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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	All MRI data was collected with a 7-Tesla Magnetom MRI Siemens scanner using Siemens commercial software
Data analysis	A custom, stand-alone code used to compile the results is accompanied with the paper. https://github.com/ulgenklc/Brain_states

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 MRI data generated in this study will be deposited in the NIH-NDA database for participants who agree to data sharing. The MRI data are available under restricted access for research use, access can be obtained via request to the study PI via the NIH-NDA. The raw data are protected and are not available due to data privacy laws. The processed fMRI data will be available upon request.

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	Sex and gender were not considered in the study design. Sex and gender are the same in this study and reported for each dataset (# of females, and # of males). All analyses were controlled for gender.
Reporting on race, ethnicity, or other socially relevant groupings	MDD (N=38) / HC (N=38) Race (Asian, White, Black or African American, More than one race, Unknown): 6,19,6,6,1 / 9,16,10,1,2 Ethnicity (Hispanic or Latino, Not Hispanic or Latino): 13,25 / 6,32
Population characteristics	fMRI dataset: Major Depressive Disorder (MDD)/Healthy Control (HC): 38/38 Age (years) mean ± standard deviation: 28.10 ± 6.68 / 30.76 ± 8.64 Sex (female:male): 21:17 / 20:18 Diffusion dataset: Major Depressive Disorder (MDD)/Healthy Control (HC): 26/27 Age (years) mean ± standard deviation: 28.42 ± 6.59 / 31.04 ± 8.00 Sex (female:male):13:13 / 13:14
Recruitment	All subjects were recruited at the Depression and Anxiety Center for Discovery and Treatment (DAC) at Icahn School of Medicine at Mount Sinai.
Ethics oversight	All data were collected under Icahn School of Medicine at Mount Sinai Institutional Review Board (studies 19-00486 and 16-01046) approved written informed consent and participants were compensated for their time.

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	This study was conducted on resting-state functional MRI (fMRI) and diffusion-weighted imaging (DWI) data collected from the same subjects. After quality control criteria were used for subject exclusion, the final resting-state fMRI dataset consisted of 38 Major Depressive Disorder (MDD) and 38 healthy controls (HC) (n=76). A subset of participants had both resting-state fMRI and DWI usable for the multi-modal structural-functional analysis, 26 MDD and 27 HC (n=53).
Data exclusions	Participants with head rotation higher than 3degree and head translation higher than 3 mm were excluded.
Replication	A replication analysis was performed and detailed in the Supplementary Information. Replication of the dynamic brain states identified in the fMRI analysis was successful. However, the association between brain states and clinical symptoms could not be replicated, likely because the replication dataset was acquired using a different MRI protocol and did not include the same clinical measures as those collected in the present study.
Randomization	Participants were assigned to case and control groups based on MDD diagnosis as described in the participants section. All analyses controlled for covariates including age, gender, and medication status using a multiple linear model approach.
Blinding	No blinding procedure was conducted in this study.

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	resting state
Design specifications	Eyes open, 10 min scan time.
Behavioral performance measures	No task was performed

Acquisition

Imaging type(s)	functional, structural, diffusion
Field strength	7 Tesla
Sequence & imaging parameters	Data were acquired at a single site on a Siemens Magnetom 7-Tesla MRI scanner. Structural T1-weighted anatomical scans were obtained using a dual-inversion magnetization prepared gradient echo (MP2RAGE) sequence with the following parameters: TR=6000ms, TE=5.14, FAs =4,5, FoV= 224 x 224mm, slice orientation = sagittal, angulation to AC-PC line, voxel size = 0.7mm isotropic. Resting state functional scans were collected via echo-planar imaging (EPI), using multi-band multi-echo with the following parameters: TR=2100ms, TEs=14.0, 37.87, 61.74ms, FA = 60, multi-band acceleration factor = 3, FoV= 200 x 200mm, slice orientation = axial, angulation to AC-PC line, phase encoding = AP, in-plane GRAPPA acceleration R=3, number of volumes = 286, Slice thickness = 1.5mm, voxel size = 1.5mm isotropic.
Area of acquisition	Whole brain

Diffusion MRI ☒ Used ☐ Not used

Parameters: Diffusion weighted imaging (DWI) data was acquired using multi-shell (b=1000, b=2000) with a high-angular-resolved single shot spin echo EPI sequence with monopolar diffusion encoding with the following parameters: TR= 4000ms, TE=62 ms, 64 directions, 10 b-values from 0-2000 s/mm2, 1.05mm isotropic resolution, whole, multi-band acceleration factor = 2, in-plane GRAPPA acceleration R=3. Paired acquisitions with reversed phase encoding in the AP/PA direction was acquired at 9 min per scan for ~40 min DWI.

Preprocessing

Preprocessing software	Multi-Echo Independent Components Analysis (ME-ICA) pipeline (https://bitbucket.org/prantikk/me-ica) version 3.20 was used for preprocessing, decomposition and denoising of the functional data.
Normalization	No normalization was used
Normalization template	No normalization was used

Noise and artifact removal	Multi-Echo Independent Components Analysis (ME-ICA) pipeline (https://bitbucket.org/prantikk/me-ica) version 3.20 was used for denoising of the functional data.
Volume censoring	No volume censoring

Statistical modeling & inference

Model type and settings	An unsupervised learning algorithm (k-medoids) with correlation distance and 'alternate' method is used via scikit-learn-extra python implementation. https://pypi.org/project/scikit-learn-extra/. More details are in the methods section of the manuscript.
Effect(s) tested	In general, age, sex and medication use is added as a covariate to the fitted regression lines. Details can be found in the Methods section.

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

Statistic type for inference (See Eklund et al. 2016)	N/A
Correction	FDR correction is applied whenever applicable.

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	Correlation as a distance metric is used to measure similarity (or distance/dissimiliarity) between different spatial fMRI maps from different time points, e.g., when implmenting the k-medoids algorithm and computing within-, between-cluster variance.
Graph analysis	Whole brain weighted structural connectivity matrices are used to compute control energy per each node in the parcellation.