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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>.

Statistics	
	es, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.
n/a Confirmed	
The exact sam	ple size (n) for each experimental group/condition, given as a discrete number and unit of measurement
A statement o	n whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
	test(s) used AND whether they are one- or two-sided ests 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
	on of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
	hesis testing, the test statistic (e.g. F , t , r) with confidence intervals, effect sizes, degrees of freedom and P value noted exact values whenever suitable.
For Bayesian a	inalysis, information on the choice of priors and Markov chain Monte Carlo settings
For hierarchic	al and complex designs, identification of the appropriate level for tests and full reporting of outcomes
Estimates of e	ffect sizes (e.g. Cohen's d , Pearson's r), indicating how they were calculated
	Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.
Software and c	ode
Policy information abou	ut <u>availability of computer code</u>
Data collection	No software and code used for data collection.
Data analysis	GraphPad Prism 6 (version 6.01), Microsoft excel 2016 (Version 1908 (Build 11929.20300))
We strongly encourage code of	om algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers. deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.
Data	
- Accession codes, uni - A list of figures that	It <u>availability of data</u> nclude a <u>data availability statement</u> . This statement should provide the following information, where applicable: que identifiers, or web links for publicly available datasets have associated raw data restrictions on data availability
The data that support the	findings of this study are available from the corresponding author upon request.
Field-speci	fic reporting
Please select the one be	elow that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.
x Life sciences	Behavioural & social sciences Ecological, evolutionary & environmental sciences

 $For a \ reference \ copy \ of \ the \ document \ with \ all \ sections, see \ \underline{nature.com/documents/nr-reporting-summary-flat.pdf}$

Life sciences study design

sclose on these points even when the disclosure is negative.
Sample size was calculated using N-query 6.0 with 80% power and 0.05 one-sided type I error to detect \sim 20% difference between mutant and control groups. Pilot studies were conducted to estimate sample size and calculate power of study.
No data were excluded.
Authors confirm that data replication was successful. Experiments were conducted with calculated sample size for two or three times to ensure reproducibility. These independent experiments were combined when possible. Authors always had more than 3 samples for histology or immunohistochemistry to replicate results.
Authors randomly allocated animals to experimental and control groups to make the experimental groups as similar as possible in all respects. In particular, the authors measured mouse body weight before the beginning of the experiment to make sure there is no weight difference between control and experimental groups.

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.

Investigators were blinded to analysis whenever it is available. In particular, immunohistochemistry images (Fig 5A, Fig 6G, Fig 7A and C) were

n/a Involved in the study	Methods	
Eukaryotic cell lines		
Palaeontology MRI-based neuroimaging		
Animals and other organisms		
Human research participants		
Clinical data		

quantified by non-study participants to reduce a possible bias.

Antibodies

Blinding

Antibodies used

UCP-1 (EMD Millipore, 662045), Akt (CST, #4056), Tyrosine hydroxylase (Santa Cruz, sc-14007), p-HSL (Ser660) (CST, #4126), HSL (CST, #4107), c-Fos (CST, #2250), pAKT (Thr308) (CST #4056), pAKT (Ser473) (CST #4060), pSTAT3 (Santa Cruz, sc-8059), STAT3 (Santa Cruz, SC-8019), a-Tubulin (Santa Cruz, sc-5286), pHSL (Ser563) (CST #4139), TuJI (beta butulin III) (Sigma T8578), POMC (Phoenix Pharmaceuticals, H-003-57), AgRP (Phoenix Pharmaceuticals, H-029-30), Sh2b1 (generated by lab).

Validation

Manufacturer's websites state all the antibodies are verified in terms of specificity, sensitivity, and reproducibility by following methods: Analysis of a large panel of cell lines with known target expression levels, Treatment of cells with appropriate kinase-specific activators and/or inhibitors, Phosphatase treatment, Correct subcellular localization or treatment-induced translocation, Comparison of results with antibody and isotype control to ensure acceptable signal-to-background ratio, Target-specific signal verified in transfected cells, knockout cells, or siRNA-treated cells, Blocking with antigen peptide to confirm elimination of specific signal, Side-by-side comparison of a new lot with previous lots to ensure lot-to-lot consistency.

Animals and other organisms

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

Laboratory animals

Authors used age-matched littermates in C57BL/6J background to improve precision and reduce variability and bias. Males and females were characterized separately to determine the potential influence of sex in data interpretations.

Wild animals

This study does not involve wild animals.

Field-collected samples

This study does not involve field-collected samples.

Ethics oversight

Animal experiments were conducted following the protocols approved by the University Committee on the Use and Care of Animals (UCUCA).

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