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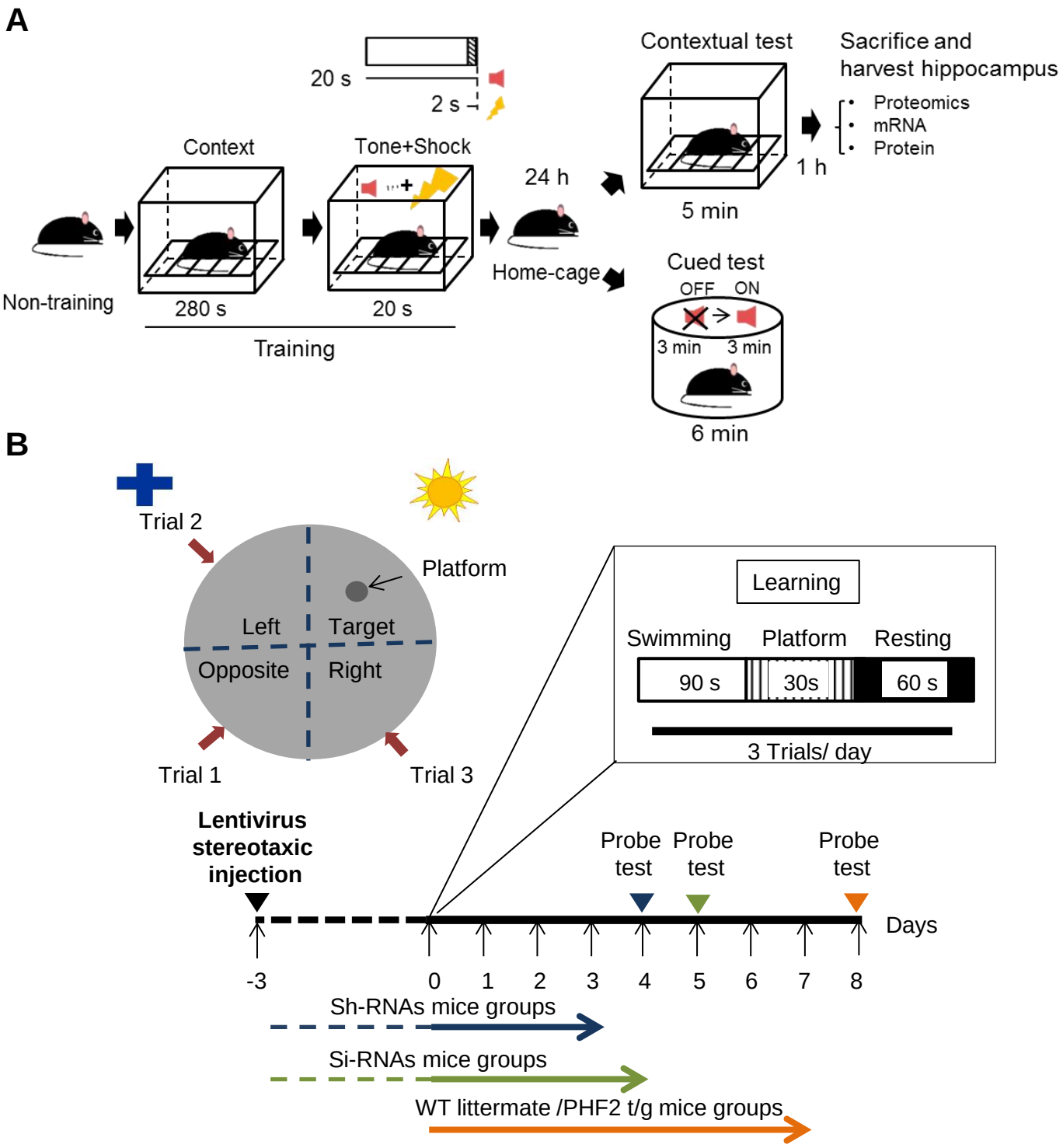
Appendix Fig S1

