UCC

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Coláiste na hOllscoile Corcaigh

Supplementary Table 2. Transgenic mice were used in this study.

Mice	Source and References
Eif2a$^{A/A}$*fTg*$^{+}$	Randal J. Kaufman[15]
Camk2α-Cre^{+}	Jackson stock no. 005359[42]
Gad2-Cre^{+}	Jackson stock no. 010802[43]
Pvalb-Cre^{+}	Jackson stock no. 008069[44]
Sst-Cre^{+}	Jackson stock no. 013044[43]
Eif2a$^{A/A}$*fTg*$^{+}$*Camk2α*-Cre^{+}	This study (see methods)
Eif2a$^{A/A}$*fTg*$^{+}$*Gad2*-Cre^{+}	This study (see methods)
Eif2a$^{A/A}$*fTg*$^{+}$*Pvalb*-Cre^{+}	This study (see methods)
Eif2a$^{A/A}$*fTg*$^{+}$*Sst*-Cre^{+}	This study (see methods)

Supplementary Table 3. a, b) Primary and secondary antibodies used in this study. All antibodies were applied in blocking buffer. All antibodies were diluted in PBS.

a) Primary antibodies

Target	Target	Dilution	Source-Cat #	Lot #	Method
eIF2α (D7D3) XP	Rabbit	1:500	Cell Signaling-5324S	5	IFC
p-eIF2α (S51)	Rabbit	1:500	Abcam-Ab32157	GR319440-11 GR319440-13	IFC
Camk2α (Cba-2)	Mouse	1:1000	Invitrogen-13-730	RA230420	IFC
PAB Camk2α	Goat	1:1000	Abcam- AB87597	GR69112-22	IFC
GAD67	Mouse	1:1000	Millipore-MAB5406	2844575	IFC
Parvalbumin	Mouse	1:1000	Sigma- P3088	016M4847V	IFC
Parvalbumin	Guinea pig	1:300	Synaptic system-195004	2-23	IFC
Somatostatin	Rat	1:100	Millipore- MAB354	3018725	IFC
Puromycin	Mouse	1:500	Kerafest-EQ0001	041416	IFC
Anti-HA-Epitope Tag	Mouse	1:1000	Biolegend-901513	B-274467	IFC, IP

b) Secondary antibodies

Target	Target	Dilution	Source-Cat #	Lot #	Method
Alexa-488	Mouse	1:400	Invitrogen-A11001	1170048	IFC
Alexa-488	Rabbit	1:400	Invitrogen-A11034	1971418	IFC
Alexa-546	Mouse	1:400	Invitrogen-A11030	1904466	IFC
Alexa-546	Rabbit	1:400	Invitrogen-A11035	1904467	IFC
Alexa Fluor 555 Alkyne	-	1:1000	Invitrogen-A20013	2126710	IFC
Alexa-647	Rat	1:400	Invitrogen-A21247	2043368	IFC
Alexa-647	Guinea Pig	1:400	Invitrogen-A21450	1979376	IFC

Supplementary Table 4. Details of statistical analyses.

Figure and # of animals or cells used	Statistical analysis, p-value summary, and $F_{(DFn, DFd)}$	Post hoc tests
Figure 1c 1. *Camk2α*-Cre^{+} ($n = 13$) 2. $Eif2a^{A/A}fTg^{+}$($n = 17$) 3. *Eif2α* $cKI^{Camk2\alpha}$ ($n = 18$)	One-way ANOVA Differences between genotypes (****, $p = 1 \times 10^{-13}$) "$F_{(2, 45)} = 493.75$"	Tukey's multiple comparisons test p-eIF2α/t-eIF2α ratio 1. *Camk2α*-Cre^{+} vs. $Eif2a^{A/A}fTg^{+}$(ns, $p = 0.7812$) 2. *Camk2α*-Cre^{+} vs. *Eif2α* $cKI^{Camk2\alpha}$ (****, $p < 10^{-4}$) 3. $Eif2a^{A/A}fTg^{+}$ vs. *Eif2α* $cKI^{Camk2\alpha}$ (****, $p < 10^{-4}$)
