

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	Data were collected using Vicon 5, Zen Black (Zeiss), Imaris (9.0.0, 64Bit, Bitplane).
Data analysis	Augur, Libra, and Magellan are available from GitHub (https://github.com/neurorestore/Augur , https://github.com/neurorestore/Libra , https://github.com/neurorestore/Magellan). Other software used for data analysis as follows: Imaris (version 9.0.0), DoubletFinder (version 2.0.3), scDbfFinder (version 1.5.18), scds (version 0.99.4), and Scrublet (version 0.2.2), Seurat (version 4.0.3), clustree (version 0.4.4), Palo (version 1.1), tricycle (version 0.99.32), speckle (version 0.0.3), ImerTest (version 3.1-3), chromVAR (version 1.12.0), ArchR (version 1.0.2), imager (version 0.41.1), RCTD (version 2.0.0), DCGA (version 1.0-2).

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](#)

Source data are provided with this paper. Sequencing data have been deposited to the Gene Expression Omnibus (GSE234774, snRNA-seq and spatial transcriptomics, and GSE230765, multiome).

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	Sample sizes are estimated based on previous physiological studies using similar animal models (Anderson et al., 2016, 2018).
Data exclusions	In mice, expression of viral vectors were confirmed post-mortem. If there was a lack of expression, the animal was excluded from behavioural analysis. Single-cell RNA sequencing libraries that did not meet quality control criteria were excluded.
Replication	All tested conditions were repeated across multiple trials and the results averaged to obtain a single-subject mean performance.
Randomization	Animals were randomly assigned to experimental groups when more than one condition was present. For within-animal comparisons every effort was made to randomize the order of conditions.
Blinding	In some cases blinding is not possible during data collection as the animals either have a SCI or do not. Animals with SCI or SCI+experimental treatment were evaluated in a blinded fashion. All statistical analysis was completed with the investigator blind to the experimental codings.

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 were: rabbit anti-GFAP (1:1000; Dako); mouse anti-GFAP (1:1000; Cell Signalling Technology), rat anti-GFAP (1:1000; ThermoFisher Scientific); rabbit anti-albumin (1:250; abcam); rabbit anti-Chat (1:200; Millipore); guinea pig anti-NeuN (1:300; Millipore); chicken anti-RFP (1:500, Novus Biologicals); rabbit anti-Chx10 (also known as Vsx2) (1:500, Novus Biologicals); rat anti-CD45 (1:100, BD Biosciences); goat anti-Sox9 (1:200, Novus Biologicals); rabbit anti-Id3 (1:500; Cell Signalling Technology); rabbit anti-PKD1L2 (1:1000; Merck Millipore). Fluorescent secondary antibodies were conjugated to Alexa 488 (green), or Alexa 405 (blue), or Alexa 555 (red), or Alexa 647 (far red) (ThermoFisher Scientific, USA). The nuclear stain was 4',6'-diamidino-2-phenylindole dihydrochloride (DAPI; 2ng/mL; Molecular Probes).

Validation

All antibodies were validated by Western blot analysis performed by the commercial source.

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

Adult male or female C57BL/6 mice (15-25 g body weight, 8-15 weeks of age) or transgenic mice were used for all experiments. Aged mice were purchased from JAX at 60 weeks of age (stock no. 000664). Vsx2Cre (MMMRRC 36672, also called Chx10Cre) transgenic mouse strain was bred and maintained on a mixed genetic background (C57BL/6).

Wild animals

No wild animals were used in the study

Reporting on sex

Both male and female mice were used in these experiments.

Field-collected samples

No field-collected samples were used in the study

Ethics oversight

All procedures and surgeries were approved by the Veterinary Office of the Canton of Geneva (Switzerland; authorization GE/145/20).

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