. P-values were corrected for multiple testing across cortical metrics (gray matter volume, cortical thickness, and surface area). P-values below the threshold of 0.001 are reported in exponential notation. Asterisks indicate significance under False Discovery Rate correction (ns, q-value > 0.05; *, q-value < 0.05; **, q-value < 0.01; ***, q-value < 0.001). Est, Estimate; CI, Confidence Interval; SE, Standard Error; df, degrees of freedom, Sig, Significance; eTIV, estimated Total Intracranial Volume; ns, non-significant.

Table S11.

Statistical summary of the linear mixed effects model assessing quadratic surface area changes between groups (Gestational Mothers, non-Gestational mothers, and Nulliparous Women) along the five experimental sessions (Session 1 to 5).

	Est.	CI 2.5%	CI 97.5%	SE	df	t value	p-value	q-value	Sig.
(Intercept)	83945.52	82359.57	85531.46	818.68	173.00	102.54	7.60e-157	7.60e-157	***
Group [Gestational Mother]	-518.61	-2320.92	1283.71	930.37	173.00	-0.56	0.578	0.578	ns
Group [non-Gestational Mother]	-30.05	-2519.90	2459.81	1285.28	173.01	-0.02	0.981	0.981	ns
Session [Linear Term]	-2624.32	-4142.90	-1105.83	777.73	666.05	-3.37	7.83e-04	0.001	**
Session [Quadratic Term]	559.27	-958.19	2076.62	777.15	666.03	0.72	0.472	0.839	ns
eTIV	3888.20	3228.18	4548.22	340.71	173.00	11.41	7.57e-23	1.14e-22	***
Age	-506.06	-1186.02	173.90	351.00	173.02	-1.44	0.151	0.151	ns
Euler Number	-76.00	-113.26	-38.75	19.08	668.79	-3.98	7.55e-05	2.26e-04	***
Inter-Session Time	173.45	-489.76	836.66	342.35	173.01	0.51	0.613	0.613	ns
Group [Gestational Mother] x Session [Linear Term]	-6218.40	-7923.15	-4513.57	873.12	666.04	-7.12	2.76e-12	8.29e-12	***
Group [non-Gestational Mother] x Session [Linear Term]	-585.09	-3138.91	1969.04	1308.03	666.09	-0.45	0.655	0.736	ns
Group [Gestational Mother] x Session [Quadratic Term]	10909.93	9200.13	12619.78	875.70	666.05	12.46	3.56e-32	5.34e-32	***
Group [non-Gestational Mother] x Session [Quadratic Term]	627.01	-1909.08	3163.40	1298.95	666.06	0.48	0.629	0.629	ns

The adjusted linear mixed effect model corresponded to Surface Area ~ *1 + Group + Session + Session^2 + Group*Session + Group*Session^2 + eTIV + Age + Euler + Inter-session Interval + (1 | participant ID)*. Statistics are shown for the fixed effects of the model. P-values were corrected for multiple testing across cortical metrics (gray matter volume, cortical thickness, and surface area). P-values below the threshold of 0.001 are reported in exponential notation. Asterisks indicate significance under False Discovery Rate correction (ns, > 0.05; *, q-value < 0.05; **, q-value < 0.01; ***, q-value < 0.001). Est, Estimate; CI, Confidence Interval; SE, Standard Error; df, degrees of freedom, Sig, Significance; eTIV, estimated Intracranial Volume; ns, non-significant.

Table S12.

Statistical summary of the linear mixed effects model assessing impact of assisted reproduction on the cortical gray matter volume trajectory over time in gestational mothers.

	Est.	CI 2.5%	CI 97.5%	SE	df	t value	p-value	Sig.
(Intercept)	457,784.15	450,156.36	465,412.01	3,893.25	123.07	117.58	2.76e-128	***
Session [Linear Term]	-73,804.12	-90,892.64	-56,717.36	8,737.77	467.27	-8.45	3.82e-16	***
Session [Quadratic Term]	169,415.86	152,417.26	186,412.83	8,691.82	467.24	19.49	2.33e-62	***
Assisted Reproduction [Yes]	4,725.21	-6,669.95	16,120.15	5,816.03	123.02	0.81	0.418	ns
Session [Linear Term] x Assisted Reproduction [Yes]	-16,066.92	-40,832.69	8,704.71	12,665.45	467.19	-1.27	0.205	ns
Session [Quadratic Term] x Assisted Reproduction [Yes]	23,802.55	-936.08	48,546.61	12,651.46	467.17	1.88	0.061	ns

The adjusted linear mixed effect model corresponded to Gray Matter Volume ~ *1 + Session + Session^2 + Session*Assisted Reproduction + Session^2*Assisted Reproduction + (1 | participant ID)*. Statistics are shown for the fixed effects of the model. Assisted Reproduction was a factor with two levels: Yes (N=69) and No (N=58). No multiple correction applied for this model. P-values below the threshold of 0.001 are reported in exponential notation. Asterisks indicate significance (ns, p-value > 0.05; *, p-value < 0.05; **, p-value < 0.01; ***, p-value < 0.001). Est, Estimate; CI, Confidence Interval; SE, Standard Error; df, degrees of freedom; Sig, Significance; ns, non-significant.

Table S13.

Statistical summary of the linear mixed effects model assessing impact of the baby's biological sex on the cortical gray matter volume trajectory over time in gestational mothers.

_	Est.	CI 2.5%	CI 97.5%	SE	df	t value	p-value	Sig.
(Intercept)	456,471.91	447,841.93	465,101.89	4,404.76	123.08	103.63	1.31e-121	***
Session [Linear Term]	-74,541.13	-93,924.33	-55,161.00	9,910.86	466.30	-7.52	2.81e-13	***
Session [Quadratic Term]	179,644.06	160,367.43	198,917.84	9,856.42	466.26	18.23	1.96e-56	***
Biological Sex [Male]	4,230.95	-7,218.97	15,680.75	5,844.02	123.04	0.72	0.470	ns
Session [Linear Term] x Biological Sex [Male]	-12,435.24	-37,610.96	12,747.13	12,875.34	466.24	-0.97	0.335	ns
Session [Quadratic Term] x Biological Sex [Male]	1,972.51	-23,137.35	27,088.51	12,841.53	466.21	0.15	0.878	ns

The adjusted linear mixed effect model corresponded to Gray Matter Volume ~ *1 + Session + Session^2 + Session*Biological Sex + Session^2*Biological Sex + (1 / participant ID)*. Statistics are shown for the fixed effects of the model. The baby's biological sex was a factor with two levels: Male (N=71) and Female (N=54). No multiple correction applied for this model. P-values below the threshold of 0.001 are reported in exponential notation. Asterisks indicate significance (ns, > 0.05; *, p-value < 0.05; **, p-value < 0.01; ***, p-value < 0.001). Est, Estimate; CI, Confidence Interval; SE, Standard Error; df, degrees of freedom, Sig, Significance; ns, non-significant.

Table S14.

Statistical summary of the linear mixed effects model assessing impact of type of parturition on the cortical gray matter volume recovery during the postpartum in gestational mothers.

	Est.	CI 2.5%	CI 97.5%	SE	df	t value	p-value	Sig.
(Intercept)	424,124.34	416,016.94	432,231.69	4,161.62	196.27	101.91	6.56e-172	***
Session	7,901.72	6,909.48	8,893.91	507.49	221.41	15.57	2.05e-37	***
Parturition Type [Scheduled C-Section]	7,636.57	-13,172.62	28,450.33	10,682.83	197.12	0.71	0.476	ns
Parturition Type [Unplanned C-Section]	-3,966.40	-18,762.90	10,830.01	7,595.50	199.75	-0.52	0.602	ns
Session x Parturition Type [Scheduled C-Section]	-976.47	-3,538.98	1,590.28	1,311.67	221.44	-0.74	0.457	ns
Session x Parturition Type [Unplanned C-Section]	359.96	-1,501.10	2,220.94	951.86	221.52	0.38	0.706	ns

The adjusted linear mixed effect model corresponded to Gray Matter Volume *~ 1 + Session (3, 4 and 5) + Parturition Type + Session*Parturition Type + (1| participant ID).* Statistics are shown for the fixed effects of the model. Parturition type was a factor with three levels: vaginal delivery (N = 74), scheduled c-section (N = 14), and unplanned c-section (N = 34). No multiple correction applied for this model. P-values below the threshold of 0.001 are reported in exponential notation. Asterisks indicate significance (ns, p-value > 0.05; *, p-value < 0.05; **, p-value < 0.01; ***, p-value < 0.001). Est, Estimate; CI, Confidence Interval; SE, Standard Error; df, degrees of freedom, Sig, Significance; ns, non-significant.

