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Reporting Summary

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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	Data were collected by the corresponding author and coauthors of the present manuscript (Drs. Cocuzza, Chopra, and Holmes), which is detailed here: [Chopra S, Cocuzza CV, Lawhead C, et al. The Transdiagnostic Connectome Project: an open dataset for studying brain-behavior relationships in psychiatry. Sci Data. 2025;12(1):923.]. This data is openly available here: https://nda.nih.gov/study.html?id=2932 and here: https://openneuro.org/datasets/ds005237. These releases provide details of collection software, including version information. Functional neuroimaging data was collected using a Siemens Magnetom 3T Prisma MR scanner and 64-channel head coil.
Data analysis	All data analyses were performed using algorithms and software openly available in the following community repository: https://github.com/HolmesLab/ClinicalNetDynamics. This includes a list (within the main README) that details all external packages or software. Human Connectome Project (HCP) pipelines, version 4.7.0, were used for minimal processing, with the following software on a 64-bit Linux operating system (RedHat RHEL version 8.8): FMRIB Software Library (FSL) version 6.0.5; FSL ICA-based xnoiseifier (FIX) version 1.06.15; FreeSurfer version 6.0.0; Connectome Workbench version 1.4.2; MATLAB version 2017b; and R version 4.3.0. All other analyses (see the GitHub repository above) were based in a Python coding environment, version 3.12.1. The primary Python toolkits and their dependencies that were used included: numpy version 1.23.5, scipy version 1.13.1, pandas 2.2.3, matplotlib version 3.9.4, and sklearn version 1.6.1.

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

TCP unprocessed and processed neuroimaging data as well as all behavioral measures are openly available here: https://nda.nih.gov/study.html?id=2932 and here: https://openneuro.org/datasets/ds005237.

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	Gender is now reported in Table 1, which reports the demographics of the dataset used in the present study. Gender was self-reported by participants and included options for male, female, non-binary, other, and prefer not to answer. Gender was not separately analyzed. In our study, we performed data splitting into discovery and validation sets to account for data leakage in supervised models (detailed in the manuscript Methods). With this, further examinations of gender would under-power analyses. However, recruitment efforts focused on comparable proportions of gender in the study sample, as was feasible. Analyses were only performed on participants who consented to open sharing of this data type, which is also in alignment with the NIH data archive (NDA) policies (where these data are shared: https://nda.nih.gov/study.html?id=2932). In the total sample, participants reported gender in the following percentages: approximately 56% female, 43% male, and <1% non-binary.
Reporting on race, ethnicity, or other socially relevant groupings	Race and ethnicity are now reported in Table 1, which reports the demographics of the dataset used in the present study. Both variables were self-reported by participants. Race included the following options: American Indian/Alaskan Native, Asian, Black or African American, More than 1 race, Native Hawaiian/Pacific Islander, Prefer not to answer, and Caucasian. Ethnicity included the following options: Hispanic or Latino, and Not Hispanic or Latino.
Population characteristics	We collected primary psychiatric diagnoses (including a category of "no diagnosis", i.e., healthy controls), using the Structured Clinical Interview for DSM-5 (SCID-5), research version. This is a structured, comprehensive, and widely used interview used by trained mental health researchers to reliably provide DSM-5-conformant diagnoses. This is reported in the Methods, Results, and Supplement of the manuscript, as well as a recent manuscript relevant to the open release of this dataset, here: [Chopra S, Cocuzza CV, Lawhead C, et al. The Transdiagnostic Connectome Project: an open dataset for studying brain-behavior relationships in psychiatry. Sci Data. 2025;12(1):923.].
Recruitment	Participants were recruited between 2019 and 2023 at Yale University in CT, USA and McLean Hospital in MA, USA. All recruitment details are extensively detailed here: [Chopra S, Cocuzza CV, Lawhead C, et al. The Transdiagnostic Connectome Project: an open dataset for studying brain-behavior relationships in psychiatry. Sci Data. 2025;12(1):923.]. In brief, researchers in these teams used IRB-approved community flyers, online advertisements, and patient referrals from participating clinicians to recruit participants from community mental health centers, local psychiatric hospitals, and online research platforms. Potential collection site differences between Yale and McLean are now addressed in the manuscript Methods and Supplement, where we did not find evidence that collection site differences were driving model performances.
Ethics oversight	Informed consent was provided to all participants, following the Institutional Review Boards (IRB) of Yale University and McLean Hospital.

