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Corresponding author(s): Costantino Iadecola

☐ 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.

Sample size was determined according to power analysis based on previous published works published by our lab on CBF regulation.

2. Data exclusions

Describe any data exclusions.

No data were excluded.

3. Replication

Describe whether the experimental findings were reliably reproduced.

All attempts at replication were successful.

4. Randomization

Describe how samples/organisms/participants were allocated into experimental groups.

Mouse randomization was based on the random number generator function (RANDBETWEEN) in Microsoft Excel software.

5. Blinding

Describe whether the investigators were blinded to group allocation during data collection and/or analysis.

Analysis was performed in a blinded fashion.

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.	Perimed and PowerLab were used for CBF measurements and MAP recording. FlowJo was used for analysis of flow cytometry experiments. Any Maze was used for collecting and analyzing behavioral experiments. Biorad Chemi Doc and Image Studio Ver 3.1 were used for collecting and analyzing immunoblots. Image J was used for analysis of ASL MRI data. IPLab was used for measurement of DAF fluorescence in experiments evaluating NO production in microvessels preparations or brain endothelial cell cultures. Graph Pad (v. 6.0) software was used for statistical analysis. Microsoft Excel was used for mouse randomization.

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.	All materials are from standard commercial sources specified in the Methods section.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).	The following commercial antibodies were injected in mice: Anti-IL-17A (Clone 17F3; bioXcell) and mouse IgG1 isotype control (Clone MOPC-21; bioXcell). The following commercial antibodies were used in flow cytometry experiments: CD45 (clone 30F-11), CD4 (clone RM4-5), TCRβ (clone H57-597), TCRγδ (clone GL3), CD11b (clone M1/70), Ly6G (clone 1A8), CD11c (clone N418), NK1.1 (clone PK136), CD19 (clone 6D5) from Biolegend and FoxP3 (clone FJK-16s) and IL-17A (clone eBio17B7) from eBiosciences. Anti-phospho-eNOS (Ser1177, #9571), anti-phospho-eNOS (Thr495, #9574) and anti-eNOS (#9572) from Cell Signaling were used to evaluate eNOS phosphorylation in microvessels preparations and brain microvascular endothelial cells. The antibodies used for western blotting experiments were validated in mice lacking eNOS.

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.	Immortalized brain mouse (bEnd.3) and human (HBEC-5i) brain endothelial cells were purchased from ATCC.
b. Describe the method of cell line authentication used.	The cell lines used in the study have been previously authenticated (please see www.atcc.org).
c. Report whether the cell lines were tested for mycoplasma contamination.	Cell lines were not tested for mycoplasma contamination.
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.	No commonly misidentified cell lines were used.

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.	The following mouse strains were used in the study: C57BL/6 (JAX), B6.129S7-Rag1tm1Mom/J (RAG1-/-, JAX Stock #002216), IL-17atm1.1(icre)Stck/J (IL-17-/-, JAX Stock #016869) and C57BL/6-IL-17atm1Bcgen/J (IL-17GFP, JAX Stock #018472). Only male mice were used in this study.

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.	The study did not involve human participants.

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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.	Please see manuscript page 19 to 22
6. Identify the instrument used for data collection.	MACSQuant Analyzer
7. Describe the software used to collect and analyze the flow cytometry data.	FlowJo
8. Describe the abundance of the relevant cell populations within post-sort fractions.	5000 endothelial cells were collected by cell-sorting and used for qRT-PCR.
9. Describe the gating strategy used.	Gating strategy is specified in the new supplemental figure. Gates were validated by TO-PRO-3 and fluorescein-diacetate labeling to identify dead and live cells, respectively. Isotype controls, single antibody-stained samples and Fluorescence Minus One controls were used to establish compensation and gating parameters.Samples were acquired and analyzed by an investigator blinded to the treatment groups.

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

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Date: 11/29/2017

Reporting Summary for MRI studies

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

Experimental design

1. Describe the experimental design.
   Resting cerebral blood flow (CBF)
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.
   n/a
3. Describe how behavioral performance was measured.
   n/a

Acquisition

4. Imaging
   a. Specify the type(s) of imaging.
   Arterial Spin Labeling MRI
   b. Specify the field strength (in Tesla).
   7.0 Tesla 70/30 Bruker Biospec small-animal MRI system with 450 mT/m gradient amplitude and a 4500 T · m−1 · s−1 slew rate
   c. Provide the essential sequence imaging parameters.
   ASL-MRI was based on a flow-sensitive alternating inversion recovery rapid acquisition with relaxation enhancement (FAIR-RARE) pulse sequence labeling the inflowing blood by global inversion of the equilibrium magnetization.
   d. For diffusion MRI, provide full detail on imaging parameters.
   n/a
5. State area of acquisition
   The resting cerebral blood flow was measured in the cortex and in the hippocampus.

Preprocessing

6. Describe the software used for preprocessing.
   Provide detail on software version and revision number, and on specific parameters (model/functions, brain extraction, segmentation, smoothing kernel size, etc.)
7. Normalization
   a. If data were normalized/standardized, describe the approach(es).
   Specify linear or non-linear and define image types used for transformation.
   b. Describe the template used for normalization/transformation.
   Specify subject space or group standardized space (e.g. original Talairach, MNI305, ICBM152).
8. Describe your procedure for artifact and structured noise removal.
   Specify motion parameters, tissue signals and physiological signals (heart rate, respiration).
9. Define your software and/or method and criteria for volume censoring and state the extent of such censoring.

Statistical modeling & inference

10. Define your 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).

11. Specify the precise effect tested.	We tested the effect of high salt diet on the resting CBF
12. Analysis	
a. Specify whether analysis is whole brain or ROI-based.	The analysis id ROI-based
b. If ROI-based, describe how anatomical locations were determined.	The resting CBF was measured in the cortex and in the hippocampus
13. State the statistic type for inference. (See Eklund et al. 2016.)	The images were analzyed by Image J and the average CBF value is reported as mL per 100g of tissue per minute.
14. Describe the type of correction and how it is obtained for multiple comparisons.	Data were analyzed by One-way ANOVA plus Tukey's test for multiple comparisons.
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