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Supplementary Materials for

GPR40 modulates epileptic seizure and NMDA receptor function

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This PDF file includes:

Supplementary Materials

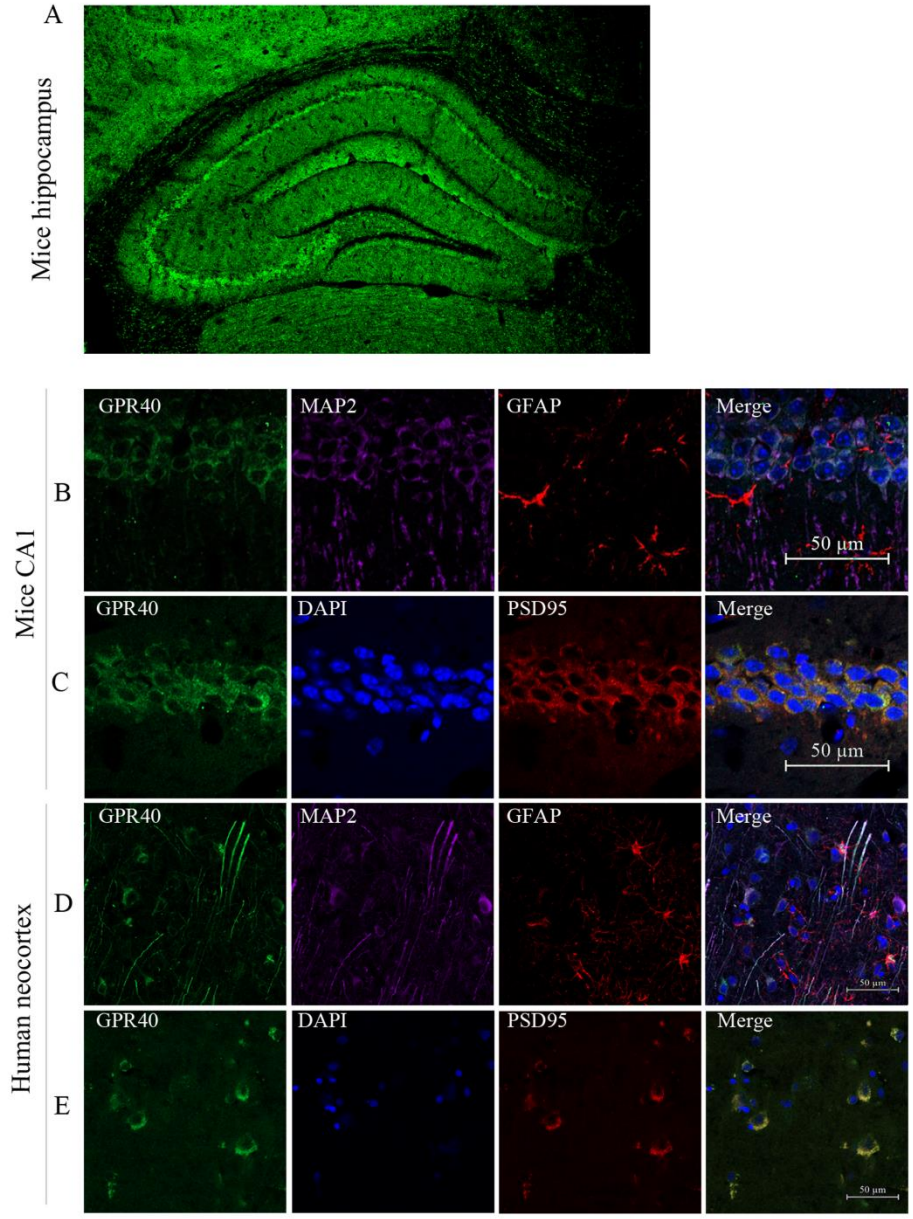

Fig. S1. Immunofluorescent labeling of GPR40 in nonepileptic brain tissues. (A) GPR40 localization in the hippocampus. **(B and C)** In hippocampal tissue from healthy mice, GPR40 colocalized with Map2 and with PSD95 but not with GFAP. **(D and E)** In the temporal neocortices from non-epileptic patients, GPR40 colocalized with Map2 and with PSD95 but not with GFAP (scale bar=50 µm).

