# 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.

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

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n/a	Confirmed
	$oxed{\boxtimes}$ 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. <i>F</i> , <i>t</i> , <i>r</i> ) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
$\boxtimes$	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
$\boxtimes$	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
	$\boxtimes$ Estimates of effect sizes (e.g. Cohen's $d$ , Pearson's $r$ ), indicating how they were calculated
	Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.
C 0:	ftware and code

### Software and code

Policy information about availability of computer code

ActiCal (Philips Respironics, Mini Mitter Company Inc., Oregon, USA) was used to collect Actigraphy data. Data collection

Data analysis

Variable extraction from cosinor analysis and data visualization were performed using Matlab R2020a (MathWorks, Natick, MA) and Python 3.9.0 (Python Software Foundation, Beaverton, OR). Statistical analyses were performed using R 4.1.0 (RStudio, Boston, MA), SAS 9.4 (SAS Institute, Cary, NC) and STATA/SE 13.0 (StataCorp LLC, College Station, TX).

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 data used in the study can be provided on request from the corresponding author.

### Human research participants

Reporting on sex and gender

The findings apply to both sexes. Sex was considered in study design with oversampling of females who are more likely to experience depression. The sex variable was used as a fixed effect and covariate in statistical analyses. The summary tables include the number of females in non-remitters vs. remitters groups.

Population characteristics

The study mostly included university age population with an average of 31 years.

Recruitment

The participants were recruited as an optional add-on from a randomized clinical trial for imaging.

Ethics oversight

Institutional Review Board of Stony Brook University (IRB #570152)

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 bel	ow 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

Behavioural & social sciences For a reference copy of the document with all sections, see <a href="nature.com/documents/nr-reporting-summary-flat.pdf">nature.com/documents/nr-reporting-summary-flat.pdf</a>

# Life sciences study design

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

Sample size

Describe how sample size was determined, detailing any statistical methods used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a rationale for why these sample sizes are sufficient.

Data exclusions

Describe any data exclusions. If no data were excluded from the analyses, state so OR if data were excluded, describe the exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established.

Replication

Describe the measures taken to verify the reproducibility of the experimental findings. If all attempts at replication were successful, confirm this OR if there are any findings that were not replicated or cannot be reproduced, note this and describe why.

Randomization

Describe how samples/organisms/participants were allocated into experimental groups. If allocation was not random, describe how covariates were controlled OR if this is not relevant to your study, explain why.

Blinding

Describe whether the investigators were blinded to group allocation during data collection and/or analysis. If blinding was not possible, describe why OR explain why blinding was not relevant to your study.

### Behavioural & social sciences study design

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

Study description

Briefly describe the study type including whether data are quantitative, qualitative, or mixed-methods (e.g. qualitative cross-sectional, quantitative experimental, mixed-methods case study).

Research sample

State the research sample (e.g. Harvard university undergraduates, villagers in rural India) and provide relevant demographic information (e.g. age, sex) and indicate whether the sample is representative. Provide a rationale for the study sample chosen. For studies involving existing datasets, please describe the dataset and source.

Sampling strategy

Describe the sampling procedure (e.g. random, snowball, stratified, convenience). Describe the statistical methods that were used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a rationale for why these sample sizes are sufficient. For qualitative data, please indicate whether data saturation was considered, and what criteria were used to decide that no further sampling was needed.

Data collection

Provide details about the data collection procedure, including the instruments or devices used to record the data (e.g. pen and paper, computer, eye tracker, video or audio equipment) whether anyone was present besides the participant(s) and the researcher, and whether the researcher was blind to experimental condition and/or the study hypothesis during data collection.

Timing

Indicate the start and stop dates of data collection. If there is a gap between collection periods, state the dates for each sample