Table S15.

Statistical summary of the linear mixed effects model assessing impact of type of breastfeeding on the cortical gray matter volume recovery during the postpartum in gestational mothers.

	Est.	CI 2.5%	CI 97.5%	SE	df	t value	p-value	Sig.
(Intercept)	428,253.47	405,927.20	450,584.28	11,463.24	197.77	37.36	1.49e-91	***
Session	8,878.03	6,074.57	11,685.93	1,435.03	217.43	6.19	3.01e-09	***
Breastfeeding Type [Exclusive Breastfeeding]	-2,320.83	-25,695.07	21,049.16	11,999.03	197.89	-0.19	0.847	ns
Breastfeeding Type [Mixed Breastfeeding]	-32,603.78	-65,078.90	-134.93	16,670.89	198.34	-1.96	0.052	ns
Session x Breastfeeding Type [Exclusive Breastfeeding]	-1,100.58	-4,042.18	1,836.85	1,503.49	217.43	-0.73	0.465	ns
Session x Breastfeeding Type [Mixed Breastfeeding]	-740.47	-4,841.42	3,354.29	2,095.95	217.45	-0.35	0.724	ns

The adjusted linear mixed effect model corresponded to Gray Matter Volume ~ 1 + Session (3, 4 and 5) + Breastfeeding Type + Session*Parturition Type + (1| participant ID). Statistics are shown for the fixed effects of the model. Breastfeeding type was a factor with three levels: no breastfeeding (N = 10), exclusive breastfeeding (N = 105), mixed breastfeeding (N = 9). No multiple correction applied for this model. P-values below the threshold of 0.001 are reported in exponential notation. Asterisks indicate significance (ns, p-value > 0.05; *, p-value < 0.05; **, p-value < 0.01; ***, p-value < 0.001). Est, Estimate; CI, Confidence Interval; SE, Standard Error; df, degrees of freedom, Sig, Significance; ns, non-significant.

Table S16.

Statistical summary of the linear mixed effects model assessing quadratic global cerebral white matter volume changes between groups (Gestational Mothers, non-Gestational mothers, and Nulliparous Women) along the five experimental sessions (Session 1 to 5).

	Est.	CI 2.5%	CI 97.5%	SE	df	t value	p-value	q-value	Sig.
(Intercept)	430439.00	418612.27	442265.74	6105.05	172.93	70.51	2.46e-129	4.92e-129	***
Group [Gestational Mother]	-8026.21	-21466.44	5414.02	6937.95	172.93	-1.16	0.249	0.498	ns
Group [non-Gestational Mother]	-4270.20	-22837.51	14297.11	9584.59	172.94	-0.45	0.656	0.656	ns
Session [Linear Term]	7859.53	-2057.89	17772.87	5078.20	665.97	1.55	0.122	0.244	ns
Session [Quadratic Term]	-3570.53	-13478.35	6337.56	5074.41	665.95	-0.70	0.482	0.561	ns
eTIV	28969.82	24047.92	33891.73	2540.73	172.93	11.40	8.13e-23	1.63e-22	***
Age	4615.33	-455.27	9685.91	2617.48	172.95	1.76	0.080	0.159	ns
Euler Number	-225.36	-468.05	18.73	124.62	668.07	-1.81	0.071	0.071	ns
Inter-Session Time	-243.41	-5189.05	4702.24	2552.98	172.94	-0.10	0.924	0.924	ns
Group [Gestational Mother] x Session [Linear Term]	-12287.87	-23418.20	-1155.19	5701.05	665.96	-2.16	0.031	0.063	ns
Group [non-Gestational Mother] x Session [Linear Term]	2948.82	-13723.63	19629.12	8540.87	665.99	0.35	0.730	0.730	ns
Group [Gestational Mother] x Session [Quadratic Term]	48457.14	37294.88	59623.65	5717.89	665.96	8.47	1.51e-16	3.02e-16	***
Group [non-Gestational Mother] x Session [Quadratic Term]	-2498.34	-19057.39	14063.65	8481.55	665.97	-0.29	0.768	0.768	ns

The adjusted linear mixed effect model corresponded to Cerebral White Matter Volume ~ *1 + Group + Session + Session^2 + Group*Session + Group*Session^2 + eTIV + Age + Euler + Inter-session Interval + (1 | participant ID)*. Statistics are shown for the fixed effects of the model. Multiple comparisons were applied across supplementary cortical metrics (white matter volume and cerebrospinal fluid). P-values below the threshold of 0.001 are reported in exponential notation. Asterisks indicate significance under False Discovery Rate correction (ns, > 0.05; *, q-value < 0.05; **, q-value < 0.01; ***, q-value < 0.001). Est, Estimate; CI, Confidence Interval; SE, Standard Error; df, degrees of freedom, Sig, Significance; eTIV, estimated Intracranial Volume; ns, non-significant.

Table S17.

Statistical summary of the linear mixed effects model assessing quadratic global cerebrospinal fluid changes between groups (Gestational Mothers, non-Gestational mothers, and Nulliparous Women) along the five experimental sessions (Session 1 to 5).

	Est.	CI 2.5%	CI 97.5%	SE	df	t value	p-value	q-value	Sig.
(Intercept)	937.67	872.59	1002.74	33.60	172.97	27.91	5.88e-66	5.88e-66	***
Group [Gestational Mother]	14.69	-59.27	88.64	38.18	172.97	0.38	0.701	0.701	ns
Group [non-Gestational Mother]	45.45	-56.74	147.63	52.75	173.09	0.86	0.390	0.656	ns
Session [Linear Term]	-49.58	-246.91	147.83	101.08	666.48	-0.49	0.624	0.624	ns
Session [Quadratic Term]	58.80	-138.42	256.05	101.01	666.28	0.58	0.561	0.561	ns
eTIV	57.34	30.25	84.42	13.98	172.97	4.10	6.32e-05	6.32e-05	***
Age	9.00	-18.91	36.91	14.41	173.22	0.62	0.533	0.533	ns
Euler Number	6.00	1.20	10.79	2.46	693.13	2.44	0.015	0.030	*
Inter-Session Time	-10.22	-37.44	17.00	14.05	173.11	-0.73	0.468	0.924	ns
Group [Gestational Mother] x Session [Linear Term]	-2.93	-224.52	218.65	113.48	666.39	-0.03	0.979	0.979	ns
Group [non-Gestational Mother] x Session [Linear Term]	-62.89	-394.98	268.84	169.99	666.83	-0.37	0.712	0.730	ns
Group [Gestational Mother] x Session [Quadratic Term]	-477.48	-699.73	-255.27	113.82	666.44	-4.20	3.10e-05	3.10e-05	***
Group [non-Gestational Mother] x Session [Quadratic Term]	-216.87	-546.64	112.63	168.82	666.55	-1.28	0.199	0.399	ns

The adjusted linear mixed effect model corresponded to: *Cerebrospinal fluid ~ 1 + Group + Session + Session^2 + Group*Session + Group*Session^2 + eTIV + Age + Euler + Inter-session Interval + (1 / participant ID).* Statistics are shown for the fixed effects of the model. P-values were corrected for multiple testing across supplementary cortical metrics (white matter volume and cerebrospinal fluid). P-values below the threshold of 0.001 are reported in exponential notation. Asterisks indicate significance under False Discovery Rate correction (ns, > 0.05; *, q-value < 0.05; **, q-value < 0.01; ***, q-value < 0.001). Est, Estimate; CI, Confidence Interval; SE, Standard Error; df, degrees of freedom, Sig, Significance; eTIV, estimated Intracranial Volume; ns, non-significant.

Table S18.

