

Double-blind peer review submissions: write DRPR and von manuscript number here : Linda B. Buck

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Last updated by author(s): YYYY-MM-DD

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.

Please do not complete any field with "not applicable" or n/a. Refer to the help text for what text to use if an item is not relevant to your study. For final submission: please carefully check your responses for accuracy; you will not be able to make changes later.

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.				
n/a	Cor	nfirmed		
\checkmark		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		
	V	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)		
<u> </u>		For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>		
/		For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings		

Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.

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

Software and code

Policy information about availability of computer code

Data collection

Statistics

Not applicable/no code provided. source and custom code used to collect the data in this study, specifying the version used OR state that no software was used.

Data analysis

STATA 8 was used to do the Mantel-Haenszel tests; described in the text asy pair, wise comparisons OR state that no software was used.

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 <u>data availability statement</u>. 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

Could not find supporting raw data, found summary of most data in supplementary material. https://www-nature-com.ezproxy.bucknell.edu/articles/nature05991#online-methods (contains link to supplementary materials)

Field-specific reporting

Please select the one belo	w 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

Life sciences study design

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

Sample size

Sample size is discussed somewhat in the beginning of the paper relating to initial work (egrhow many chemicals were tested and how many showed significant results. However sample size for antidepressant experiements can only be found in online supplementa material

Data exclusions

I'm not clear on the data exclusion policy for individuals that died immediately. There is a quote in online methods that makes me think that they were thrown out whether exclusion criteria were pre-established

Replication

This experiment provides enough information to replicate it but some of the details are unclear (eg why unequal drug+ and druggroups and different number of experiments for differnet scenarios ced, note this and describe why.

Randomization

Not clear about what role lineage of Quelegans played: Also unclear if pseudoreplication happened within a well plate or well (several individuals in oone well and each plate recieved a particual treatmens.

Blinding

No data or information was presented on this group allocation during data collection and/or analysis. If blinding was not possible, describe why OR explain why blinding was not relevant to your study.

Behavioural & social sciences study design

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

Study description

Briefly describe the study type including whether data are quantitative, qualitative, or mixed-methods (e.g. qualitative cross-sectional, quantitative experimental, mixed-methods case study).

Research sample

State the research sample (e.g. Harvard university undergraduates, villagers in rural India) and provide relevant demographic information (e.g. age, sex) and indicate whether the sample is representative. Provide a rationale for the study sample chosen. For studies involving existing datasets, please describe the dataset and source.

Sampling strategy

Describe the sampling procedure (e.g. random, snowball, stratified, convenience). Describe the statistical methods that were used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a rationale for why these sample sizes are sufficient. For qualitative data, please indicate whether data saturation was considered, and what criteria were used to decide that no further sampling was needed.

Data collection

Provide details about the data collection procedure, including the instruments or devices used to record the data (e.g. pen and paper, computer, eye tracker, video or audio equipment) whether anyone was present besides the participant(s) and the researcher, and whether the researcher was blind to experimental condition and/or the study hypothesis during data collection.

Timing

Indicate the start and stop dates of data collection. If there is a gap between collection periods, state the dates for each sample cohort.

Data exclusions

If no data were excluded from the analyses, state so OR if data were excluded, provide the exact number of exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established.

Non-participation

State how many participants dropped out/declined participation and the reason(s) given OR provide response rate OR state that no participants dropped out/declined participation.

Randomization

If participants were not allocated into experimental groups, state so OR describe how participants were allocated to groups, and if allocation was not random, describe how covariates were controlled.

Ecological, evolutionary & environmental sciences study design

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

Study description

Briefly describe the study. For quantitative data include treatment factors and interactions, design structure (e.g. factorial, nested, hierarchical), nature and number of experimental units and replicates.

Research sample

Describe the research sample (e.g. a group of tagged Passer domesticus, all Stenocereus thurberi within Organ Pipe Cactus National Monument), and provide a rationale for the sample choice. When relevant, describe the organism taxa, source, sex, age range and any manipulations. State what population the sample is meant to represent when applicable. For studies involving existing datasets, describe the data and its source.

Sampling strategy

Note the sampling procedure. Describe the statistical methods that were used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a rationale for why these sample sizes are sufficient.