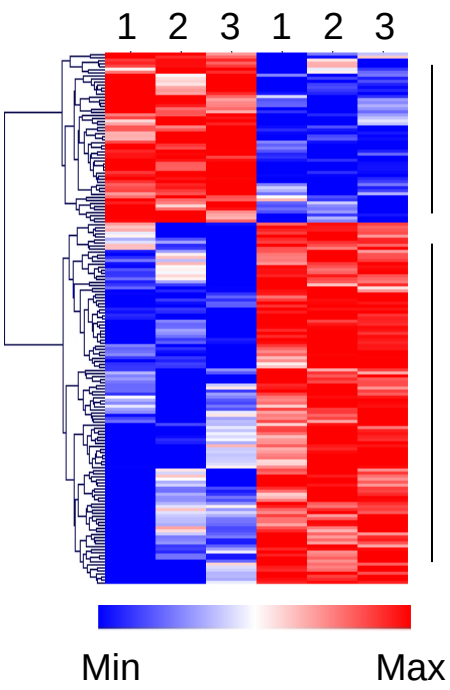


Appendix Fig S1. Behavioral diagrams

(A) Diagram of the apparatus used for contextual fear conditioning test. Mice were trained for the contextual fear conditioning (a tone shock, 80 db, 2 kHz, 20 s; a foot shock, 2 s, 0.7 mA/sec constant current) and tested 24 h later. **(B)** Diagram of the apparatus used for Morris water maze test.

Appendix Fig S2

A



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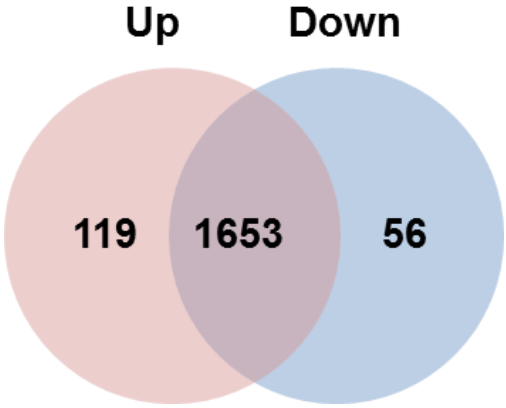


