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Initial submission	Revised version	Final submission

# **Reporting Summary**

Nature Research 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 Research policies, see <u>Authors & Referees</u> and the <u>Editorial Policy Checklist</u>.

Please do not complete any field with "not applicable" or n/a. Refer to the help text for what text to use if an item is not relevant to your study. For final submission: please carefully check your responses for accuracy; you will not be able to make changes later.

## Statistical parameters

When statistical analyses are reported,	, confirm that the following	items are present in the re	elevant location (e.g. f	igure legend,	table legend	d, main
text, or Methods section).						

II/a	(0)	minied
	$ \mathbf{V} $	The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement
	$ \mathbf{V} $	An indication of whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
	V	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.
	$ \mathbf{V} $	A description of all covariates tested
		A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
	V	A full description of the statistics including <u>central tendency</u> (e.g. means) or other basic estimates (e.g. regression coefficient) AND <u>variation</u> (e.g. standard deviation) or associated <u>estimates of uncertainty</u> (e.g. confidence intervals)
	V	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.
X		For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
X		For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
X		Estimates of effect sizes (e.g. Cohen's d, Pearson's r), indicating how they were calculated
	$\bigvee$	Clearly defined error bars State explicitly what error bars represent (e.g. SD, SE, CI)

Our web collection on statistics for biologists may be useful.

## Software and code

Policy information about availability of computer code

Data collection

No software was used for data collection.

Data analysis

GraphPad Prism V 7.04

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/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

## Data

Policy information about availability of data

All manuscripts must include a <u>data availability statement</u>. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on request.

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Please select the b	pest 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
Life scie	nces study design
All studies must di	sclose on these points even when the disclosure is negative.
Sample size	Sample sizes were based on prior experience with in vitro and in vivo experiments
Data exclusions	No data were excluded
Replication	For in vitro studies, experimental replicates and biological replicates were performed. For in vivo studies, all data are reported. Biologic replicates were >3. More than a single investigator performed experiments. Attempts at replication were successful
Randomization	Mice were randomly assigned to treatment group, controlling for age, gender and weight. In vitro treatments were randomly assigned, controlling for experimental variables including well location on plate, timing, etc.
Blinding Investigators analyzing animal data were blinded to treatment.	
Behavio	ural & social sciences study design
All studies must di	sclose on these points even when the disclosure is negative.
Study descriptio	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 strates	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 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.

# Ecological, evolutionary & environmental sciences study design

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

participants dropped out/declined participation.

allocation was not random, describe how covariates were controlled.

Study description

Non-participation

Randomization

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.

State how many participants dropped out/declined participation and the reason(s) given OR provide response rate OR state that no

If participants were not allocated into experimental groups, state so OR describe how participants were allocated to groups, and if

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 work, collec	tion and transport
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 and import/export  Describe the efforts you have made to access habitats and to collect and import/export your samples in a responsion in compliance with local, national and international laws, noting any permits that were obtained (give the name authority, the date of issue, and any identifying information).	
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 & experimental systems	Methods	
n/a Involved in the study	n/a Involved in the study	
Unique biological materials X ChIP-seq		
Antibodies	X Flow cytometry	
☐ ☑ Eukaryotic cell lines ☑ ☑ MRI-based neuroimaging		
X   Palaeontology		
Animals and other organisms		
Human research participants		

## Unique biological materials

Policy information about <u>availability of materials</u>

Obtaining unique materials

The RNA aptamers are unique materials and the sequence is provided in the manuscript and can be obtained commercially.

## **Antibodies**

Antibodies used

Antibodies are commercially available and supplier, catalog number and dilution are available in manuscript text.

Validation	Recombinant proteins were used when available as positive controls. Negative controls for immunostaining consisted of processing in the absence of primary antibodies.		
Eukaryotic cell lines			
Policy information about <u>cell li</u>	<u>nes</u>		
Cell line source(s)	ATCC, CRL-2922, Manassas, VA		
Authentication	Cells were purchased for use in these studies and no authentication after receipt from supplier.		
Mycoplasma contamination	Cell line was tested routinely tested for mycoplasma and confirmed to be negative.  None.		
Commonly misidentified line (See ICLAC register)			
Palaeontology			
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).		
Specimen deposition	Indicate 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 confirm t  Animals and other of	hat the raw and calibrated dates are available in the paper or in Supplementary Information.  Organisms		
Policy information about studi	es involving animals; ARRIVE guidelines recommended for reporting animal research		
Laboratory animals	Mus musculus, BALB/cJ from Jax Labs, males, 8-12 weeks of age.		
Wild animals			
Field-collected samples			
Human research pa	rticipants		
Policy information about studi	es involving human research participants		
Population characteristics	Human participants were used for collection of blood from male and female healthy donors, 20-60 years of age		
Recruitment  Subjects were recruited from healthy donors in university setting.			
ChIP-seq			
Data deposition  Confirm that both raw ar	nd 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 publication.

For "Initial submission" or "Revised version" documents, provide reviewer access links. For your "Final submission" document, provide a link to the deposited data.

Files in database submission

Provide a list of all files available in the database submission.

Genome browser session (e.g. UCSC)

Provide a link to an anonymized genome browser session for "Initial submission" and "Revised version" documents only, to enable peer review. Write "no longer applicable" for "Final submission" documents.

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, catalog number, clone name, and lot number.
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 at 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: 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 Describe the sample preparation, detailing the biological source of the cells and any tissue processing steps used. Sample preparation Instrument Identify the instrument used for data collection, specifying make and model number. Describe the software used to collect and analyze the flow cytometry data. For custom code that has been deposited into a Software 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. Describe the gating strategy used for all relevant experiments, specifying the preliminary FSC/SSC gates of the starting cell Gating strategy population, indicating where boundaries between "positive" and "negative" staining cell populations are defined. Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.

## Magnetic resonance imaging

Behavioral performance measures

## Experimental design

Indicate task or resting state; event-related or block design. Design type

Specify the number of blocks, trials or experimental units per session and/or subject, and specify the length of each trial Design specifications

or block (if trials are blocked) and interval between trials.

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

Specify: functional, structural, diffusion, perfusion. Imaging type(s)

Field strength Specify in Tesla

Sequence & imaging parameters 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.

State whether a whole brain scan was used OR define the area of acquisition, describing how the region was determined. Area of acquisition

Diffusion MRI Used	Not used		
Preprocessing			
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 & inference			
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 <u>Eklund et al. 2016</u> )	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 connective	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.).		
Multivariate modeling and predictive	analysis  Specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.		

