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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	BrainLab iPlan Stereotaxy 3.0, Python 3.5 and 3.7, FSL 6.0, NeuroPace Programmer software v1.8.0.21
Data analysis	The code and data used to produce the results and figures in this paper are available at https://github.com/ScangosLab/closed_loop_mdd

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 data that support the findings in this report are available within the report itself, the source data, and within our publicly available GitHub Repository. Raw neural signals are freely 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	The sample size is N=1 in this case report.
Data exclusions	No data relevant to the case report was excluded.
Replication	All code was reviewed for accuracy by at least 2 people. All analyses were reproduced successfully. Code to reproduce the figures and analyses are available at: https://github.com/ScangosLab/closed_loop_mdd
Randomization	The data is not randomized as it is a n=1 case-report.
Blinding	The patient was blinded during the sham controlled stimulation studies. Investigators were usually but not always blinded. Blinding was broken during some sessions for safety reasons. We have subsequently added a second physician to each session so that blinding can be maintained.

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	The patient was a 36 yo woman with severe treatment resistant depression.
Recruitment	The patient contacted our center about participation in a clinical trial of closed-loop DBS (PRESIDIO trial). The patient's physician had heard about the trial and brought it up to the patient in her clinic appointment. She then contacted us about the possiblity of participating. Patients who choose to participate in this study may have a higher tolerance for risk, have more medical knowledge, or have stronger personality disorder traits. They may be more affluent with greater access to or ability to use the internet, or psychiatrists at academic centers who know more about brain stimulation as a treatment option. Due to the inclusion criteria, participants may have depression characterized by greater mood reactivity. As a result, it is possible that closed-loop therapy may be successful only for certain types of depression.
Ethics oversight	The United States Food and Drug Administration (FDA) and the Institutional Review Board (IRB) at University of California, San Francisco approved this protocol. We also work with a neurologist who specializes in ethics of deep brain stimulation.

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	NCT04004169
Study protocol	Please see https://clinicaltrials.gov/ct2/show/NCT04004169. We can provide the study protocol upon reasonable request.
Data collection	Data were collected and analyzed between October 2019 and Jan 2021. Data were collected at the University of California, San Francisco School of Medicine. Specifically, they were collected in a laboratory setting at Langley Porter Psychiatric Hospital and Clinic and in the Epilepsy Monitoring Unit at Moffitt-Long Hospital. Self-report mood ratings were also collected by the patient at home.
Outcomes	The primary and secondary outcomes were pre-defined in our protocol that was submitted to the U.S. Food and Drug Administration and Institutional Review Board at University of California, San Francisco. The measures were logged in ClinicalTrials.gov (https://clinicaltrials.gov/ct2/show/NCT04004169) prior to enrollment of our first subject. We selected the Montgomery Asberg Depression Rating Scale (MADRS) as our primary outcome measure because it is one of the most widely used measures of depression in clinical trials. We additionally utilized visual analog scales and a 6-question version of the Hamilton Depression Rating Scale because these scales have been used previously to assess depression symptoms on a shorter timescale. The MADRS scale was administered by a physician. The remaining scales were administered using RedCap on an iPad in the laboratory or at home. Scores and time of administration were downloaded from RedCap onto a secure server where neural data was also stored.