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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.

- 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

The EMG recording (sensors placed on the right abductor pollicis bevis) is real-time analyzed using a companion Spike 2 software that uses prewritten software to determine whether muscle activation occurred (>150uV) and changes the output of the TMS capacitor to the next probabilistic intensity based on parametric estimation via sequential testing (PEST) protocol.

Data analysis

All statistics were completed in IBM SPSS 25.

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. The data are not publicly available due to containing information that could compromise research participant privacy. Please e-mail authors to request deidentified data and we will respond to any reasonable requests.
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

Behavioural & social sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description

Quantitative study design exploring the effects of zero gravity on the brain. This was a longitudinal, multi-visit trial investigating cortical excitability in various gravity states.

Research sample

We recruited 10 healthy adults (5 men, mean age = 41.0) in this multi-visit TMS cortical excitability experiment conducted in simulated zero gravity (0G) environment induced by parabolic flight (Zero Gravity Corporation, USA). Inclusion/exclusion criteria were as follows: Age between 25–61 years old, familiarity with TMS equipment, a baseline resting motor threshold lower than 90% of total machine output, no personal or familial history of seizures, no medications that would reduce seizure threshold, no metal implanted in the body above the level of the neck, no motion sickness on Earth. One of the 10 participants had prior zero gravity experience. All others were unexperienced fliers who had limited to expert levels of TMS training and familiarity with the onboard TMS and MEP acquisition equipment. Nine out of 10 participants were right handed; handedness was not anticipated to impact rMT values as we used a within-subjects, repeated-measures design.

Sampling strategy

We enrolled 10 individuals due to the limitation on the number of zero gravity fliers. 10 participants was the maximum number of seats we had on the parabolic flight airplane.

Data collection

All data collection was recorded in real-time on the computers that administered the stimulation paradigm. Back-up data was recorded using pen and paper in case there were technical issues on the flight.

Timing

We collected data on three separate days. The first two days served as baselines confirmation of stable neurophysiological signatures at earth gravity. These baselines were spread one week apart. The third visit was conducted on flight day, with three repeated measures.

Data exclusions

No data was excluded during any of the Earth gravity rMT attempts (100 baseline attempts (5 per subject/visit), 30 pre-flight attempts (3 per subject), and 30 post-flight attempts (3 per subject)). During Zero Gravity, 10 of the 50 rMT attempts were rejected in-flight due to poor quality acquisition determined by the computer operator and secondarily confirmed digitally post-flight by one rater trained in Spike 2 software. Each participant had at least 3, and up to 5, clean zero gravity rMT acquisitions.

Non-participation

N/A

Randomization

Participants were divided into two teams of 5 individuals (Team A and B) and each team was assigned their own closed-loop TMS system. Both systems had identical hardware and software. The two teams were roughly equivalent in age (Team A – mean = 42.8 years, Team B – mean = 39.2) and gender (Team A – 2 female, Team B – 3 female).

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 |

Antibodies

Describe all antibodies used in the study; as applicable, provide supplier name, catalog number, clone name, and lot number.
**Eukaryotic cell lines**

**Policy information about cell lines**

| Cell line source(s) | State the source of each cell line used. |
|---------------------|------------------------------------------|
| **Authentication**  | Describe the authentication procedures for each cell line used OR declare that none of the cell lines used were authenticated. |
| **Mycoplasma contamination** | Confirm that all cell lines tested negative for mycoplasma contamination OR describe the results of the testing for mycoplasma contamination OR declare that the cell lines were not tested for mycoplasma contamination. |
| Commonly misidentified lines (See ICLAC register) | Name any commonly misidentified cell lines used in the study and provide a rationale for their use. |

**Palaeontology and Archaeology**

**Specimen provenance** Provide provenance information for specimens and describe permits that were obtained for the work (including the name of the issuing authority, the date of issue, and any identifying information).

**Specimen deposition** Indicate where the specimens have been deposited to permit free access by other researchers.

**Dating methods** If new dates are provided, describe how they were obtained (e.g. collection, storage, sample pretreatment and measurement), where they were obtained (i.e. lab name), the calibration program and the protocol for quality assurance OR state that no new dates are provided.

**Ethics oversight** Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.

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

**Animals and other organisms**

**Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research**

| Laboratory animals | For laboratory animals, report species, strain, sex and age OR state that the study did not involve laboratory animals. |
| Wild animals | Provide details on animals observed in or captured in the field; report species, sex and age where possible. Describe how animals were caught and transported and what happened to captive animals after the study (if killed, explain why and describe method; if released, say where and when) OR state that the study did not involve wild animals. |
| Field-collected samples | For laboratory work with field-collected samples, describe all relevant parameters such as housing, maintenance, temperature, photoperiod and end-of-experiment protocol OR state that the study did not involve samples collected from the field. |
| Ethics oversight | Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not. |

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

**Human research participants**

**Policy information about studies involving human research participants**

| Population characteristics | See Above |
| Recruitment | Recruited via word of mouth within the Medical University of South Carolina community in Charleston, SC |
| Ethics oversight | MUSC Institutional Review Board for Human Research (IRB) - Pro00084982 |

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 | Provide the trial registration number from ClinicalTrials.gov or an equivalent agency. |
Study protocol
Note where the full trial protocol can be accessed OR if not available, explain why.

Data collection
Describe the settings and locales of data collection, noting the time periods of recruitment and data collection.

Outcomes
Describe how you pre-defined primary and secondary outcome measures and how you assessed these measures.

