nature portfolio

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| Last undated by author(s). | Eah 2 2023 |

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 <u>Editorial Policies</u> and the <u>Editorial Policy Checklist</u>.

| Sta | atistics | | | | | | |
|--|---|---|--|--|--|--|--|
| For | all statistical ar | nalyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section. | | | | | |
| n/a | Confirmed | | | | | | |
| | \sum 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 descript | tion of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons | | | | | |
| | A full deso | cription of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient tion (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 Give <i>P</i> values as exact values whenever suitable. | | | | | | |
| X | For Bayes | ian analysis, information on the choice of priors and Markov chain Monte Carlo settings | | | | | |
| X | For hierar | chical 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 | | | | | | |
| | ' | Our web collection on <u>statistics for biologists</u> contains articles on many of the points above. | | | | | |
| So | ftware an | d code | | | | | |
| Poli | cy information | about <u>availability of computer code</u> | | | | | |
| Da | Data collection No custom software were used. We used HEKA PatchMaster 2.7, Striatech OptoDrum and Zeiss ZEN for data collection. | | | | | | |
| Da | Data analysis No custom software were used. We used Igor Pro 7, Microsoft Excel and ImageJ Fiji for data 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

Datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Human research participants

| Poli | cv int | formation a | ıbout stud | ies invo | lving | human | research | partici | pants and | d Sex and | Gend | ler in | Research | ٦. |
|------|--------|-------------|------------|----------|-------|-------|----------|---------|-----------|-----------|------|--------|----------|----|
| | | | | | | | | | | | | | | |

| Reporting | on | SPX | and | gende |
|-----------|----|-----|-----|-------|

Use the terms sex (biological attribute) and gender (shaped by social and cultural circumstances) carefully in order to avoid confusing both terms. Indicate if findings apply to only one sex or gender; describe whether sex and gender were considered in study design whether sex and/or gender was determined based on self-reporting or assigned and methods used. Provide in the source data disaggregated sex and gender data where this information has been collected, and consent has been obtained for sharing of individual-level data; provide overall numbers in this Reporting Summary. Please state if this information has not been collected. Report sex- and gender-based analyses where performed, justify reasons for lack of sex- and gender-based analysis.

Population characteristics

Describe the covariate-relevant population characteristics of the human research participants (e.g. age, genotypic information, past and current diagnosis and treatment categories). If you filled out the behavioural & social sciences study design questions and have nothing to add here, write "See above."

Recruitment

Describe how participants were recruited. Outline any potential self-selection bias or other biases that may be present and how these are likely to impact results.

Ethics oversight

Identify the organization(s) that approved the study protocol.

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. |
|---------------------------|---|----------|---|
| X Life sciences | Behavioural & social sciences | | Ecological, evolutionary & environmental sciences |

For a reference copy of the document with all sections, see <u>nature.com/documents/nr-reporting-summary-flat.pdf</u>

Life sciences study design

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

| Sample size | Sample sizes were mainly estimated form previous experience in experiments using similar experimental techniques. |
|-----------------|--|
| Data exclusions | No data were excluded from the analysis. |
| Replication | All data sets were presented with sample size as well as measure of variance. |
| Randomization | Animals were randomly allocated to treatment groups with no pre-selection criteria. We did not discriminate between male and female animals. |
| Blinding | Experiments were processed without human bias wherever possible (e.g. automated OMR tracking). |

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 | | | |
| Antibodies | ChIP-seq | | | |
| Eukaryotic cell lines | ⊠ Flow cytometry | | | |
| Palaeontology and archaeology | MRI-based neuroimaging | | | |
| Animals and other organisms | | | | |
| Clinical data | | | | |
| Dual use research of concern | | | | |
| | | | | |

Antibodies

Antibodies used anti-tRFP (Evrogen; AB234)

Validation This antibody has been validated previously and labeling of target cell populations in this study were as expected and published.

Eukaryotic cell lines

Policy information about <u>cell lines and Sex and Gender in Research</u>

Cell line source(s)

Authentication

Robust GPCR triggered GIRK currents confirms the description of this cell line.

Mycoplasma contamination

Routine mycoplasma tests of all our cell lines confirmed no mycoplasma infection.

Commonly misidentified lines (See ICLAC register)

N/A

Animals and other research organisms

Policy information about <u>studies involving animals</u>; <u>ARRIVE guidelines</u> recommended for reporting animal research, and <u>Sex and Gender in</u> <u>Research</u>

Laboratory animals

Mice; C3H/HeOuJ (rd1) and C57BL/6J (WT) strains.

Wild animals

N/A

Reporting on sex

The did not discriminate research animals based on sex.

Field-collected samples

N/A

Ethics oversight

Cantonal Veterinary Authority of Bern.

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