

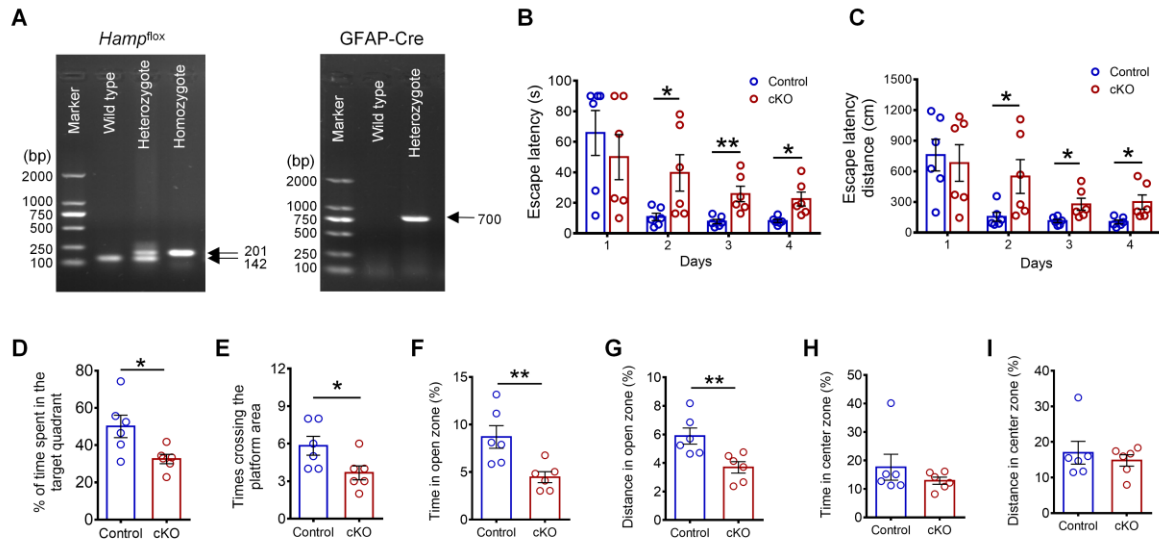
## Supplementary tables and figures

**Table S1.** Primer sequences for genotyping.

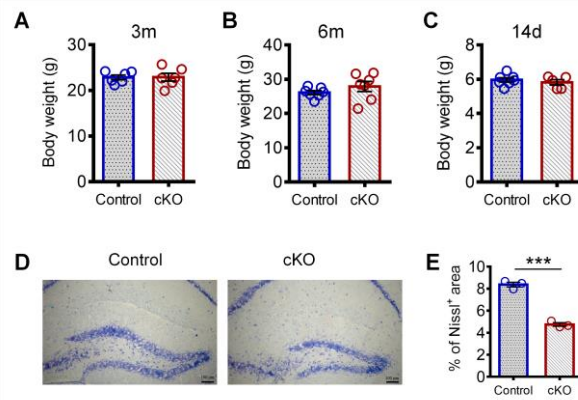
Primers	Sequences (5'-3')
<i>Hamp</i> <sup>fl<sup>ox</sup></sup> forward	GTAGGGTCTGATAAGTGAAGCCAG
<i>Hamp</i> <sup>fl<sup>ox</sup></sup> reverse	AGCACAAAGGCTTATAGCACATTC
GFAP-Cre forward	TAGCCCACTCCTTCATAAAGCCCT
GFAP-Cre reverse	GCTAAGTGCCTTCTCTACACC
Nestin-Cre forward	CCTTCCTGAAGCAGTAGAGCA
Nestin-Cre reverse	GCCTTATTGTGGAAGGACTG

**Table S2.** Primer sequences for qRT-PCR.

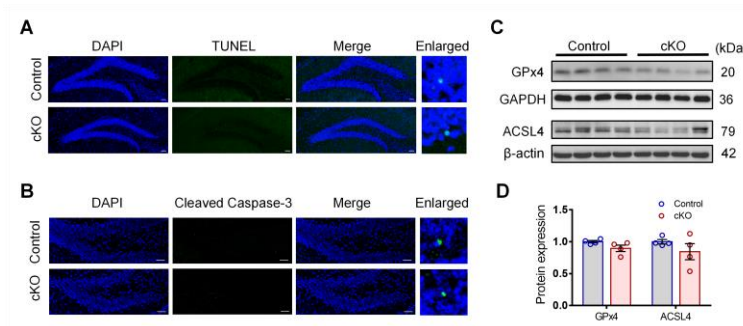
Genes	Forward (5'-3')	Reverse (5'-3')
<i>GAPDH</i>	TGACTTCAACAGCGACACCCA	CACCCTGTTGCTGTAGCCAAA
<i>Hamp</i>	CTGAGCAGCACACCTATCTC	TGGCTCTAGGCTATGTTTGC
<i>TNF-<math>\alpha</math></i>	CACCATGAGCACAGAAAGCA	TAGACAGAAGAGCGTGGTGG
<i>IL-6</i>	CTGCAAGAGACTTCCATCCAG	AGTGGTATAGACAGGTCTGTTGG
<i>BDNF</i>	CTGTATCAAAAGGCCAACTGAA	GTGTCTATCCTTATGAATCGCCA
<i>NGF</i>	ACTGGACTAAACTTCAGCATTCC	GGGCAGCTATT GGTGCAGTA