Analysis of variance between two nested models analyzing global cerebral white matter volume changes through time (Linear Model vs. Quadratic Model)

	npar	AIC	BIC	logLik	deviance	Chisq	Df	Pr(>Chisq)
Model A. Linear Model	12	17,017.37	17,074.34	-8,496.68	16,993.37			
Model B. Quadratic Model	15	16,778.53	16,849.74	-8,374.26	16,748.53	244.84	3	8.54e-53

Model A corresponds to the following linear mixed effect model: *Cerebral white matter volume ~ 1 + Group + Session + Group*Session + eTIV + Age + Euler + Inter-session Interval + (1 / participant ID)*. Model B corresponds to the following linear mixed effect model: *Cerebral white matter volume ~ 1 + Group + Session + Session^2 + Group*Session + Group*Session^2 + eTIV + Age + Euler + Inter-session Interval + (1 / participant ID).* Both models were fitted with a maximum likelihood estimation. P-values below the threshold of 0.001 are reported in exponential notation. npar, number of parameters in the model; AIC, Akaike Information Criterion; BIC; Bayesian Information Criterion; logLik, Log-likelihood of the model; deviance, measure of goodness of fit for each model; Chisq, Chi-squared statistic; Df, degrees of freedom, Pr(>Chisq), p-value associated with the chi-square test.

Table S19.

Analysis of variance between two nested models analyzing global cerebrospinal fluid changes through time (Linear Model vs. Quadratic Model)

	npar	AIC	BIC	logLik	deviance	Chisq	Df	Pr(>Chisq)
Model A. Linear Model	12	9,701.28	9,758.26	-4,838.64	9,677.28			
Model B. Quadratic Model	15	9,644.26	9,715.48	-4,807.13	9,614.26	63.02	3	1.33e-13

Model A corresponds to the following linear mixed effect model: *Cerebrospinal fluid ~ 1 + Group + Session + Group*Session + eTIV + Age + Euler + Inter-session Interval + (1 / participant ID)*. Model B corresponds to the following linear mixed effect model: *Cerebrospinal fluid ~ 1 + Group + Session + Session^2 + Group*Session + Group*Session^2 + eTIV + Age + Euler + Inter-session Interval + (1 / participant ID).* Both models were fitted with a maximum likelihood estimation. P-values below the threshold of 0.001 are reported in exponential notation. npar, number of parameters in the model; AIC, Akaike Information Criterion; BIC; Bayesian Information Criterion; logLik, Log-likelihood of the model; deviance, measure of goodness of fit for each model; Chisq, Chi-squared statistic; Df, degrees of freedom, Pr(>Chisq), p-value associated with the chi-square test.

Table S20.

Statistical summary of the linear mixed effects model assessing nested cortical gray matter volume trajectories over time, based on their functional location using Yeo's 7-Networks, in first-time gestational mothers.

	Est.	CI 2.5%	CI 97.5%	SE	df	t value	p-value	Sig.
(Intercept)	28,398.87	27,745.39	29,052.36	333.42	883.99	85.18	0.00e+00	***
Session [Linear Term]	-10,212.15	-11,456.04	-8,968.27	634.65	3,334.18	-16.09	3.65e-56	***
Session [Quadratic Term]	27,129.75	25,877.02	28,382.48	639.16	3,334.32	42.45	3.80e-315	***
Networks [DMN + FP]	14,588.86	13,387.92	15,789.80	612.73	884.00	23.81	3.32e-97	***
eTIV	1,449.71	894.83	2,004.59	283.11	883.99	5.12	3.74e-07	***
Age	-477.54	-1,027.30	72.22	280.50	884.11	-1.70	0.089	ns
Euler Number	-41.35	-68.49	-14.21	13.85	3,342.82	-2.99	0.003	**
Inter-Session Time	103.12	-434.15	640.39	274.12	884.10	0.38	0.707	ns
Networks [DMN + FP] x Session [Linear Term]	-16,830.25	-19,151.94	-14,508.55	1,184.56	3,334.15	-14.21	1.59e-44	***
Networks [DMN + FP] x Session [Quadratic Term]	22,893.02	20,574.91	25,211.13	1,182.73	3,334.13	19.36	3.44e-79	***

The adjusted linear mixed effect model corresponded to *Cortical Volume ~ Nested Networks + Session + Session^2 + Session* Nested Networks + Session^2*Nested Networks + eTIV + Age + Euler + Inter-session Interval + (1 / participant ID / Yeo Networks).* No multiple comparison correction applied for this model. Statistics are shown for the fixed effects of the model. P-values below the threshold of 0.001 are reported in exponential notation. Asterisks indicate significance (ns, p-value > 0.05; *, p-value < 0.05; **, p-value < 0.01; ***, p-value < 0.001). Est, Estimate; CI, Confidence Interval; SE, Standard Error; df, degrees of freedom, Sig, Significance; ns, non-significant.

Table S21.

Statistical summary of the linear mixed effects model assessing a single cortical gray matter volume trajectory over time for all of Yeo's 7-Networks, in first-time gestational mothers.

	Est.	CI 2.5%	CI 97.5%	SE	df	t value	p-value	Sig.
(Intercept)	32,567.12	31,855.03	33,279.20	363.31	884.99	89.64	0.00e+00	***
Session [Linear Term]	-15,020.75	-16,161.65	-13,879.85	582.10	3,336.14	-25.80	4.98e-134	***
Session [Quadratic Term]	33,671.36	32,518.45	34,824.28	588.23	3,336.29	57.24	0.00e+00	***
eTIV	1,449.71	739.26	2,160.17	362.48	884.99	4.00	6.88e-05	***
Age	-477.55	-1,181.44	226.34	359.14	885.08	-1.33	0.184	ns
Euler Number	-41.28	-70.71	-11.85	15.02	3,342.33	-2.75	0.006	**
Inter-Session Time	103.13	-584.77	791.03	350.98	885.07	0.29	0.769	ns

The adjusted linear mixed effect model corresponded to *Cortical Volume* $\sim$ *Session* + *Session*^{2} + *eTIV* + *Age* + *Euler* + *Inter-session Interval* + *(1 | participant ID / Yeo Networks).* Statistics are shown for the fixed effects of the model. No multiple comparison correction applied for this model. P-values below the threshold of 0.001 are reported in exponential notation. Asterisks indicate significance (ns, p-value > 0.05; *, p-value < 0.05; **, p-value < 0.01; ***, p-value < 0.001). Est, Estimate; CI, Confidence Interval; SE, Standard Error; df, degrees of freedom, Sig, Significance; ns, non-significant.

Table S22.

Statistical summary of the linear mixed effects model assessing whole-brain modularity changes between session (1,4,5) and groups (Gestational Mothers, non-Gestational mothers, and Nulliparous Women)

	Est.	CI 2.5%	CI 97.5%	SE	df	t value	p-value	Sig.
(Intercept)	0.39	0.37	0.41	0.01	448.64	44.44	1.96e-166	***
Group [Gestational Mother]	0.01	-0.01	0.03	0.01	444.21	0.52	0.604	ns
Group [non-Gestational Mother]	-0.01	-0.04	0.02	0.02	456.60	-0.57	0.571	ns
Session 4	-0.01	-0.03	0.02	0.01	310.86	-0.48	0.630	ns
Session 5	-0.01	-0.04	0.01	0.01	336.11	-1.17	0.244	ns
FWD	0.000	-0.01	0.01	0.003	346.89	0.03	0.974	ns
Age	-0.003	-0.01	0.002	0.003	174.23	-1.16	0.248	ns
Inter-Session Time	-0.002	-0.01	0.004	0.003	178.49	-0.67	0.503	ns
Group [Gestational Mother] x Session 4	-0.02	-0.05	0.001	0.01	310.84	-1.87	0.063	ns
Group [non-Gestational Mother] x Session 4	0.01	-0.02	0.05	0.02	311.27	0.75	0.454	ns
Group [Gestational Mother] x Session 5	-0.01	-0.04	0.01	0.01	337.23	-0.91	0.365	ns
Group [non-Gestational Mother] x Session 5	0.02	-0.03	0.06	0.02	348.66	0.70	0.484	ns

The adjusted linear mixed effect model corresponded to: *Whole-brain modularity ~ 1 + Group + Session + Group*Session + Age + FWD + Inter-session Interval + (1 | participant ID).* Statistics are shown for the fixed effects of the model. No multiple comparison correction applied for this model. P-values below the threshold of 0.001 are reported in exponential notation. Asterisks indicate significance (ns, > 0.05; *, p-value < 0.05; **, p-value < 0.01; ***, p-value < 0.001). Est, Estimate; CI, Confidence Interval; SE, Standard Error; df, degrees of freedom, Sig, Significance; FWD, Frame-Wise Displacement; ns, non-significant.

