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	Open source: Python 3.9 Commercial software: We used hardware manufactured by Blackrock Microsystems (along with the associated firmware and the NeuroPort Central Suite software package (version 7.0.6), the proprietary software suite used to control their hardware) to acquire and pre-process data from the neural implant. Custom code: We used a real-time software package (referred to as rtNSR; described in prior literature that is referenced in the current manuscript) to process neural data in real time
Data analysis	Open source: - torch==1.13.1 - pyaudio=0.2.14 Custom code: We used custom scripts and modules to analyze the neural data and implementing real-time prediction and avatar animation. Relevant code to replicate the main findings of this study will be made available upon publication in a public GitHub repository at the following URL: https://github.com/cheoljun95/streaming.braindecoder

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

Data relevant to this study is accessible under restricted access according to our clinical trial protocol. This enables us to share de-identified information with researchers from other institutions but prohibits us from publicly making it available. Access can be granted upon reasonable request. Requests for data can be sent to Dr. Edward Chang at edward.chang@ucsf.edu. Responses can be expected within 3 weeks. Any data provided must be kept confidential and cannot be shared with others unless approval is obtained from Dr. Edward Chang. The original and updated clinical protocols are attached as supplementary materials to this paper. To protect the participant's anonymity, any information that could identify her will not be part of the shared data, specifically her personalized voice synthesizer (a generic voice model will be provided instead). Source data to recreate the figures in the manuscript will be publicly released upon publication. All ECoG neural data is available in the Harvard Dataverse at the following DOI: https://doi.org/10.7910/DVN/8TQKC8. The EMG dataset is available at the following DOI: https://doi.org/10.5281/ZENODO.4064409. The MEA dataset is available at the following DOI: https://doi.org/10.5061/dryad.x69p8czpq.

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	The single participant in the study is female. Sex and gender effects were not researched in this study.
Reporting on race, ethnicity, or other socially relevant groupings	*Please specify the socially constructed or socially relevant categorization variable(s) used in your manuscript and explain why they were used. Please note that such variables should not be used as proxies for other socially constructed/relevant variables (for example, race or ethnicity should not be used as a proxy for socioeconomic status).* *Provide clear definitions of the relevant terms used, how they were provided (by the participants/respondents, the researchers, or third parties), and the method(s) used to classify people into the different categories (e.g. self-report, census or administrative data, social media data, etc.)* *Please provide details about how you controlled for confounding variables in your analyses.*
Population characteristics	The single participant in the study is a female of age 47 at the start of the study with severe spastic quadriparesis and anarthria caused by brainstem stroke.
Recruitment	Participants with motor impairments secondary to neurological disorders were recruited from stroke, ALS, and Neurology clinics at UCSF. Prior to study enrollment, researchers conduct an informal phone interview to go through study information and schedule an in-person visit. This in-person office visit is then followed by three additional outpatient screening visits. We follow an iterative enrollment process, and allow the participant to learn about the study more during each visit. During the first visit, the participant has the study explained to them in detail, and has the chance to ask any questions. Should the participant wish to continue, the next in-person visit will include a physical exam and further screening to determine eligibility. After this visit, an MRI and CT of the brain is obtained for future surgical planning and eligibility purposes. As part of general presurgical testing, an ECG and chest X-ray are also obtained. The third follow-up visit is included to review this data and address any participant questions before enrollment in the clinical trial. To be eligible for enrollment, participants must fit specific clinical characteristics (see attached clinical protocol for full inclusion and exclusion criteria). As this eligibility criteria is quite specific, we do not expect any significant self-selection bias in this study, due to the fact that participants who enroll will not differ from those who choose not to enroll in any relevant clinical characteristics. After implantation, she was compensated $50 per session up to an annual maximum of $5,000.
Ethics oversight	The Food and Drug Administration approved the investigational use of the neural implant device, and the study's protocol was approved by the Institutional Review Board at the University of California, San Francisco. The study protocol was approved by the National Institute on Deafness and Communication Disorders at the NIH.

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	Sample sizes for tests were determined by the amount of available data with the participant. The amount of data collected with the

Sample size	participant was dependent on our estimation of how much data (e.g. how many trials of the tasks) would be required to reasonably estimate the measurements of interest and perform statistical comparisons.
Data exclusions	For latency and speed analyses, five trials and two trials for the 50-phrase-AAC sentence set and 1024-word-General sentence set, respectively, had a detection time occurring at least 500 ms before the go-cue and were excluded from latency analyses. These trials would have detections which occurred before the model could have received neural samples. For the 50-phrase-AAC sentence set, two trials where no audio was emitted were also excluded. These trials were included for error rate calculations.
Replication	Our decoding strategy successfully generalized to other modalities, participants, and across several types of architectures, which is extremely promising for replication. However, this does not provide definitive evidence of reproducibility. True replication of the results might require real-time deployment in multiple participants.
Randomization	Randomization was not critical to this single-participant-per-modality study.
Blinding	Because the goal of the study was to demonstrate the feasibility of a naturalistic brain-to-speech brain-computer interface controlled by a paralyzed person's silent-speech attempts, blinding was not relevant to this study.

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

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	Clinicaltrials.gov NCT03698149
Study protocol	The single participant in the study is a female of age 47 at the start of the study with severe spastic quadriparesis and anarthria caused by brainstem stroke. The original and updated clinical protocols are attached as supplementary materials to this paper.
Data collection	Data collection occurred in the participant's living room. The clinical trial began in November 2018, however this participant was recruited and enrolled in the study following implantation of the study device during September 2022 at UCSF Medical Center. The currently approved duration of the larger clinical trial is 6 years. This is with the expectation that all 8 patients will be recruited in the first 4-5 years and all other activities including data collection, device development, and analysis will be completed in 6 years. Further information on data collection procedures can be found in the attached clinical-trial protocol.
Outcomes	This clinical trial is a phase I single-center early feasibility study to evaluate the long term potential of ECoG-based neural interfaces to control advanced neuroprotheses for motor and communication restoration. This is a low participant enrollment, exploratory clinical trial, therefore secondary outcomes were not pre-defined. Our primary, pre-definied endpoint is to assess the safety and efficacy of the trial device. This is stated in the protocol as "Feasibility of control of a wearable exoskeleton device and a communication interface." With this primary end-point in mind, and with the exploratory nature of the trial guiding future directions, a variety of analysis and testing methods will be explored with trial participants throughout the trial to assess the efficacy of an ECoG based neural interface for motor and communication restoration.

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.*