C

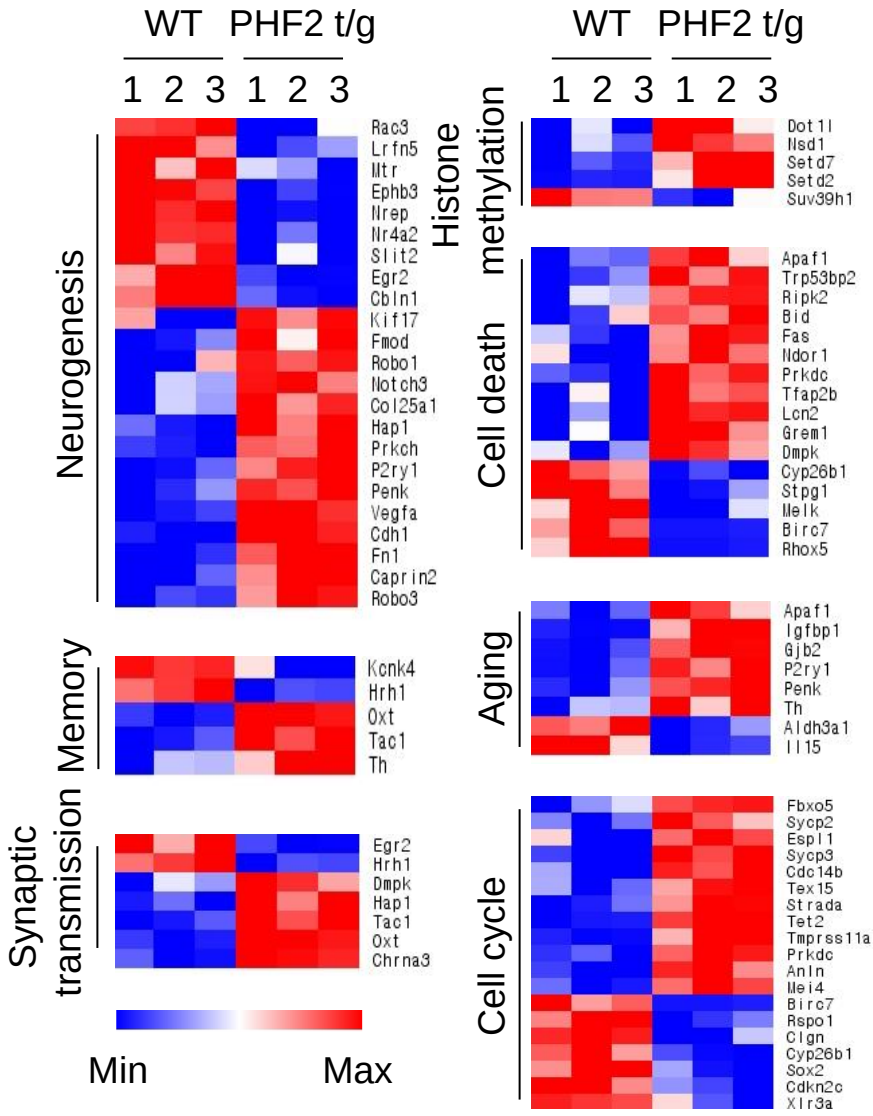
Up regulation

Category	Gene	P value
collagen fibril organization	4	0.002
signal transduction	17	0.006
positive regulation of cell proliferation	9	0.023
eating behavior	3	0.025
maternal aggressive behavior	2	0.025
cell-cell signaling	4	0.029
negative regulation of cell adhesion mediated by integrin	2	0.032
proteolysis	9	0.034
negative regulation of BMP signaling pathway	3	0.035
osteoblast differentiation	4	0.036

Down regulation

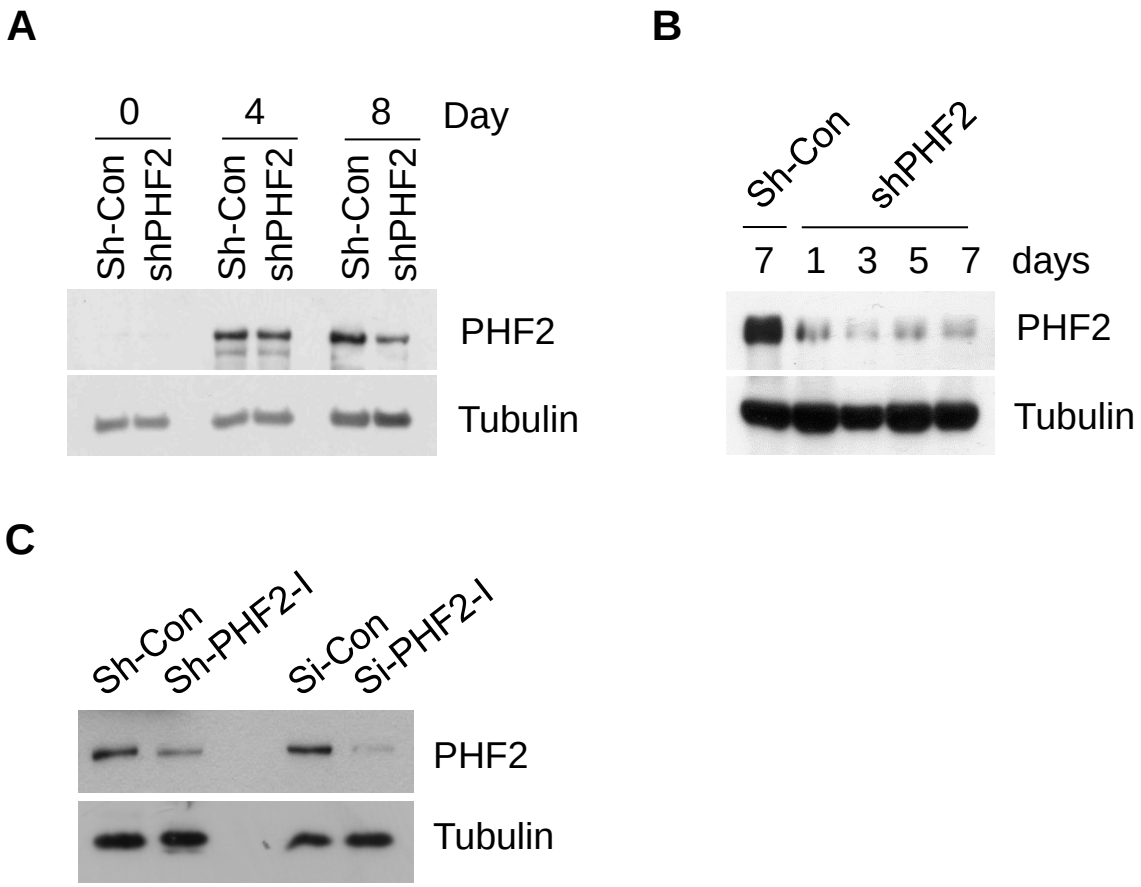
Category	Gene	adjP
cellular response to interferon-gamma	5	0.001
lymphocyte chemotaxi	4	0.001
monocyte chemotaxis	4	0.001
chemokine-mediated signaling pathway	4	0.001
neutrophil chemotaxis	4	0.001
activation of GTPase activity	4	0.001
cellular response to interleukin-1	4	0.001
positive regulation of ERK1 and ERK2 cascade	4	0.001
T cell costimulation	5	0.001
cellular response to tumor necrosis factor	4	0.003