Table S23.

Statistical summary of the linear mixed effects model assessing system segregation, within-network modularity and mean participation coefficient changes between session (1,4,5) and groups (Gestational Mothers, non-Gestational mothers, and Nulliparous Women)

Metrics/Network	Term	Est.	CI 2.5%	CI 97.5%	SE	df	t value	p-value	q-value	Sig.
System segregation										
Visual Network										
	Grupo [Gestational Mother] x Session 4	-0.75	-1.98	0.48	0.63	305.28	-1.19	0.235	0.379	ns
	Grupo [non-Gestational Mother] x Session 4	-0.77	-2.62	1.07	0.95	305.72	-0.82	0.415	0.888	ns
	Grupo [Gestational Mother] x Session 5	-0.11	-1.45	1.24	0.69	331.80	-0.16	0.875	0.911	ns
	Grupo [non-Gestational Mother] x Session 5	-0.71	-2.84	1.40	1.09	343.32	-0.65	0.514	0.976	ns
Somatomotor Network										
	Grupo [Gestational Mother] x Session 4	-0.50	-0.83	-0.16	0.17	302.64	-2.87	0.004	0.091	ns
	Grupo [non-Gestational Mother] x Session 4	-0.20	-0.71	0.31	0.26	303.13	-0.78	0.439	0.888	ns
	Grupo [Gestational Mother] x Session 5	-0.18	-0.55	0.20	0.19	320.69	-0.93	0.355	0.868	ns
	Grupo [non-Gestational Mother] x Session 5	0.32	-0.27	0.91	0.30	328.25	1.04	0.297	0.976	ns
Dorsal attention Network										
	Grupo [Gestational Mother] x Session 4	-0.17	-1.00	0.65	0.42	303.71	-0.41	0.682	0.895	ns
	Grupo [non-Gestational Mother] x Session 4	0.97	-0.27	2.21	0.64	304.18	1.52	0.130	0.888	ns
	Grupo [Gestational Mother] x Session 5	-0.58	-1.49	0.33	0.47	326.77	-1.24	0.215	0.868	ns
	Grupo [non-Gestational Mother] x Session 5	-0.60	-2.03	0.84	0.74	336.64	-0.81	0.418	0.976	ns
Ventral attention Network										
	Grupo [Gestational Mother] x Session 4	1.11	0.15	2.07	0.49	307.58	2.25	0.025	0.166	ns
	Grupo [non-Gestational Mother] x Session 4	0.42	-1.03	1.87	0.74	308.04	0.57	0.572	0.888	ns

Table S23.

Statistical summary of the linear mixed effects model assessing system segregation, within-network modularity and mean participation coefficient changes between session (1,4,5) and groups (Gestational Mothers, non-Gestational mothers, and Nulliparous Women)

Metrics/Network	Term	Est.	CI 2.5%	CI 97.5%	SE	df	t value	p-value	q-value	Sig.
	Grupo [Gestational Mother] x Session 5	-0.06	-1.12	1.00	0.54	329.54	-0.12	0.907	0.911	ns
	Grupo [non-Gestational Mother] x Session 5	0.03	-1.64	1.70	0.86	338.89	0.03	0.976	0.976	ns
Limbic Network										
	Grupo [Gestational Mother] x Session 4	7.36	-3.77	18.34	5.73	187.39	1.29	0.200	0.351	ns
	Grupo [non-Gestational Mother] x Session 4	6.03	-10.12	22.22	8.41	197.18	0.72	0.474	0.888	ns
	Grupo [Gestational Mother] x Session 5	10.04	-1.76	21.72	6.09	195.68	1.65	0.101	0.868	ns
	Grupo [non-Gestational Mother] x Session 5	13.40	-4.21	31.16	9.18	187.51	1.46	0.146	0.976	ns
Frontoparietal Network										
	Grupo [Gestational Mother] x Session 4	2.48	-1.04	6.01	1.81	309.94	1.37	0.171	0.327	ns
	Grupo [non-Gestational Mother] x Session 4	0.01	-5.30	5.30	2.72	310.22	0.003	0.998	0.998	ns
	Grupo [Gestational Mother] x Session 5	0.98	-2.90	4.84	1.99	334.30	0.49	0.624	0.911	ns
	Grupo [non-Gestational Mother] x Session 5	-0.75	-6.86	5.34	3.13	344.82	-0.24	0.811	0.976	ns
Default Network										
	Grupo [Gestational Mother] x Session 4	1.24	-0.05	2.53	0.66	310.63	1.87	0.063	0.166	ns
	Grupo [non-Gestational Mother] x Session 4	-0.52	-2.46	1.42	1.00	311.09	-0.52	0.604	0.888	ns
	Grupo [Gestational Mother] x Session 5	0.87	-0.55	2.29	0.73	332.88	1.19	0.235	0.868	ns
	Grupo [non-Gestational Mother] x Session 5	-0.54	-2.78	1.70	1.15	342.35	-0.47	0.638	0.976	ns
Modularity										
Visual Network										
	Grupo [Gestational Mother] x Session 4	0.04	0.001	0.08	0.02	308.09	1.99	0.048	0.166	ns

Table S23.

Statistical summary of the linear mixed effects model assessing system segregation, within-network modularity and mean participation coefficient changes between session (1,4,5) and groups (Gestational Mothers, non-Gestational mothers, and Nulliparous Women)

Metrics/Network	Term	Est.	CI 2.5%	CI 97.5%	SE	df	t value	p-value	q-value	Sig.
	Grupo [non-Gestational Mother] x Session 4	0.03	-0.03	0.09	0.03	308.51	1.02	0.308	0.888	ns
	Grupo [Gestational Mother] x Session 5	0.02	-0.02	0.07	0.02	336.00	0.89	0.372	0.868	ns
	Grupo [non-Gestational Mother] x Session 5	0.02	-0.05	0.09	0.04	348.18	0.46	0.647	0.976	ns
Somatomotor Network										
	Grupo [Gestational Mother] x Session 4	-0.02	-0.04	0.003	0.01	302.07	-1.71	0.088	0.204	ns
	Grupo [non-Gestational Mother] x Session 4	-0.01	-0.04	0.02	0.02	302.55	-0.60	0.549	0.888	ns
	Grupo [Gestational Mother] x Session 5	-0.002	-0.03	0.02	0.01	322.95	-0.19	0.847	0.911	ns
	Grupo [non-Gestational Mother] x Session 5	0.005	-0.03	0.04	0.02	331.80	0.24	0.812	0.976	ns
Dorsal attention Network										
	Grupo [Gestational Mother] x Session 4	0.005	-0.03	0.04	0.02	307.81	0.25	0.803	0.932	ns
	Grupo [non-Gestational Mother] x Session 4	0.01	-0.05	0.07	0.03	308.27	0.32	0.746	0.888	ns
	Grupo [Gestational Mother] x Session 5	0.01	-0.03	0.05	0.02	330.49	0.40	0.689	0.911	ns
	Grupo [non-Gestational Mother] x Session 5	0.04	-0.03	0.10	0.03	340.17	1.16	0.248	0.976	ns
Ventral attention Network										
	Grupo [Gestational Mother] x Session 4	0.000	-0.03	0.03	0.02	310.71	-0.01	0.993	0.993	ns
	Grupo [non-Gestational Mother] x Session 4	-0.03	-0.08	0.01	0.02	311.14	-1.42	0.156	0.888	ns
	Grupo [Gestational Mother] x Session 5	0.005	-0.03	0.04	0.02	337.03	0.28	0.777	0.911	ns
	Grupo [non-Gestational Mother] x Session 5	-0.02	-0.07	0.03	0.03	348.43	-0.70	0.487	0.976	ns
Limbic Network										

Table S23.

