Sample size A minimum biological sample size of n=3-5 were performed with technical triplicates within each biological replicate

All experiments were replicated at least three times with reported standard statistical measurements (mean, SD, SEM). Differences were considered significant at p<0.05.

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

Life sciences study design

Replication

Study description

Sampling strategy

Data collection

Non-participation

Randomization

Research sample

Sampling strategy

Timing and spatial scale

Timing

Data exclusions No data were excluded in any of our experimental analysis.

Randomization No randomization was needed for any of our experimental analysis.

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

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

Study description

| Briefly describe the study. For quantitative data include treatment hierarchical), nature and number of experimental units and rep.

Investigators were blinded in the process of all data processing and analysis

Behavioural & social sciences study design

nature research

Corresponding author(s): Anthony Gramolin Last updated by author(s): Dec 4, 2019

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 <u>Authors & Referees</u> and the <u>Editorial Policy Checklist</u>.

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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

on <u>statistics for biologists</u> contains articles on many of the pa

Software and code Data collection

Policy information about <u>availability of computer code</u>

nms or software that are central to the research but not yet described in published literature, software must be made aw in a community repository (e.g. GitHub). See the Nature Research <u>guidelines for submitting code & software</u> for further

Data

Data exclusions

Reproducibility

Randomization Blinding

Field conditions

Disturbance

on about availability of data

Policy information about <u>availability of data</u>
All manuscripts ust include a <u>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

The authors declare that all supporting data are available within the article and supplementary files. Source data containing associated raw data are provided as a Source Data file.

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

(these choices, If there is a gap between collection periods, state the dates for each sample the data are taken

If no data were excluded from the analyses, state so OR if data were excluded, describe the exclusions and the rationale be indicating whether exclusion criteria were pre-established.

Behavioural & social sciences Ecological, evolutionary & environmental sciences

Palaeontology Specimen provenance

Specimen deposition Dating methods

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

Animals and other organisms

Human research participants

Population characteristics

Recruitment

Ethics oversight

Clinical data

Study protocol

Policy information about <u>studies involving animals</u>; <u>ARRIVE guidelines</u> recommended for reporting animal research

Laboratory animals Adult male 6-8 week old CD1 mice (Jackson Labs) were used in our study Field-collected samples

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

Policy information about clinical studies
All manuscripts should comply with the ICMUE guidelines for publication of clinical research and a completed CONSORT checkles must be included with all submass

All experimental procedures involving animals were approved by the University of Toronto Animal Use and Care Committee; all animal experiments were conducted in accordance with the animal care guidelines. Note that full information on the approval of the study protocol must also be provided in the manuscript.

Policy information about studies involving human research participants

Reporting for specific materials, systems and methods

Flow cytometry

MRI-based neuroimaging

Materials & experimental systems

Methods n/a Involved in the study n/a Involved in the study

Did the study involve field work? Yes No

Field work, collection and transport

Eukaryotic cell lines

Palaeontology
Animals and other organisms

Human research participants

Clinical data

Antibodies Validation

Antibodies used

All antibody used in the study are listed and described in detail in the Methods section under Antibodies

Eukaryotic cell lines

Cell line source(s)

Mycoplasma contamination Confirm that all cell lines tested negative for mycoplasma contamination OR description of the cell lines were not tested for mycoplasma.

Data collection Outcomes

Clinical trial registration

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

ChIP-seq

Data deposition

Confirm that both raw and final processed data have been deposited in a public database such as GEO.

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

Peak calling parameters

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.

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 Identify the instrument used for data collection, specifying make and model number. Instrument Describe the software used to collect and analyze the flow cytometry data. For custom community repository, provide accession details. Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.

Magnetic resonance imaging

Experimental design Indicate task or resting state; event-related or block design Design type 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. Design specifications Behavioral performance measures

Specify the pulse sequence type (gradient echo, spin echo, etc.), imaging type (EPI, spiral, etc.), field of view slice thickness, orientation and TE/TR/flip angle. Sequence & imaging parameters Area of acquisition Diffusion MRI Used ☐ Not used Preprocessing Preprocessing software 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 rationals for lock of normalization. Normalization Normalization template Noise and artifact removal 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 Specify type of analysis: Whole brain ROI-based Both Specify voxel-wise or cluster-wise and report all relevant parameters for cluster-wise methods Describe the type of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte (cario), Correction Models & analysis n/a Involved in the study Functional and/or effective connectivi

Graph analysis
Multivariate modeling or predictive analysis

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

Graph analysis Multivariate modeling and predictive analysis

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