nature neuroscience

Corresponding Author:	Sonenberg N and Amir S	# Main Figures:	5
Manuscript Number:	NN-A50637B	# Supplementary Figures:	6
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		# Supplementary Videos:	0

Reporting Checklist for Nature Neuroscience

This checklist is used to ensure good reporting standards and to improve the reproducibility of published results. For more information, please read Reporting Life Sciences Research.

Please note that in the event of publication, it is mandatory that authors include all relevant methodological and statistical information in the manuscript.

▶ Statistics reporting, by figure

- Please specify the following information for each panel reporting quantitative data, and where each item is reported (section, e.g. Results, & paragraph number).
- Each figure legend should ideally contain an exact sample size (n) for each experimental group/condition, where n is an exact number and not a range, a clear definition of how n is defined (for example x cells from x slices from x animals from x litters, collected over x days), a description of the statistical test used, the results of the tests, any descriptive statistics and clearly defined error bars if applicable.
- · For any experiments using custom statistics, please indicate the test used and stats obtained for each experiment.
- Each figure legend should include a statement of how many times the experiment shown was replicated in the lab; the details of sample collection should be sufficiently clear so that the replicability of the experiment is obvious to the reader.
- For experiments reported in the text but not in the figures, please use the paragraph number instead of the figure number.

Note: Mean and standard deviation are not appropriate on small samples, and plotting independent data points is usually more informative. When technical replicates are reported, error and significance measures reflect the experimental variability and not the variability of the biological process; it is misleading not to state this clearly.

		TEST US	TEST USED n		DESCRIPTIVE S' (AVERAGE, VARIA	-	P VALUE		DEGREES OF FREEDOM & F/t/z/R/ETC VALUE			
	FIGURE NUMBER	WHICH TEST?	SECTION & PARAGRAPH #	EXACT VALUE	DEFINED?	SECTION & PARAGRAPH #	REPORTED?	SECTION & PARAGRAPH #	EXACT VALUE	SECTION & PARAGRAPH #	VALUE	SECTION & PARAGRAPH #
example	1a	one-way ANOVA	Fig. legend	9, 9, 10, 15	mice from at least 3 litters/group	Methods para 8	error bars are mean +/- SEM	Fig. legend	p = 0.044	Fig. legend	F(3, 36) = 2.97	Fig. legend
example	results, para 6	unpaired t- test	Results para 6	15	slices from 10 mice	Results para 6	error bars are mean +/- SEM	Results para 6	p = 0.0006	Results para 6	t(28) = 2.808	Results para 6
+	1b	one-way ANOVA	Fig.1 legend	6,6,6,8,6, 8	6-8 mice from each group	Fig.1 b	error bars are mean +/- SEM	Fig.1 legend	p=0.000	Fig.1 legend	F(5,34)=15.913	Fig.1 legend