Statistical summary of the linear mixed effects model assessing system segregation, within-network modularity and mean participation coefficient changes between session (1,4,5) and groups (Gestational Mothers, non-Gestational mothers, and Nulliparous Women)

Metrics/Network	Term	Est.	CI 2.5%	CI 97.5%	SE	df	t value	p-value	q-value	Sig.
	Grupo [Gestational Mother] x Session 4	-0.02	-0.14	0.10	0.06	164.97	-0.29	0.775	0.932	ns
	Grupo [non-Gestational Mother] x Session 4	-0.05	-0.23	0.13	0.09	176.83	-0.55	0.580	0.888	ns
	Grupo [Gestational Mother] x Session 5	0.01	-0.12	0.14	0.07	171.11	0.12	0.908	0.911	ns
	Grupo [non-Gestational Mother] x Session 5	-0.05	-0.24	0.15	0.10	161.10	-0.48	0.634	0.976	ns
Frontoparietal Network										
	Grupo [Gestational Mother] x Session 4	-0.05	-0.09	-0.003	0.02	306.80	-2.06	0.040	0.166	ns
	Grupo [non-Gestational Mother] x Session 4	-0.04	-0.10	0.03	0.03	307.09	-1.07	0.287	0.888	ns
	Grupo [Gestational Mother] x Session 5	-0.02	-0.07	0.03	0.02	331.42	-0.75	0.454	0.911	ns
	Grupo [non-Gestational Mother] x Session 5	0.003	-0.07	0.08	0.04	342.07	0.07	0.947	0.976	ns
Default Network										
	Grupo [Gestational Mother] x Session 4	-0.05	-0.09	0.002	0.02	311.63	-1.87	0.062	0.166	ns
	Grupo [non-Gestational Mother] x Session 4	0.01	-0.06	0.09	0.04	312.06	0.38	0.703	0.888	ns
	Grupo [Gestational Mother] x Session 5	-0.07	-0.12	-0.01	0.03	336.67	-2.45	0.015	0.311	ns
	Grupo [non-Gestational Mother] x Session 5	-0.02	-0.11	0.06	0.04	347.45	-0.57	0.569	0.976	ns
mean Participation Coefficient										
Visual Network										
	Grupo [Gestational Mother] x Session 4	0.04	0.000	0.07	0.02	298.77	1.94	0.054	0.166	ns
	Grupo [non-Gestational Mother] x Session 4	-0.02	-0.07	0.04	0.03	299.23	-0.55	0.581	0.888	ns
	Grupo [Gestational Mother] x Session 5	0.03	-0.01	0.07	0.02	323.66	1.41	0.160	0.868	ns

Table S23.

Statistical summary of the linear mixed effects model assessing system segregation, within-network modularity and mean participation coefficient changes between session (1,4,5) and groups (Gestational Mothers, non-Gestational mothers, and Nulliparous Women)

Metrics/Network	Term	Est.	CI 2.5%	CI 97.5%	SE	df	t value	p-value	q-value	Sig.
	Grupo [non-Gestational Mother] x Session 5	-0.01	-0.07	0.06	0.03	334.41	-0.17	0.861	0.976	ns
Somatomotor Network										
	Grupo [Gestational Mother] x Session 4	0.01	-0.01	0.04	0.01	307.10	0.87	0.386	0.580	ns
	Grupo [non-Gestational Mother] x Session 4	-0.002	-0.04	0.04	0.02	307.58	-0.12	0.903	0.998	ns
	Grupo [Gestational Mother] x Session 5	0.002	-0.03	0.03	0.01	327.51	0.13	0.899	0.911	ns
	Grupo [non-Gestational Mother] x Session 5	-0.02	-0.07	0.02	0.02	336.13	-0.92	0.356	0.976	ns
Dorsal attention Network										
	Grupo [Gestational Mother] x Session 4	0.01	0.000	0.03	0.01	307.84	1.91	0.057	0.166	ns
	Grupo [non-Gestational Mother] x Session 4	0.000	-0.02	0.02	0.01	308.32	0.03	0.975	0.998	ns
	Grupo [Gestational Mother] x Session 5	0.01	-0.01	0.02	0.01	328.05	1.12	0.265	0.868	ns
	Grupo [non-Gestational Mother] x Session 5	-0.01	-0.03	0.01	0.01	336.58	-0.72	0.471	0.976	ns
Ventral attention Network										
	Grupo [Gestational Mother] x Session 4	-0.001	-0.01	0.01	0.01	311.26	-0.14	0.888	0.932	ns
	Grupo [non-Gestational Mother] x Session 4	-0.03	-0.05	-0.005	0.01	311.69	-2.43	0.016	0.331	ns
	Grupo [Gestational Mother] x Session 5	0.01	-0.01	0.02	0.01	337.10	0.69	0.493	0.911	ns
	Grupo [non-Gestational Mother] x Session 5	-0.01	-0.04	0.01	0.01	348.26	-1.20	0.232	0.976	ns
Limbic Network										
	Grupo [Gestational Mother] x Session 4	0.02	-0.004	0.05	0.01	313.19	1.63	0.104	0.218	ns
	Grupo [non-Gestational Mother] x Session 4	0.01	-0.03	0.05	0.02	313.62	0.42	0.672	0.888	ns

Table S23.

Statistical summary of the linear mixed effects model assessing system segregation, within-network modularity and mean participation coefficient changes between session (1,4,5) and groups (Gestational Mothers, non-Gestational mothers, and Nulliparous Women)

Metrics/Network	Term	Est.	CI 2.5%	CI 97.5%	SE	df	t value	p-value	q-value	Sig.
	Grupo [Gestational Mother] x Session 5	0.002	-0.02	0.03	0.01	337.72	0.18	0.860	0.911	ns
	Grupo [non-Gestational Mother] x Session 5	0.01	-0.04	0.05	0.02	348.25	0.27	0.790	0.976	ns
Frontoparietal Network										
	Grupo [Gestational Mother] x Session 4	0.001	-0.01	0.02	0.01	309.77	0.16	0.873	0.932	ns
	Grupo [non-Gestational Mother] x Session 4	-0.003	-0.03	0.02	0.01	310.24	-0.30	0.761	0.888	ns
	Grupo [Gestational Mother] x Session 5	0.001	-0.02	0.02	0.01	330.10	0.11	0.911	0.911	ns
	Grupo [non-Gestational Mother] x Session 5	-0.004	-0.03	0.02	0.01	338.68	-0.28	0.781	0.976	ns
Default Network										
	Grupo [Gestational Mother] x Session 4	0.01	-0.01	0.03	0.01	312.70	0.52	0.601	0.841	ns
	Grupo [non-Gestational Mother] x Session 4	0.01	-0.02	0.04	0.02	313.16	0.71	0.480	0.888	ns
	Grupo [Gestational Mother] x Session 5	-0.01	-0.03	0.01	0.01	333.77	-0.97	0.333	0.868	ns
	Grupo [non-Gestational Mother] x Session 5	-0.002	-0.04	0.03	0.02	342.69	-0.12	0.907	0.976	ns

The adjusted linear mixed effect model corresponded to: *Functional Metric ~ 1 + Group + Session + Group*Session + Age + FWD + Inter-session Interval + (1 / participant ID).* Statistics are shown for the interaction terms of the model. P-values were corrected for multiple testing across cortical metrics (system segregation, within-network modularity, and mean participation coefficient) and Networks (visual, somatomotor, dorsal attention, ventral attention, limbic, frontoparietal, and default mode network). Brain parcellations and its correspondence to Yeo's 7 large-scale functional networks were done using Shaefer's 400 parcellations atlas (14). Asterisks indicate significance under False Discovery Rate correction (ns, q-value > 0.05; *, q-value < 0.05; **, q-value < 0.01; ***, q-value < 0.001). Est, Estimate; CI, Confidence Interval; SE, Standard Error; df, degrees of freedom, Sig, Significance; FWD, Frame-Wise Displacement, ns, non-significant.

Table S24.