Figure 1e 1. *Camk2α*-Cre^{+} ($n = 7$) 2. $Eif2a^{A/A}fTg^{+}$ ($n = 8$) 3. *Eif2α* $cKI^{Camk2\alpha}$ ($n = 8$)	Two-way ANOVA (alpha 0.05) Interaction (***, $p = 7.2 \times 10^{-4}$) "$F_{(2, 40)} = 8.72$" Naive and 24 h (****, $p < 10^{-5}$) "$F_{(1, 40)} = 226.8$" Genotype effect (***, $p = 7.5 \times 10^{-4}$) "$F_{(2, 40)} = 8.66$"	Tukey's multiple comparisons test 24 h 1. *Camk2α*-Cre^{+} vs. $Eif2a^{A/A}fTg^{+}$ (ns, $p = 0.98$) 2. *Camk2α*-Cre^{+} vs. *Eif2α* $cKI^{Camk2\alpha}$ (****, $p = 5.6 \times 10^{-5}$) 3. $Eif2a^{A/A}fTg^{+}$ vs. *Eif2α* $cKI^{Camk2\alpha}$ (****, $p = 1.6 \times 10^{-5}$)
Figure 1f 1. *Camk2α*-Cre^{+} ($n = 7$) 2. $Eif2a^{A/A}fTg^{+}$ ($n = 8$) 3. *Eif2α* $cKI^{Camk2\alpha}$ ($n = 8$)	Two-way ANOVA (alpha 0.05) Interaction (***, $p = 1.1 \times 10^{-4}$) "$F_{(2, 40)} = 11.55$" Pre-CS and 24 h CS (****, $p < 10^{-5}$) "$F_{(1, 40)} = 249.6$" Genotype effect (****, $p = 4.1 \times 10^{-8}$)"$F_{(2, 40)} = 26.81$"	Tukey's multiple comparisons test 24 h CS 1. *Camk2α*-Cre^{+} vs. $Eif2a^{A/A}fTg^{+}$ (ns, $p = 0.67$) 2. *Camk2α*-Cre^{+} vs. *Eif2α* $cKI^{Camk2\alpha}$ (****, $p < 10^{-5}$) 3. $Eif2a^{A/A}fTg^{+}$vs. *Eif2α* $cKI^{Camk2\alpha}$ (****, $p < 10^{-5}$)
Figure 1g, h (E-LTP); **Extended Data Figure 3m** 1. AAV9.*Camk2α*.eGFP (*Camk2α*-eGFP) • Baseline ($n = 8$) • 30 min ($n = 8$) • 180 min ($n = 8$) 2. AAV9.*Camk2α*.Cre (*Camk2α*-Cre) • Baseline ($n = 8$) • 30 min ($n = 8$) • 180 min ($n = 8$)	Two-way RM ANOVA Time × Genotype effect (*, $p = 0.013$) "$F_{(2, 28)} = 5.1$" Time (****, $p < 10^{-4}$) "$F_{(2, 28)} = 42.15$" Genotype effect (**, $p = 6.2 \times 10^{-3}$) "$F_{(1, 14)} = 10.36$" Two-way RM ANOVA Time × Genotype effect (*, $p = 0.016$) "$F_{(2, 14)} = 5.65$" Time (****, $p < 10^{-4}$) "$F_{(2, 14)} = 38.2$" Genotype effect (*, $p = 0.024$) "$F_{(1, 7)} = 8.2$"	Tukey's multiple comparisons tests AAV9.*Camk2α*.eGFP 1. Baseline vs. 30 min (***, $p = 3 \times 10^{-4}$) 2. Baseline vs. 180 min (ns, $p = 0.3029$) 3. 30 min vs. 180 min (*, $p = 0.0134$) AAV9.*Camk2α*.Cre 1. Baseline vs. 30 min (****, $p < 10^{-4}$) 2. Baseline vs. 180 min (****, $p < 10^{-4}$) 3. 30 min vs. 180 min (*, $p = 0.0159$) Sidak's multiple comparisons test AAV9.*Camk2α*.eGFP vs AAV9.*Camk2α*.Cre 1. Baseline (ns, $p = 0.99$) 2. 30 min (**, $p = 4.6 \times 10^{-3}$); Extended Data Figure 3m 3. 180 min (**, $p = 3.9 \times 10^{-3}$); Figure 1h
Figure 1k 1. AAV9.*Camk2α*.eGFP ($n = 8$) 2. AAV9.*Camk2α*.Cre ($n = 8$)	Kolmogorov–Smirnov test for inter-event intervals of mEPSCs (****, $p < 10^{-4}$) Kolmogorov-Smirnov D = 0.2938	
Figure 1k (inset) 1. AAV9.*Camk2α*.eGFP ($n = 8$) 2. AAV9.*Camk2α*.Cre ($n = 8$)	Unpaired t test with Welch's correction mEPSC Frequency $t_{7.59} = 3.2$, *, $p = 0.0135$	
Figure 1l 1. AAV9.*Camk2α*.eGFP ($n = 8$) 2. AAV9.*Camk2α*.Cre ($n = 7$)	Kolmogorov–Smirnov test for Amplitude of mEPSCs (****, $p < 10^{-4}$) Kolmogorov-Smirnov D = 0.4064	
