

Supplementary Materials

Fig. S1. Numbers of NeuN-positive cells and doublecortin (DCX)-positive cells in the hippocampal DG region.

Fig. S2. The role of CXCR7 in regulating mIPSCs in dentate GCs in the epilepsy model.

Fig. S3. The role of CXCR7 in regulating the AMPAR-mediated synaptic currents in dentate GCs in the mouse model of epilepsy.

Fig. S4. Schematic showing the design of the experiment for determining the effects of SL327 on the levels of phosphorylated ERK1/2, NR2A expression and NR2A-mediated synaptic events in response to the altered expression of CXCR7 in the mouse model of KA-induced epilepsy.

Fig. S5. The expression levels of CXCR4, CXCL11, and CXCL12 in the hippocampus of the KA-induced epilepsy mouse model and in the brain tissues of patients with TLE.

Fig. S6. The possible role of CXCR7 in regulating the levels of phosphorylated PLC- γ 1, PI3K, Akt, and STAT3.

Fig. S7. NMDAR-mEPSC recordings of brain slices from the control and KA-induced epilepsy groups in the absence or presence of pertussis toxin (PT, a G-protein blocker, 1 μ g/mL in a recording pipette).

Table S1. Clinical characteristics of TLE patients.

Table S2. Clinical characteristics of control patients.

Table S3. P values of Figure 6 (D, E, and G) and Figure 7B.

