nature portfolio

Corresponding author(s): Óscar Vilarroya

Last updated by author(s): Nov 20, 2024

Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☐	☒	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	Qualtrics XM, Philips Ingenia CX 3 Tesla
Data analysis	MRI preprocessing was performed with Freesurfer version 7.2. rs-fMRI processing was performed with a Nipype pipeline implemented in Python (version 3.9.7). Statistical analyses were performed in Rstudio (version 2023.06.0+421), under R version 4.3.1, with the following libraries: lmer (version 1.1.33) for LME models, including global neuroanatomical, functional connectomics, neuropsychological and hormonal data; emmeans (version 1.8.7) for computing estimated marginal means for assessing contrasts among modeled factors; stats (version 4.3.1) for assessing quadratic effects in neuroanatomical and hormonal data, to apply FDR corrections, and to perform pearson and Spearman correlations between neuroanatomical and neuropsychological or hormonal data; and mediation (version 4.5.0) for the mediation analysis. Vertex-wise FDR-corrected maps were computed using the lme_mass_FDR function included in the MATLAB's LME vertex-wise tool distributed within FreeSurfer. Figures were plotted using ggplot2 R library. The in-house Rscript also used the following libraries: htmltools (version 0.5.5), tydiverse (version 2.0.0), readxl (version 1.4.3), kableExtra (version 1.3.4.9000), doBy (version 4.6.17), ggpurb (version 0.6.0), corrplot (version 0.92), dyplr (version 1.1.2), MASS (version 7.3.60), flextable (version 0.9.4), officer (version 0.6.3), sjPlot (version 2.8.14). Vertex-wise analyses were plotted using the R library fsbrain (version 0.5.4).

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

The study materials, data, and analysis scripts will be made openly available on a GitHub repository. The raw and processed MRI images of the study participants will be made available upon reasonable request to the corresponding author.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	The subjects of this study were pregnant and non-pregnant females who self-identified as women. Therefore, sex- and gender-based analyses were not applicable.
Reporting on race, ethnicity, or other socially relevant groupings	No information with regard to race or ethnicity was collected.
Population characteristics	Eligible subjects were females in their reproductive years. Our final experimental sample consisted of 127 first-time gestational mothers (mean age ± sd = 33.67 ± 4.04 years), 20 non-gestational mothers (mean age ± sd = 32.15 ± 3.53 years), and 32 nulliparous women (mean age ± sd = 30.38 ± 3.23 years). Except for one, all non-gestational mothers of the final sample were partners of women from the gestational mothers group. Exclusion criteria included being over 45 years old, being pregnant at the pre-conception session, previous pregnancies beyond the first trimester, current major neurological or psychiatric disorders assessed by the MINI International Neuropsychiatric Interview, intake of psychiatric medication, and MRI incompatibilities. Gestational mothers and their non-gestational partners who did not achieve pregnancy after the first MRI session were discontinued from the study.
Recruitment	Participants were recruited in the Barcelona area through word-of-mouth, local hospitals, and social media ads.
Ethics oversight	This research was approved by the Ethics Committee at the Hospital del Mar Research Institute (Ref: 2017/7450/I), the Hospital Clínic de Barcelona (Ref: HCB/2018/0357), and the Hospital Universitari Quirón Dexeus (Ref: 7/2/2017), in accordance with the Declaration of Helsinki guidelines. All participants signed a consent form before participating in the study and received monetary compensation for their participation.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☐ Life sciences ☒ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Behavioural & social sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description	We used a quantitative longitudinal case-control study assessing first-time gestational mothers (N=127) along five sessions: (1) pre-conception, (2) at 18 weeks of pregnancy (mean ± sd = 18.25 ± 0.94 weeks), (3) at 34 weeks of pregnancy (mean ± sd = 34.20 ± 0.90 weeks), (4) at one month postpartum (mean ± sd = 1.09 ± 0.27 months), and (5) at six months postpartum (mean ± sd = 6.05 ± 0.32 months). First-time gestational mothers were also compared to a group of non-gestational mothers (N=20) and nulliparous women (N=32) who completed all visits at similar time points.
Research sample	Our research sample comprised women living around the Barcelona area, willing to participate in our study, and most of them were recruited through social media. These women were in their thirties and representative of the Spanish pregnant population.
Sampling strategy	The sampling of participants was done using a convenience sampling procedure. Our sample size is based on: a) the birth success rate of each conception method obtained in our previous study (40% for non-assisted; 44% for AI after 4 cycles; 25% for IVF initiated cycle) (Hoekzema et al., 2017), as well as on the Spanish Fertility Society reports (https://www.registrosef.com/); b) the estimation of the final sample size required to capture the effects sizes obtained in our previous study (Hoekzema et al., 2017).

Data collection	Neuroimaging data: Philips Ingenia CX 3T MRI scanner. Demographic, obstetric, and neuropsychological questionnaires: auto-administered via Qualtrics. MINI international neuropsychiatric interview: administered on the day of the study visit by a clinical psychologist. Urine samples: collected the night before the study visit. The study visits included the participant, a clinical psychologist, and an MRI technician. Due to the objectives and design of the study, data collection, and analysis were not performed blind to the conditions of the experiments.
Timing	Data collection started in April 2020 and ended in September 2023
Data exclusions	We only included participants who had completed at least sessions 1,3, and 4 (138 gestational mothers, 22 non-gestational mothers, and 33 nulliparous women). From this sample, we excluded 9 participants who met our mental health exclusion criteria, one because of being pregnant at session 1 (pre-pregnancy session) and 4 because of having an unusable MRI image from either session 1, 3, or 4.
Non-participation	Five participants did not return to the fifth session due to loss of interest.
Randomization	Randomization is not applicable to this study since group allocation was decided upon the status of the participants (gestational mothers, non-gestational mothers, and nulliparous women).

