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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	No software were used in data collection.
Data analysis	ZEN, ImageJ, Aperio ImageScope were used for basic image processing which included normalization by size, magnification, and optical settings. MATLAB v9.5.0.9 was used for metabolic and myelin data analysis. RadiAnt DICOM Viewer, PMOD v3.8, and Microview software were used for CT and MRI image processing. GraphPad Prism v7 were used for statistical analysis. Clampfit 10.2 and OriginPro8 were utilized for electrophysiology data processing.

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 from the corresponding author 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

Life sciences study design

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

Sample size	During the process of technology development (i.e., surgical approach, vascular isolation, device configuration, perfusate formulation, etc.) and the final study described herein, approximately 300 postmortem pig brains were utilized from USDA-approved food production facilities. Once the technology was optimized and stark differences in tissue integrity were observed in pilot studies, 32 independent brains underwent BEx perfusion, data from which are presented herein. Out of these 32 BEx-perfused brains, the sample size (including the matched sample number of brains subjected to 1h PMI, 10h PMI, and CP conditions) used for each analysis is delineated within either each respective figure legend or in the further information in the Methods. No statistical test was used a priori to determine the sample size. A posteriori power was computed for all group comparisons and resulted in a beta value for all analyses above 0.9.
Data exclusions	Data from the postmortem pig brains that were used for the development and optimization of this technology (i.e., surgical approach, vascular isolation, device configuration, perfusate formulation, etc.) were not included in this manuscript. Furthermore, data from surgical and technical errors leading to confounded perfusion parameters were also excluded.
Replication	All procedures, drugs, chemicals, compounds and technologies applied to the brains were standardized as best as possible for every step and automated, when possible, for reliable replication.
Randomization	All pigs were selected based on a standardized criteria of breed (Yorkshire) and weight (~50-75 kg) and age (6-8 months of age). Experiments were organized (i.e. which experimental condition was going to be performed) several days in advance with the food processing facility to ensure that the personnel reserved animals of the established criteria. At the day of the experiment, animals were randomly selected by the facility personnel, and assigned to each experimental condition.
Blinding	Group allocation was conducted as described above. Data collection was performed by independent investigators. Prior to data analysis, immunohistological and histological images were randomized and analyzed by independent, blinded observers as described in the methods section.

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

The antibodies utilized herein are as follows:
IBA1 (rabbit anti-iba1; 1:1000; Wako; 019-19741; Lot: PTR2404)
GFAP (mouse anti-GFAP; 1:500; Sigma; G3893; Clone: G-A-5; Lot: 096M4849V)
RBFOX3/NeuN (rabbit anti-NeuN; 1:2000; Abcam; ab177487; Lot: GR249899-56)
cleaved Caspase-3 (rabbit anti-actCASP3; 1:200; CST; 9661S; Lot: 45)
MBP (rat anti-MBP; 1:200; BioRad; MCA409S; Clone 12; 160223)
Neurogranin (NRGN) (sheep anti-NRGN; 1:50; R&D systems; AF7947; Lot: CHRO011)
GAD1 (goat anti-GAD1; 1:50; R&D systems; AF2086; Lot: KRD0216081).

Validation	We have extensive experience in validating and utilizing the antibodies described in this study, as previously reported in Sousa, AMM et al., (Science 2017; PMID: 29170230), Onorati, M. et al., (Cell Reports 2016; PMID: 27568284), Olmos-Serrano, JL. et al., (Neuron 2016; PMID: 26924435), Daniele, SG. et al., (Science Signaling 2015; PMID: 25969543). These antibodies listed below are commonly used by members of our laboratory. Additional information on the specificity cross-reactivity can be found on the manufacturer's website, along with links to key publications. For antibodies that do not come with manufacturers' porcine validation: IBA-1 antibody has been validated in a porcine model of traumatic brain injury (PMID: 28081963). For Neurogranin and GAD1 antibodies, the staining pattern is consistent with our previous laboratory findings and is consistent with the staining pattern in the species validated by the manufacturer.

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	No laboratory animals were utilized in this study.
Wild animals	No wild animals were utilized in this study.
Field-collected samples	No field-collected samples were utilized in this study.
Ethics oversight	All of the research was conducted on the post-mortem brains which were procured from a local food production facility as described above. No animal was used strictly for research, but instead animal heads were collected after the animal was sacrificed for food production according to USDA guidelines. For all experimental groups, domestic pigs (S. scrofa domesticus; 6-8 months of age [~50-75 kg]) raised for food production were used. We discussed the experiments detailed within this manuscript with the Institutional Animal Care and Use Committee at Yale University. The Committee concluded that the study was exempt from procedures and protocols pertaining to vertebrate research since the tissues utilized were a product of food production and deemed postmortem.

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