Timing	cohort.
Data exclusions	If no data were excluded from the analyses, state so OR if data were excluded, provide the exact number of exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established.
Non-participation	State how many participants dropped out/declined participation and the reason(s) given OR provide response rate OR state that no participants dropped out/declined participation.
Randomization	If participants were not allocated into experimental groups, state so OR describe how participants were allocated to groups, and if allocation was not random, describe how covariates were controlled.
	volutionary & environmental sciences study design
all studies must disclose or	n these points even when the disclosure is negative.
Study description	Briefly describe the study. For quantitative data include treatment factors and interactions, design structure (e.g. factorial, nested, hierarchical), nature and number of experimental units and replicates.
Research sample	Describe the research sample (e.g. a group of tagged Passer domesticus, all Stenocereus thurberi within Organ Pipe Cactus National Monument), and provide a rationale for the sample choice. When relevant, describe the organism taxa, source, sex, age range and any manipulations. State what population the sample is meant to represent when applicable. For studies involving existing datasets, describe the data and its source.
Sampling strategy	Note the sampling procedure. Describe the statistical methods that were used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a rationale for why these sample sizes are sufficient.
Data collection	Describe the data collection procedure, including who recorded the data and how.
Timing and spatial scale	Indicate the start and stop dates of data collection, noting the frequency and periodicity of sampling and providing a rationale for these choices. If there is a gap between collection periods, state the dates for each sample cohort. Specify the spatial scale from which the data are taken
Data exclusions	If no data were excluded from the analyses, state so OR if data were excluded, describe the exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established.
Reproducibility	Describe the measures taken to verify the reproducibility of experimental findings. For each experiment, note whether any attempts to repeat the experiment failed OR state that all attempts to repeat the experiment were successful.
Randomization	Describe how samples/organisms/participants were allocated into groups. If allocation was not random, describe how covariates were controlled. If this is not relevant to your study, explain why.
Blinding	Describe the extent of blinding used during data acquisition and analysis. If blinding was not possible, describe why OR explain why blinding was not relevant to your study.
Did the study involve field	d work?

### Field work, collection and transport

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Field conditions	Describe the study conditions for field work, providing relevant parameters (e.g. temperature, rainfall).
Location	State the location of the sampling or experiment, providing relevant parameters (e.g. latitude and longitude, elevation, water depth).
Access & import/export	Describe the efforts you have made to access habitats and to collect and import/export your samples in a responsible manner and in compliance with local, national and international laws, noting any permits that were obtained (give the name of the issuing authority, the date of issue, and any identifying information).
	the date of issue, and any identifying informations.
Disturbance	Describe any disturbance caused by the study and how it was minimized.

# 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 & experime	ental s	ystems Methods		
n/a Involved in the study	n/a Involved in the study			
Antibodies		ChIP-seq		
Eukaryotic cell lines		Flow cytometry		
Palaeontology and a	archaeol	ogy MRI-based neuroimaging		
Animals and other of	organism	S		
Clinical data				
Dual use research o	f concer	n		
Antibodies				
Antibodies used	Describe all antibodies used in the study; as applicable, provide supplier name, catalog number, clone name, and lot number.			
Validation		be the validation of each primary antibody for the species and application, noting any validation statements on the acturer's website, relevant citations, antibody profiles in online databases, or data provided in the manuscript.		
Eukaryotic cell lin	es			
Policy information about <u>ce</u>	ell lines	and Sex and Gender in Research		
Cell line source(s)		State the source of each cell line used and the sex of all primary cell lines and cells derived from human participants or vertebrate models.		
Authentication		Describe the authentication procedures for each cell line used OR declare that none of the cell lines used were authenticated.		
Mycoplasma contaminat	ion	Confirm that all cell lines tested negative for mycoplasma contamination OR describe the results of the testing for mycoplasma contamination OR declare that the cell lines were not tested for mycoplasma contamination.		
Commonly misidentified (See ICLAC register)	lines	Name any commonly misidentified cell lines used in the study and provide a rationale for their use.		
Palaeontology an	d Arc	chaeology		
Specimen provenance	Provide provenance information for specimens and describe permits that were obtained for the work (including the name of the issuing authority, the date of issue, and any identifying information). Permits should encompass collection and, where applicable, export.			
Specimen deposition	Indicat	e where the specimens have been deposited to permit free access by other researchers.		
Dating methods	If new dates are provided, describe how they were obtained (e.g. collection, storage, sample pretreatment and measurement), where they were obtained (i.e. lab name), the calibration program and the protocol for quality assurance OR state that no new dates are provided.			
Tick this box to confir	m that	the raw and calibrated dates are available in the paper or in Supplementary Information.		
Ethics oversight	Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.			
Note that full information on t	he appro	oval of the study protocol must also be provided in the manuscript.		
Animals and other	rroc	oarch organisms		
Animals and othe				
Policy information about <u>st</u> <u>Research</u>	udies ir	nvolving animals; ARRIVE guidelines recommended for reporting animal research, and <u>Sex and Gender in</u>		
Laboratory animals	For lab	oratory animals, report species, strain and age OR state that the study did not involve laboratory animals.		
Wild animals	Provide details on animals observed in or captured in the field; report species and age where possible. Describe how animals were caught and transported and what happened to captive animals after the study (if killed, explain why and describe method; if released, say where and when) OR state that the study did not involve wild animals.			
Reporting on sex	Provide	e if findings apply to only one sex; describe whether sex was considered in study design, methods used for assigning sex. e data disaggregated for sex where this information has been collected in the source data as appropriate; provide overall are in this Reporting Summary. Please state if this information has not been collected. Report sex-based analyses where		