		TEST US	SED		n		DESCRIPTIVE S (AVERAGE, VARIA		P VALUE		DEGREES OF FREEDOM & F/t/z/R/ETC VALUE	
	FIGURE NUMBER	WHICH TEST?	SECTION & PARAGRAPH #	EXACT VALUE	DEFINED?	SECTION & PARAGRAPH #	REPORTED?	SECTION & PARAGRAPH #	EXACT VALUE	SECTION & PARAGRAPH #	VALUE	SECTION & PARAGRAPH #
+	1c	one-way ANOVA	Fig.1 legend	4,3,3,3,3,	3-4 mice for each time point	Fig.1 legend	error bars are mean +/- SEM	Fig.1 legend	p=0.000	Fig.1 legend	F(5,13)=10.141	Fig.1 legend
+	1e	one-way ANOVA	Fig.1 legend	6,6,4,4	4-6 mice from each group	Fig.1 e	error bars are mean +/- SEM	Fig.1 legend	p=0.000	Fig.1 legend	F(3,16)=103.220	Fig.1 legend
+	1g	one-way ANOVA	Fig.1 legend	4,4,4,4,4,	4 mice for each time point	Fig.1 legend	error bars are mean +/- SEM	Fig.1 legend	p=0.000	Fig.1 legend	F(5,18)=18.964	Fig.1 legend
+	2d	Student's t- test	Fig.2 legend	12,18	12 WT mice and 18 KI mice	Fig.2d	error bars are mean +/- SEM	Fig.2 legend	CT15: p=0.002 CT22: p=0.000	Fig.2 legend	CT15: F(1,28)=13.100 CT22: F(1,28)=21.702	Fig.2 legend
+	2e	Student's t- test	Fig.2 legend	12,18	12 WT mice and 18 KI mice	Fig.2d	error bars are mean +/- SEM	Fig.2 legend	D1-8: p=0.000 D9-22: p=0.000 D23-26: p=0.000	Fig.2 legend	D1-8: F(1,28)=33.165 D9-22 F(1,28)=17.843 D23-26 F(1,28)=21.726	Fig.2 legend
+	3b	Student's t- test	Fig.3 legend	9,14,15, 26,5,5,9, 14	Numbers are indicated in the figure	Fig.3b	error bars are mean +/- SEM	Fig.3 legend	T21:p=0.03 T22:p=0.000 T26:p=0.272 T27:p=0.042	Fig.3 legend	T21: F(1,21)=5.448 T22: F(1,39)=39.493 T26: F(1,8)=1.389 T27: F(1,21)=4.690	Fig.3 legend
+	3c	X2 test	Fig.3 legend	9,14,15,2 6,5,5,9,1 4	Numbers are indicated in the figure	Fig.3b	Percentage	Fig.3 legend	T21:p=0.052 T22:p=0.000 T26:p=1.000 T27:p=0.042	Fig.3 legend	df=1 T21:X2=4.407 T22:X2=17.564 T26:X2=0 T27:X2=4.707	Fig.3 legend
+	4a	one-way ANOVA	Fig.4 legend	6,6,6,6,6, 6,6,6,6,6, 6,6	6 WT or KI mice for each time point	Fig.4 legend	error bars are mean +/- SEM	Fig.4 legend	p=0.000	Fig.4 legend	F(11,60)=22.698	Fig.4 legend
+	4b	one-way ANOVA	Fig.4 legend	6,6,6,6,6, 6,6,6,6,6, 6,6	6 WT or KI mice for each time point	Fig.4 legend	error bars are mean +/- SEM	Fig.4 legend	p=0.000	Fig.4 legend	F(11,60)=28.840	Fig.4 legend
+	4d	one-way ANOVA	Fig.4 legend	10,10,8,8	20 WT mice and 16 KI mice	Fig.4 d	error bars are mean +/- SEM	Fig.4 legend	p=0.000	Fig.4 legend	F(3,32)=8.049	Fig.4 legend
+	4f	one-way ANOVA	Fig.4 legend	10,10,10, 12	20 WT mice and 22 KI mice	Fig.4 legend	error bars are mean +/- SEM	Fig.4 legend	p=0.000	Fig.4 legend	F(3,38)=67.135	Fig.4 legend
+	4h	one-way ANOVA	Fig.4 legend	3,3,3	3 WT MEFs,3 KI MEFs for each time point	Fig.4 legend	error bars are mean +/- SEM	Fig.4 legend	p=0.000	Fig.4 legend	F(5,12)=394.178	Fig.4 legend
+	4i	one-way ANOVA	Fig.4 legend	3,3,3	3 WT MEFs,3 KI MEFs for each time point	Fig.4 legend	error bars are mean +/- SEM	Fig.4 legend	p=0.000	Fig.4 legend	F(5,12)=36.576	Fig.4 legend

+ -	5b	one-way ANOVA	Fig.5 legend	3,3,3,	3WT mice, 3 heterozygous(HET) and 3 homozygous (KI) KI mice	Results Para 11	error bars are mean +/- SEM	Result s Para 11	PER1: p=0.000 PER2:p=0.000 CLOCK: p=0.074 BMAL1: p=0.074 CRY1: p=0.172 CRY2: p=0.429 p-eIF4E: p=0.000	Results Para 11	PER1: F(2,6)=130.360 PER2: F(2,6)=135.16 CLOCK: F(2,6)=4.154 BMAL1: F(2,6)=4.160 CRY1 F(2,6)=2.395 CRY2 F(2,6)=0.979 p-elF4E: F(2,6)=511.440	Results Para 11
+	5d	Student's t- test	Fig.5 legend	3,3	3 WT MEFs,3 KI MEFs	Results Para 12	error bars are mean +/- SEM	Result s Para 12	Per1: p=0.000 Per2:p=0.000 Control: p=0.510	Results Para 12	Per1: F(1,4)=294.000 Per2: F(1,4)=291.84 Control: F(1,4)=0.521	Results Para 12
+ -	5f	one-way ANOVA	Fig.5 legend	3,3,3,3	3WT MEFs for each concentration	Results Para 12	error bars are mean +/- SEM	Result s Para 12	Per1: p=0.000 Per2:p=0.000 Control: p=0.407	Fig.5 legend	Per1: F(3,8)=126.016 Per2: F(3,8)=42.225 Control: F(3,8)=1.091	Results Para 12

▶ Representative figures

1. Are any representative images shown (including Western blots and immunohistochemistry/staining) in the paper?

If so, what figure(s)?

2. For each representative image, is there a clear statement of how many times this experiment was successfully repeated and a discussion of any limitations in repeatability?