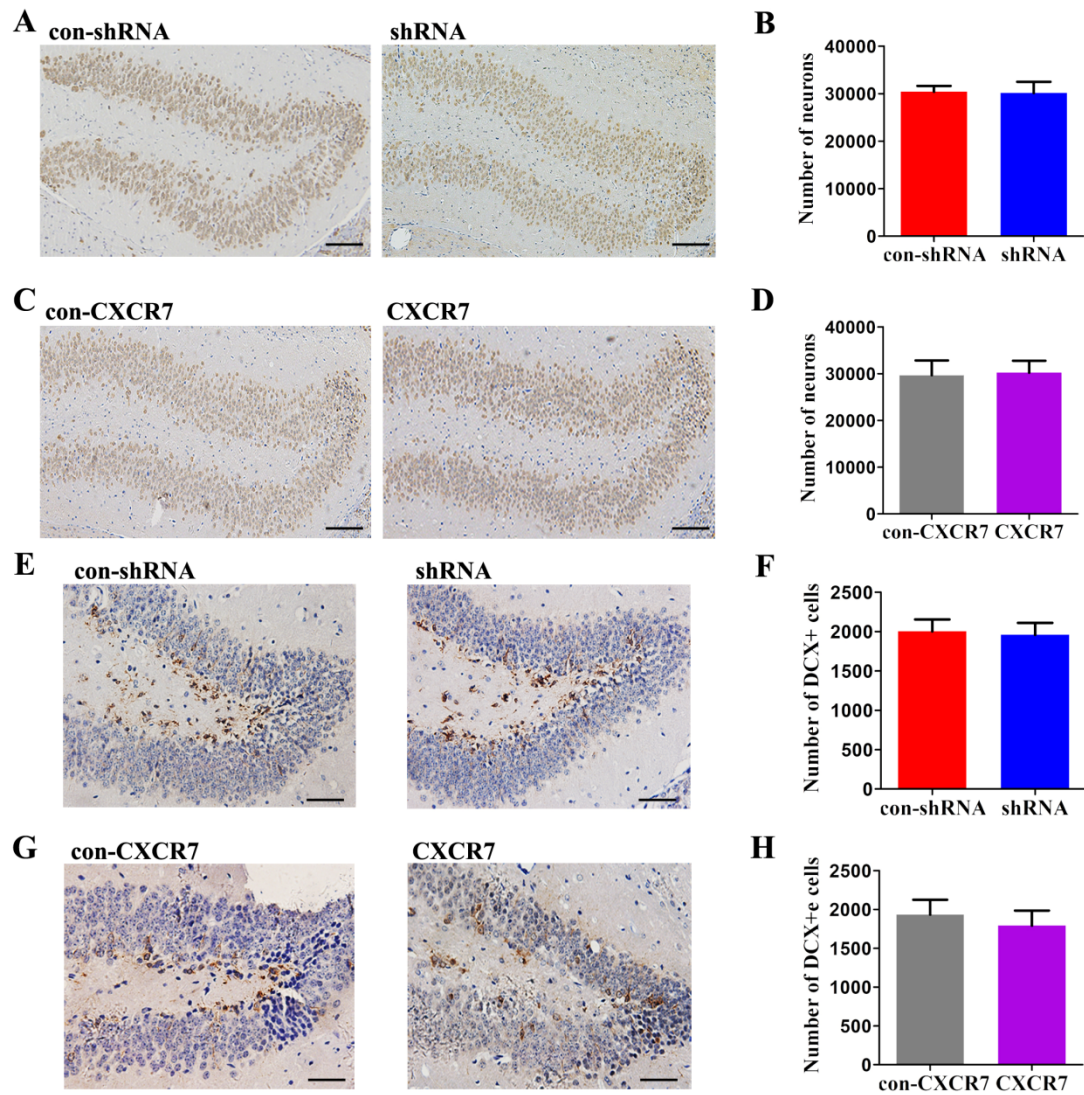


Fig. S1. Numbers of NeuN-positive cells and doublecortin (DCX)-positive cells in the hippocampal DG region. (A-D) NeuN-positive cells: (A) representative images of NeuN-positive cells (brown staining) in the DG region of the con-shRNA and shRNA groups (scale bar = 100 μ m), and (B) corresponding quantitative analyses of the number of NeuN-positive cells; (C) representative images of NeuN-positive cells in the DG region of con-CXCR7 group and CXCR7 group (scale bar = 100 μ m), and (D) corresponding quantitative analyses of the number of NeuN-positive cells (n = 4 per group). (E-H) DCX-positive cells: (E) representative images of DCX-positive cells

(brown staining) in the DG region of the con-shRNA and shRNA groups (scale bar = 50 μ m), and (F) corresponding quantitative analyses of the number of DCX-positive cells; (G) representative images of DCX-positive cells in the DG region of the con-CXCR7 and CXCR7 groups (scale bar = 50 μ m), and (H) corresponding quantitative analyses of the number of DCX-positive cells (n = 4 per group). Student's t-test.

