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Reporting Summary

Nature Research 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 Research policies, see Authors & Referees 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	*Provide a description of all commercial, open source and custom code used to collect the data in this study, specifying the version used OR state that no software was used.*
Data analysis	Codes used to analyze and plot the results are available as Supplementary Software (SupplementarySoftware.zip) and github (https://github.com/thewonlab/HAR). R Libraries and programs used in the manuscript were described in the Methods.

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/reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research 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 list of figures that have associated raw data
- A description of any restrictions on data availability

Hi-C data from fetal brain are available through GEO and dbGaP under the accession number GSE77565 and phs001190.v1.p1, respectively. Hi-C data from adult brain are available through https://www.synapse.org//#!Synapse:syn4921369/wiki/ 390671 and the PsychENCODE knowledge portal http://resource.psychencode.org/. Promoter-based interaction maps for fetal brain and adult brain are available in Supplementary Tables 22-23 of Won et al. and the PsychENCODE knowledge portal, respectively.

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

Life sciences study design

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

Sample size	We used publicly available (1) Hi-C datasets in the fetal and adult brain and (2) previously defined human-specific evolutionary elements. The sample size was described in the previous studies. For functional validation results (Figure 4), we described the sample size (N).
Data exclusions	No data were excluded during the analysis.
Replication	We did not replicate our Hi-C findings, since previous papers reporting the Hi-C datasets (Won et al., Nature 2016; Wang et al., Science 2018) have performed extensive integrative analyses to confirm the validity of Hi-C datasets. For functional validation results (Figure 4), we described sample size (N) for replication.
Randomization	We used publicly available (1) Hi-C datasets in the fetal and adult brain and (2) previously defined human-specific evolutionary elements. Therefore, we did not need to perform randomization.
Blinding	We were not blinded during the analysis, but we don't expect bias as all results follow strict statistical criteria applied to all elements in the same manner. We have used the same standard procedure to process data. For Figure

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
☒	☐ Animals and other organisms
☒	☐ Human research participants
☒	☐ Clinical data

Methods

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