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	The openly available dataset used in this study was the Transdiagnostic Connectome Project (TCP), see here: [Chopra S, Cocuzza CV, Lawhead C, et al. The Transdiagnostic Connectome Project: an open dataset for studying brain-behavior relationships in psychiatry. Sci Data. 2025;12 (1):923.]. The full TCP dataset included N=241 and the present study examined n=219 of these participants. Given that some fMRI data was missing for select participants, the study of n=219 was the optimal number to include as many participants as possible, while only dropping 1 resting-state fMRI run (and keeping 3 other resting-state fMRI runs). This is further detailed in the manuscript Methods and Supplement.
Data exclusions	In addition to the sample size considerations above, select behavioral measures were excluded on the basis of a missingness threshold before

	imputation. This is now detailed in the Methods, and we followed best practices in the literature on imputation of these types of cognitive, behavioral, and clinician-assisted measures. A large number of measures remained after these exclusions: a total of 110 behavioral measures were examined.
Replication	We did not perform traditional replication analyses given sample size constraints. However, we used a strict data splitting scheme to ensure that information was not leaked across training, test, and validation sets of our data. Further, we have now added text to the Discussion that characterizes the unique nature of this dataset (e.g., there are few, if any, other comparable datasets available with a rich set of behavioral and neuroimaging measures, as well as such an extensively transdiagnostic cohort). This portion of the Discussion enthusiastically encourages future data collection efforts, with explicit mention of replication and generalizability.
Randomization	Randomization was relevant to the portion of our study that split data into discovery (train and test) and validation sets. Here, we ensured that discovery and validation sets had comparable percentages of participants from (1) Yale and McLean collection sites, and (2) each SCID-5 psychiatric diagnosis group. Aside from these 2 constraints, participants were randomly assigned to each set. This is detailed in the manuscript Methods and Supplement.
Blinding	Blinding was not relevant to our study because this was not a clinical trial with participants allocated to varying treatment groups. We performed no experimental manipulation based on participant grouping, therefore there were no biases requiring blinding to mitigate.

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

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	This study does not meet the definition of a clinical trial provided by the ICMJE. However, clinically-relevant variables were used, including SCID-V psychiatric diagnoses. All data is available in the NIH data archive, collection #3552.
Study protocol	This study does not meet the definition of a clinical trial provided by the ICMJE. However, the dataset (including processing protocols) is extensively detailed here: [Chopra S, Cocuzza CV, Lawhead C, et al. The Transdiagnostic Connectome Project: an open dataset for studying brain-behavior relationships in psychiatry. Sci Data. 2025;12(1):923.].
Data collection	Data was collected between November 2019 and March 2023 at Yale University Department of Psychology, FAS Brain Imaging Center in New Haven, Connecticut, USA; and McLean Hospital Brain Imaging Center in Belmont, Massachusetts, USA. Following recruitment, there were 3 sessions: (1) clinician-assisted interviews and surveys with trained mental health researchers; in-person, (2) MRI and cognitive assessment batteries; in-person, and (3) cognitive and behavioral assessments and scales; online.
Outcomes	This study does not meet the definition of a clinical trial provided by the ICMJE. However, primary psychiatric diagnoses were established by the Structured Clinical Interview for DSM-5 (SCID-5), research version.

Plants

Seed stocks	The Plants category under Materials & experimental systems was deemed n/a above.
Novel plant genotypes	The Plants category under Materials & experimental systems was deemed n/a above.
Authentication	The Plants category under Materials & experimental systems was deemed n/a above.

Magnetic resonance imaging

Experimental design

Design type	3 resting-state fMRI runs and 3 task-state fMRI runs. Task-state fMRI included 2 block design tasks: the Stroop task and the Emotional Faces task.
Design specifications	Each resting-state fMRI run was 6.5 minutes in duration; each Stroop task fMRI run was 6.8 minutes; and the Emotional Faces task fMRI was 6.6 minutes. The Stroop task consisted of 78 trials per run; congruent and incongruent conditions, displaying stimuli for 0.25 seconds each. There was a variable interstimulus interval of 2.25–8.25 seconds and a pre-run fixation of 2 s. The Emotional Faces task had 109 trials consisting of a cue for 2.88–3 seconds every 5 trials, followed by stimulus presentation for 1.8–2 seconds, and a variable interstimulus interval of 0.96–0.99 seconds. There was a pre-run countdown of 6 seconds. There were face and shape trials evenly represented throughout the run. In both tasks, response times varied and responses were permitted after stimulus presentation (via button box).
Behavioral performance measures	Behavioral quality control was performed previously for this dataset; see here: [Chopra S, Cocuzza CV, Lawhead C, et al. The Transdiagnostic Connectome Project: an open dataset for studying brain-behavior relationships in psychiatry. Sci Data. 2025;12(1):923.].