Figure 1l (inset) 1. AAV9.*Camk2α*.eGFP ($n = 8$) 2. AAV9.*Camk2α*.Cre ($n = 7$)	Unpaired t test with Welch's correction mEPSC Amplitude $t_{12.19} = 3.64$, **, $p = 3.3 \times 10^{-3}$	
Figure 1n 1. AAV9.*Camk2α*.eGFP ($n = 9$) 2. AAV9.*Camk2α*.Cre ($n = 11$)	Kolmogorov–Smirnov test for inter-event intervals of mIPSCs (****, $p < 10^{-4}$) Kolmogorov-Smirnov D = 0.2333	
Figure 1n (inset) 1. AAV9.*Camk2α*.eGFP ($n = 9$) 2. AAV9.*Camk2α*.Cre ($n = 11$)	Unpaired t test with Welch's correction mIPSC Frequency $t_{16.71} = 2.22$, *, $p = 0.04$	
Figure 1o 1. AAV9.*Camk2α*.eGFP ($n = 9$) 2. AAV9.*Camk2α*.Cre ($n = 11$)	Kolmogorov–Smirnov test for Amplitude of mIPSCs (ns, $p = 0.073$) Kolmogorov-Smirnov D = 0.1294	
Figure 1o (inset) 1. AAV9.*Camk2α*.eGFP ($n = 9$) 2. AAV9.*Camk2α*.Cre ($n = 11$)	Unpaired t test with Welch's correction mIPSC Amplitude $t_{12.69} = 0.75$, ns, $p = 0.47$	
Figure 2b 1. *Sst*-Cre^{+} ($n = 4$) 2. *Eif2α* cKI^{Sst} ($n = 5$)	Unpaired t test with Welch's correction P-eIF2α/t-eIF2α ratio $t_{5.79} = 4.73$, **, $p = 3.6 \times 10^{-3}$	
Figure 2c 1. *Sst*-Cre^{+} ($n = 7$) 2. *Eif2α* cKI^{Sst} ($n = 9$)	Two-way ANOVA (alpha 0.05) Interaction (****, $p = 3.3 \times 10^{-5}$) "$F_{(1, 28)} = 24.41$" Naive and 24 h (****, $p < 10^{-5}$) "$F_{(1, 28)} = 264.6$" Genotype effect (***, $p = 1.5 \times 10^{-4}$) "$F_{(1, 28)} = 19.19$"	Sidak's multiple comparisons test 24 h 1. *Sst*-Cre^{+} vs. *Eif2α* cKI^{Sst} (****, $p < 10^{-5}$)
Figure 2d 1. *Sst*-Cre^{+} ($n = 7$) 2. *Eif2α* cKI^{Sst} ($n = 9$)	Two-way ANOVA (alpha 0.05) Interaction (*, $p = 0.024$) "$F_{(1, 28)} = 5.68$" Pre-CS and 24 h CS (****, $p < 10^{-4}$) "$F_{(1, 28)} = 204.6$" Genotype effect (*, $p = 0.014$) "$F_{(1, 28)} = 6.86$"	Sidak's multiple comparisons test 24 h 1. *Sst*-Cre^{+} vs. *Eif2α* cKI^{Sst} (**, $p = 2.9 \times 10^{-3}$)

Figure 2e, f (E-LTP); Extended Data Figure 7f 1. *Sst*-Cre$^+$ • Baseline ($n = 9$) • 30 min ($n = 9$) • 180 min ($n = 9$) 2. *Eif2α* cKI^{Sst} • Baseline ($n = 9$) • 30 min ($n = 9$) • 180 min ($n = 8$)	Mixed-effects model (REML) Time × Genotype effect (**, $p = 0.0089$) "$F_{(2, 31)} = 5.53$" Time (****, $p < 10^{-4}$) "$F_{(2, 31)} = 23.70$" Genotype effect (*, $p = 0.021$) "$F_{(1, 16)} = 6.54$" Mixed-effects model (REML) Time × Genotype effect (**, $p = 7.5 \times 10^{-3}$) "$F_{(2, 15)} = 6.9$" Time (****, $p < 10^{-4}$) "$F_{(2, 16)} = 19.68$" Genotype effect (*, $p = 0.0214$) "$F_{(1, 8)} = 8.134$"	Tukey's multiple comparisons tests *Sst*-Cre$^+$ 1. Baseline vs. 30 min (**, $p = 1.3 \times 10^{-3}$) 2. Baseline vs. 180 min (ns, $p = 0.99$) 3. 30 min vs. 180 min (**, $p = 1.8 \times 10^{-3}$) *Eif2α* cKI^{Sst} 1. Baseline vs. 30 min (****, $p < 10^{-4}$) 2. Baseline vs. 180 min (***, $p = 1 \times 10^{-4}$) 3. 30 min vs. 180 min (ns, $p = 0.65$) Sidak's multiple comparisons tests *Sst*-Cre$^+$ vs. *Eif2α* cKI^{Sst} 1. Baseline (ns, $p = 0.9998$) 2. 30 min (ns, $p = 0.2539$); Extended Data Figure 7f 3. 180 min (***, $p = 7 \times 10^{-4}$); Figure 2f
