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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 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	For all measurements, the same MRS protocol was used. A 10 cm single tuned 31P surface coil (Philips Health Care, Best, the Netherlands) earlier used in the phantom experiments was also used in vivo. he code used to analyse the data is publicly available on: 10.5281/zenodo.13834427. A statement referring to this reposit is added to the manuscript.
Data analysis	Spectra were fitted with an in-house developed MATLAB script (MATLAB 2018b, The MathWorks, Inc.)

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 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

The data that support the findings of this study are available from the corresponding author upon reasonable 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	N=5 for Reproducibility, n=8 for in vivo validation with temporal ischemia, n=28 for group comparison
Data exclusions	No data was excluded
Replication	In vivo reproducibility tests of NAD metabolite quantification using DEMz HB editing before and after repositioning showed a coefficient of variation (CV) of 7.5% ± 3.0% for fitted NAD+ amplitudes (1.1 ± 0.1 A.U.) between both acquisitions. The sum of NADH and NAD+ showed a CV of 5.5% ± 2.6% (1.4 ± 0.1 A.U.), NADH a CV of 21.8% ± 7.6% (0.3 ± 0.1 A.U.) and the ratio of NAD+/NADH a CV of 23.3% ± 9.4% (4.8 ± 1.6).
Randomization	the study does not include any intervention, so randomization does not apply
Blinding	the study does not include any intervention, so blinding does not apply to the in vivo data. The analysis of the data was performed in a blinded fashion

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
☐	☒ Human research participants
☐	☒ Clinical data
☒	☐ Dual use research of concern

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Human research participants

Policy information about studies involving human research participants

Population characteristics	PAll participants recruited for this study provided informed consent. Eight healthy lean (BMI: 18-25 kg/m2, age: 18-40 years) male and female participants were included. Exclusion criteria were MRI-contraindications, uncontrolled hypertension, impaired liver function, kidney insufficiency, engagement in exercise for more than 3 h per week, unstable body weight (weight gain or loss more than 5 kg in the previous 3 months), excessive alcohol consumption (males > 4 units/day, females > 3 units/day), use of anti-coagulants, and use of other medication known to interfere with the outcome parameters/patient safety. Coagulation, kidney and liver functions were assessed by blood sample analysis for prothrombin time (PT), partial thromboplastin time (aPTT), international normalized ratio (INR) creatinine, aspartate aminotransferase (ASAT), and alanine aminotransferase (ALAT).
Recruitment	Participants were recruited in the community of Maastricht and its surroundings through advertisements placed on the Maastricht University campus, in newspapers, supermarkets, and at sports clubs.
Ethics oversight	The study was conducted in accordance with the principles of the declaration of Helsinki and approved by the Ethics Committee of the Maastricht University. All participants provided their written informed consent.

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

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	For all in vivo measurements, participants provided informed consent and study protocols were approved by the local medical ethical review committee. Trial monitoring was performed by the Clinical Trial Center Maastricht, The Netherlands. The studies were registered at the Netherlands trial register with identifier NL8888 and at clinical trials.gov with identifier NCT03666013 and NCT04907110.
Study protocol	The trial protocol can be asseced on clinicaltrails.gov and in the submitted paper
Data collection	The in vivo measurements in humans was conducted at the Metabolic Research Unit within the Maastricht University Medical Centre in The Netherlands.
Outcomes	For the in vivo validation of our data, we compared NAD measurements in old active versus inactive volunteers.