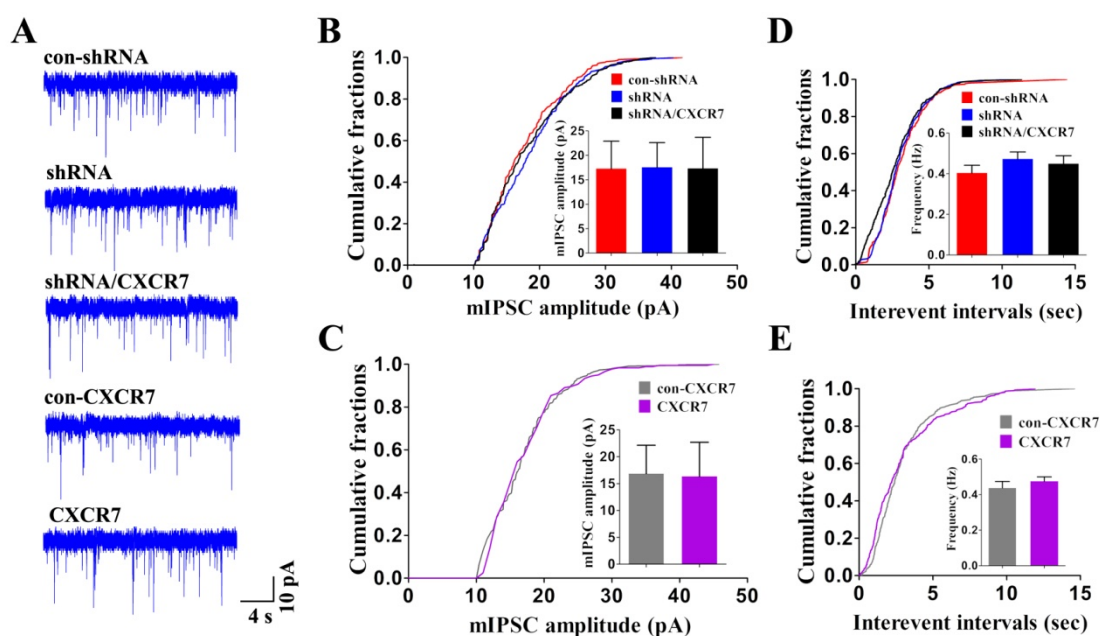


Fig. S2. The role of CXCR7 in regulating mIPSCs in dentate GCs in the epilepsy model. (A) Representative images of mIPSCs in each group and statistical analyses of the amplitude (B) and frequency (D) of the mIPSCs in the con-shRNA, shRNA, and shRNA/CXCR7 groups (n = 5 per group). Statistical analyses of the amplitude (C) and frequency (E) of the mIPSCs in the con-CXCR7 and CXCR7 groups are also shown (n = 5 per group). One-way ANOVA with a post hoc Bonferroni test for column data; Kolmogorov–Smirnov test for cumulative fraction data.