Figure 2i 1. *Sst*-Cre$^+$ ($n = 9$) 2. *Eif2α* cKI^{Sst} ($n = 7$)	Kolmogorov–Smirnov test for inter-event intervals of mEPSCs (ns, $p > 0.99$) Kolmogorov-Smirnov D = 0.031	
Figure 2i (Inset) 1. *Sst*-Cre$^+$ ($n = 9$) 2. *Eif2α* cKI^{Sst} ($n = 7$)	Unpaired t test with Welch's correction mEPSC Frequency $t_{11.85} = 0.05$, ns, $p = 0.96$	
Figure 2j 1. *Sst*-Cre$^+$ ($n = 9$) 2. *Eif2α* cKI^{Sst} ($n = 7$)	Kolmogorov–Smirnov test for Amplitude of mEPSCs (ns, $p = 0.25$) Kolmogorov-Smirnov D = 0.1143	
Figure 2j (Inset) 1. *Sst*-Cre$^+$ ($n = 9$) 2. *Eif2α* cKI^{Sst} ($n = 7$)	Unpaired t test with Welch's correction mEPSC Amplitude $t_{10.69} = 0.52$, ns, $p = 0.61$	
Figure 2l 1. *Sst*-Cre$^+$ ($n = 8$) 2. *Eif2α* cKI^{Sst} ($n = 8$)	Kolmogorov–Smirnov test for inter-event intervals of mIPSCs (ns, $p = 0.99$) Kolmogorov-Smirnov D = 0.05	
Figure 2l (Inset) 1. *Sst*-Cre$^+$ ($n = 8$) 2. *Eif2α* cKI^{Sst} ($n = 8$)	Unpaired t test with Welch's correction mIPSC Frequency $t_{13.57} = 0.98$, ns, $p = 0.34$	
Figure 2m 1. *Sst*-Cre$^+$ ($n = 8$) 2. *Eif2α* cKI^{Sst} ($n = 8$)	Kolmogorov–Smirnov test for Amplitude of mIPSCs (****, $p < 10^{-4}$) Kolmogorov-Smirnov D = 0.25	
Figure 2m (Inset) 1. *Sst*-Cre$^+$ ($n = 8$) 2. *Eif2α* cKI^{Sst} ($n = 8$)	Unpaired t test with Welch's correction mIPSC Amplitude $t_{14} = 3.14$, **, $p = 7.2 \times 10^{-3}$	
Figure 2p 1. *Sst*-Cre$^+$ (Saline) ($n = 7$) 2. *Sst*-Cre$^+$ (CNO) ($n = 8$) 3. *Eif2α* cKI^{Sst} (Saline) ($n = 6$) 4. *Eif2α* cKI^{Sst} (CNO) ($n = 8$)	Two-way ANOVA (alpha 0.05) Interaction (****. $p < 10^{-4}$) "$F_{(3, 50)} = 10.17$" 24 h Saline/CNO (****, $p < 10^{-4}$) "$F_{(1, 50)} = 543.5$" Genotype effect (****, $p < 10^{-4}$) "$F_{(3, 50)} = 13.7$"	Sidak's multiple comparisons test 24 h 1. *Sst*-Cre$^+$ (Saline) vs. *Sst*-Cre$^+$ (CNO) (*, $p = 0.037$) 2. *Sst*-Cre$^+$ (Saline) vs. eIF2α$^{A/A}$ cKI^{Sst} (Saline) (****, $p < 10^{-4}$) 3. eIF2α$^{A/A}$ cKI^{Sst} (Saline) vs. eIF2α$^{A/A}$ cKI^{Sst} (CNO) (***, $p = 2 \times 10^{-4}$)
Extended Data Figure 1c Excitatory neurons 1. Naïve ($n = 6$, mean 12 neurons) 2. 15 min post-FC ($n = 6$, mean 12 neurons)	Unpaired t test with Welch's correction, $t_{9.8} = 2.31$, *, $p = 0.044$	
Extended Data Figure 1d PVALB +ve neuron 1. Naïve ($n = 6$, mean 10-11 neurons) 2. 15 min post-FC ($n = 6$, mean 10-11 neurons)	Unpaired t test with Welch's correction, $t_{9.17} = 0.112$, ns, $p = 0.9129$	
Extended Data Figure 1e SST +ve neuron 1. Naïve ($n = 6$, mean 6-7 neurons) 2. 15 min post-FC ($n = 6$, mean 6-7 neurons)	Unpaired t test with Welch's correction, $t_{9.44} = 2.43$, *, $p = 0.037$	