Dual use research of concern
Policy information about dual use research of concern

Hazards
Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

No □ Yes
☐ Public health
☐ National security
☐ Crops and/or livestock
☐ Ecosystems
☐ Any other significant area

Experiments of concern
Does the work involve any of these experiments of concern:

No □ Yes
☐ Demonstrate how to render a vaccine ineffective
☐ Confer resistance to therapeutically useful antibiotics or antiviral agents
☐ Enhance the virulence of a pathogen or render a nonpathogen virulent
☐ Increase transmissibility of a pathogen
☐ Alter the host range of a pathogen
☐ Enable evasion of diagnostic/detection modalities
☐ Enable the weaponization of a biological agent or toxin
☐ Any other potentially harmful combination of experiments and agents

ChIP-seq
Data deposition
☐ Confirm that both raw and final processed data have been deposited in a public database such as GEO.
☐ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links
May remain private before publication.
For "Initial submission" or "Revised version" documents, provide reviewer access links. For your "Final submission" document, provide a link to the deposited data.

Files in database submission
Provide a list of all files available in the database submission.

Genome browser session
Provide a link to an anonymized genome browser session for "Initial submission" and "Revised version" documents only, to enable peer review. Write "no longer applicable" for "Final submission" documents.

Methodology

Replicates
Describe the experimental replicates, specifying number, type and replicate agreement.

Sequencing depth
Describe the sequencing depth for each experiment, providing the total number of reads, uniquely mapped reads, length of reads and whether they were paired- or single-end.

Antibodies
Describe the antibodies used for the ChIP-seq experiments; as applicable, provide supplier name, catalog number, clone name, and lot number.

Peak calling parameters
Specify the command line program and parameters used for read mapping and peak calling, including the ChIP, control and index files used.
Flow Cytometry

Plots

Confirm that:

- The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).
- The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).
- All plots are contour plots with outliers or pseudocolor plots.
- A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation

Describe the sample preparation, detailing the biological source of the cells and any tissue processing steps used.

Instrument

Identify the instrument used for data collection, specifying make and model number.

Software

Describe the software used to collect and analyze the flow cytometry data. For custom code that has been deposited into a community repository, provide accession details.

Cell population abundance

Describe the abundance of the relevant cell populations within post-sort fractions, providing details on the purity of the samples and how it was determined.

Gating strategy

Describe the gating strategy used for all relevant experiments, specifying the preliminary FSC/SSC gates of the starting cell population, indicating where boundaries between "positive" and "negative" staining cell populations are defined.

☐ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.

Magnetic resonance imaging

Experimental design

Design type

Indicate task or resting state; event-related or block design.

Design specifications

Specify the number of blocks, trials or experimental units per session and/or subject, and specify the length of each trial or block (if trials are blocked) and interval between trials.

Behavioral performance measures

State number and/or type of variables recorded (e.g. correct button press, response time) and what statistics were used to establish that the subjects were performing the task as expected (e.g. mean, range, and/or standard deviation across subjects).

Acquisition

Imaging type(s)

Specify: functional, structural, diffusion, perfusion.

Field strength

Specify in Tesla

Sequence & imaging parameters

Specify the pulse sequence type (gradient echo, spin echo, etc.), imaging type (EPI, spiral, etc.), field of view, matrix size, slice thickness, orientation and TE/TR/flip angle.

Area of acquisition

State whether a whole brain scan was used OR define the area of acquisition, describing how the region was determined.

Diffusion MRI

☐ Used

☐ Not used

Preprocessing

Preprocessing software

Provide detail on software version and revision number and on specific parameters (model/functions, brain extraction, segmentation, smoothing kernel size, etc.).

Normalization

If data were normalized/standardized, describe the approach(es): specify linear or non-linear and define image types used for transformation OR indicate that data were not normalized and explain rationale for lack of normalization.

Normalization template

Describe the template used for normalization/transformation, specifying subject space or group standardized space (e.g.)
### Normalization template

(Original Talairach, MNI305, ICBM152) or indicate that the data were not normalized.

### Noise and artifact removal

Describe your procedure(s) for artifact and structured noise removal, specifying motion parameters, tissue signals and physiological signals (heart rate, respiration).

### Volume censoring

Define your software and/or method and criteria for volume censoring, and state the extent of such censoring.

### Statistical modeling & inference

#### Model type and settings

Specify type (mass univariate, multivariate, RSA, predictive, etc.) and describe essential details of the model at the first and second levels (e.g. fixed, random or mixed effects; drift or auto-correlation).

#### Effect(s) tested

Define precise effect in terms of the task or stimulus conditions instead of psychological concepts and indicate whether ANOVA or factorial designs were used.

#### Specify type of analysis:

- [ ] Whole brain
- [ ] ROI-based
- [ ] Both

#### Statistic type for inference

Specify voxel-wise or cluster-wise and report all relevant parameters for cluster-wise methods.

(See Eklund et al. 2016)

#### Correction

Describe the type of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte Carlo).

### Models & analysis

**n/a** Involved in the study

- [ ] Functional and/or effective connectivity
- [ ] Graph analysis
- [ ] Multivariate modeling or predictive analysis

#### Functional and/or effective connectivity

Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).

#### Graph analysis

Report the dependent variable and connectivity measure, specifying weighted graph or binarized graph, subject- or group-level, and the global and/or node summaries used (e.g. clustering coefficient, efficiency, etc.).

#### Multivariate modeling and predictive analysis

Specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.