Descriptive table of all the steroid metabolites analyzed

Steroid Family	Metabolite	Horm. Concentration (Baseline)	Horm. Concentration (18 prg. weeks)	Horm. Concentration (32 prg. weeks)	Horm. Concentration (1 month postpartum)	Est.	p-value	q-value	Sig.
ESTROGENS									
	estriol 3-sulfate	-2.17 (1.13)	3.28 (1.40)	4.99 (1.00)	-2.94 (1.37)	-81.84	9.22e-82	5.53e-81	***
	estriol 16a-glucuronide	-1.93 (2.62)	4.48 (1.17)	6.15 (0.52)	-2.34 (2.02)	-99.14	2.18e-62	6.54e-62	***
	estrone sulfate	-0.02 (1.81)	4.71 (1.59)	5.27 (1.44)	-0.33 (1.40)	-57.18	2.62e-50	5.24e-50	***
	estriol 3-glucuronide	-0.62 (3.33)	4.24 (1.25)	5.66 (0.69)	-2.65 (1.56)	-85.71	6.24e-46	9.36e-46	***
	estrone glucuronide	1.76 (1.23)	4.28 (0.94)	5.12 (0.81)	0.07 (1.52)	-46.28	9.55e-43	1.15e-42	***
	estradiol 3-sulfate	-2.87 (2.11)	0.55 (1.55)	1.30 (1.68)	-5.41 (1.23)	-52.08	2.16e-32	2.16e-32	***
PROGESTOGENS									
	5a-pregnanediol 3b,20a bisulfate	2.38 (1.20)	6.12 (0.90)	7.27 (0.58)	1.86 (1.31)	-55.67	2.60e-63	3.12e-62	***
	pregnanediol 3-glucuronide	6.03 (1.09)	9.62 (0.68)	10.40 (0.35)	6.65 (0.59)	-39.18	1.61e-61	9.67e-61	***
	5b-pregnanediol 3a,20a 20-sulfate	2.51 (1.17)	3.45 (0.83)	4.00 (0.72)	-0.21 (0.86)	-37.99	8.08e-42	3.23e-41	***
	5a-pregnanediol 3b,20a 20-sulfate + 5b-pregnanediol 3b,20a 20-sulfate	1.54 (1.35)	2.13 (0.99)	2.37 (0.96)	-1.08 (1.13)	-34.98	9.69e-34	2.91e-33	***
	pregn-5-enediol 3b,20a bisulfate a	4.69 (0.90)	5.71 (0.95)	6.34 (0.71)	4.36 (0.87)	-16.38	8.25e-22	1.65e-21	***
	pregn-5-enediol 3b,20a bisulfate b	4.69 (0.90)	5.71 (0.95)	6.34 (0.71)	4.36 (0.87)	-16.38	8.25e-22	1.65e-21	***
	5a-pregnanediol 3a,20a 20-sulfate	-0.34 (2.04)	0.84 (0.91)	2.09 (0.82)	-1.60 (1.44)	-38.93	1.66e-21	2.85e-21	***
	pregn-5-enediol 3b-sulfate, 20a-glucuronide	3.56 (0.83)	3.77 (0.85)	4.03 (0.74)	2.50 (0.74)	-15.64	3.24e-21	4.86e-21	***
	pregn-5-enetriol 3b,17,20a bisulfate	2.78 (0.72)	2.94 (1.01)	3.45 (0.81)	2.42 (0.93)	-9.84	1.38e-08	1.84e-08	***

	pregnenolone sulfate	-2.52 (1.48)	-0.43 (1.28)	-0.03 (1.57)	-1.48 (1.66)	-13.79	8.37e-05	1.00e-04	***
	pregn-5-enediol 3b,20a 20-sulfate	1.00 (0.84)	-0.01 (0.72)	-0.14 (0.68)	-0.42 (0.60)	-4.31	0.008	0.009	**
	pregn-5-enediol 3b,20a 3-sulfate	0.76 (0.70)	-0.04 (0.69)	-0.11 (0.65)	-0.39 (0.62)	-3.67	0.014	0.014	*
CORTICOIDS									
	11-dehydrocorticosterone sulfate	1.23 (0.75)	3.34 (0.54)	4.06 (0.49)	2.18 (0.65)	-18.57	3.01e-34	5.73e-33	***
	20a-dihydrocortisone	1.83 (0.85)	2.50 (0.78)	3.14 (0.71)	0.86 (0.70)	-20.60	1.54e-23	1.46e-22	***
	corticosterone 21-sulfate	1.22 (0.98)	2.75 (0.68)	3.83 (0.48)	1.89 (0.93)	-19.13	1.64e-19	1.04e-18	***
	cortisol 21-sulfate	0.64 (1.26)	2.60 (0.75)	3.77 (0.66)	1.52 (0.97)	-20.77	2.06e-18	9.81e-18	***
	cortisone 21-sulfate	-0.56 (1.00)	1.21 (0.77)	2.22 (0.69)	-0.04 (0.94)	-17.18	3.19e-17	1.21e-16	***
	20b-dihydrocortisone	1.02 (0.82)	1.35 (0.85)	1.92 (0.72)	-0.01 (0.89)	-17.38	1.99e-15	6.31e-15	***
	Cortisone	2.66 (0.85)	3.45 (0.64)	3.93 (0.61)	2.67 (0.77)	-13.02	2.11e-11	5.72e-11	***
	11-dehydrocosrticosterone	-2.84 (1.28)	-2.34 (1.13)	-1.77 (0.85)	-3.56 (1.43)	-18.70	1.27e-10	3.01e-10	***
	Cortisol	-0.03 (1.30)	0.58 (0.93)	0.75 (0.99)	-0.40 (1.07)	-14.45	7.42e-07	1.57e-06	***
	tetrahydrocortisone 3-glucuronide	6.98 (0.68)	6.72 (0.58)	7.24 (0.70)	7.21 (0.48)	7.31	1.83e-06	3.48e-06	***
	b-Cortolone	1.06 (0.71)	1.37 (0.60)	1.85 (0.60)	0.97 (0.60)	-7.19	3.92e-06	6.77e-06	***
	a-Cortolone	1.40 (0.75)	1.67 (0.69)	2.03 (0.62)	1.09 (0.55)	-6.96	4.72e-06	7.48e-06	***
	5a-dihydrocortisol	-2.76 (0.78)	-3.27 (0.78)	-3.39 (0.87)	-2.92 (0.67)	4.64	0.011	0.016	*
	5b-tetrahydrocortisol	1.34 (0.77)	1.05 (0.75)	1.41 (0.69)	1.56 (0.79)	4.56	0.028	0.039	*
	Cortol 4	-0.48 (1.98)	-0.67 (1.06)	-0.70 (1.08)	-0.09 (0.89)	3.55	0.219	0.277	ns
	5b-tetrahydrocortisone	2.12 (1.15)	0.80 (1.29)	1.29 (0.91)	0.76 (1.16)	-1.33	0.649	0.770	ns
	5a-tetrahydrocortisone	0.84 (2.00)	0.57 (1.13)	-0.04 (1.45)	0.25 (1.38)	0.94	0.770	0.813	ns
	Cortol 1	-0.99 (1.99)	-0.94 (1.09)	-1.58 (1.26)	-1.25 (0.86)	-1.00	0.741	0.813	ns