Extended Data Figure 1k Excitatory neurons 1. Naïve ($n = 6$, mean 12 neurons) 2. 15 min post-FC ($n = 6$, mean 12 neurons)	Unpaired t test with Welch's correction, $t_{8.14} = 2.85$, *, $p = 0.021$	
Extended Data Figure 1l PVALB +ve neuron	Unpaired t test with Welch's correction, $t_{9.99} = 0.23$, ns, $p = 0.823$	

1. Naïve (n = 6, mean 6 neurons) 2. 15 min post-FC (n = 6, mean 6 neurons)		
Extended Data Figure 1m SST +ve neuron 1. Naïve (n = 6, mean 5 neurons) 2. 15 min post-FC (n = 6, mean 5 neurons)	Unpaired t test with Welch's correction, $t_{(9.09)} = 2.33$, *, $p = 0.044$	
Extended Data Figure 2c 1. *Camk2α*-Cre$^+$ (n = 8) 2. *Eif2a*$^{A/A}$*fTg*$^+$ (n = 7) 3. *Eif2α* cKI^{Camk2α} (n = 8)	Two-way ANOVA (alpha 0.05) Interaction (ns, $p = 0.31$) "$F_{(2, 40)} = 1.19$" Naive and 1 h (****, $p < 10^{-5}$) "$F_{(1, 40)} = 366.57$" Genotype effect (ns, $p = 0.39$) "$F_{(2, 40)} = 0.97$"	Tukey's multiple comparisons test 1 h 1. *Camk2α*-Cre$^+$ vs. *Eif2a*$^{A/A}$*fTg*$^+$ (ns, $p = 0.91$) 2. *Camk2α*-Cre$^+$ vs. *Eif2α* cKI^{Camk2α} (ns, $p = 0.27$) 3. *Eif2a*$^{A/A}$*fTg*$^+$ vs. *Eif2α* cKI^{Camk2α} (ns, $p = 0.14$)
Extended Data Figure 2d 1. *Camk2α*-Cre$^+$ (n = 8) 2. *Eif2a*$^{A/A}$*fTg*$^+$ (n = 8) 3. *Eif2α* cKI^{Camk2α} (n = 8)	Two-way ANOVA (alpha 0.05) Interaction (ns, $p = 0.86$) "$F_{(2, 42)} = 0.16$" Pre-CS and 1 h CS (****, $p < 10^{-5}$) "$F_{(1, 42)} = 186.3$" Genotype effect (ns, $p = 0.63$) "$F_{(2, 42)} = 0.46$"	Tukey's multiple comparisons test 1 h CS 1. *Camk2α*-Cre$^+$ vs. *Eif2a*$^{A/A}$*fTg*$^+$ (ns, $p = 0.99$) 2. *Camk2α*-Cre$^+$ vs. *Eif2α* cKI^{Camk2α} (ns, $p = 0.68$) 3. *Eif2a*$^{A/A}$*fTg*$^+$vs. *Eif2α* cKI^{Camk2α} (ns, $p = 0.60$)
Extended Data Figure 2g 1. AAV9.*Camk2α*.eGFP (n = 26) 2. AAV9.*Camk2α*.Cre (n = 27)	Unpaired t test with Welch's correction $t_{(50.43)} = 6.08$, ****, $p = 1.59 \times 10^{-7}$	
Extended Data Figure 2i 1. *Camk2α*-Cre$^+$ (n = 8) 2. *Eif2a*$^{A/A}$*fTg*$^+$ (n = 9) 3. *Eif2α* cKI^{Camk2α} (n = 8)	Two-way ANOVA (alpha 0.05) Interaction (***, $p = 4 \times 10^{-4}$) "$F_{(2, 44)} = 9.41$" Naive and 24 h (****, $p < 10^{-4}$) "$F_{(1, 44)} = 632.2$" Genotype effect (****, $p = 3.73 \times 10^{-5}$) "$F_{(2, 44)} =$ 12.97"	Tukey's multiple comparisons test 24 h 1. *Camk2α*-Cre$^+$ vs. *Eif2a*$^{A/A}$*fTg*$^+$ (ns, $p = 0.89$) 2. *Camk2α*-Cre$^+$ vs. *Eif2α* cKI^{Camk2α} (****, $p < 10^{-4}$) 3. *Eif2a*$^{A/A}$*fTg*$^+$ vs. *Eif2α* cKI^{Camk2α} (****, $p < 10^{-4}$)