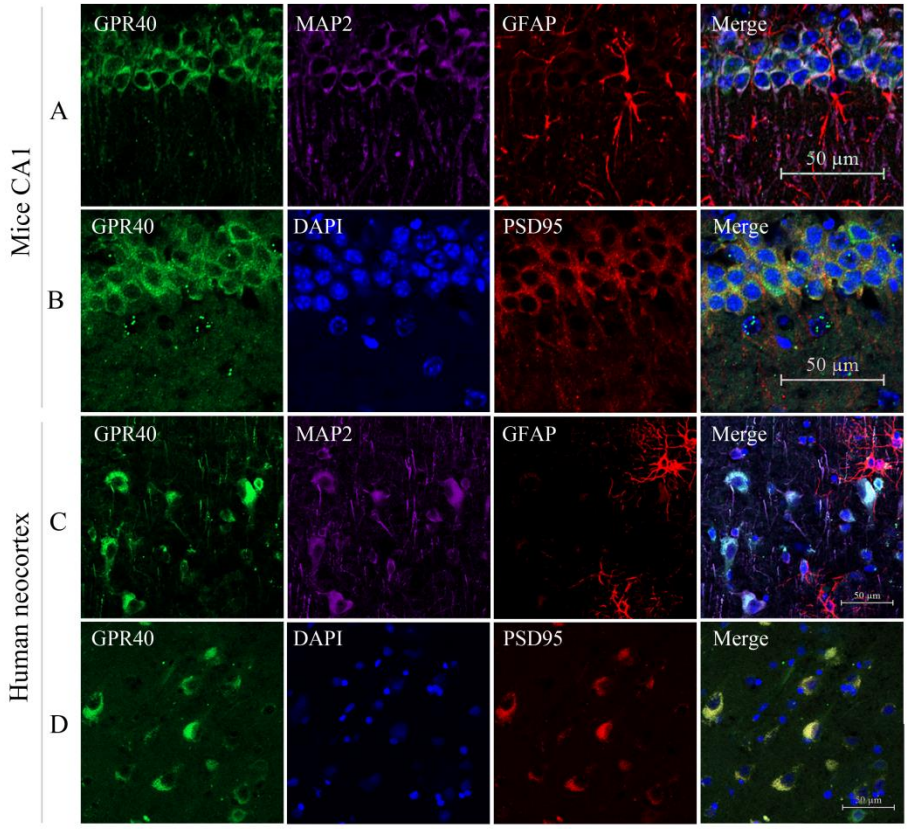

Fig. S2. Immunofluorescent labeling of GPR40 in epileptic tissues. (A and B) In hippocampal tissue from a mouse TLE model, GPR40 colocalized with Map2 and with PSD95 but not with GFAP. **(C and D)** In the temporal neocortices from TLE patients, GPR40 colocalized with Map2 and with PSD95 but not with GFAP (scale bar=50 µm).

