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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 (*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	Zen imaging software (Zeiss) to record calcium transients and for acquiring microscopy images. pClamp11 (Molecular Devices) for electric stimulations of roots and nerves and patch clamp recording. LinLab2 (Scientifica) for temperature-controlled stimulations.
Data analysis	MATLAB (MathWorks) custom code to analyze calcium imaging data. Codes can be found in the following repository: https://github.com/FGabrielli/Negm_et_al-codes. Python custom code for algorithmic inference of neuronal plasticity. Clampfit11 (Molecular Devices) for patch clamp recording analysis Fiji 1.54 for analyzing microscopy images GraphPad Prism 9.0 for statistical analysis and graphs. CorelDRAW X7 for making figures.

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

Raw data not provided in the main text or supplementary materials are available in the data source file or from the corresponding author upon request.

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	*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 if 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.*
Reporting on race, ethnicity, or other socially relevant groupings	*Please specify the socially constructed or socially relevant categorization variable(s) used in your manuscript and explain why they were used. Please note that such variables should not be used as proxies for other socially constructed/relevant variables (for example, race or ethnicity should not be used as a proxy for socioeconomic status).* *Provide clear definitions of the relevant terms used, how they were provided (by the participants/respondents, the researchers, or third parties), and the method(s) used to classify people into the different categories (e.g. self-report, census or administrative data, social media data, etc.)* *Please provide details about how you controlled for confounding variables in your analyses.*
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 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

Life sciences study design

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

Sample size	Sample sizes were determined using Gpower analysis with a significance level of 0.05 and a power of 0.80 based on previous studies using ex vivo spinal cord preparations and 2-photon calcium imaging in similar experimental contexts. The number of samples (animals, slices and neurons analyzed per condition) was chosen to ensure reproducibility across biological replicates, yet allowing reliable statistical comparisons between groups. For each condition (control, disinhibition, and nerve injury), data were collected from at least 5 animals per condition.
Data exclusions	No data were excluded from the analyses unless recordings were technically compromised (e.g., motion artifacts, loss of focus, or incomplete imaging stacks). These exclusion criteria were pre-established before analysis. For all experiments, ROUT test for outliners was performed, and data points identified as statistical outliers were excluded when applicable.
Replication	We successfully replicated several behavioral experiments related to neuropathy models previously reported in the literature, observing results closely consistent with prior findings. All our key findings were independently replicated in at least n = 5 separate experiments from different animals. Pharmacological disinhibition experiments were repeated in separate preparations and yielded consistent results. Nerve injury–induced changes were also confirmed across multiple animals.
Randomization	Animals were randomly assigned to the experimental groups (control, sham, or nerve injury) and data collection and analysis were performed

under identical experimental conditions to control for potential confounds. No covariates (e.g., age, sex, weight) differed systematically between groups.

Blinding

Data collection and analysis was performed blind to experimental groups. During dorsal root stimulation experiments, image acquisition and signal processing, experimenters were unaware of whether the sample belonged to control, sham or nerve-injured conditions. Blinding during the ex vivo preparation experiments was not always possible due to the presence of a visible cuff implant around the sciatic nerve, which was accessible for the experimenter but the use of standardized stimulation protocols described in materials and methods and analysis blinding minimized bias.

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

antibody - supplier - catalog number
Guinea Pig anti-NeuN Merck Millipore -ABN90
Goat anti-Pax2- R&D Systems- AF3364
Mouse anti-NF200- Sigma- N0142
Rabbit anti-CGRP- BMA Biomedicals- T4032
conjugated IB4-488- ThermoFisher Scientific- I21411
Donkey DyLight 405 Anti-Mouse IgG (H+L) -Jackson ImmunoResearch -715-475-150
Donkey Alexa Fluor®488 Anti-Rabbit IgG (H+L) - Jackson ImmunoResearch -711-545-152
Cy™3 Donkey Anti-Mouse IgG (H+L)- Jackson ImmunoResearch -715-165-150
Cy™3 Donkey Anti-Goat IgG (H+L)- Jackson ImmunoResearch- 705-165-147
Cy™5 Donkey Anti-Guinea Pig IgG (H+L)- Jackson ImmunoResearch- 706-175-148
Alexa 647 Donkey Anti-Rabbit IgG (H+L)- Jackson ImmunoResearch -711-605-152