Extended Data Figure 2j 1. *Camk2α*-Cre$^+$ (n = 8) 2. *Eif2a*$^{A/A}$*fTg*$^+$ (n = 8) 3. *Eif2α* cKI^{Camk2α} (n = 8)	Two-way ANOVA (alpha 0.05) Interaction (**, $p = 1.4 \times 10^{-3}$) "$F_{(2, 42)} = 7.74$" Pre-CS and 24 h CS (****, $p < 10^{-4}$) "$F_{(1, 42)} = 330.6$" Genotype effect (**, $p = 1.5 \times 10^{-3}$) "$F_{(2, 42)} = 7.64$"	Tukey's multiple comparisons test 24 h CS 1. *Camk2α*-Cre$^+$ vs. *Eif2a*$^{A/A}$*fTg*$^+$ (ns, $p = 0.72$) 2. *Camk2α*-Cre$^+$ vs. *Eif2α* cKI^{Camk2α} (****, $p < 10^{-4}$) 3. *Eif2a*$^{A/A}$*fTg*$^+$ vs. *Eif2α* cKI^{Camk2α} (***, $p = 3 \times 10^{-4}$)
Extended Data Figure 2k 1. *Camk2α*-Cre$^+$ (n = 10) 2. *Eif2a*$^{A/A}$*fTg*$^+$ (n = 10) 3. *Eif2α* cKI^{Camk2α} (n = 10)	Two-way ANOVA (alpha 0.05) Interaction (ns, $p = 0.59$) "$F_{(2, 54)} = 0.53$" Outer and Inner zone (****, $p < 10^{-5}$) "$F_{(1, 54)} = 200$" Genotype effect (ns, $p > 0.99$) "$F_{(2, 54)} = 5.6 \times 10^{-12}$"	Tukey's multiple comparisons test Outer 1. *Camk2α*-Cre$^+$ vs. *Eif2a*$^{A/A}$*fTg*$^+$ (ns, $p = 0.76$) 2. *Camk2α*-Cre$^+$ vs. *Eif2α* cKI^{Camk2α} (ns, $p = 0.98$) 3. *Eif2a*$^{A/A}$*fTg*$^+$ vs. *Eif2α* cKI^{Camk2α} (ns, $p = 0.86$) Inner 1. *Camk2α*-Cre$^+$ vs. *Eif2a*$^{A/A}$*fTg*$^+$ (ns, $p = 0.76$) 2. *Camk2α*-Cre$^+$ vs. *Eif2α* cKI^{Camk2α} (ns, $p = 0.98$) 3. *Eif2a*$^{A/A}$*fTg*$^+$ vs. *Eif2α* cKI^{Camk2α} (ns, $p = 0.86$)
Extended Data Figure 2l 1. *Camk2α*-Cre$^+$ (n = 10) 2. *Eif2a*$^{A/A}$*fTg*$^+$ (n = 10) 3. *Eif2α* cKI^{Camk2α} (n = 10)	One-way ANOVA Total distance (ns, $p = 0.83$) "$F_{(2, 27)} = 0.19$"	Tukey's multiple comparisons tests Total distance 1. *Camk2α*-Cre$^+$ vs. *Eif2a*$^{A/A}$*fTg*$^+$ (ns, $p = 0.87$) 2. *Camk2α*-Cre$^+$ vs. *Eif2α* cKI^{Camk2α} (ns, $p = 0.99$) 3. *Eif2a*$^{A/A}$*fTg*$^+$ vs. *Eif2α* cKI^{Camk2α} (ns, $p = 0.85$)
Extended Data Figure 3c 1. AAV9.*Camk2α*.eGFP (n = 7) 2. AAV9.*Camk2α*.Cre (n = 10)	Two-way ANOVA (alpha 0.05) Interaction (*, $p = 0.029$) "$F_{(1, 30)} = 5.27$" Naive and 24 h (****, $p < 10^{-5}$) "$F_{(1, 30)} = 61.24$" Genotype effect (*, $p = 0.03$) "$F_{(1, 30)} = 5.19$"	Sidak's multiple comparisons test 24 h AAV9.*Camk2α*.eGFP vs. AAV9.*Camk2α*.Cre (**, $p = 5.9 \times 10^{-3}$)
Extended Data Figure 3d 1. AAV9.*Camk2α*.eGFP (n = 10) 2. AAV9.*Camk2α*.Cre (n = 9)	Unpaired t test with Welch's correction $t_{(13.19)} = 2.72$, *, $p = 0.017$	
Extended Data Figure 3e 1. AAV9.*Camk2α*.eGFP (n = 8) 2. AAV9.*Camk2α*.Cre (n = 8)	Two-way ANOVA (alpha 0.05) Interaction (ns, $p = 0.85$) "$F_{(1, 28)} = 0.038$" Pre-CS and 24 h CS (****, $p < 10^{-4}$) "$F_{(1, 28)} = 104.75$" Genotype effect (ns, $p = 0.67$) "$F_{(1, 28)} = 0.18$"	Sidak's multiple comparisons test 24 h CS AAV9.*Camk2α*. eGFP vs. AAV9.*Camk2α*.Cre (ns, $p = 0.89$)