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☐	☒ MRI-based neuroimaging

Plants

Seed stocks	*Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.*
Novel plant genotypes	*Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.*
Authentication	*Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.*

Magnetic resonance imaging

Experimental design

Design type	High-resolution T1-weigthed anatomical Magnetic Resonance Imaging; resting state functional Magnetic Resonance Imaging.
Design specifications	Since this is a structural MRI and resting-state fMRI sequence, no blocks, trials, or experimental units are applicable.
Behavioral performance measures	Since this is a structural MRI and resting-state fMRI sequence, behavioral performances are not applicable.

Acquisition

Imaging type(s)	Structural and functional
Field strength	3T
Sequence & imaging parameters	We acquired three-dimensional T1-weighted images on a 3 Tesla Philips Ingenia CX with a Head-and-Neck 32-channel coil. We used a Turbo Field Echo (TFE) sequence in sagittal orientation and the following parameters: Voxel size = 0.75x0.75x1mm3; field of view (FOV) = 240 x 240 x 180 mm3; echo time (TE) = 4.6 ms; repetition time (TR) = 9.9/2300 ms; prepulse delay = 900 ms; flip angle (FA) = 8º; acceleration factor = 1.9; percent sampling = 78%; acquisition time = 259 s. We obtained rs-fMRI images on the same 3 Tesla Philips Ingenia CX with a Head-and-Neck 32-channel coil. We acquired T2*-weighted whole-brain single shot echo-planar images (EPIs, with 225 images, the first three, 26 serving as dummy scans to account for T1 saturation effects equilibration) with the following parameters: TR = 1.6 s; TE = 35 ms; Flip Angle = 75°; Field of View = 240 x 240 x 138 mm; voxel size = 3 × 3 mm; 46 slices; and slice thickness = 3 mm. Subsequently, two extra images were acquired to address image distortions induced by the magnetic field. These images were acquired using single-shot spin-echo EPI sequences in opposing phase encoding directions—one with phase encoding in the anterior-posterior direction and the other with phase encoding in the posterior-anterior direction. Each image comprised two volumes with the same spatial resolution and matrix dimensions as the resting-state images and the acquisition parameters were TR = 1600 ms; TE = 35 ms; and a flip angle = 90º.
Area of acquisition	Whole brain

Diffusion MRI ☐ Used ☒ Not used

Preprocessing

Preprocessing software	Structural MRI: FreeSurfer (V 7.2.0) longitudinal stream (https://surfer.nmr.mgh.harvard.edu/fswiki/LongitudinalProcessing), which comprises a cross-sectional processing of the images, a creation of a base within-subject template, and a longitudinal processing of the images using the template. Resting-state fMRI: Nipype pipeline implemented in Python (version 3.9.7), which involved a fieldmap intensity correction, head motion realignment, spatial co-registration and normalization, 8 mm-FWHM spatial smoothing, and temporal filtering (0.009–0.08 Hz). Six head motion parameters, signals from white matter, and cerebrospinal fluid were regressed from the images to control for head motion and physiological noises.
Normalization	Structural MRI global analyses: -Normalization to create the within-subject template (non-linear spherical surface registration) Structural MRI vertex-wise analyses: -Normalization to create the within-subject template (non-linear spherical surface registration) -Normalization to fsaverage (non-linear spherical surface registration) Resting-state fMRI: - Normalization to MNI space
Normalization template	Structural MRI global analyses: Within-subject space (native space) Structural MRI vertex-wise analyses: fsaverage space to achieve a vertex-correspondance among subjects Resting-state fRMI: MNI152Lin6Asym template from FSL
Noise and artifact removal	Structural MRI: Freesurfer's recon-all inhomogeneity correction. The normalization to fsaverage was smoothed with a 10mm full-width-at-half-maximum Gaussian kernel filter. Resting-state fMRI: using FSL, six head motion parameters, signals from white matter, and cerebrospinal fluid were regressed from the images to control for head motion and physiological noises.
Volume censoring	Volume censoring was not appliable.

Statistical modeling & inference

Model type and settings	Linear mixed effect (LME) models with random intercepts with covariates
Effect(s) tested	We computed group and session differences using LME Models

Specify type of analysis: ☒ Whole brain ☐ ROI-based ☐ Both

Statistic type for inference (See Eklund et al. 2016)	vertex-wise
Correction	False Discovery Rate correction (alpha<5 %, P<0.05)

Models & analysis

n/a	Involved in the study
☐	☐ Functional and/or effective connectivity
☐	☒ Graph analysis
☐	☐ Multivariate modeling or predictive analysis

Functional and/or effective connectivity

Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).

Graph analysis

For our graph analysis, we computed metrics related to network integration/segregation and distinctiveness, including whole-brain and within-network modularity, mean participation coefficient, and systemsegregation. All the metrics were calculated for each subject and session (1, 4, and 5) over a range of weighted, undirected matrices. Then, we calculated the averaged composite index across all the costs. We applied a null model comparison using a network rewiring approach and calculated the same graph theory metrics on the randomized matrices (i.e., null graph theory metrics). Finally, we corrected our metrics by subtracting the values obtained from the null graph theory metrics at a subject level. These were the values used in our analyses.

Multivariate modeling and predictive analysis

Specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.