Validation

Antibody Validation and source information
Guinea Pig anti-NeuN (Merck Millipore, ABN90) Validated by the manufacturer for immunofluorescence in mouse tissue. Widely used as a neuronal marker; staining restricted to neuronal nuclei and perikarya, consistent with published literature (e.g., Baptiste Lacoste et al. Neuron, 83(5), 1117-1130 (2014-08-27). Expected labeling pattern confirmed in this study Peirs et al. “Dorsal Horn Circuits for Persistent Mechanical Pain.” Neuron vol. 87,4 (2015): 797-812. doi:10.1016/j.neuron.2015.07.029.
Goat anti-Pax2 (R&D Systems, AF3364) Manufacturer validated for immunohistochemistry and immunofluorescence in Mouse samples. Pax2 expression pattern observed here (inhibitory interneurons in the dorsal horn) matches previous reports Peirs et al. “Dorsal Horn Circuits for Persistent Mechanical Pain.” Neuron vol. 87,4 (2015): 797-812. doi:10.1016/j.neuron.2015.07.029 and Ishibashi, Tadayuki et al. “Selective Involvement of a Subset of Spinal Dorsal Horn Neurons Operated by a Prodynorphin Promoter in Aβ Fiber-Mediated Neuropathic Allodynia-Like Behavioral Responses in Rats.” Frontiers in molecular neuroscience vol. 15 911122. 23 Jun. 2022, doi:10.3389/fnmol.2022.911122.
Mouse anti-NF200 (Sigma, N0142) Validated for immunofluorescence in mouse and rat. NF200 is a marker of large myelinated fibers; expected labeling observed in the dorsal root and superficial dorsal horn, consistent with previous literature (e.g.,Kim, Y S et al. “Expression of vesicular glutamate transporters in transient receptor potential melastatin 8 (TRPM8)-positive dental afferents in the mouse.” Neuroscience vol. 303 (2015): 378-88. doi:10.1016/j.neuroscience.2015.07.013).
Rabbit anti-CGRP (BMA Biomedicals, T4032) Manufacturer validated for immunofluorescence in mouse and rat. CGRP labeling observed in small-diameter sensory fibers, consistent with published data (e.g., Grosu, Andreea Violeta et al. “Dorsal root ganglia CSF1+ neuronal subtypes have different impact on macrophages and microglia after spared nerve injury.” Journal of the peripheral nervous system : JPNS vol. 29,4 (2024): 514-527. doi:10.1111/jns.12674).
Conjugated IB4-488 (ThermoFisher Scientific, I21411) IB4 binding is a standard marker for non-peptidergic C-fibers; conjugate validated by the manufacturer. Expected pattern in lamina II confirmed in this study; Guo, Changxiong et al. “Pain and itch coding mechanisms of polymodal sensory neurons.” Cell reports vol. 42,11 (2023): 113316. doi:10.1016/j.celrep.2023.113316.

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	Wild-type (WT) adult C57BL/6J mice were obtained from Janvier Labs (Saint Berthevin, France). Transgenic lines included VGLUT2Cre (Vglut2-ires-Cre; RRID: IMSR_JAX:016963), R26lsl-tdTomato (Ai14; RRID: IMSR_JAX:007914), and R26lsl-GCaMP6f (Ai95; RRID: IMSR_JAX:028865) obtained from The Jackson Laboratory (Bar Harbor, ME, USA), as well as PKCγCreERT2 mice provided by Dr. David Ginty (Harvard University, Boston, USA) and Dr. Emmanuel Bourinet (Institut de Génomique Fonctionnelle, Montpellier, France). Double-heterozygous VGLUT2Cre/+; R26lsl-GCaMP6f/+ mice were used for calcium imaging experiments, while VGLUT2Cre/+; R26lsl-tdTomato/+ and PKCγCreERT2/+; R26lsl-tdTomato/+ mice were used for anatomical and immunohistochemical analyses. Both male and female mice aged 4–8 weeks were used. No significant sex differences were observed, and data from both sexes were pooled.
Wild animals	The study did not involve wild animals.
Reporting on sex	Both male and female mice aged 4–8 weeks were used. Sex was not considered as a biological variable in this study, and both sexes were pooled in the analysis.
Field-collected samples	The study did not involve samples collected from the field.
Ethics oversight	All animal procedures followed the ethical guidelines of the International Association for the Study of Pain and ethical guidelines of the Directive 2010/63/UE of the European Parliament on the protection of animals used for scientific purpose, and were approved by the local ethical committee C2EA-02 and the ministère de L'Enseignement Supérieur, de la Recherche et de l'Innovation (authorization project 11837-2017101816028463V5).

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

Plants

Seed stocks	*Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.*
Novel plant genotypes	*Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.*
Authentication	*Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.*