nature portfolio

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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	No software was used.
Data analysis	No software was used for data collection. We performed data analyses using the Cellenics® platform, accessible at the GitHub repository (https://github.com/hms-dbmi-cellenics), GraphPad Prism 9 software (GraphPad Software Inc., San Diego, USA), Imaris software (v.9.5, Bitplane), Image J, Clampex software (version 11.2, Molecular Devices), and Zen Black or Zen Blue software (ZEISS Microscopy Software).

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

Sequence data have been deposited at the NIH GEO database under accession code GSE240815 (https://0-www-ncbi-nlm-nih-gov.brum.beds.ac.uk/geo/query/acc.cgi?acc=GSE240815). The raw mass spectrometry proteomics data have been deposited to the ProteomeXchange Consortium via the PRIDE partner repository with the dataset identifier PXD044572 (http://www.ebi.ac.uk/pride/archive/projects/PXD044572). Source data are provided as a Source Data file.

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	No human data was used.
Reporting on race, ethnicity, or other socially relevant groupings	No human data was used.
Population characteristics	No human data was used.
Recruitment	No human data was used.
Ethics oversight	No human data was used.

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	For IHC, at least n=6 per group were included; for transmission electron microscopy, n=4 per group were included; for compound action potential, n=3 per group were included; for proteomics, at least n=3 per group were included; and for single-cell RNA-seq, n=4 per group were included.
Data exclusions	In the single-cell RNA-seq experiment, sample number 3 had to be excluded from the analysis due to irremediable technical problems during sample preparation.
Replication	The n for each experiment is indicated in the figure caption. Each n represents a biological replicate, with a minimum of three replicates per group used. Number of technical replicates are also reported in the figure caption and ranges from 1-14.
Randomization	Mice were purchased from a vendor and randomly allocated into specific diet, treatment/control groups.
Blinding	The researchers were not blinded, as it was essential to know which diet/stimulation was needed.

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
[ ]	[x] Antibodies
[x]	[ ] Eukaryotic cell lines
[x]	[ ] Palaeontology and archaeology
[ ]	[x] Animals and other organisms
[x]	[ ] Clinical data
[x]	[ ] Dual use research of concern
[x]	[ ] Plants

Methods

n/a	Involved in the study
[x]	[ ] ChIP-seq
[x]	[ ] Flow cytometry
[x]	[ ] MRI-based neuroimaging

Antibodies

Antibodies used

The primary antibodies used were: anti-MOG (1:500, AB32760, Abcam), anti-MBP (1:300, MCA409S, BioRad), anti-APCCC1 (1:50, OP80, Sigma-Aldrich), anti-PDGFRα (1:50, AF1062, R&D Systems), anti-OLIG2 (1:200, MABN50, Sigma-Aldrich), anti-Ki67 (1:500, 14569882, Thermo Fisher), anti-IBA1 (1:500, 234004, SYSY), anti-GFAP (1:500, 130300, Thermo Fisher), anti-GPX4 (1:200, ab25066, Abcam), anti-HMGB1 (1:200, ab18256, Abcam), anti-MAP2 (1:500, 822501, BioLegend), anti-SYN1 (1:500, D12G5, Cell Signaling Technology), anti-SHANK3 (1:500, 162304, Synaptic Systems), anti-EAAT1 (1:50, ab181036, Abcam), anti-ALDH1A1 (1:200, AF5869, R&D Systems), anti-C1Q (1:500, ab182451, Abcam), anti-C3 (1:500, 11862, Abcam), anti-RUNX1 (1:100, sc-365644, Santa Cruz Biotechnology), anti-MOBP (1:50, Thermo Fisher), and anti-PVALB (1:300, ab11427, Abcam), anti-ANKG (1:500, 386005, SySy); anti-NFH (1:1000, ab4680, Abcam), anti-HSP70 (1:100, PA5-77828, Thermo Fisher) and anti-SOX10 (1:100, 703439, Thermo Fisher). For staining of E06, CD16/CD32 Fc blocking antibody (1:500, 553141, BD) and 0.1% fish gelatin blocking agent were added to the blocking solution. Sections were washed with PBS, and stained with Alexa Fluor 488, 594, or 647 conjugated secondary antibodies in PBS, for 2h at RT. The secondary antibodies used were: anti-rabbit IgG Alexa 488 conjugated (1:500, A-21206, Thermo Fisher), anti-rat IgG Alexa 488 conjugated (1:500, A-21208, Thermo Fisher), anti-mouse IgG Alexa 488 conjugated (1:500, A-28175, Thermo Fisher), anti-rabbit IgG Alexa 594 conjugated (1:500, A-11037, Thermo Fisher), anti-mouse IgG Alexa 594 conjugated (1:500, A-11032, Thermo Fisher), anti-guinea pig IgG Alexa 594 conjugated (1:500, A-11076, Thermo Fisher), anti-chicken IgY Alexa 647 conjugated (1:500, A-21449, Thermo Fisher), anti-rat IgG Alexa 647 conjugated (1:500, A-21247, Thermo Fisher) and anti-mouse IgG Alexa 647 conjugated (1:500, A-28181, Thermo Fisher).

Validation

All antibodies were commercial and had been validated by their manufacturers. The optimal concentration was determined in the laboratory and is described in the study.

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

Male C57BL/6J mice (12 weeks old), were obtained from the Jackson Laboratory (https://www.jax.org/) while aged male C57BL/6J mice (25 months old) were sourced from the National Institute of Health (NIH) (https://www.nia.nih.gov/research/dab/aged-rodent-colonies). The mice were housed in groups of four based on a standard cycle of 12-hour light/12-hour dark, with weekly cage maintenance.

Wild animals

None.

Reporting on sex

No sex- and gender-based analyses were performed because we sought to understand if multisensory gamma stimulation could affect myelination while avoiding potential gender-related factors. Future studies will include both sexes.

Field-collected samples

None.

Ethics oversight

All experimental procedures were conducted following the approval of the Committee for Animal Care of the Division of Comparative Medicine at the Massachusetts Institute of Technology and the Institutional Animal Care and Use Committee (protocol nº 0621-033-24).

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

Plants

Seed stocks	Not used.
Novel plant genotypes	Not used.
Authentication	N/A