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Corresponding author(s): Scott Russo

☐ Initial submission ☐ Revised version ☒ Final submission

Life Sciences Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form is intended for publication with all accepted life science papers and provides structure for consistency and transparency in reporting. Every life science submission will use this form; some list items might not apply to an individual manuscript, but all fields must be completed for clarity.

For further information on the points included in this form, see Reporting Life Sciences Research. For further information on Nature Research policies, including our data availability policy, see Authors & Referees and the Editorial Policy Checklist.

Experimental design

1. Sample size

   Describe how sample size was determined. — Methods - Statistical Analysis section, page 38-39

2. Data exclusions

   Describe any data exclusions. — Methods - Statistical Analysis section, page 38-39

3. Replication

   Describe whether the experimental findings were reliably reproduced. — Methods - Statistical Analysis section, page 38-39

4. Randomization

   Describe how samples/organisms/participants were allocated into experimental groups. — Methods - Statistical Analysis section, page 38-39

5. Blinding

   Describe whether the investigators were blinded to group allocation during data collection and/or analysis. — Methods - Statistical Analysis section, page 38-39

   Note: all studies involving animals and/or human research participants must disclose whether blinding and randomization were used.

6. Statistical parameters

   For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or in the Methods section if additional space is needed).

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.)
☐	☒ A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ A statement indicating how many times each experiment was replicated
☐	☒ The statistical test(s) used and whether they are one- or two-sided (note: only common tests should be described solely by name; more complex techniques should be described in the Methods section)
☐	☒ A description of any assumptions or corrections, such as an adjustment for multiple comparisons
☐	☒ The test results (e.g. *P* values) given as exact values whenever possible and with confidence intervals noted
☐	☒ A clear description of statistics including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range)
☐	☒ Clearly defined error bars

See the web collection on statistics for biologists for further resources and guidance.

Software

Policy information about availability of computer code

7. Software

Describe the software used to analyze the data in this study.	Methods - Statistical Analysis section, page 38-39

For manuscripts utilizing custom algorithms or software that are central to the paper but not yet described in the published literature, software must be made available to editors and reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). *Nature Methods* guidance for providing algorithms and software for publication provides further information on this topic.

Materials and reagents

Policy information about availability of materials

8. Materials availability

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a for-profit company.	N/A

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).	Citations are included on page 27 and 28

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.	N/A
b. Describe the method of cell line authentication used.	N/A
c. Report whether the cell lines were tested for mycoplasma contamination.	N/A
d. If any of the cell lines used are listed in the database of commonly misidentified cell lines maintained by ICLAC, provide a scientific rationale for their use.	N/A

Animals and human research participants

Policy information about studies involving animals; when reporting animal research, follow the ARRIVE guidelines

11. Description of research animals

Provide details on animals and/or animal-derived materials used in the study.	Methods - mice section, page 22

Policy information about studies involving human research participants

12. Description of human research participants

Describe the covariate-relevant population characteristics of the human research participants.	Methods - Human postmortem tissue collection, page 32

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Flow Cytometry Reporting Summary

Form fields will expand as needed. Please do not leave fields blank.

Data presentation

For all flow cytometry data, confirm that:

☒ 1. The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☒ 2. 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).

☒ 3. All plots are contour plots with outliers or pseudocolor plots.

☒ 4. A numerical value for number of cells or percentage (with statistics) is provided.