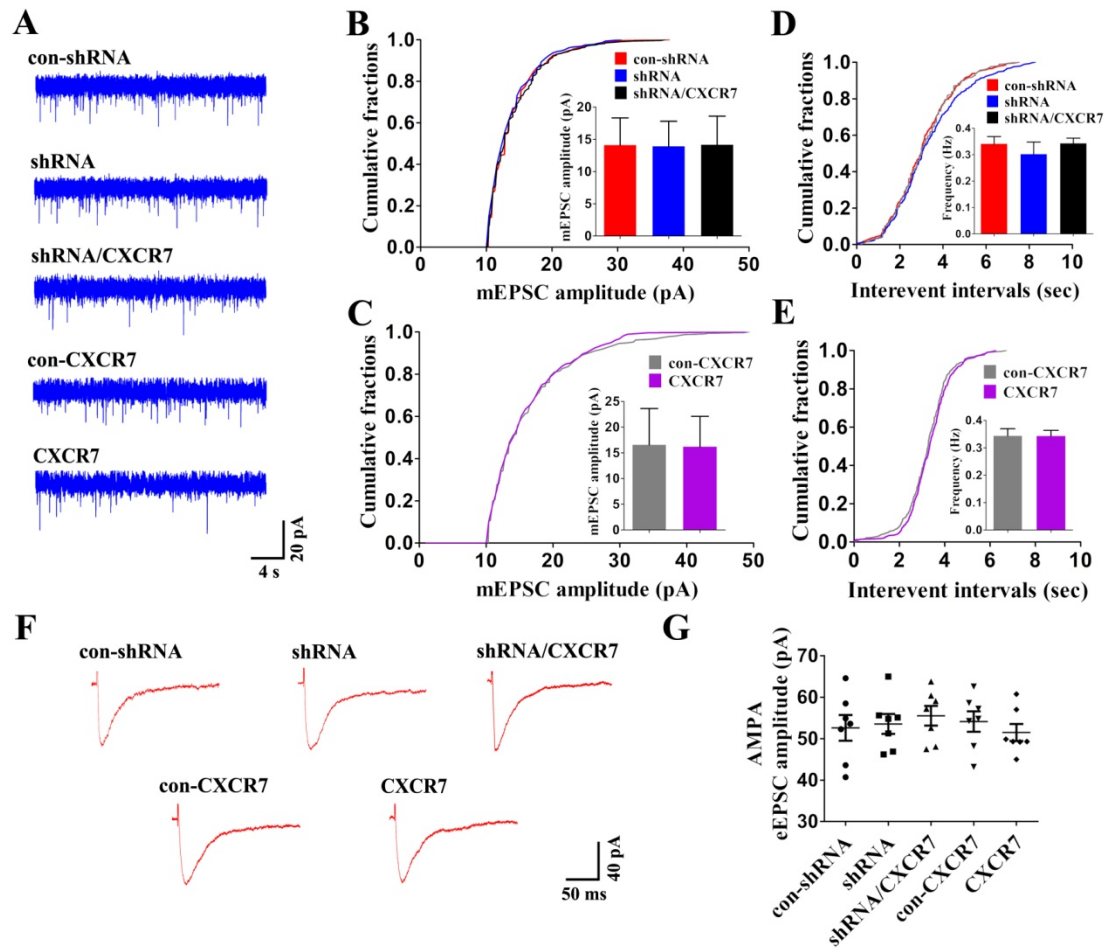


Fig. S3. The role of CXCR7 in regulating the AMPAR-mediated synaptic currents in dentate GCs in the mouse model of epilepsy. AMPAR-mEPSCs: (A) representative images of AMPAR-mEPSCs in each group and statistical analyses of the amplitude (B) and frequency (D) of AMPAR-mEPSCs in the con-shRNA, shRNA, and shRNA/CXCR7 groups. Statistical analyses of the amplitude (C) and frequency (E) of AMPAR-mEPSCs in the con-CXCR7 and CXCR7 groups are also shown ($n = 5$ per group). (F) AMPAR-eEPSCs: representative images of AMPAR-eEPSCs in each group and (G) statistical analyses of the amplitude of AMPAR-eEPSCs ($n = 7$ per group). One-way ANOVA with a post hoc Bonferroni test for column data;

Kolmogorov–Smirnov test for cumulative fraction data.

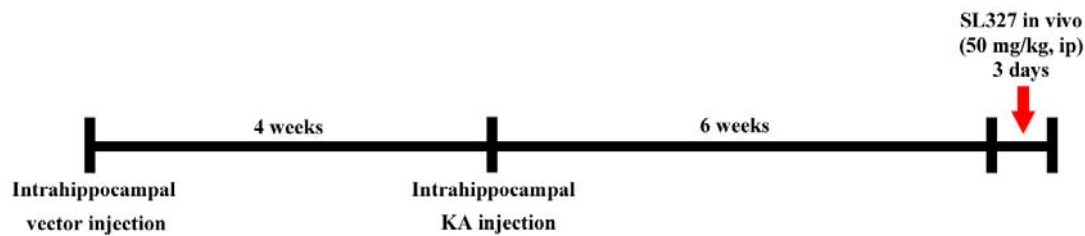


Fig. S4. Schematic showing the design of the experiment for determining the effects of SL327 on the levels of phosphorylated ERK1/2, NR2A expression and NR2A-mediated synaptic events in response to the altered expression of CXCR7 in the mouse model of KA-induced epilepsy.

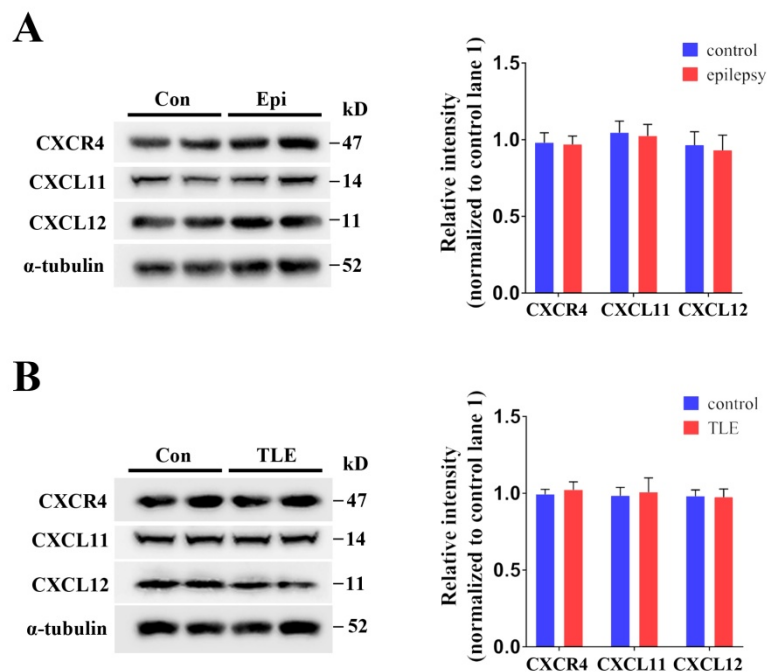


Fig. S5. The expression levels of CXCR4, CXCL11, and CXCL12 in the hippocampus of the mouse model with KA-induced epilepsy and in the brain tissues

of patients with TLE. (A) Representative images of western blotting analyses of the hippocampus from mice subjected to the KA-induced epilepsy model and the corresponding statistical analysis (n = 5 per group). (B) Representative images of western blotting analyses of brain tissues from patients with TLE and the corresponding statistical analysis (n = 6 per group). Student's t-test was used in the statistical analyses.