Extended Data Figure 3f 1. AAV9.*Camk2α*.eGFP (n = 10) 2. AAV9.*Camk2α*.Cre (n = 10)	Two-way ANOVA (alpha 0.05) Interaction (ns, $p = 0.94$) "$F_{(1, 36)} = 5.1 \times 10^{-3}$" Outer and Inner zone (****, $p < 10^{-4}$) "$F_{(1, 36)} = 121.27$" Genotype effect (ns, $p > 0.99$) "$F_{(1, 36)} = 3.63 \times 10^{-9}$"	Sidak's multiple comparisons test Outer 1. AAV9.*Camk2α*.eGFP vs. AAV9.*Camk2α*.Cre (ns, $p = 0.99$) Inner 1. AAV9.*Camk2α*.eGFP vs. AAV9.*Camk2α*.Cre (ns, $p = 0.99$)
Extended Data Figure 3h 1. AAV9.*Camk2α*.eGFP (n = 9) 2. AAV9.*Camk2α*. Cre (n = 9)	Two-way ANOVA (alpha 0.05) Interaction (**, $p = 5.3 \times 10^{-3}$) "$F_{(1, 32)} = 8.95$" Naive and 24 h (****, $p < 10^{-4}$) "$F_{(1, 32)} = 310.89$" Genotype effect (**, $p = 1.6 \times 10^{-3}$) "$F_{(1, 32)} = 11.92$"	Sidak's multiple comparisons test 24 h AAV9.*Camk2α*.eGFP vs. AAV9.*Camk2α*.Cre (***, $p = 10^{-4}$)
Extended Data Figure 3i 1. AAV9.*Camk2α*.eGFP (n = 10) 2. AAV9.*Camk2α*.Cre (n = 9)	Unpaired t test with Welch's correction $t_{(12.2)} = 3.42$, **, $p = 4.9 \times 10^{-3}$	
Extended Data Figure 3j	Two-way ANOVA (alpha 0.05)	Sidak's multiple comparisons test

1. AAV9.*Camk2α*.eGFP (*n* = 9) 2. AAV9.*Camk2α*.Cre (*n* = 9)	Interaction (*, $p = 0.027$) "$F_{(1, 32)} = 5.38$" Pre-CS and 24 h CS (****, $p < 10^{-5}$) "$F_{(1, 32)} = 150.2$" Genotype effect (**, $p = 1.5 \times 10^{-3}$) "$F_{(1, 32)} = 12.01$"	24 h CS AAV9.*Camk2α*.eGFP vs. AAV9.*Camk2α*.Cre (***, $p = 5 \times 10^{-4}$)
Extended Data Figure 3k 1. AAV9.*Camk2α*.eGFP (*n* = 10) 2. AAV9.*Camk2α*.Cre (*n* = 10)	Two-way ANOVA (alpha 0.05) Interaction (ns, $p = 0.68$) "$F_{(1, 36)} = 0.17$" Outer and Inner zone (****, $p < 10^{-5}$) "$F_{(1, 36)} = 160.1$" Genotype effect (ns, $p > 0.99$) "$F_{(1, 36)} = 8.3 \times 10^{-9}$"	Sidak's multiple comparisons test Outer 1. AAV9.*Camk2α*.eGFP vs. AAV9.*Camk2α*.Cre (ns, $p = 0.95$) Inner 1. AAV9.*Camk2α*.eGFP vs. AAV9.*Camk2α*.Cre (ns, $p = 0.95$)
Extended Data Figure 3n, o (L-LTP) 1. AAV9.*Camk2α*.eGFP • Baseline (*n* = 7) • 30 min (*n* = 7) • 180 min (*n* = 7) 2. AAV9.*Camk2α*.Cre • Baseline (*n* = 8) • 30 min (*n* = 8) • 180 min (*n* = 8)	Two-way RM ANOVA Time × Genotype effect (ns, $p = 0.92$) "$F_{(2, 26)} = 0.08$" Time (****, $p < 10^{-4}$) "$F_{(2, 26)} = 32.6$" Genotype effect (ns, $p = 0.79$) "$F_{(1, 13)} = 0.071$" Mixed-effects model (REML) Time × Genotype effect (ns, $p = 0.9245$) "$F_{(2, 11)} = 0.079$" Time (****, $p < 10^{-4}$) "$F_{(2, 14)} = 32.6$" Genotype effect (ns, $p = 0.7981$) "$F_{(1, 7)} = 0.071$"	Tukey's multiple comparisons tests AAV9.*Camk2α*.eGFP 1. Baseline vs. 30 min (****, $p < 10^{-4}$) 2. Baseline vs. 180 min (**, $p = 7.1 \times 10^{-3}$) 3. 30 min vs. 180 min (ns, $p = 0.061$) AAV9.*Camk2α*.Cre 1. Baseline vs. 30 min (****, $p < 10^{-4}$) 2. Baseline vs. 180 min (**, $p = 4.1 \times 10^{-3}$) 3. 30 min vs. 180 min ns, $p = 0.12$) Sidak's multiple comparisons test AAV9.*Camk2α*.eGFP vs AAV9.*Camk2α*.Cre 1. Baseline (ns, $p = 0.99$) 2. 30 min (ns, $p = 0.96$) 3. 180 min (ns, $p = 0.99$); (Extended Data Figure 3o)