performed, justify reasons for lack of sex-based analysis.

Field-collected samples

For laboratory work with field-collected samples, describe all relevant parameters such as housing, maintenance, temperature, photoperiod and end-of-experiment protocol OR state that the study did not involve samples collected from the field.

Ethics oversight

Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.

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

Advancing Personalized Antidepressant Treatment Using PET/MRI, ClinicalTrials.gov: NCT02623205. This actigraphy study was an optional add-on to this clinical trial.

Study protocol

This actigraphy study was an optional add-on to this clinical trial. The Study Protocol can be accessed at:  $https://clinicaltrials.gov/ProvidedDocs/05/NCT02623205/Prot\_SAP\_000.pdf$ 

Data collection

The motor activity data was acquired as an optional component of a randomized, placebo-controlled, double-blind, single-site trial of the SSRI escitalopram with brain imaging. Briefly, 77 participants completed the trial after 8 discontinued, 57 of whom opted for actigraphy. The clinical and demographic variables were measured at Stony Brook University and the Actigraphy data was collected at the participants' living environment between 7/5/2017 and 03/13/2020.

Outcomes

Depression severity was quantified by trained raters using the 17-item Hamilton Depression Rating Scale (HDRS) before initiating treatment, and at the end of the first and eighth week of treatment.

The primary outcomes were:

For ANOVA models:

- 1. Change in depression from pretreatment values after the first week of treatment [ $\Delta$ HDRS1 = In(Week1-HDRS/ Week0-HDRS) = In(Week1-HDRS) In(Week0-HDRS)]
- 2. Change in depression from pretreatment values after the eighth week [ $\Delta$ HDRS8 = In(Week8-HDRS/ Week0-HDRS)] = In(Week8-HDRS) In(Week0-HDRS)]

For multivariate logistic regression:

The binary outcome was remitter (free of depression, vs. non-remitter) designated a priori as at least 50% reduction in depression, which is a score of ≤ 7 on the 17-item Hamilton Depression Rating Scale (HDRS), after eight weeks of treatment.

### Dual use research of concern

Policy information about <u>dual use research of concern</u>

### Hazards

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

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

Experiments of concer			
Does the work involve an	of these experiments of concern:		
No Yes			
Demonstrate how to render a vaccine ineffective			
Confer resistance t	Confer resistance to therapeutically useful antibiotics or antiviral agents		
Enhance the virule	Enhance the virulence of a pathogen or render a nonpathogen virulent		
Increase transmiss	ility of a pathogen		
Alter the host rang	of a pathogen		
Enable evasion of o	Enable evasion of diagnostic/detection modalities		
Enable the weapor	ration of a biological agent or toxin		
Any other potentia	y harmful combination of experiments and agents		
ChIP-seq			
Data deposition			
•	and final processed data have been deposited in a public database such as <u>GEO</u> .		
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 public	For "Initial submission" or "Revised version" documents, provide reviewer access links. provide a link to the deposited data.	For your "Final submission" document,	
Files in database submiss	Provide a list of all files available in the database submission.		
Genome browser session (e.g. <u>UCSC</u> )	Provide a link to an anonymized genome browser session for "Initial submission" and "Fenable peer review. Write "no longer applicable" for "Final submission" documents.	'evised version" documents only, to	
Methodology			
Replicates	Describe the experimental replicates, specifying number, type and replicate agreement.		
Sequencing depth	Describe the sequencing depth for each experiment, providing the total number of reads, uniquely mapped reads, length of reads and whether they were paired- or single-end.		
Antibodies	Describe the antibodies used for the ChIP-seq experiments; as applicable, provide supplier name number.	e, catalog number, clone name, and lot	
Peak calling parameters	Specify the command line program and parameters used for read mapping and peak calling, including the ChIP, control and index files used.		
Data quality	Describe the methods used to ensure data quality in full detail, including how many peaks are a	t FDR 5% and above 5-fold enrichment.	
Software	Describe the software used to collect and analyze the ChIP-seq data. For custom code that has been deposited into a community repository, provide accession details.		
Flow Cytometry			
Plots			
Confirm that:			
	e marker and fluorochrome used (e.g. CD4-FITC).		
		s an analysis of identical markers)	
	rly visible. Include numbers along axes only for bottom left plot of group (a 'group' is	an analysis of lucillical fildikers).	
	ots with outliers or pseudocolor plots.		
A numerical value for	umber of cells or percentage (with statistics) is provided.		
Methodology			
Sample preparation	Describe the sample preparation, detailing the biological source of the cells and any tiss	sue processing steps used.	
Instrument	Identify the instrument used for data collection, specifying make and model number.		