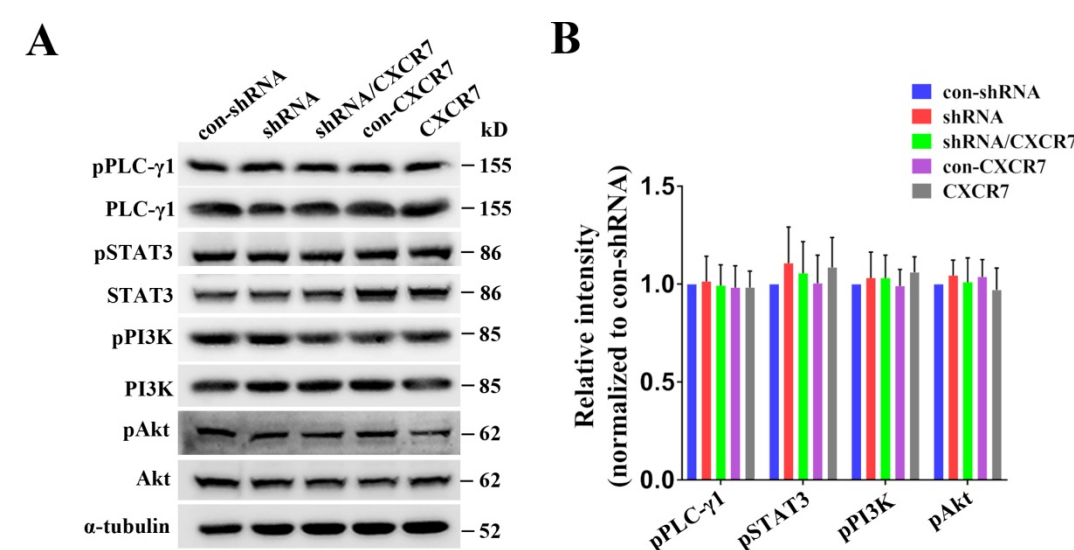


Fig. S6. The possible role of CXCR7 in regulating the levels of phosphorylated PLC- γ 1, PI3K, Akt, and STAT3 (A-B). (A) Representative images of western blotting analyses and (B) the corresponding statistical analysis (n = 5 per group). One-way ANOVA with a post hoc Bonferroni test.

