

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 [Authors & Referees](#) 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

Fiji ImageJ was used to track mouse position in the behavioural experiments. The code used is available upon request. Imaris x64 v 9.0.2 was used for the measurement of the area and cFos positive neurons in the regions analyzed.

Data analysis

Customized code in R (version 3.3.3) program was used to analyze data in the behavioral experiments. Custom R code is available upon request. For the analysis of the behaviour and cFos levels, GraphPad Prism 6 was used to generate graphs and statistics.

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. 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 [data availability statement](#). 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

All data supporting the findings of this study are available upon request.

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 calculate the sample size. Sample size was determined based on our experience and the sample size used in similar studies.
Data exclusions	Animals in which histological examination showed that optrodes and/or viral targeting were in the incorrect location were excluded from analysis after behavioural tests. The exclusion criteria was pre-established.
Replication	All the behavioral experiments were repeated at least once. Each group of 4 mice was first tested and then at least another attempt was performed for each group to confirm the result in a different behavioral session. In particular, the experimental group of mice CS+US, was repeated 5 times (total of 18 mice) to confirm the result. All attempts at replication were successful.
Randomization	The odors presented in the behavioural test were presented in random order, as described in the manuscript. All mice were assigned to different experimental conditions randomly.
Blinding	Investigators were blind to group allocation in experiments involving the analysis of cFos expression.

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
☐	☒ Animals and other organisms
☒	☐ Human research participants
☒	☐ Clinical data

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used	TH, chicken, 1:1000, Aves Labs, Inc. c-Fos, rabbit, 1:500, SC-52; Santa Cruz Biotechnology, Santa Cruz, CA anti-GFP, chicken, 1:2000, Aves Lab 1020 Alexa Fluor 568 goat anti-chicken secondary antibody, 1:500, Invitrogen Alexa 568 or 633 goat anti-rabbit secondary antibody, 1:500, Invitrogen Alexa Fluor 633, anti-chicken secondary antibody, 1:500, Invitrogen
Validation	-TH, chicken (Aves Labs, Inc., CAT# TYH) IHC and ICC in adult brain mice (http://www.aveslab.com/wp-content/uploads/catalog.pdf) -c-Fos, rabbit (SC-52; Santa Cruz Biotechnology), WB, IHC, IF in mice (http://datasheets.scbt.com/sc-52.pdf) PMID: # 29296070, 25970608 and 25975181 -anti-GFP, chicken (CAT# GFP, Aves Lab 1020), WB and IHC in mice cortex (http://www.aveslab.com/wp-content/uploads/catalog.pdf) -Alexa Fluor 568 goat anti-chicken secondary antibody, (CAT# A-11041, Invitrogen), ICC, Flow, IF and IHC (https://www.thermofisher.com/antibody/product/Goat-anti-Chicken-IgY-H-L-Secondary-Antibody-Polyclonal/A-11041), 15 references including PMID: #27579481 and #27779190 -Alexa 568 goat anti-rabbit secondary antibody, (Cat # A-11011, Invitrogen), Flow, ICC and IF HepG2 cells (https://www.thermofisher.com/antibody/product/Goat-anti-Rabbit-IgG-H-L-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A-11011), 147 references including PMID: #28032400 -Alexa 633 goat anti-rabbit secondary antibody, (Cat # A-21071, Invitrogen), Flow, ICC, IF in HepG2 cells (https://www.thermofisher.com/antibody/product/Goat-anti-Rabbit-IgG-H-L-Highly-Cross-Adsorbed-Secondary-Antibody-Polyclonal/)

A-21071), 28 references including PMID: #27897178

-Alexa Flour 633, anti-chicken secondary antibody, (Cat # A-21103, Invitrogen), ICC, IF and IHC (<https://www.thermofisher.com/antibody/product/Goat-anti-Chicken-IgY-H-L-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A-211030>), 4 references including PMID: #23658173

Animals and other organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research

Laboratory animals

Two lines of mice were used in these experiments:

1. WT mice were F1 derived from a cross between C57BL/6NTac and 129S6/SvEvTac mice (Taconic Farms, Germantown, NY).
2. transgenic mice that express a channelrhodopsin2-YFP fusion protein in M72-expressing OSNs (M72-ChR2 mice, Jackson Laboratory). Mice were 8-9 weeks of age at the start of all experiments. Both male and female mice were used in all experiments

Wild animals

This study did not involve wild animals.

Field-collected samples

This study did not involve samples collected from the field.

Ethics oversight

All procedures were approved by Hospital for Sick Children Animal Care and Use Committee and conducted in accordance with Canadian Council on Animal Care (CCAC) and US National Institutes of Health (NIH) guidelines on Care and Use of Laboratory Animals.

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