Acquisition

Imaging type(s)	Functional
Field strength	3T
Sequence & imaging parameters	Functional imaging: spin echo sequence with fieldmaps in both AP and PA directions. EPI imaging. TR=800 ms; TR=37 ms; flip angle=52°; voxel size = 2mm^3; multiband acceleration factor=8.
Area of acquisition	Whole brain.

Diffusion MRI ☐ Used ☒ Not used

Preprocessing

Preprocessing software	The Human Connectome Project (HCP) minimal processing pipelines, version 4.7.0, available here: https://github.com/Washington-University/HCPpipelines (includes versioning of all dependencies).
Normalization	Nonlinear registration via FNIRT to map anatomical data to a standard space (MNI152); as well as MSM-All to map functional data to a dense, surface-based template (FSLR). This creates what HCP calls a “grayordinate” space of vertices (instead of voxels). The whole brain consists of approximately 91K vertices and the cortex 64K vertices.
Normalization template	The "MNINonlinear" template was used, which is also known as the MNI-ICBM152 Nonlinear series 2009c,. and MNI152NLin2009cAsym.
Noise and artifact removal	We used HCP’s ICA-FIX denoising algorithm for all data; this accounts for sources of noise from movement, scanner drift, and physiologically based artifact. FIX classifiers that were trained on HCP data (which we closely matched with respect to scanner protocol) were used during denoising; motion parameters in x/y/z translational and rotational spaces, as well as their derivatives, were used. Data was also demeaned and detrended.
Volume censoring	After minimal processing, we skipped the first 5 frames in each fMRI run.

Statistical modeling & inference

Model type and settings	The main model used was a nu-support vector classification (NuSVC), using all default parameters provided by scikit-learn (Python). The predictors (X) included features of brain network dynamics that were given by applying non-negative matrix factorization to across-cognitive-state functional connectivity estimates. The outcomes (y) were 4 different approaches to characterizing psychiatric symptom structure across individuals in the sample, including: (1) case-control status, (2) primary diagnosis grouping, (3) strict symptom fingerprints, and (4) fuzzy symptom fingerprints. The latter 3 models were multiclass

classifications.

Effect(s) tested

We tested whether each NuSVC model accurately classified symptom structures (the 4 types of outcome measures listed above) against an empirically-based chance level. Empirical chance was given by nonparametric permutation testing where null distributions contained 1000 estimates.

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

Statistic type for inference

(See Eklund et al. 2016)

Our main analyses included a metric for the entire connectome (per fMRI run) quantifying the extent that each participant exhibited across-state network dynamics, or significant shifting in network weights; these were the predictors of the NuSVC model described above.

Correction

We followed Nichols and Holmes (2001) nonparametric permutation testing which builds an empirically based null model (sometimes also called "max-T" testing).

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

Whole-brain (cortex and subcortex) functional connectivity estimated with product-moment correlations.

Graph analysis

FC was based on weighted, undirected graphs for each fMRI run, which were later submitted to non-negative matrix factorization to uncover hidden dynamic state shifts in FC estimates. We included 2 supporting analyses that used traditional graph metrics: network efficiency and system segregation.

Multivariate modeling and predictive analysis

We used non-negative matrix factorization (NMF) to estimate brain network dynamics. Using this approach, across-state FC data were decomposed into a features matrix of subgraph estimates (basis set) and a coefficient matrix that quantify how much each subgraph was expressed per fMRI run and per participant. The subgraphs matrix were used for graph analyses and the coefficients matrix were used for classification models. For all supervised portions of these analyses, or otherwise when parameters needed to be tuned (e.g., empirically based optimization of k, which is the number of subgraphs used in NMF): the discovery dataset was used for training and test, while the validation set was completely held out until downstream analyses were run (i.e., the main reporting in the manuscript).