D



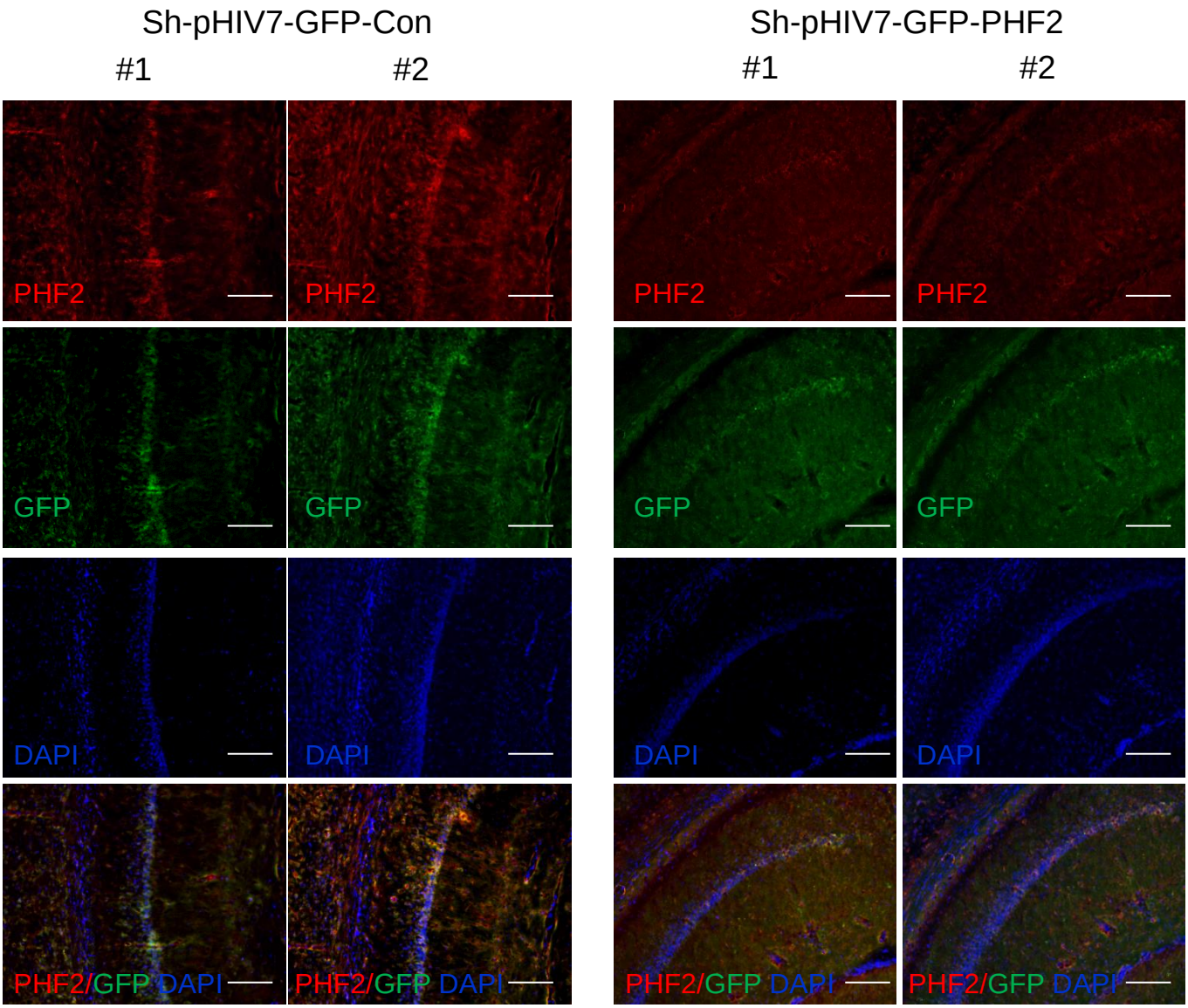
Appendix Fig S2. QuantSeq analysis in the hippocampus of WT and PHF2 t/g. (A) Heat map depicts the changes in gene expression between WT and PHF2 t/g hippocampal tissue. (B) Venn diagrams show the number of genes that were upregulated or down regulated between WT and PHF2 t/g. (C) KEGG analysis of genes up-regulated or down-regulated in WT and PHF2 t/g mice. (D) Heat map of 7 groups of genes from the KEGG analysis in panel A. P values were calculated using a hypergeometric test (raw P value) and adjusted by multiple testing (adjusted P values).

