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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	All intra-operative data was recorded using the Neuro Omega (Alpha Omega) integrated software in its clinical micro-electrode recording system. Human MRI images were acquired using Prisma System VEC11C (Siemens).
Data analysis	Data analysis of all neural data were performed using custom analysis code written in MATLAB R2020a/b and R2021a/b. Diffusion High definition fiber tracking was performed using DSI-Studio. Electrode reconstructions was performed using DSI-studio and Compumedics Neuroscan's Curry software (v.9). All figures were rendered in Adobe Illustrator CC v26.0 - v26.3.1.

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

The main data supporting the results in this study are available within the paper and its Supplementary Information. All data generated in this study and software will be uploaded in a public repository upon acceptance of the manuscript. Raw data will be available upon reasonable request to the corresponding author.

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	Data comes from the first 3 enrolled subjects in our study: 3 female subjects. We do not expect gender to influence the affect of stimulation
Reporting on race, ethnicity, or other socially relevant groupings	Data comes from the first three enrolled subjects in our study, all of Caucasian decent. Race was collected from hospital electronic medical records and self-reported by the subjects. Race/ethnic identity did not factor into our study or serve as proxies for other variables.
Population characteristics	We enrolled 3 female human subjects (RNS01, RNS02, RNS03, ages 46, 26, 21, respectively). They were all undergoing RNS implantation of the centromedian nucleus of the thalamus for treatment of drug resistent generalized epilepsy.
Recruitment	Subjects signed an informed consent whose content were approved by the IRB of the University of Pittsburgh. Patients were recruited through referral from Dr. Gonzalez-Martinez. As there was only one study group, recruitment was not subject to self-selection bias.
Ethics oversight	All intra-operative procedures were approved by the University of Pittsburgh Institutional Review Board (STUDY21060089).

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	No statistical methods were used to pre-determine sample sizes. All data was analyzed in all subjects independently and no formal statistical comparison between populations was performed. Data comes from the first 3 enrolled subjects in our study and no other subject was excluded from the analysis.
Data exclusions	No data was excluded
Replication	The reproducibility of experimental finding was confirmed across the three human subjects.
Randomization	No randomization was introduced in our experiments. Since no formal statistical comparisons were required in our study and all human subjects. were independently analyzed, no randomization was necessary and the same protocol was performed on all human subjects.
Blinding	The investigators were blinded to experimental condition while processing the data

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

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.

Magnetic resonance imaging

Experimental design

Design type	Anatomical Scan and Diffusion Weighted Imaging
Design specifications	No trial, single session
Behavioral performance measures	Subjects did not perform any behavioral tasks while undergoing MRI.

Acquisition

Imaging type(s)	structural/diffusion
Field strength	Human: 3T
Sequence & imaging parameters	Structural- (MPRAGE) sequence (TR = 2300 ms; TE = 2.9 ms; FoV = 256 × 256 mm2; 192 slices, slice thickness = 1.0 mm, in-plane resolution = 1.0 × 1.0 mm); Diffusion: diffusion spectrum imaging scheme to capture a total of 257 diffusion samples. The maximum b-value used was 4000 s/mm² and the in-plane resolution and slice thickness were 2 mm.
Area of acquisition	Whole brain scan

Diffusion MRI ☒ Used ☐ Not used

Parameters: The diffusion spectrum imaging scheme to capture a total of 257 diffusion samples. The maximum b-value used was 4000 s/mm² and the in-plane resolution and slice thickness were 2 mm.

Preprocessing

Preprocessing software	Diiffusion tensor estimation and tractography were performed using DSI studio (http://dsi-studio.labsolver.org).
Normalization	The diffusion data were reconstructed in the MNI space using q-space diffeomorphic reconstruction.
Normalization template	The diffusion data were reconstructed in the MNI space using q-space diffeomorphic reconstruction.
Noise and artifact removal	Scans provided strong signal to noise ratio and no artifacts were observed.
Volume censoring	Subjects remained sufficiently still, no volume censoring was required.

Statistical modeling & inference

Model type and settings	Does not apply, only DTI analysis was performed
Effect(s) tested	No effects were tested, analysis was performed at the individual subject level

Specify type of analysis: ☒ Whole brain ☐ ROI-based ☐ Both

Statistic type for inference (See Eklund et al. 2016)	No statistical inferences were used, analysis was performed at the individual subject level
Correction	No corrections were used, analysis was performed at the individual subject level

Models & analysis

n/a	Involved in the study
☒	☐ Functional and/or effective connectivity
☒	☐ Graph analysis
☒	☐ Multivariate modeling or predictive analysis