Data collection	Describe the data collection procedure, including who recorded the data and how.				
Timing and spatial scale	Indicate the start and stop dates of data collection, noting the frequency and periodicity of sampling and providing a rationale for these choices. If there is a gap between collection periods, state the dates for each sample cohort. Specify the spatial scale from which the data are taken				
Data exclusions	If no data were excluded from the analyses, state so OR if data were excluded, describe the exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established.				
Reproducibility	Describe the measures taken to verify the reproducibility of experimental findings. For each experiment, note whether any attempts to repeat the experiment failed OR state that all attempts to repeat the experiment were successful.				
Randomization Describe how samples/organisms/participants were allocated into groups. If allocation was not random, describe how covarious controlled. If this is not relevant to your study, explain why.					
Blinding Describe the extent of blinding used during data acquisition and analysis. If blinding was not possible, describe why OR explain we blinding was not relevant to your study.					
Did the study involve field	work? Yes No				
Field work, collect	tion and transport				
Field conditions	Describe the study conditions for field work, providing relevant parameters (e.g. temperature, rainfall).				
Location	State the location of the sampling or experiment, providing relevant parameters (e.g. latitude and longitude, elevation, water depth).				
Access and import/export	Describe the efforts you have made to access habitats and to collect and import/export your samples in a responsible manner and in compliance with local, national and international laws, noting any permits that were obtained (give the name of the issuing authority, the date of issue, and any identifying information).				
Disturbance	Describe any disturbance caused by the study and how it was minimized.				
Reporting fo	r specific materials, systems and methods				
	uthors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, vant 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 & experime	ntal systems Methods				
n/a Involved in the study	n/a Involved in the study				
Antibodies	ChIP-seq				
Eukaryotic cell lines	Flow cytometry				
✓ Palaeontology	MRI-based neuroimaging				
Animals and other o	rganisms				
Human research par	ticipants				
Clinical data					
Antibodies					
Antibodies used	Describe all antibodies used in the study; as applicable, provide supplier name, catalog number, clone name, and lot number.				
Validation	Describe the validation of each primary antibody for the species and application, noting any validation statements on the manufacturer's website, relevant citations, antibody profiles in online databases, or data provided in the manuscript.				
Eukaryotic cell lines					
Policy information about <u>cell lines</u>					
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 contaminati	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.				

Palaeontology

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.

Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.

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

Describe the covariate-relevant population characteristics of the human research participants (e.g. age, gender, genotypic information, past and current diagnosis and treatment categories). If you filled out the behavioural & social sciences study design questions and have nothing to add here, write "See above."

Recruitment

Describe how participants were recruited. Outline any potential self-selection bias or other biases that may be present and how these are likely to impact results.

Ethics oversight

Identify the organization(s) that approved the study protocol.

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.

ChIP-seq

Data deposition

	Confirm that both	raw and fina	I processed data	have been	deposited in a	public database	such as GEO.
_			•			'	

Confirm that you	have deposited of	or provided	access to graph files	(e.g. BED fil	es) for the ca	lled peaks.

Data access links					
Data access links May remain private before publication	For "Initial submission" or "Revised version" documents, provide reviewer access links. For your "Final submission" documents, 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 (e.g. <u>UCSC</u>)	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.				
1ethodology					
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.				
Data quality	Describe the methods used to ensure data quality in full detail, including how many peaks are at FDR 5% and above 5-fold enrichment.				
Software	Describe the software used to collect and analyze the ChIP-seq data. For custom code that has been deposited into a community repository, provide accession details.				
low Cytometry					
lots					
Confirm that:					
The axis labels state the	marker and fluorochrome used (e.g. CD4-FITC).				
	visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers)				
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All plots are contour plot A numerical value for nu lethodology Sample preparation Instrument Software	visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers) is with outliers or pseudocolor plots. The provided of cells or percentage (with statistics) is provided. Describe the sample preparation, detailing the biological source of the cells and any tissue processing steps used. Identify the instrument used for data collection, specifying make and model number. 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.				
All plots are contour plot	visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers) is with outliers or pseudocolor plots. mber of cells or percentage (with statistics) is provided. Describe the sample preparation, detailing the biological source of the cells and any tissue processing steps used. Identify the instrument used for data collection, specifying make and model number. 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. Describe the abundance of the relevant cell populations within post-sort fractions, providing details on the purity of the samples				

Magnetic resonance imaging

Experimental design

Design specifications

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

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 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.				
Sequence & imaging parameters					
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				
Parameters Specify # of	directions, b-values, whether single shell or multi-shell, and if cardiac gating was 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. 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	e				
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	e brain ROI-based Both				
Anatomi	cal location(s) Describe how anatomical locations were determined (e.g. specify whether automated labeling algorithms or probabilistic atlases were used).				
Statistic type for inference (See <u>Eklund et al. 2016</u>)	Specify voxel-wise or cluster-wise and report all relevant parameters for cluster-wise methods.				
Correction	scribe the type of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte				
Models & analysis					
n/a Involved in the study Functional and/or effective connectivity Graph analysis Multivariate modeling or predictive analysis					
Functional and/or effective connect	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.).				



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

metrics.

Multivariate modeling and predictive analysis