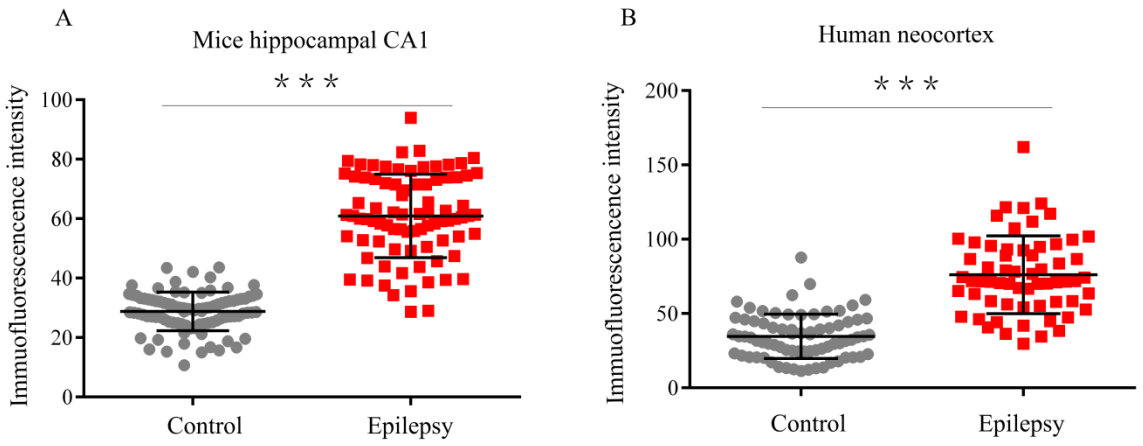

Fig. S3. Immunofluorescence intensity of GPR40 in epileptic and nonepileptic brain tissues. (A) GPR40 immunoreactivity was increased in the hippocampal CA1 region of mice from the KA-induced model compared with controls (Control n=93, Epilepsy n=73). **(B)** GPR40 immunoreactivity was increased in the neocortex of TLE patients compared with non-epileptic controls (Control n=74, Epilepsy n=62). Data are shown as the means ± s.e.m.; Student's t-test, ***p < 0.001.

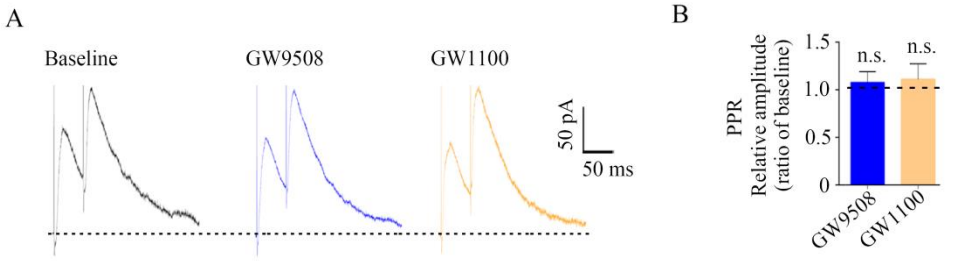

Fig. S4. GPR40 has no effect on PPR for NMDA-mediated EPSCs. (A and B) Representative traces of the PPR for NMDA-mediated EPSCs and summary of the PPR among the groups. For the analysis, n=6 in each group. The effect of each treatment was normalized to the baseline; error bars represent the mean ± s.e.m.; n.s., not significant, paired t-test.

