nature research

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Last updated by author(s): Feb 18, 2021

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.

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	Ethovision ® 11 software was used for mouse mobility studies for back mounted devices. ANY-maze video tracking system (Stoelting Co.) was used for mouse mobility studies for head mounted devices. ABAQUS (ABAQUS Analysis User's 554 Manual 2016) was used for mechanical simulation. Ansys HFSS (Ansys HFSS 13 User's 566 14 guide) was used for electromagnetic modeling. COMSOL 5.2a (Equation Based Modeling User's guide) was used for optical and thermal modeling. OceanView 2.0.7 was used to collect optical light intensity. Mediso Nucline v2.01 was used to collect MicroCT imaging data. Raspberry Pi Camera v2 (Raspberry Pi Foundation) was used for video acquisition in behavioral experiments.
Data analysis	Group statistical analyses were done using GraphPad Prism 7 software (GraphPad, LaJolla, CA). All image data were analyzed by using FIJI (ImageJ 1.52p) (Schindelin et al., 2012). Social and place preference behavior was analyzed by Toxtrac (Version 2.90) (Rodriguez, A., et al., 2018). Multi-subject social interaction and preference behaviors were analyzed by BORIS (v. 7.9.8) (Friard, O., et al., 2016) Mouse mobility data for back mounted devices were analyzed with Ethovision software (Noldus Information Technology; Leesburg, VA). Mouse mobility data for head mounted devices were analyzed with ANY-maze video tracking system (Stoelting Co.). Data on mouse body deformation were analyzed in Matlab (R2018b). Estimation of mouse back mobility was done with Deeplabcut (2.1) (Mathis et al, 2018). Plots were generated in OriginPro2019. MicroCT imaging data were analyzed with Amira v2020.2. All computer code generated during and/or used in the current study is available on https://github.com/A-VazquezGuardado/Real-time_control_Optogenetics.

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

Raw data generated during the current study are available from the corresponding author on reasonable request. The data analyzed in the current study are available on https://github.com/A-VazquezGuardado/Real-time_control_Optogenetics

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	Required sample sizes were estimated based on previous report of published results and our past experience performing similar experiments. No statistical methods were used to pre-determine sample sizes but our sample sizes are similar to those reported in previous publications (Shin et al, 2017; Kingsbury et al, 2019; Wu et al, 2021)
Data exclusions	Data from failed devices were excluded from the analysis.
Replication	The number of replicates for each experiment were reported in the paper and the method section. All experiments were repeated at least twice. All attempts at replication were successful.
Randomization	Animals were randomly assigned to treatment groups. All samples were randomly assigned to experimental groups.
Blinding	Whenever possible, data were analyzed blind to condition. For social interaction analysis during synchronized/desynchronized stimulation, investigators were not blinded to the stimulation patterns since the indicator LEDs displayed the information. All other experiments were analyzed blind to conditions. The investigators were blinded to group assignment during data collection

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

Antibodies used	Primary antibody rabbit anti-c-Fos (1:10000; Synaptic Systems, Goettingen, Germany) was used in this study. For evaluation of biocompatibility, rabbit anti-GFAP (1:1000, ab7260, abcam, Cambridge, United Kingdom), rabbit anti-IBA1 (1:1000, ab178846, abcam), and rabbit anti-Hemoglobin subunit alpha (1:500, ab92492, abcam) were used. Alexa Fluor 647-conjugated secondary antibodies against rabbit (Life Technologies, Carlsbad, CA) were diluted at 1:500.
Validation	All antibodies are commercially available and validated in multiple studies. Complete information is available in the data sheets on the manufacturer's website. Rabbit anti-c-Fos was tested with HELA cells +/- tetradecanoylphobol-13-acetate. Control peptide is available on the vendor website (Cat. No. 226003, synaptic systems). According to the manufacturer's website, rabbit anti-GFAP

specifically recognizes mammalian GFAP on western blots and immunocytochemically. It detects a band of 55kDa corresponding to GFAP and also a GFAP derived 48kDa band. Rabbit anti-IBA1 is a rabbit monoclonal antibody generated with synthetic peptide within Mouse Iba1 aa 100 to the C-terminus. Anti-Hemoglobin subunit alpha antibody is monoclonal, generated with synthetic peptide corresponding to Human Hemoglobin subunit alpha aa 50-150. Rabbit anti-c-Fos is specific for c-fos and has been internally validated in the lab across several studies.

Animals and other organisms

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

Laboratory animals	C57/B6 and B6.SJL-Slc6a3tm1.1(cre)Bkmn/J adult male and female mice (postnatal days 21-100) were used in this study. Only male mice were used for multi-subject social interaction experiments. Approximately equal numbers of males and females were used for other experiments. All mice were group-housed before surgery and singly housed after surgery, with standard feeding, light-dark cycle, and enrichment procedures; littermates were randomly assigned to conditions. C57/B6 mice and male Sprague-Dawley rats (250 - 300g; postnatal days 60 - 70) were used in MicroCT imaging experiments.
Wild animals	No wild animals were used in the study.
Field-collected samples	No field collected samples were used in the study.
Ethics oversight	Animals were handled according to protocols approved by the Animal Care and Use Committees in Northwestern University, US Army Research Laboratory and Washington University.

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

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