Software	Describe the software used to collect and analyze the flow cytometry data. For custom code that has been deposited into a community repository, provide accession details.		
Cell population abundance	Describe the abundance of the relevant cell populations within post-sort fractions, providing details on the purity of the samples and how it was determined.		
Gating strategy	Describe the gating strategy used for all relevant experiments, specifying the preliminary FSC/SSC gates of the starting cell population, indicating where boundaries between "positive" and "negative" staining cell populations are defined.		
Tick this box to confirm that	at a figure exemplifying the gating strategy is provided in the Supplementary Information.		
Magnetic resonance	imaging		
Experimental design			
Design type	Indicate task or resting state; event-related or block design.		
Design specifications	Specify the number of blocks, trials or experimental units per session and/or subject, and specify the length of each trial or block (if trials are blocked) and interval between trials.		
Behavioral performance meas	State number and/or type of variables recorded (e.g. correct button press, response time) and what statistics were used to establish that the subjects were performing the task as expected (e.g. mean, range, and/or standard deviation across subjects).		
Acquisition			
Imaging type(s)	Specify: functional, structural, diffusion, perfusion.		
Field strength	Specify in Tesla		
Sequence & imaging parameter	Specify the pulse sequence type (gradient echo, spin echo, etc.), imaging type (EPI, spiral, etc.), field of view, matrix size, slice thickness, orientation and TE/TR/flip angle.		
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		
reprocessing			
Preprocessing software	Provide detail on software version and revision number and on specific parameters (model/functions, brain extraction, segmentation, smoothing kernel size, etc.).		
Normalization	If data were normalized/standardized, describe the approach(es): specify linear or non-linear and define image types used for transformation OR indicate that data were not normalized and explain rationale for lack of normalization.		
Normalization template	Describe the template used for normalization/transformation, specifying subject space or group standardized space (e.g. original Talairach, MNI305, ICBM152) OR indicate that the data were not normalized.		
Noise and artifact removal	Describe your procedure(s) for artifact and structured noise removal, specifying motion parameters, tissue signals and physiological signals (heart rate, respiration).		
Volume censoring	Define your software and/or method and criteria for volume censoring, and state the extent of such censoring.		
Statistical modeling & infe	rence		
Model type and settings	Specify type (mass univariate, multivariate, RSA, predictive, etc.) and describe essential details of the model at the first and second levels (e.g. fixed, random or mixed effects; drift or auto-correlation).		
Effect(s) tested	Define precise effect in terms of the task or stimulus conditions instead of psychological concepts and indicate whether ANOVA or factorial designs were used.		
Specify type of analysis:	Whole brain ROI-based Both		
Statistic type for inference (See Eklund et al. 2016)	Specify voxel-wise or cluster-wise and report all relevant parameters for cluster-wise methods.		
Correction	Describe the type of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte Carlo).		

### 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	Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).
Graph analysis	Report the dependent variable and connectivity measure, specifying weighted graph or binarized graph, subject- or group-level, and the global and/or node summaries used (e.g. clustering coefficient, efficiency, etc.).