

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 (<i>n</i>) 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 <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
☒	☐ 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>
☒	☐ 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 <i>d</i> , Pearson's <i>r</i>), 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	For imaging data: ZEN black 3.7 Software was used with Zeiss Axio Observer Z1 Microscope systems. For behavioral data: Retention latencies were manually scored.
Data analysis	Analysis Software: Image J 1.48 Software, SPSS version 27, R project version 4.1.1, nf-core/smrnaseq v2.2.4, FastQC v0.11.9,Trim Galore! v0.6.6, Bowtie1 v1.3.0, Bowtie2 v2.3.5, mirtrace v1.0.1, MultiQC v1.9, UNIX V7, edgeR v3.32.1, mirtop v0.4.20, MiRDeep2 v0.1.3. No original code was used for analysis.

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](#)

Data is available at 10.5281/zenodo.15496898

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

N/A

Reporting on race, ethnicity, or other socially relevant groupings

N/A

Population characteristics

N/A

Recruitment

N/A

Ethics oversight

N/A

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](https://www.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

No statistical methods were used to pre-determine sample sizes. The choice of sample sizes is based on standard practices on the field and our lab (Atucha & Roozendaal, 2015; Atucha et al., PNAS, 2017; Roozendaal & Mirone, Psychoneuroendocrinology)

Data exclusions

All exclusion criteria were pre-established. Animals that did not react to the footshock during training were excluded, since the shock might not have been delivered. Animals with brain lesions due to brain infusions or off-target infusions were excluded. Samples with significantly different PCR efficiency were excluded from the averages.

Replication

To minimize batch-to-batch variations, different groups were trained simultaneously e.g. control vs norepinephrine or antagomir. Thus, experiments were repeated at least twice and all replications were successful.

Randomization

Data collection and the assignment of groups for individual animals in all experiments was done in a random or blocked manner to guarantee that groups were equally distributed both in behavioral and molecular experiments. These groups were subject to identical procedures.

Blinding

Data collection and analysis were performed blind to the conditions of the experiments.

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

Antibodies

Antibodies used	Primary antibodies: rabbit anti-CREB (Cell Signaling, Cat#9197S, Clone#48H2); rabbit anti(ser-133)-pCREB (Cell Signalling, Cat#9198L, Clone#87G3). Secondary antibody: donkey anti-Rabbit IgG (H+L), Alexa Fluor 488 (Thermo Fisher, Cat#A21206, RRID#AB_2535792)
Validation	CREB and pCREB have been extensively validated: ChIP assays, Luciferase assays and application (WB, IP, IHC, IF, F, ChIP, C& R), Guzowski & McGaugh, PNAS, 1997. The secondary Antibody Alexa Fluor 488 has been validated with ICC and IF on rat primary cortical neurons and applied (Fornari et al., 2012).

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)	HEK293 cell line (CRL1573, ATCC; https://www.atcc.org/products/crl-1573)
Authentication	Authentication was performed with Short Tandem Repeat (STR) analysis by ATCC (https://www.atcc.org/products/crl-1573)
Mycoplasma contamination	ATCC confirmed negative mycoplasma testing (https://www.atcc.org/products/crl-1573)
Commonly misidentified lines (See ICLAC register)	N/A

Animals and other research organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research, and [Sex and Gender in Research](#)

Laboratory animals	Male adult Sprague-Dawley rats (280-320 g at the time of surgery) from Charles River Breeding Laboratories (Kisslegg, Germany) were kept individually in a temperature-controlled (22 °C vivarium room and maintained on a 12-h:12-h light:dark regimen (7:00-19:00 h light on) with ad libitum access to food and water.
Wild animals	This study does not include wild animals.
Reporting on sex	We restricted our study to male animals because it was built on previous experiments and settings optimized for male rats only (Atucha et al., PNAS, 2017; Atucha & Roozendaal, 2015). Female rats would require different experimental settings due sex-specific differences in stress effects on memory (Bangasser et al., 2016)
Field-collected samples	This study does not involve samples collected from the field.
Ethics oversight	All experimental procedures were in compliance with European Union Directive 2010/63/EU and approved by the Central Authority for Scientific procedures on Animals (CCD), The Hague, The Netherlands and /or Institutional Animal Care and Use Committee of Radboud University, Nijmegen, The Netherlands.

Note that full information on the approval of the study protocol must also be provided in the manuscript.