If so, where is this reported (section, paragraph #)?

Yes, Figs 1a,1d and 1f; Figs 2a,2b and 2c; Figs 3a; Figs 4c,4e and 4g; Figs 5a and 5e.

Yes, in the respective sections of "Results" and "Figure legends".

▶ Statistics and general methods

1. Is there a justification of the sample size?

If so, how was it justified?

Where (section, paragraph #)?

Even if no sample size calculation was performed, authors should report why the sample size is adequate to measure their effect size.

2. Are statistical tests justified as appropriate for every figure?

Where (section, paragraph #)?

a. If there is a section summarizing the statistical methods in the methods, is the statistical test for each experiment clearly defined? The sample size was determined according to customary practice in the field.

The statistical tests were selected according to customary practice in the field.

Yes, in the "Methods" section, paragraph11.

	b.	Do the data meet the assumptions of the specific statistical test you chose (e.g. normality for a parametric test)?	Yes, in the "Methods" section, paragraph11.
		Where is this described (section, paragraph #)?	
	C.	Is there any estimate of variance within each group of data?	N/A
		Is the variance similar between groups that are being statistically compared?	
		Where is this described (section, paragraph #)?	
	d.	Are tests specified as one- or two-sided?	Two-sided.
	e.	Are there adjustments for multiple comparisons?	Yes, multiple comparisons were made by ANOVA, followed by the Student-Newman-Keuls test for individual comparisons.
3.	Are crite	ria for excluding data points reported?	N/A
	Was this	criterion established prior to data collection?	
	Where is	this described (section, paragraph #)?	
4.		ne method of randomization used to assign subjects (or to the experimental groups and to collect and process data.	N/A
	If no ran	domization was used, state so.	
	Where d	oes this appear (section, paragraph #)?	
5	ls a state	ement of the extent to which investigator knew the group	N/A
٥.		n during the experiment and in assessing outcome included?	
	If no blin	ding was done, state so.	
	Where (s	section, paragraph #)?	
6.		riments in live vertebrates, is a statement of compliance with uidelines/regulations included?	Yes, in the "Methods" section, paragraph1.
	Where (s	section, paragraph #)?	
7.	Is the sp	ecies of the animals used reported?	Yes, in the "Methods" section, paragraph1.
		section, paragraph #)?	
8.		rain of the animals (including background strains of KO/ ic animals used) reported?	Yes, in the "Methods" section, paragraph1.
		section, paragraph #)?	
9.	Is the se	x of the animals/subjects used reported?	Yes, in the "Methods" section, paragraph1.
	Where (s	section, paragraph #)?	
10.	Is the ag	e of the animals/subjects reported?	Yes, in the "Methods" section, paragraph2.
	Where (s	section, paragraph #)?	

11. For animals housed in a vivarium, is	the light/dark cycle reported?	Yes, in the "Methods" section, paragraph2.
Where (section, paragraph #)?		
12. For animals housed in a vivarium, is animals per cage) reported? Where (section, paragraph #)?	the housing group (i.e. number of	No, in the "Methods" section, paragraph5.
13. For behavioral experiments, is the tiddark cycle)?	me of day reported (e.g. light or	Yes, in the "Methods" section, paragraph2.
Where (section, paragraph #)?		
14. Is the previous history of the animals administration, surgery, behavioral to Where (section, paragraph #)?		N/A
a. If multiple behavioral tests group of animals, is this rep Where (section, paragraph)	ported?	N/A
15. If any animals/subjects were exclude	ed from analysis, is this reported?	N/A
Where (section, paragraph #)?		
a. How were the criteria for e		N/A
b. Specify reasons for any dis animals at the beginning a	crepancy between the number of nd end of the study.	N/A
Where is this described (se	ection, paragraph #)?	
▶ Reagents		
1. Have antibodies been validated for u (assay and species)?	use in the system under study	Yes, the information is in the citations #12,20,26 and 30.
a. Is antibody catalog numbe		Yes, in the table in the "Methods" section.
Where does this appear (se	ection, paragraph #)!	

Yes, in the "Results" section, paragraph #8 and #9.

b. Where were the validation data reported (citation,

supplementary information, Antibodypedia)?
Where does this appear (section, paragraph #)?