Methodological details

5. Describe the sample preparation.	Blood was collected by submandibular vein bleed into EDTA-lined tubes (Sarstedt) 100 uL blood was transferred into FACS buffer (PBS w/o Ca2+ Mg2+ supplemented with 2% heat inactivated FBS and 5mM EDTA), and red blood cells (RBC) were lysed in 1× RBC Lysis solution (eBioscience). For brain leukocyte isolation, mice were deeply anesthetized with a lethal dose of choral hydrate and transcardially perfused with PBS. Brain was removed and one forebrain hemisphere (without olfactory bulb) was minced, incubated in phenol-red free DMEM supplemented with 2% heat inactivated FBS, 10mM HEPES and Collagenase type IV (0.4 mg/mL) for 15 min and then passed through a 19G blunt syringe to obtain a homogeneous cell suspension. Mononuclear cells were separated with a 40% Percoll gradient. Isolated cells were surface stained in FACS buffer for 20-30 min on ice with the following antibodies: CD11b (clone M1/70, eBioscience), F4/80 (clone CI: A3-1, BioRad), CD45 (clone 30F11, eBioscience), MHC II (clone M5/114.15.2, eBioscience), CD3e (clone 145-2C11, Biolegend), Gr-1 (clone RB6-8C5, Biolegend), CD115 (clone AFS98, eBioscience).
6. Identify the instrument used for data collection.	BD LSR II Fortessa
7. Describe the software used to collect and analyze the flow cytometry data.	Data were collected using BD FACSDiva software and analyzed with FlowJo software (Tree Star).
8. Describe the abundance of the relevant cell populations within post-sort fractions.	N/A
9. Describe the gating strategy used.	ccr2RFP+ monocytes were gated as single, live, CD11b+ F4/80+ ccr2RFP+ cx3cr1GFP-. cx3cr1GFP+ microglia were gated as single, live, CD11b+ F4/80+ ccr2RFP- cx3cr1GFP+.

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

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MRI Studies Reporting Summary

Form fields will expand as needed. Please do not leave fields blank.

Experimental design

1. Describe the experimental design.	Gd-DTPA perfusion scan were compared to baseline scans. The mice received a baseline scan followed by an injection of Gd-DTPA (.3mmol/kg) with a volume of 0.1ml. The Repeat scan was obtained 25 mins after injection as described in the Material and Methods section, page 34.
2. 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.	Each mouse was scanned once 25 mins after Gd-DTPA injection for 15 minutes.
3. Describe how behavioral performance was measured.	Behavioral phenotype of stressed mice was performed using the social interaction test as described in the Material and Methods, page 23 and 24.

Acquisition

4. Imaging	
a. Specify the type(s) of imaging.	T1
b. Specify the field strength (in Tesla).	7 Tesla
c. Provide the essential sequence imaging parameters.	FLASH sequence, TE=4ms, TR=304ms, 4 Averages, Flip angle=75 degrees. FOV=20mm, 256x256, Slice thickness=0.5mm, 32 slices
d. For diffusion MRI, provide full details of imaging parameters.	No diffusion was acquired
5. State area of acquisition.	New York

Preprocessing

6. Describe the software used for preprocessing.	Post injection images were reconstructed using the same scaling factor (gain) as the pre-injection scan. Subsequently an in-house script was used to convert from Raw Bruker format to Nifti format. In-house software based on Matlab V2013 (Mathworks Inc, Natick, MA) was used to extract Region of Interests (ROI) from the images.
7. Normalization	
a. If data were normalized/standardized, describe the approach(es).	N/A
b. Describe the template used for normalization/ transformation.	N/A
8. Describe your procedure for artifact and structured noise removal.	N/A
9. Define your software and/or method and criteria for volume censoring, and state the extent of such censoring.	N/A

Statistical modeling & inference

10. Define your model type and settings.	Series of ROI mean values were normalized to the unstressed control group average and compared for each brain region.
11. Specify the precise effect tested.	ROI values were compared for each brain region using one-way ANOVA and Bonferroni's Multiple Comparison Test. Correlation between individual ROI values and social interaction ratio was evaluated using Pearson's test.
12. Analysis	
a. Specify whether analysis is whole brain or ROI-based.	ROI means were obtained for the bilateral Prefrontal cortex, Nucleus Accumbens, Striatum, Hippocampus, Thalamus, Somatosensory Cortex, Insular Cortex
b. If ROI-based, describe how anatomical locations were determined.	ROI positions were visually identified
13. State the statistic type for inference. (See Eklund et al. 2016.)	N/A
14. Describe the type of correction and how it is obtained for multiple comparisons.	N/A
15. Connectivity	
a. For functional and/or effective connectivity, report the measures of dependence used and the model details.	N/A
b. For graph analysis, report the dependent variable and functional connectivity measure.	N/A
16. For multivariate modeling and predictive analysis, specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.	N/A