nature portfolio

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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	The following packages and software were used for data collection: Cell Ranger (v3.1.0 and v6.1.1).
Data analysis	Data Analysis: Data analysis was performed using R (v4.0.1), RStudio (v1.4.1717) and Python (v3.8.10). Key R packages included: Seurat (v4.3.0.1), SeuratObject (v4.1.3), SeuratWrappers, SeuratDisk, torch, SummarizedExperiment (v1.30.2), ggplot2 (v3.4.2), future(v1.32.0), scratch.hicat (v1.0.0), scratch.vis (v0.0.210), scratch.io (v0.1.0), slingshot, monocle(v2.0), sctransform(v0.3.5), SingleCellExperiment (v1.24.0), rhdf5 (v2.44.0), HDF5Array (v1.28.1), scSeqComm (v1.0), OmnipathR (v3.10.1), graphite, stringr (v1.5.0), corrplot (v0.92), nat, Rcpp (v1.0.10), RcppParallel (v5.1.7), RInside, scico (v1.4.0), circlize (v0.4.15), ggnewscale (v0.4.9), ggformula, viridis(v0.6.3), RcolorBrewer (v1.1.3), ggridges (v0.5.4), clusterProfiler (v4.10.1), org.Mm.eg.db (v3.18.0), enrichplot (v1.22.0), simplifyEnrichment, presto, scCustomize, factoextra (v1.0.7), NbClust, ggpubr (v0.6.0), ggeasy (v0.1.4), ggthemes (v4.2.4), ggrepel (v0.9.3), data.table (v1.14.8), dplyr (v1.1.2), tibble (v3.2.1), tidyverse (v2.0.0), reshape2 (v1.4.4), pbapply (v1.7.0), pbmcapply (v1.5.1), DescTools (0.99.49), SCISSORs, MatrixGenerics (v1.12.2), plyr (v1.8.8), MetaMarkers, scales (v1.2.1), paletteer (v1.5.0), gplots (v3.1.3), scubi, rgl (v1.1.3), car (v3.1.2), gridExtra (v2.3), ComplexHeatmap (v2.16.0), heatmaply (v1.4.2), ggsankey (v0.0.99999), plotly (v4.10.2), reticulate (v1.30), patchwork (v1.1.2), and conflicted (v1.2.0). Python packages included: tqdm, matplotlib (v3.1.2), mpl_toolkits, numpy (v1.17.4), pandas (v0.25.3), scipy, ngauge, and Scrublet. The code used for data analysis in this manuscript is available on demand during review and will be put on Github Shiny App – scLRsomatoDev: The following software and packages were used to build the Shiny app: Docker, shiny (v4.0.3), remotes, ggplot2 (v3.4.2), add2ggplot (v0.3.0), ggnewscale (v0.4.9, data.table (v1.14.8), bslib (v0.5.0), esquisse (v1.1.2), DT (v0.28), shinyWidgets (v0.7.6), circlize (v0.4.15), scales (v1.2.1), graphics (v4.3.2), dplyr (v1.1.2), plotly (v4.10.2), heatmaply (v1.4.2), magick (v2.7.4), shinycssloaders (v1.0.0), reshape2 (v1.4.4), plyr (v1.8.8), datamods (v1.4.1), paletteer (v1.5.0), scico (v1.4.0), cowplot (v1.1.1), ggeasy (v0.1.4), ggthemes (v4.2.4), grDevices (v4.3.2), stringr (v1.5.0), BiocManager (v1.30.21), ComplexHeatmap (v2.16.0), rhdf5(v2.44.0), HDF5Array (v1.28.1), SummarizedExperiment (v1.30.2), scratch.hicat (v1.0.0), scratch.io (v1.0.0), and scratch.vis (v1.0.0).

Raw sc/snRNA-seq data generated in this study are available in the ArrayExpress database under accession E-MTAB-16260, and bulk RNA-seq data are available under accession E-MTAB-16355 (https://www.ebi.ac.uk/biostudies/arrayexpress/studies). Processed data, QC outputs, and derived RDS files are deposited on Zenodo (https://zenodo.org/records/11634657). Interactive exploration of inferred signaling networks is available through the scLRSomatoDev Shiny application at https://sclrsomatodev.online/.

All scripts used for data preprocessing, quality control, ligand–receptor inference, ontology annotation, and enrichment analysis were written in R and Python. The complete codebase, including custom functions and documentation, is publicly available on Zenodo (https://zenodo.org/records/11634657). Additional documentation and tutorials are provided online:
Documentation: https://cortical-interactome.github.io/scLRSomatoDev-Docs/
Video tutorials: https://www.youtube.com/playlist?list=PLyfGSyn6Q6UY82ccuHRZQmRchVx6DskfJ

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

Data availability
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Code availability
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Documentation: https://cortical-interactome.github.io/scLRSomatoDev-Docs/
Video tutorials: https://www.youtube.com/playlist?list=PLyfGSyn6Q6UY82ccuHRZQmRchVx6DskfJ

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	NA
Reporting on race, ethnicity, or other socially relevant groupings	NA
Population characteristics	NA
Recruitment	NA
Ethics oversight	NA

