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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	Custom scripts, primarily MATLAB-based, some C++ and Simulink. All are available via GitHub (links under 'Data analysis' below).
Data analysis	Analysis code is available at https://github.com/tne-lab/MSIT-Nature-Biomedical-Engineering. The closed-loop neurostimulation system has been released as open-source code and documented, and the neural decoding and state-space modeling engines have similarly been released for open download (https://github.com/TRANSFORM-DBS/Encoder-Decoder-Paper and https://github.com/Eden-Kramer-Lab/COMPASS).

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

The main data supporting the results in this study are available within the paper and its Supplementary Information. Pre-processed and anonymized neural and behavioural data are available through Zenodo at https://zenodo.org/record/5083120#.YOhvWehKiUk and https://zenodo.org/record/5085197#.YOhtouhKiUk.

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	We performed exhaustive sampling for all available participants during the study period. We carried out post-hoc power calculations to verify we had adequate power for the key reported effects.
Data exclusions	Neural data were excluded from channels or trials contaminated by artefacts. These were determined by pre-established rules described in detail in Methods.
Replication	This experiment is a replication of a prior report of similar effects in a different human-subjects population (but now adds the capability for closed-loop control). We believe this verifies reproducibility.
Randomization	Randomization was not relevant, as we employed a within-subjects design.
Blinding	Blinding was not relevant, as we employed a within-subjects design. The investigators working directly with the participant could not be blinded because the neurostimulation is obvious on the recording traces to anyone with training, and because all researchers needed to know the experimental condition to maintain participant safety in case of emergency.

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

Human research participants

Policy information about studies involving human research participants

Population characteristics	Twenty-one participants (age range: 19–57; mean age: 35; female: 12/21; left-handed: 5/21) with long-standing pharmacoresistant complex partial seizures.
Recruitment	All participants who underwent neurosurgery for epilepsy during the study period were approached. There were no known systematic sources of bias.
Ethics oversight	Informed consent and all other ethical aspects of the study were approved and monitored by the Partners Institutional Review Board.

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