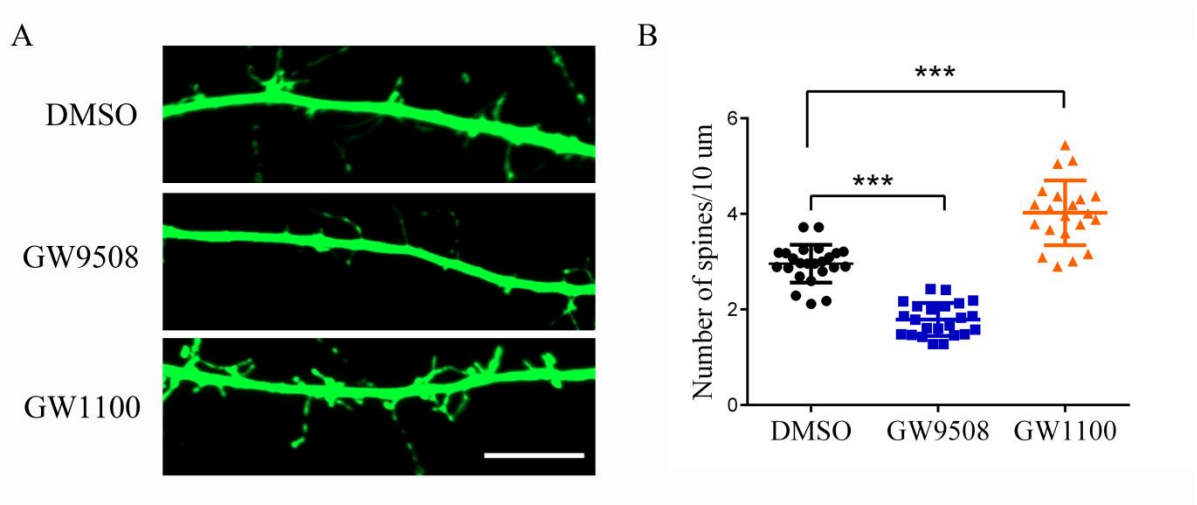

Fig. S5. GPR40 regulates spine density. (A) Representative confocal images showing the spine density on cultured hippocampal neurons after treatment with 0.1% DMSO, GW9508 (20 μM) or GW1100 (20 μM), scale bar = 10 μm. **(B)** The summarized result of the spine density (DMSO n=24, GW9508 n=23, GW1100 n=21, one-way ANOVA followed by Tukey's test, ***$p < 0.001$).

Table S1. Clinical characteristics of epileptic patients in this study.

Case	Gender/Age (years)	Course (years)	AEDs before surgery	Resection tissue	Neuropathological diagnosis
EP 1	M/25	11	PB, VPA, LTG	RTN	G, NL
EP 2	F/30	11	VPA, PB, PHT, TPM	LTN	G, NL
EP 3	M/18	15	PHT, PB, CBZ, VPA	RTN	G
EP 4	M/22	18	VPA, CBZ, PHT	LTN	NL, G
EP 5	F/26	7	CBZ, VPA, TPM	LTN	G
EP 6	F/36	10	PB, CBZ, VPA, OXC	RTN	NL, G
EP 7	F/12	5	CBZ, TPM, LTG,	LTN	NL, G
EP 8	F/21	8	TPM, VPA, CBZ	LTN	G
EP 9	F/23	6	TPM, CBZ, VPA	RTN	G
EP 10	F/20	7	VPA, OXC, PB	RTN	NL, G
EP 11	M/9	6	CBZ, PB, LTG	LTN	NL
EP 12	F/33	15	OXC, CBZ, TPM, PB	LTN	NL, G
EP 13	F/14	5	CBZ, LTG, TPM,	RTN	NL,
EP 14	F/18	13	CBZ, VPA, TPM	LTN	NL, G
EP 15	F/25	14	VPA, CBZ, LTG	LTN	NL
EP 16	F/24	6	CBZ, VPA, TPM	LTN	G
EP 17	M/20	7	VPA, TPM, PB	RTN	G, NL
EP 18	F/14	9	VPA, CBZ, PB	RTN	NL, G
EP 19	M/21	6	CBZ, VPA, TPM, PHT	RTN	NL
EP 20	M/39	10	CBZ, VPA, TPM	LTN	NL, G

EP=epilepsy patients; C=control; F=female; M=male; AEDs=antiepileptic drugs; CBZ=carbamazepine; VPA=valproate; TPM= topiramate; PHT=phenytoin; PB=phenobarbital; LTG=lamotrigine; OXC=oxcarbazepine; LTN=left temporal neocortex; RTN=right temporal neocortex; G=gliosis; NL=neuron loss.

Table S2. Clinical characteristics of control individuals with brain trauma.

Case	Gender/Age (years)	Mechanism of injury	GCS score	Time to surgical intervention (hours)	Resection tissue	Neuropathological diagnosis
TBI 1	M/11	MVA	7	15	LTN	N
TBI 2	F/38	Fall	7	20	LTN	N
TBI 3	M/40	MVA	5	15	LTN	N
TBI 4	F/34	Stumble	8	17	LTN	N
TBI 5	M/30	MVA	6	11	RTN	N
TBI 6	F/17	MVA	7	18	RTN	N
TBI 7	M/11	MVA	9	22	RTN	N
TBI 8	M/25	MVA	5	12	RTN	N
TBI 9	F/8	Stumble	6	15	LTN	N
TBI 10	M/20	MVA	7	19	RTN	N

TBI= traumatic brain injury; F=female; M=male; MVA=motor vehicle accident; GCS= Glasgow Coma Scale; LTN=left temporal neocortex; RTN=right temporal neocortex; N=relative normal.