2. If cell lines were used to reflect the properties of a particular tissue or disease state, is their source identified?	Yes, in the citation #15.
Where (section, paragraph #)?	
a. Were they recently authenticated?	No, because it is a standard cell line as stated in citation #15.
Where is this information reported (section, paragraph #)?	
▶ Data deposition	
Data deposition in a public repository is mandatory for: a. Protein, DNA and RNA sequences b. Macromolecular structures c. Crystallographic data for small molecules d. Microarray data	
Deposition is strongly recommended for many other datasets for which strawailable here. We encourage the provision of other source data in supplemental Dryad.	
We encourage publication of Data Descriptors (see Scientific Data) to maxim	mize data reuse.
1. Are accession codes for deposit dates provided?	N/A
Where (section, paragraph #)?	
► Computer code/software	
Any custom algorithm/software that is central to the methods must be supplime of publication. However, referees may ask for this information at any t	
Identify all custom software or scripts that were required to conduct the study and where in the procedures each was used.	N/A
 If computer code was used to generate results that are central to the paper's conclusions, include a statement in the Methods section under "Code availability" to indicate whether and how the code can be accessed. Include version information as necessary and any restrictions on availability. 	N/A
▶ Human subjects	
	(
1. Which IRB approved the protocol?	N/A
Where is this stated (section, paragraph #)?	

N/A

2. Is demographic information on all subjects provided?

Where (section, paragraph #)?

3.	Is the number of human subjects, their age and sex clearly defined? Where (section, paragraph #)?	N/A
4.	Are the inclusion and exclusion criteria (if any) clearly specified? Where (section, paragraph #)?	N/A
5.	How well were the groups matched? Where is this information described (section, paragraph #)?	N/A
6.	Is a statement included confirming that informed consent was obtained from all subjects?	N/A
	Where (section, paragraph #)?	
7.	For publication of patient photos, is a statement included confirming that consent to publish was obtained?	N/A
	Where (section, paragraph #)?	
• f	MRI studies	
	papers reporting functional imaging (fMRI) results please ensure that thormation is clearly provided in the methods:	nese minimal reporting guidelines are met and that all this
1.	Were any subjects scanned but then rejected for the analysis after the data was collected?	N/A
	If yes, is the number rejected and reasons for rejection described?	N/A
	Where (section, paragraph #)?	
2.	Is the number of blocks, trials or experimental units per session and/ or subjects specified?	N/A
	Where (section, paragraph #)?	
3.	Is the length of each trial and interval between trials specified?	N/A
4.	Is a blocked, event-related, or mixed design being used? If applicable, please specify the block length or how the event-related or mixed design was optimized.	N/A
5.	Is the task design clearly described?	N/A
	Where (section, paragraph #)?	
6.	How was behavioral performance measured?	N/A
7.	Is an ANOVA or factorial design being used?	N/A

8. For data acquisition, is a whole brain scan used?	N/A
If not, state area of acquisition.	
a. How was this region determined?	N/A
9. Is the field strength (in Tesla) of the MRI system stated?	N/A
a. Is the pulse sequence type (gradient/spin echo, EPI/spiral)	N/A
stated?	IV/A
b. Are the field-of-view, matrix size, slice thickness, and TE/TR/	N/A
flip angle clearly stated?	
 Are the software and specific parameters (model/functions, smoothing kernel size if applicable, etc.) used for data processing and 	N/A
pre-processing clearly stated?	
11. Is the coordinate space for the anatomical/functional imaging data	N/A
clearly defined as subject/native space or standardized stereotaxic space, e.g., original Talairach, MNI305, ICBM152, etc? Where (section,	
paragraph #)?	
12. If there was data normalization/standardization to a specific space	N/A
template, are the type of transformation (linear vs. nonlinear) used and image types being transformed clearly described? Where (section,	
paragraph #)?	
13. How were anatomical locations determined, e.g., via an automated	N/A
labeling algorithm (AAL), standardized coordinate database (Talairach daemon), probabilistic atlases, etc.?	
daemon), probabilistic atlases, etc.:	
14. Were any additional regressors (behavioral covariates, motion etc)	N/A
used?	
15. Is the contrast construction clearly defined?	N/A
16. Is a mixed/random effects or fixed inference used?	N/A
a. If fixed effects inference used, is this justified?	N/A
a. If fixed effects fillerence used, is this justified:	NyA
17. Were repeated measures used (multiple measurements per subject)?	N/A
a. If so, are the method to account for within subject	N/A
correlation and the assumptions made about variance clearly stated?	
deally stated:	
18. If the threshold used for inference and visualization in figures varies, is	N/A
this clearly stated?	
19. Are statistical inferences corrected for multiple comparisons?	N/A

a. If not, is this labeled as uncorrected?	N/A
20. Are the results based on an ROI (region of interest) analysis?	N/A
a. If so, is the rationale clearly described?	N/A
b. How were the ROI's defined (functional vs anatomical localization)?	N/A
21. Is there correction for multiple comparisons within each voxel?	N/A
22. For cluster-wise significance, is the cluster-defining threshold and the corrected significance level defined?	N/A

▶ Additional comments

Additional Comments