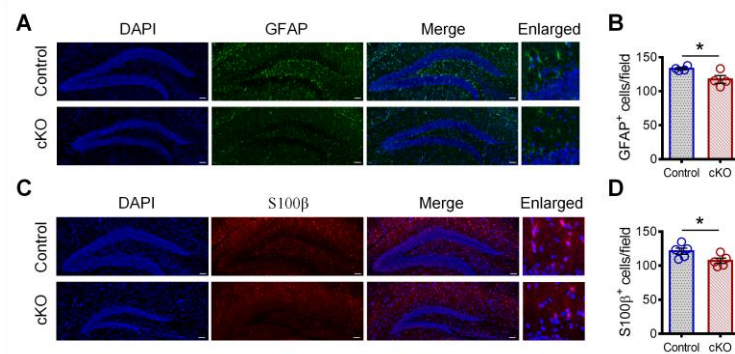
**Figure S1. Genotyping and behavioral tests of *Hamp<sup>GFAP</sup>* cKO and control mice.** **A** PCR amplification for identifying the bands of *Hamp<sup>lox/lox</sup>* (homozygote: one band at 201 bp; heterozygote: two bands at 201 bp and 142 bp; wildtype allele: one band at 142 bp) and GFAP-Cre (with cre: 700 bp; wildtype: no band). **B-E** In the Morris water maze test, the escape latency (**B**) and distance (**C**) during the training stage, and the percentage of time spent in the target quadrant (**D**) and number of times crossing the platform (**E**) of the 6-month-old *Hamp<sup>GFAP</sup>* cKO and control mice were analyzed. **F-I** In the elevated plus maze test, the percentages of time (**F**) and distance (**G**) spent in the open zone, and the percentages of time (**H**) and distance (**I**) in the center area of the 3-month-old *Hamp<sup>GFAP</sup>* cKO and control mice were analyzed. Data were expressed as mean  $\pm$  SEM,  $n = 6$  per group. \* $p < 0.05$  and \*\* $p < 0.01$ .



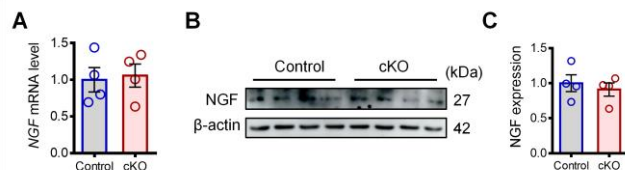
**Figure S2. Body weights and the Nissl staining results of the *Hamp<sup>GFAP</sup>* cKO and control mice.** **A-C** The body weights of 3-month-old (**A**,  $n = 6$ ), 6-month-old (**B**,  $n = 7$ ), and 14-day-old (**C**,  $n = 7$  and 5) *Hamp<sup>GFAP</sup>* cKO and control mice were determined. **D-E** Representative Nissl staining images (**D**) and quantification (**E**) in the 3-month-old *Hamp<sup>GFAP</sup>* cKO and control mice ( $n = 3$ ). Data were expressed as mean  $\pm$  SEM. \*\*\* $p < 0.001$ .



**Figure S3. Detection of apoptosis and ferroptosis levels in the hippocampus of *Hamp<sup>GFAP</sup>* cKO and control mice.** A-B TUNEL staining (A) and cleaved Caspase-3 immunostaining (B) for detecting apoptotic cells in the hippocampal DG of 3-month-old *Hamp<sup>GFAP</sup>* cKO and control mice (scale bar: 50  $\mu$ m). C-D Western blot images (C) and quantification (D) of GPx4 and ACSL4 expression levels in the hippocampus of 3-month-old *Hamp<sup>GFAP</sup>* cKO and control mice ( $n = 4$  per group, GAPDH and  $\beta$ -actin as the internal reference). Data were expressed as mean  $\pm$  SEM.



**Figure S4. Immunostaining for astrocytes in the hippocampus of *Hamp<sup>GFAP</sup>* cKO and control mice.** A-B Representative immunostaining images for GFAP (A) and quantification (B) in the hippocampal DG of 3-month-old *Hamp<sup>GFAP</sup>* cKO and control mice (scale bar: 50  $\mu$ m,  $n = 4$  per group). C-D Representative immunostaining images for S100 $\beta$  (C) and quantification (D) in the hippocampal DG of 14-day-old *Hamp<sup>GFAP</sup>* cKO and control mice (scale bar: 50  $\mu$ m,  $n = 5$  per group). Data were expressed as mean  $\pm$  SEM. \* $p < 0.05$ .



**Figure S5. Detection of *NGF* mRNA and protein levels in the hippocampus of *Hamp<sup>GFAP</sup>* cKO and control mice.** A qRT-PCR results of *NGF* expression in the hippocampus of 3-month-old *Hamp<sup>GFAP</sup>* cKO and control mice ( $n = 4$  per group). B-C Western blot images (B) and quantification (C) of *NGF* expression levels in the hippocampus of 3-month-old *Hamp<sup>GFAP</sup>* cKO and control mice ( $n = 4$  per group;  $\beta$ -actin as the internal reference). Data were expressed as mean  $\pm$  SEM.