Appendix Fig S3



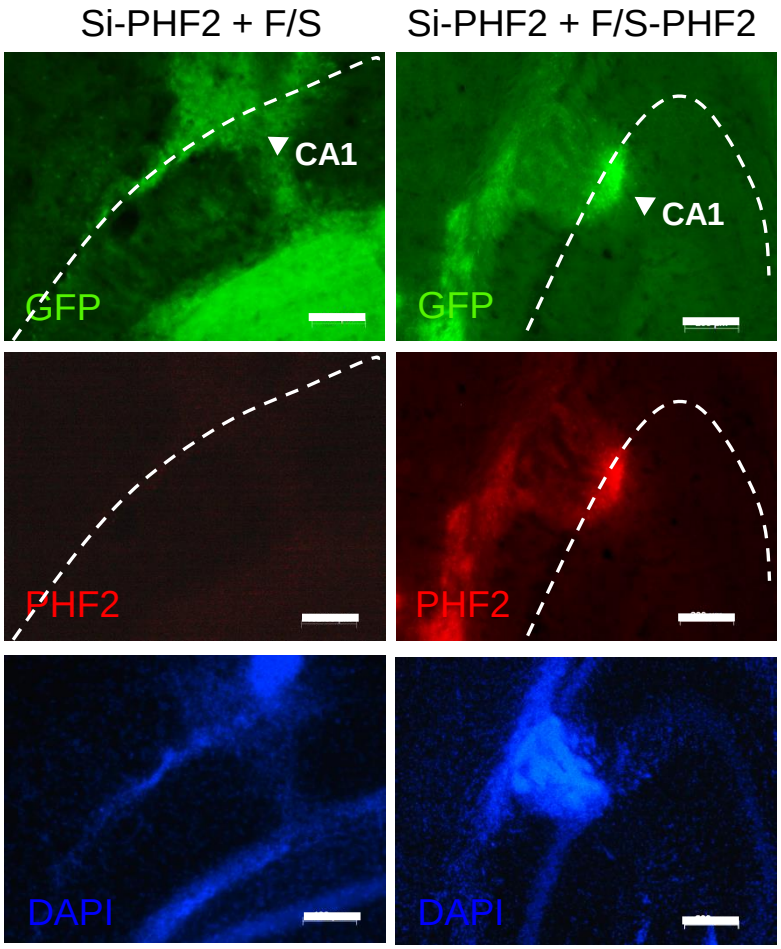
Appendix Fig S3. Reduced expression of PHF2 by sh-PHF2 or si-PHF2. (A) Time-dependent knocked-down expression of PHF2 by transfection of sh-PHF2 lentivirus into primary neurons. (B) Knocked-down expression of PHF2 in hippocampus at the indicated time after stereotactic injection of sh-PHF2 lentivirus into CA1 region. (C) Knocked-down expression of PHF2 in hippocampus on the third day after stereotactic injection of shRNA or siRNA into CA1 region.

