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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	No software was used for data collection.
Data analysis	We released a software package which allows the central analyses in this paper to be performed quickly and easily, the "spatiotemporal" Python package, which can be installed through pip or downloaded at https://github.com/murraylab/spatiotemporal. Analysis utilized Python 3.6 with the libraries numpy 1.19.5, scipy 1.5.4, bctpy 0.5.0, pingouin 0.3.8, and paranoid-scientist 0.2.2.

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 HCP data are available at: https://www.humanconnectome.org/study/hcp-young-adult. The Human Connectome Project with Global Signal Regression (HCP-

GSR) dataset was derived from the same data as the HCP dataset. The Yale-TRT data are available at: http://fcon_1000.projects.nitrc.org/indi/retro/yale_trt.html. The Cam-CAN data are available at: https://www.cam-can.org/index.php?content=dataset. The LSD data and Psilocybin data are available upon request.

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender	Our sample consisted of both males and females, but effects of sex were not analyzed in our current study.
Population characteristics	The HCP dataset consisted of subjects aged 22-37; the Yale-TRT dataset aged 27-56; the Cam-CAN dataset aged 18-88; the LSD dataset aged 20-34; and the Psilocybin dataset aged 20-40. No other population characteristics were analyzed.
Recruitment	Participants were recruited using diverse strategies to achieve goals which were not relevant to the current study, such as related sibling pairs for the HCP data. Recruitment strategy is unlikely to impact our conclusions.
Ethics oversight	All participants provided written informed consent statements before participation in the study. The HCP data were acquired using protocols approved by the Washington University institutional review board. The Yale-TRT data were collected with approval by the Yale University institutional review board. The Cam-CAN data were collected with approval by the Cambridgeshire 2 Research Ethics Committee. The LSD and Psilocybin data were collected with approval by the Cantonal Ethics Committee of Zurich, and the Swiss Federal Office of Public Health, Bern, Switzerland, authorized the use of LSD and Psilocybin in humans.

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 did not perform sample size calculations, and instead used all data available from the respective datasets.
Data exclusions	HCP: 33 subjects were excluded from the GSR analysis due to non-convergence of the preprocessing pipeline. Cam-CAN: Six subjects and one cerebellar region were excluded due to missing data. Yale TRT: No subjects were excluded. LSD: One subject was excluded due to failed registration. Psilocybin: One subject was excluded due to missing data.
Replication	We replicated our results on five different datasets, as described in the paper.
Randomization	In the LSD and Psilocybin data, the order of experimental sessions (drug and placebo) was randomised. The randomisation was balanced and completed by a study nurse who had no other role in the trial.
Blinding	The LSD and Psilocybin datasets were double-blinded. No other group allocation was performed in this study, so no other blinding was necessary.

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

Methods

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

Magnetic resonance imaging

Experimental design

Design type	Resting state
Design specifications	HCP dataset: four 14.5 minute scans per subject on two different days, TR=720. Yale-TRT dataset: 24 six-minute scans per subject spread across four days, TR=1000. Cam-CAN dataset: one 8.5 minute scan per subject, TR=1970. LSD dataset: Two 10 minute scans for each of the three treatment groups in each subject, TR=2500. Psilocybin dataset: three 10 minute scans for both treatment groups, TR=2430.
Behavioral performance measures	Behavioural performance measures are not applicable to this study.

Acquisition

Imaging type(s)	Functional
Field strength	3T
Sequence & imaging parameters	All scans were acquired using a Gradient-Echo Echo-Planar Imaging (EPI) sequence. Full details are provided in the respective publications. Parameters are: HCP: 72 slices, TR = 720 ms, TE = 33.10 ms, multiband factor = 8, flip angle = 52, voxel size = 2 x 2 x 2 mm, FOV = 208 x 180 x 144 mm; TRT: 75 slices, TR = 1000 ms, TE = 30 ms, flip angle = 55, voxel size = 2 x 2 x 2 mm; Cam-CAN: 32 slices, slice thickness of 3.7 mm with an interslice gap of 20%, TR = 1970 ms, TE = 30 ms, flip angle = 78, FOV = 192 x 192 mm; voxel size = 3 x 3 x 4.44 mm; LSD: 45 slices, TR = 2500 ms, TE = 27 ms, field of view = 240 x 240 mm, voxel size = 3 x 3 x 3 mm; sensitivity-encoding reduction factor = 2.0; Psi: 45 slices, TR = 2430 ms, TE = 27 ms, slice thickness = 3 mm, field of view = 240 x 240 mm; voxel size = 3 x 3 x 3 mm; sensitivity-encoding reduction factor = 2.0.
Area of acquisition	Whole brain

Diffusion MRI ☐ Used ☒ Not used

Preprocessing

Preprocessing software	HCP data, LSD data, and Psilocybin data were preprocessed with the HCP minimal preprocessing pipeline and the Connectome Workbench suite. Yale TRT data were preprocessed with BioImage Suite. Cam-CAN data were processed with Automatic Analysis 4.2.
Normalization	HCP data, LSD data, and Psilocybin data used surface-based analysis. Yale TRT: Data were normalized to MNI template through affine and non-linear transformation. Cam-CAN: Normalization to MNI template through affine transformation.
Normalization template	MNI
Noise and artifact removal	HCP: Motion correction was performed, and data were denoised using ICA-FIX, and high-pass filtered at 0.01 hz. A 2 mm spatial smoothing was applied on the cortical surface constrained to the parcel. The first 100 timepoints were discarded. Yale TRT: Motion correction was performed with SPM5, and data were spatially smoothed with a 2.5 mm gaussian filter. Nuisance regression was performed, including linear, quadratic, and cubic drift, a 24-parameter model of motion, mean cerebrospinal fluid signal, and mean white matter signal. Cam-CAN: We also applied a second-order Butterworth low-pass filter at half the Nyquist frequency (0.127 Hz) to account for high-frequency motion artifacts. LSD and Psilocybin: Nuisance regression was performed, including mean ventricle signal, white matter, and motion parameters. Motion scrubbing was applied to remove the frames with the highest movement. All measurements of temporal autocorrelation accounted for the scrubbing.
Volume censoring	Performed only for LSD and Psilocybin data. Frames were removed which satisfied one of the following criteria: (a) the sum of displacement across all six rigid body movement correction parameters exceeded 0.5 mm (assuming 50 mm cortical

sphere radius); (b) RMS of differences in intensity between current and preceding frame normalized by frame intensity which exceeded 1.6 times the median across scans.

Statistical modeling & inference

Model type and settings: We used the following models, as described in detail in the paper: Spatiotemporal, TA-only, SA-only, Intrinsic timescale with SA, Homogeneous TA, eigensurrogate, phase randomisation, Zalesky matching, edge reshuffle, economical clustering.

Effect(s) tested: We tested the models' ability to reproduce graph metrics.

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

Statistic type for inference (See Eklund et al. 2016): We used spatial and temporal autocorrelation statistics, defined in the paper.

Correction: Where applicable, we used Bonferroni correction for multiple comparisons.

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: FC was computed using Pearson correlation

Graph analysis: Weighted and binarized subject-level graphs were analyzed. Connectivity measures for weighted graphs: mean-FC, var-FC, kurt-FC, nodal mean-FC, nodal var-FC, nodal kurt-FC. Connectivity measures for binarized graphs: assortativity, clustering coefficient, local efficiency, global efficiency, modularity (Newman-Girvan Q), transitivity, nodal degree, nodal betweenness centrality.