	Cortol 2	2.34 (0.95)	1.48 (0.77)	1.37 (0.80)	1.47 (0.72)	-0.14	0.938	0.938	ns
ANDROGENS									
	epitestosterone sulfate	0.28 (0.62)	3.53 (0.74)	5.18 (0.57)	0.02 (0.63)	-51.23	5.98e-85	7.17e-84	***
	androst-5-enediol 3b,17b bisulfate	4.47 (1.06)	3.77 (1.16)	3.46 (1.04)	4.41 (1.33)	13.51	2.95e-11	1.77e-10	***
	16b-hydroxydehydroandrosterone 3-sulfate	2.68 (0.97)	5.08 (0.94)	5.52 (0.99)	3.95 (1.01)	-12.82	1.30e-10	5.21e-10	***
	androsterone glucuronide + etiocholanolone glucuronide	7.02 (0.68)	7.90 (0.53)	7.44 (0.68)	7.89 (0.53)	4.57	8.12e-04	0.002	**
	epitestosterone glucuronide	4.77 (0.59)	5.04 (0.61)	4.85 (0.58)	5.00 (0.66)	3.61	0.003	0.008	**
	epiandrosterone sulfate	0.81 (1.53)	3.51 (1.17)	2.65 (1.24)	3.26 (1.05)	7.48	0.008	0.017	*
	16a-hydroxydehydroandrosterone 3-sulfate	3.42 (1.19)	5.73 (1.03)	5.36 (1.21)	4.84 (1.07)	-5.56	0.019	0.033	*
	etiocholanolone sulfate	2.00 (1.29)	4.50 (0.87)	4.05 (1.04)	4.69 (0.86)	4.68	0.042	0.064	ns
	dehydroepiandrosterone sulfate	4.13 (1.50)	4.66 (2.59)	2.32 (3.40)	3.82 (2.68)	8.20	0.077	0.102	ns
	androst-5-enediol bisulfate	4.59 (1.02)	4.80 (1.04)	5.30 (1.07)	4.57 (1.15)	-3.76	0.088	0.106	ns
	androsterone sulfate	2.91 (1.17)	5.27 (0.87)	4.62 (1.19)	4.83 (0.90)	2.33	0.309	0.337	ns
	androstenedione	-0.78 (0.71)	-0.71 (0.72)	-1.01 (0.70)	-1.21 (0.63)	-0.61	0.648	0.648	ns

Steroid metabolites grouped by families. Hormonal concentrations are represented in their logarithmic form and corrected to their creatinine levels. Mean hormonal concentration and standard deviation per session, correspond to steroid levels in gestational mothers. The *trajectory* of each metabolite was estimated with the following linear mixed effect model: Hormonal Concentration ~ Group + Session + Session^2 + Group*Session + Group*Session^2 + Age + BMI + Inter-session Interval+ (1 | participant ID). Estimate (Est.) corresponds to the estimate of the Group [Gestational Mother] x Session [Quadratic Term]. P-values below the threshold of 0.001 are reported in exponential notation. Asterisks indicate significance under False Discovery Rate correction (ns, q-value > 0.05; *, q-value < 0.05; **, q-value < 0.01; ***, q-value < 0.001). P-values were corrected for multiple testing within each steroid family using FDR (estrogens, progestogens, corticoids, and androgens). A quadratic trajectory was determined when there was a significant q-value for the Group [Gestational Mother] x Session [Quadratic Term] interaction. Est, estimate; Sig, significance; ns, non-significant.

Table S25

Longitudinal correlations between steroid hormones concentrations and cortical gray matter volume trajectories from before pregnancy to one month postpartum in gestational mothers.

Steroid Family	Compound	Correlation Coefficient	p-value	q-value	Sig.
Estrogens					
	estriol 3-sulfate	-0.32	0.001	0.006	**
	estrone sulfate	-0.24	0.016	0.049	*
	estriol 3-glucuronide	0.21	0.032	0.065	ns
	estradiol 3-sulfate	-0.17	0.087	0.130	ns
	estrone glucuronide	0.11	0.265	0.318	ns
	estriol 16a-glucuronide	-0.02	0.867	0.867	ns
Progestogens					
	pregnenolone sulfate	-0.15	0.148	0.560	ns
	pregn-5-enediol 3b,20a 20-sulfate	0.13	0.193	0.560	ns
	pregn-5-enediol 3b,20a 3-sulfate	0.10	0.302	0.560	ns
	pregn-5-enediol 3b,20a bisulfate a	0.07	0.467	0.560	ns
	pregn-5-enediol 3b,20a bisulfate b	0.07	0.467	0.560	ns
	pregn-5-enediol 3b-sulfate, 20a-glucuronide	-0.10	0.304	0.560	ns
	pregn-5-enetriol 3b,17,20a bisulfate	-0.08	0.450	0.560	ns
	5a-pregnanediol 3a,20a 20-sulfate	0.09	0.398	0.560	ns
	5b-pregnanediol 3a,20a 20-sulfate	0.18	0.072	0.560	ns
	5a-pregnanediol 3b,20a 20-sulfate + 5b-pregnanediol 3b,20a 20-sulfate	0.10	0.305	0.560	ns
	pregnanediol 3-glucuronide	0.04	0.669	0.730	ns
	5a-pregnanediol 3b,20a bisulfate	-0.02	0.811	0.811	ns
Corticoids					
	11-dehydrocorticosterone sulfate	-0.11	0.281	0.865	ns
	20a-dihydrocortisone	-0.11	0.286	0.865	ns
	20b-dihydrocortisone	-0.10	0.309	0.865	ns
	5b-tetrahydrocortisol	0.14	0.165	0.865	ns
	tetrahydrocortisone 3-glucuronide	0.14	0.175	0.865	ns
	5a-dihydrocortisol	-0.09	0.391	0.913	ns
	11-dehydrocosrticosterone	-0.04	0.706	0.988	ns
	b-Cortolone	0.06	0.571	0.988	ns
	cortisone 21-sulfate	0.04	0.665	0.988	ns

Table S25

Longitudinal correlations between steroid hormones concentrations and cortical gray matter volume trajectories from before pregnancy to one month postpartum in gestational mothers.

Steroid Family	Compound	Correlation Coefficient	p-value	q-value	Sig.
	Cortisone	-0.06	0.532	0.988	ns
	a-Cortolone	0.00	0.978	0.993	ns
	corticosterone 21-sulfate	0.01	0.919	0.993	ns
	cortisol 21-sulfate	0.01	0.933	0.993	ns
	Cortisol	0.00	0.993	0.993	ns
Androgens					
	androst-5-enediol 3b,17b bisulfate	0.20	0.044	0.156	ns
	epitestosterone sulfate	-0.22	0.027	0.156	ns
	16b-hydroxydehydroandrosterone 3-sulfate	-0.08	0.428	0.749	ns
	epiandrosterone sulfate	-0.09	0.365	0.749	ns
	16a-hydroxydehydroandrosterone 3-sulfate	-0.05	0.617	0.785	ns
	epitestosterone glucuronide	0.04	0.673	0.785	ns
	androsterone glucuronide + etiocholanolone glucuronide	-0.02	0.841	0.841	ns

Steroid metabolites are grouped by families. Spearman correlation coefficient is the product of a simple correlation between the quadratic coefficients in percentage of gray matter volume change and each steroid metabolite. Correlations were only assessed for those metabolites with a significant quadratic trajectory (described in the previous table). P-values were corrected for multiple testing using FDR within each steroid family (estrogens, progestogens, corticoids, and androgens). Asterisks indicate significance under False Discovery Rate correction (ns, q-value > 0.05; *, q-value < 0.05; **, q-value < 0.01; ***, q-value < 0.001). Sig, Significance; ns, non-significant.

Table S26

Correlations between the percentage of cortical gray matter volume change during pregnancy/postpartum, and antenatal/postnatal maternal attachment.

	R	CI 2.5%	CI 97.5%	df	t value	p-value	q-value	Sig.
Antenatal Intensity of Preoccupation - % GM Volume Change (S1 to S3)	0.13	-0.05	0.29	125	1.42	0.157	0.251	ns
Antenatal Attachment Quality - % GM Volume Change (S1 to S3)	0.15	-0.02	0.32	125	1.73	0.085	0.212	ns
Postnatal Absence of Hostility - % GM Volume Change (S1 to S3)	0.24	0.04	0.41	96	2.37	0.020	0.079	ns
Postnatal Attachment Quality - % GM Volume Change (S1 to S3)	0.05	-0.15	0.25	96	0.48	0.629	0.785	ns
Postnatal Pleasure in Interaction - % GM Volume Change (S1 to S3)	0.01	-0.19	0.20	96	0.05	0.957	0.957	ns
Postnatal Absence of Hostility - % GM Volume Change (S3 to S5)	0.29	0.10	0.46	96	3.00	0.003	0.028	*
Postnatal Attachment Quality - % GM Volume Change (S3 to S5)	0.16	-0.04	0.35	96	1.63	0.106	0.212	ns
Postnatal Pleasure in Interaction - % GM Volume Change (S3 to S5)	-0.04	-0.24	0.16	96	-0.40	0.687	0.785	ns

The associations were assessed as separate Pearson's correlations between *Attachment and % gray matter volume change*. Antenatal attachment was measured at 34 weeks of pregnancy (i.e., Session 3). Postnatal attachment was measured at 6 months postpartum (i.e., Session 5). P-values were corrected for multiple testing applied across the eight tested associations. Asterisks indicate significance under False Discovery Rate correction (ns, q-value > 0.05; *, q-value < 0.05; **, q-value < 0.01; ***, q-value < 0.001). R, Pearson correlation coefficient; CI, Confidence Interval; df, degrees of freedom, Sig, Significance; S1; Session1; S3, Session 3; S5; Session 5.