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

Life sciences study design

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

Sample size	We generated five single-cell RNA-sequencing (scRNA-seq) libraries and two multiplexed single-nucleus RNA-sequencing (snRNA-seq) libraries, the latter incorporating barcoded antibodies. All libraries were prepared using the 10x Genomics platform. In total, we obtained 58,027 high-quality cells, with cell counts ranging from approximately 9,000 to 16,000 per time point, across six postnatal developmental stages of the somatosensory cortex. Sample size was determined based on the goal of capturing key developmental transitions in cortical neurons, while balancing experimental cost, technical feasibility, and downstream analytical requirements. No formal statistical method was used to pre-determine sample size. Additional developmental time points were incorporated from publicly available datasets.
Data exclusions	To retain only high-quality cells in sequencing experiments, we applied the following filtering criteria: • Cells with >10% mitochondrial gene expression were excluded. • Cells with a log10(number of detected genes) outside three double median absolute deviations (doubleMAD) from the population median were excluded (with a minimum gene count threshold of 500). • Cells with a log10(number of detected UMIs) below three doubleMADs of the population median were also removed. • We plotted log10(nFeature_RNA) vs. log10(nCount_RNA) and fitted a linear regression model between these variables. Cells lying above an offset of -0.09 from this regression line were removed. • Doublets were identified and removed using the Scrublet package. • After cell type annotation, only cells classified as glutamatergic or GABAergic neurons were retained for downstream analyses to align with the study's focus.
Replication	Most of the datasets used in this study were obtained from publicly available sources. For specific time points that were not available, we generated additional data by pulling dissociated cells from multiple animals in a single-cell experiment to represent that time point.
Randomization	No randomization was applied. Covariates were not controlled as they were not relevant to the goals of this analysis and were not statistically assessed.
Blinding	Blinding was not performed. All analyses were conducted uniformly across samples in reproducible ways. As such, blinding was not expected to reduce bias in this context.

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

Antibodies

Antibodies used	rabbit anti-Parvalbumin (1:1000, Swant), chicken anti-GFP (1:500, Aves), rabbit anti-Synaptotagmin 2 (SYT2) (1:100, DSHB), mouse IgG2a anti-SYT2 (DSHB, 1:100), and rabbit anti-SPTBN4 (Thermofisher, 1:1000). rabbit anti-CBLN4 (Invitrogen, PA5-36472) and anti-Mouse GLUD1 (Proteintech, 67026-1-Ig) or anti-CBLN4 and goat anti-NEO1 (Biotechne, AF1079) co-immunolabeling before application of Rabbit Plus and Mouse Minus or Rabbit Plus and Goat Minus probes, respectively (Merck, Duolink).
Validation	Validation was based on manufacturer-provided data and a review of the literature for the antibodies

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	NA

Authentication	NA
Mycoplasma contamination	NA
Commonly misidentified lines (See ICLAC register)	NA

Palaeontology and Archaeology

Specimen provenance	NA
Specimen deposition	NA
Dating methods	NA

☐ Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.

Ethics oversight	NA

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

Animals and other research organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in Research

Laboratory animals	Mice (Mus musculus) were group-housed (2–5 mice per cage) with same-sex littermates under a 12-hour light–dark cycle, with ad libitum access to food and water. Animals were bred and maintained on a mixed SVeV-129/C57BL/6N background. Samples were collected at six postnatal stages: P0, P2, P5, P8, P16, and P30.
Wild animals	No wild animals were used in this study
Reporting on sex	Sex was not considered in the experimental design and the sample use for P0, P2, P5, P8, P16, and P30 are a mixe of male/female.
Field-collected samples	No field-collected samples were used in this study.
Ethics oversight	Animal experiments were conducted in accordance with European Communities Council Directives and approved by French ethical committees (Comité d'Ethique pour l'expérimentation animale no. 14; permission number: 62-12112012, Apafis #21683-2019073011285386v4)

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

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	NA
Study protocol	NA
Data collection	NA
Outcomes	NA

Dual use research of concern

Policy information about dual use research of concern

Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

No	Yes	
☒	☐	Public health
☒	☐	National security
☒	☐	Crops and/or livestock
☒	☐	Ecosystems
☒	☐	Any other significant area

Experiments of concern

Does the work involve any of these experiments of concern:

No	Yes	
☒	☐	Demonstrate how to render a vaccine ineffective
☒	☐	Confer resistance to therapeutically useful antibiotics or antiviral agents
☒	☐	Enhance the virulence of a pathogen or render a nonpathogen virulent
☒	☐	Increase transmissibility of a pathogen
☒	☐	Alter the host range of a pathogen
☒	☐	Enable evasion of diagnostic/detection modalities
☒	☐	Enable the weaponization of a biological agent or toxin
☒	☐	Any other potentially harmful combination of experiments and agents

Plants

Seed stocks	NA
Novel plant genotypes	NA
Authentication	NA

ChIP-seq

Data deposition

☐ Confirm that both raw and final processed data have been deposited in a public database such as GEO.

☐ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links *May remain private before publication.*	NA
Files in database submission	NA
Genome browser session (e.g. UCSC)	NA

Methodology

Replicates	NA
Sequencing depth	NA
Antibodies	NA
Peak calling parameters	NA
Data quality	NA
Software	NA

Flow Cytometry

Plots

Confirm that:

☐ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☐ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

☐ All plots are contour plots with outliers or pseudocolor plots.

☐ A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	NA
Instrument	NA
Software	NA
Cell population abundance	NA
Gating strategy	NA

☐ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.

Magnetic resonance imaging

Experimental design

Design type	NA
Design specifications	NA
Behavioral performance measures	NA

Acquisition

Imaging type(s)	NA
Field strength	NA
Sequence & imaging parameters	NA
Area of acquisition	*State whether a whole brain scan was used OR define the area of acquisition, describing how the region was determined.*

Diffusion MRI ☐ Used ☒ Not used

Preprocessing

Preprocessing software	NA
Normalization	NA
Normalization template	NA
Noise and artifact removal	NA
Volume censoring	NA

Statistical modeling & inference

Model type and settings	NA
Effect(s) tested	NA

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

Statistic type for inference	NA

(See Eklund et al. 2016)

Correction	NA

Models & analysis

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