Appendix Fig S4



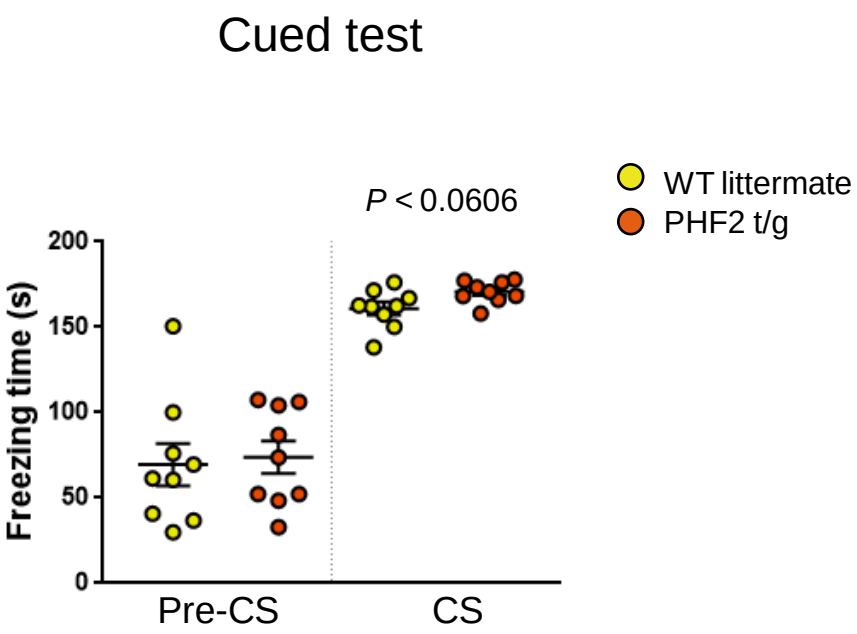
Appendix Fig S4. Immunofluorescence analysis of the PHF2 levels in the hippocampus. Immunofluorescence staining of indicated proteins after stereotaxic injection of the indicated lentiviral particles into bilateral hippocampus CA1 of WT mice. Scale bar, 100 μm.

Appendix Fig S5



Appendix Fig S5. Immunofluorescence analysis of PHF2 protein in the hippocampus. Stereotaxic injection of Si-PHF2 and F/S or F/S-PHF2 into bilateral hippocampus CA1 of WT mice. Scale bar, 100 μm.

Appendix Fig S6



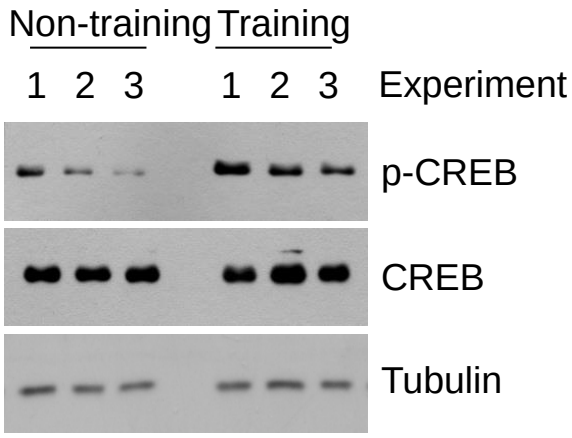
Appendix Fig S6. Cued dependent memory formation in WT or PHF2 t/g mice. The training consisted of a 280 s exposure of mice to the conditioning box (context) followed by a tone (80 db, 2 kHz, 20 s). And a foot shock (0.7 mA/sec constant current) was administered during the last 2 s of tone presentation and co-terminated with the tone. Approximately 24 hours after training, each mice were re-exposed to a novel context for 3 min followed by an additional 3-min exposure to a tone. Freezing was recorded every 1min for 6 min.

Data format: Data are represented as the mean values ± SEM (n = 9). Data were analyzed using unpaired, two-sided Student's t-test.