Table S27

Mediation analyses assessing the effect of mental health variables (well-being, stress, and depression) on the association between the percentage of gray matter volume recovery during postpartum and the absence of hostility at six months postpartum.

Mental Health		Est.	CI 2.5%	CI 97.5%	p-value	q-value	Sig.
Wellbeing							
	ACME	0.15	0.05	0.27	0.002	0.006	ns
	ADE	0.14	-0.02	0.29	0.087	0.088	ns
	Total Effect	0.29	0.12	0.45	0.002	0.002	**
	Prop. Mediated	0.51	0.22	1.13	0.003	0.008	**
Stress							
	ACME	0.09	0.002	0.19	0.044	0.066	ns
	ADE	0.21	0.05	0.35	0.014	0.022	*
	Total Effect	0.29	0.12	0.45	0.002	0.002	**
	Prop. Mediated	0.29	0.01	0.71	0.045	0.069	ns
Depression							
	ACME	0.04	-0.01	0.11	0.166	0.166	ns
	ADE	0.25	0.08	0.39	0.005	0.014	*
	Total Effect	0.29	0.11	0.44	0.001	0.002	**
	Prop. Mediated	0.13	-0.08	0.39	0.167	0.167	ns

Mediation analyses results. Multiple testing correction was applied across the three tested mediation analyses. ACME is the average causal mediate effect (i.e., the effect of the mediator alone). ADE corresponds to the average direct effect (i.e., unmediated effect). The total effect is the sum of the ACME and ADE. The proportion mediated represents the proportion of the predictor's effect on the response variable that passes through the mediator. P values were corrected for multiple testing across all tested mediations (well-being, stress, and depression). Asterisks indicate significance under False Discovery Rate correction (ns, q-value > 0.05; *, q-value < 0.05; **, q-value < 0.01; ***, q-value < 0.001). Est, Estimate; CI, Confidence Interval; Sig, Significance; ns, non-significant

Table S28.

Standards and their MS-characteristics used in determination of phase II steroid metabolites.

Steroid metabolite identified	Corresponding compound	Supplier	Ion transition (m/z → m/z)	CE [eV]
	Standards			
Estrone sulfate	estrone sulfate	c	349→269	30
Estrone glucuronide	estrone glucuronide	b	445→269	30
Estradiol 3-sulfate, 17b-glucuronide	estradiol 3-sulfate, 17β-glucuronide	h	263→351	15
Estradiol 3-sulfate	estradiol 3-sulfate	b	351→271	30
Estriol 3-sulfate	estriol 3-sulfate	e	367→287	35
Estriol 3-glucuronide	estriol 3-glucuronide	e	463→287	30
Estriol 16a-glucuronide	estriol 16α-glucuronide	e	463→287	30
Pregnenolone sulfate	pregnenolone sulfate	b	395→97	30
Pregn-5-enediol 3b,20a bisulfate	pregn-5-ene-3β,20S-diol 3β,20α-bisulfate	g	238→379	15
Pregn-5-enediol 3b-sulfate, 20a-glucuronide	pregn-5-ene-3β,20S-diol 3β-sulfate 20α-glucuronide	h	286→397	15
Pregn-5-enediol 3b,20a 3-sulfate	pregn-5-ene-3β,20S-diol 3β-sulfate	i	397→97	30
Pregn-5-enediol 3b,20a 20-sulfate	pregn-5-ene-3β,20S-diol 20α - sulfate	i	397→97	30
Pregn-5-enetriol 3b,17,20a bisulfate	pregn-5-ene-3β,17,20S-diol 3β,20α - bisulfate	i	246→395	15
5a-Pregnanediol 3b,20a bisulfate	5α-pregnane-3β,20α-diol 3β,20α - bisulfate	g	239→381	15
5a-Pregnanediol 3a,20a 20-sulfate	5α-pregnane-3α,20α-diol 20α - sulfate	i	399→97	40
5a-Pregnanediol 3b,20a 20-sulfate + 5b-pregnanediol 3b,20a 20-sulfate	5α-pregnane-3β,20α-diol 20α - sulfate	i	399→97	40
	5β-pregnane-3β,20α-diol 20α - sulfate	i		
5b-Pregnanediol 3a,20a 20-sulfate	5β-pregnane-3α,20α-diol 20α-sulfate	i	399→97	40
Pregnanediol 3-glucuronide	5β-pregnane-3α,20α-diol 3α-glucuronide	b	495→75	30
Dehydroepiandrosterone sulfate	androst-5-en-3β-ol-17-one 3β-sulfate	c	367→97	30
16b-Hydroxydehydroandrosterone 3-sulfate	androst-5-ene-3β-16β-diol-17-one 3β-sulfate	i	383→97	30
16a-Hydroxydehydroandrosterone 3-sulfate	androst-5-ene-3β-16α-diol-17-one 3β-sulfate	b	383→97	30
Androst-5-enediol 3b,17b bisulfate	androst-5-ene-3β,17β-diol 3β,17β bisulfate	g	224→351	15
Androst-5-enediol bisulfate	androst-5-ene-3α,17β-diol bisulfate	i	224→351	15
Epitestosterone sulfate	epitestosterone sulfate	a	367→97	30
Epitestosterone glucuronide	epitestosterone glucuronide	a	463→75	30
Epiandrosterone sulfate	epiandrosterone sulfate	b	369→97	35
Androsterone sulfate	androsterone sulfate	a	369→97	35
Etiocholanolone sulfate	etiocholanolone sulfate	a	369→97	35
Androsterone glucuronide + etiocholanolone glucuronide	androsterone glucuronide	a	465→75	30
	etiocholanolone glucuronide	a		
11-Dehydrocorticosterone sulfate	11-dehydrocorticosterone sulfate	i	423→97	30
Corticosterone 21-sulfate	corticosterone 21-sulfate	b	425→97	30
Cortisol 21-sulfate	cortisol 21-sulfate	d	441→97	30
Tetrahydrocortisone 3-glucuronide	5α-tetrahydrocortisone 3-glucuronide	f	539→509	30
Cortisone 21-sulfate	cortisone 21-sulfate	b	439→97	30

Internal standards (ISTD)				
ISTD-Gluc_1	androsterone-d4 glucuronide	a	469→75	30
ISTD- Gluc _2	epitestosterone-d4 glucuronide	a	467→75	35
ISTD-Sulf_1	estradiol-d4 3-sulfate	d	354→274	30
ISTD- Sulf _2	3-S{^{18}O}$_3$-epiandrosterone-sulfate	g	375→103	35
ISTD- Sulf _3	epitestosterone-d3 sulfate	a	370→98	35
ISTD-biSulf_1	17-S{18O}3-5α-androstane-3α,17β-diol bisulfate	g	228→359	15
ISTD-biSulf_2	17-S{^{18}O}$_3$-5α-androstane-3β,17β-diol bisulfate	g	228→359	15
ISTD-SulfGluc	3-S{^{18}O}$_3$-5α-androstane-3β,17β-diol 3β-sulfate, 17β -glucuronide	h	276→377	15

a - Australian National Measurement Institute (Pymble, Australia).
b - Steraloids (Newport, RI, USA).
c - Merk (Sigma-Aldrich, Burlington, MA, USA).
d - TRC-Canada (Toronto Research Chemicals, Toronto, Canada).
e - kindly provided by Prof. C. Shackelton from UCSF Benioff Children's Hospital Oakland Research Institute.
f - kindly gifted by Dr. Lorna C Gilligan from University of Birmingham.
g – quantitatively synthesized on customer demand, according to published methodology (60).
h – quantitatively synthesized on customer demand, according to published methodology (61).
i - qualitatively synthesized *in-house* at small scale based on earlier described methodology (60).

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