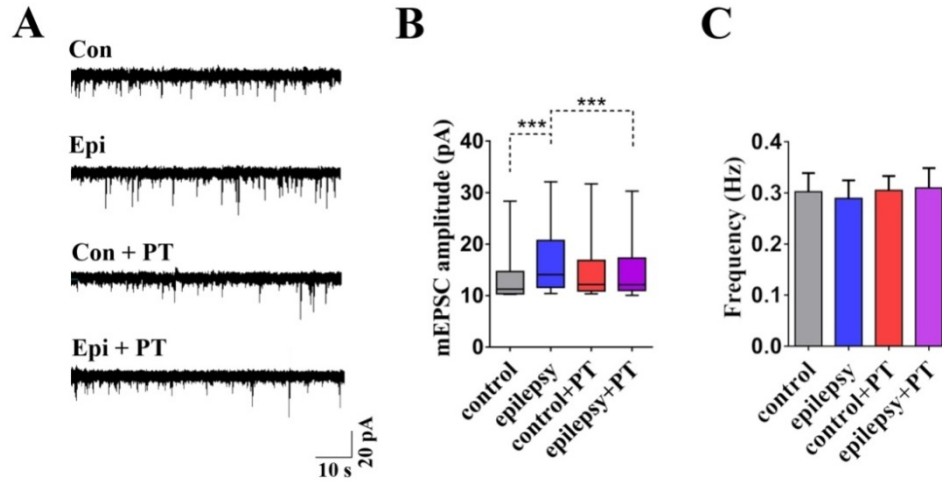


Fig. S7. NMDAR-mEPSC recordings of brain slices from the control and KA-induced epilepsy groups in the absence or presence of pertussis toxin (PT, a G-protein blocker, 1 μ g/mL in a recording pipette) (A-C). (A) Representative images of NMDAR-mEPSCs in each group; statistical analyses of the amplitude (B) and frequency (C) of the NMDAR-mEPSCs in the control group, epilepsy group (KA-induced mouse model of epilepsy), control + PT group, and epilepsy + PT group ($n = 6$ per group). The amplitude of NMDAR-mEPSCs in the epilepsy group was significantly higher than that in the control group ($p < 0.001$); the amplitude of NMDAR-mEPSCs in the epilepsy + PT group was lower than that in the epilepsy group ($p < 0.001$); and there was no significant difference in the amplitude of NMDAR-mEPSCs between the control + PT group and the epilepsy + PT group. Kruskal-Wallis one-way ANOVA test was used in the statistical analyses of the amplitude, *** $p < 0.001$; one-way ANOVA with a post hoc Bonferroni test was used in the statistical analyses of the frequency.

Table S1. Clinical characteristics of TLE patients

No	Sex	Age at surgery (years)	Course (years)	AEDs before surgery	Resected tissue	Pathologic result
1	M	29	4	CBZ, VPA, CLZ	LTN	G, NL
2	M	27	4	CBZ, VPA, PHT	LTN	G, NL
3	M	29	16	CBZ, VPA, TPM	RTN	G, NL, ND
4	M	39	7	CBZ, PHT, VPA	RTN	G, NL, ND
5	F	22	11	OXC, VPA, TPM	RTN	G, NL, ND
6	M	23	6	CBZ, PHT, TPM	RTN	G, NL
7	F	35	17	CBZ, VPA, CLZ, TPM	LTN	G, NL, ND
8	F	25	8	VPA, CBZ, PHT	LTN	G, NL
9	F	18	6	OXC, VPA, LTG	LTN	G, NL

F: female, M: male, AEDs: anti-epileptic drugs, CBZ: carbamazepine, VPA: valproic acid, PHT: phenytoin, CLZ: clonazepam, LTG: lamotrigine, OXC: oxcarbazepine, TPM: topiramate, LTN: left temporal neocortex, RTN: right temporal neocortex, G: gliosis, NL: neuronal loss, ND: neuronal degeneration.

Table S2. Clinical characteristics of control patients

No.	Sex	Age	Disease diagnosis	Resected tissue	Pathologic result
1	M	49	Brain trauma	RTN	Normal
2	F	31	Brain trauma	RTN	Normal
3	F	22	Brain trauma	LTN	Normal
4	M	17	Brain trauma	RTN	Normal
5	M	23	Brain trauma	LTN	Normal
6	F	21	Brain trauma	RTN	Normal
7	M	28	Brain trauma	LTN	Normal
8	F	15	Brain trauma	LTN	Normal
9	F	31	Brain trauma	RTN	Normal

F: female, M: male, LTN: left temporal neocortex, RTN: right temporal neocortex.

Table S3. P values of Figure 6 (D, E, and G) and Figure 7B in main text.

*Comparisons	p-value p-ERK1	of p-ERK2	of p-value membrane NR2A	of p-value NR2A eEPSCs
shRNA compared with con-shRNA	< 0.001	< 0.001	< 0.001	< 0.001
shRNA/CXCR7 compared with shRNA	0.017	0.036	0.032	0.006
CXCR7 compared with con-CXCR7	< 0.001	< 0.001	< 0.001	< 0.001
con-shRNA/Vehicle compared with con-shRNA/SL327	< 0.001	< 0.001	< 0.001	< 0.001
shRNA/CXCR7/Vehicle compared with shRNA/CXCR7/SL327	< 0.001	0.006	0.046	0.005
con-CXCR7/Vehicle compared with con-CXCR7/SL327	< 0.001	< 0.001	< 0.001	< 0.001
CXCR7/Vehicle compared with CXCR7/SL327	< 0.001	< 0.001	< 0.001	< 0.001

*Statistical analysis with two-way ANOVA with a post hoc Bonferroni test.