A

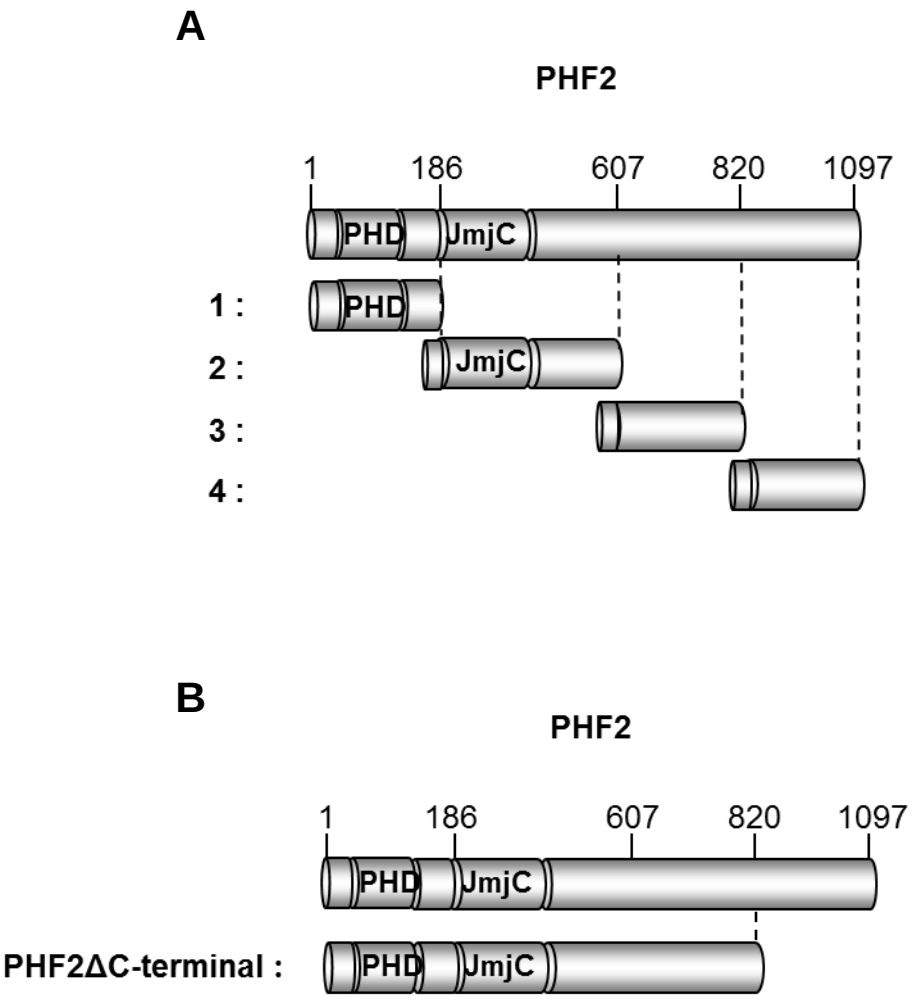
Transcription factors		
Up	Activator	CREB
		TCF4
		GTF2I
		STAT6
		JUNB
		PBX3
	Inhibitor	MEF2A
		STAT1
Down	Activator	MEF2D
		ATF2
		JUND
	Inhibitor	STAT3

B



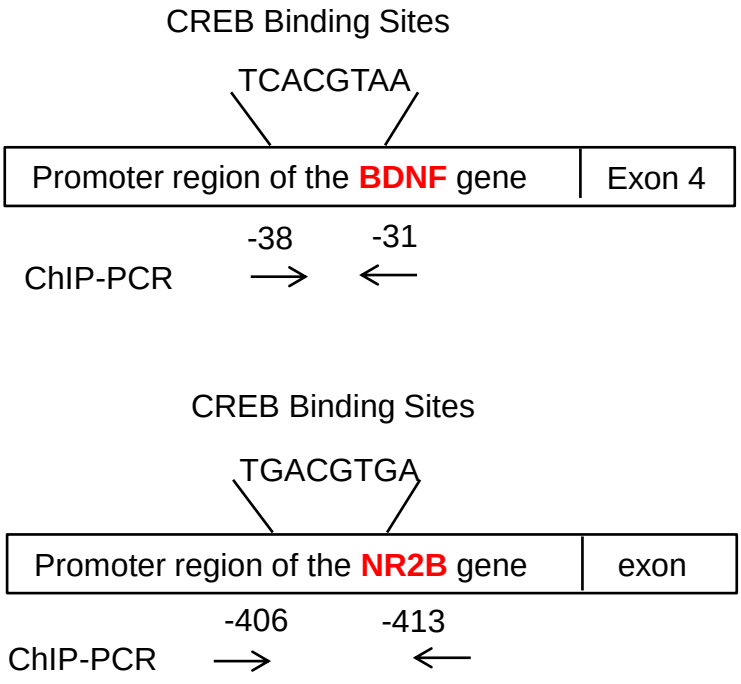
Appendix Fig S7. Post-training induces activation of CREB in hippocampus. (A) The table represents selection of transcription factors differentially upregulated or downregulated in hippocampal lysate from CFC trained mice. (B) Immunoblotting assay of phosphorylated CREB and total CREB. Trained mice showed increase in p-CREB levels.

Appendix Fig S8



Appendix Fig S8. Schematic representation of PHF2 domain structure. (A) The domain structure of F/S-tagged PHF2 fragments. (B) The deletion mutant of PHF2 C-terminal region (PHF2ΔC).

Appendix Fig S9



Appendix Fig S9. CRE sequence of the BDNF and NR2B promoter.

Appendix Table S1. Nucleotide sequences of siRNAs and shRNAs used in knock- down experiments.

Purposes	Targets	Sequences (5' to 3')
shRNAs	Control	CUAGCAAAAACGCUGAGUACUUCGAAAUGUCCUCGAGGACAUUUC GAAGUACUCAGCGCC
	Phf2-I	CUAGCAAAAACGUGGCUAUUAAAGUGUUCUACUCGAGUAGAACAC UUUAAUAGCCACGCC
	Phf2-II	GGCCGGCGTGGCUAUUAAAGUGUUCUACUCGA GUAGAACACUUU AAUAGCCACGUUUUUG
siRNA	Non-target	UUGAGCAAUUCACGUUCAUUU
	Phf2-I	CACUUCUUCCCUUUCUUCUUGCUCCCA

Appendix Table S2. Primers used in real-time PCR and ChIP assays.

	Gene	Forward primers (5’ to 3’)	Reverse primers (5’ to 3’)
RT-qPCR	*Bdnf*	ATGCCGCAAACATGTCTATGAG	TGACCCACTCGCTAATACTGTCA
	CamKIIα	ACCCTGGCCTGGTCCTTCAATG	AGCCATCCTCACCACTATGCTGG
	Cdk5	GGCTAAAAACCGGGAAACTC	CCATTGCAGCTGTCGAAATA
	Creb	TCAGGGTACTACCATTC	TTCAGCAGGCTGTGTAGGAA
	C-fos	TTCCTGGCAATAGCGTGTTC	TTCAGACCACCTCGACAATG
	Egr1	CGAGCGAACAACCCTATGAG	CATTATTCAGAGCGATGTCAGAAA
	Glur1	TTTTCTAGGTGCGGTTGTGG	CCT TTGGAGAACTGGGAACA
	Glur2	AAGGAGGAAAGGGAAACGAG	CCGAAGTGGAAAACTGAACC
	Npas4	GCTATACTCAGAAGGTCCAGAAGGC	TCAGAGAATGAGGGTAGCACAGC
	Nr2b	TCTGCCTTCTTAGAGCCATTCAG	AGACAGCTACAGCAGAGAC
	Psd95	ATTCCCAGCAAACGGCG	ACTGAACCTGACCGTACAGGCCTTTA ACCTTGACCACTCTCCCTTTGGAGAC TGGGAACA
	Phf2	TGCCCGAACTGCGAGAAAACCC	TTTCACGTCCGGTGTTGGCCC
	Shank3	CTGCACATCTGTGCCCTCTA	AAGCTCAAAGTTCCCTGCAA
	Trkb	GTGGTGTCATTAGTAGGTTCTTTGTT TT	ACTGAACCTGACCGTACAGAGTT TGGGTCTTTGCTGCC
ChIP PCR	*Bdnf*	TGATCATCACTCACGACCACG	CAGCCTCTCTGAGCCAGTTACG
	Nr2b	CGCTGCTATTCCTTCTTGCT	CCCTCACTCCCACTGCTAAG
	Gapdh	CCTGCTTATCCAGTCCTAGCTA	AAATGAGGCGGGTCCAAAG