Extended Data Figure 3p 1. AAV9.*Camk2α*.eGFP (*n* = 8) 2. AAV9.*Camk2α*.Cre (*n* = 6)	Two-way ANOVA (alpha 0.05) Interaction (ns, $p = 0.83$) "$F_{(3, 48)} = 0.29$" Paired-pulse ratio (ns, $p = 0.11$) "$F_{(3, 48)} = 2.14$" Genotype effect (ns, $p = 0.84$) "$F_{(1, 48)} = 0.041$"	Sidak's multiple comparisons test Pulse interval 1. 20 - 110 (ms) (ns, $p \geq 0.87$)
Extended Data Figure 3r 1. AAV9.*Camk2α*.eGFP (*n* = 8) 2. AAV9.*Camk2α*.Cre (*n* = 12)	Unpaired t test with Welch's correction Resting membrane potential $t_{(16.59)} = 2.28$, *, $p = 0.036$	
Extended Data Figure 3s 1. AAV9.*Camk2α*.eGFP (*n* = 8) 2. AAV9.*Camk2α*.Cre (*n* = 10)	Unpaired t test with Welch's correction Input resistance $t_{(14.63)} = 0.72$, ns, $p = 0.48$	
Extended Data Figure 3t 1. AAV9.*Camk2α*.eGFP (*n* = 8) 2. AAV9.*Camk2α*.Cre (*n* = 9)	Unpaired t test with Welch's correction F/I gain $t_{(13)} = 0.56$, ns, $p = 0.58$	
Extended Data Figure 6d 1. *Gad2*-Cre$^+$ (*n* = 8) 2. *Eif2a*$^{A/A}$*fTg*$^+$ (*n* = 7) 3. *Eif2α* cKI *Gad2* (*n* = 11)	One-way ANOVA Differences between genotypes (****, $p = 5.83 \times 10^{-10}$) "$F_{(2, 23)} = 61.6$"	Tukey's multiple comparisons test p-eIF2α/t-eIF2α ratio 1. *Gad2*-Cre$^+$ vs. *Eif2a*$^{A/A}$*fTg*$^+$ (ns, $p = 0.68$) 2. *Gad2*-Cre$^+$ vs. *Eif2α* cKI^{Gad2} (****, $p < 10^{-6}$) 3. *Eif2a*$^{A/A}$*fTg*$^+$ vs. *Eif2α* cKI^{Gad2} (****, $p < 10^{-6}$)
Extended Data Figure 6e 1. *Gad2*-Cre$^+$ (*n* = 10) 2. *Eif2a*$^{A/A}$*fTg*$^+$ (*n* = 7) 3. *Eif2α* cKI^{Gad2} (*n* = 8)	Two-way ANOVA (alpha 0.05) Interaction (ns, $p = 0.86$) "$F_{(2, 44)} = 0.15$" Naive and 1 h (****, $p < 10^{-5}$) "$F_{(1, 44)} = 412.6$" Genotype effect (ns, $p = 0.92$)"$F_{(2, 44)} = 0.084$"	Tukey's multiple comparisons test 1 h 1. *Gad2*-Cre$^+$ vs. *Eif2a*$^{A/A}$*fTg*$^+$ (ns, $p = 0.88$) 2. *Gad2*-Cre$^+$ vs. *Eif2α* cKI^{Gad2} (ns, $p = 0.98$) 3. *Eif2a*$^{A/A}$*fTg*$^+$ vs. *Eif2α* cKI^{Gad2} (ns, $p = 0.81$)
Extended Data Figure 6f 1. *Gad2*-Cre$^+$ (*n* = 7) 2. *Eif2a*$^{A/A}$*fTg*$^+$ (*n* = 6) 3. *Eif2α* cKI^{Gad2} (*n* = 8)	Two-way ANOVA (alpha 0.05) Interaction (*, $p = 0.012$) "$F_{(2, 36)} = 5.05$" Naive and 24 h (****, $p < 10^{-5}$) "$F_{(1, 36)} = 294.7$" Genotype effect (**, $p = 2 \times 10^{-3}$) "$F_{(2, 36)} = 7.41$"	Tukey's multiple comparisons test 24 h 1. *Gad2*-Cre$^+$ vs. *Eif2a*$^{A/A}$*fTg*$^+$ (ns, $p = 0.35$) 2. *Gad2*-Cre$^+$ vs. *Eif2α* cKI^{Gad2} (****, $p = 7.3 \times 10^{-5}$) 3. *Eif2a*$^{A/A}$*fTg*$^+$ vs. *Eif2α* cKI^{Gad2} (**, $p = 0.0083$)
Extended Data Figure 6g 1. *Gad2*-Cre$^+$ (*n* = 10) 2. *Eif2a*$^{A/A}$*fTg*$^+$ (*n* = 6) 3. *Eif2α* cKI^{Gad2} (*n* = 8)	Two-way ANOVA (alpha 0.05) Interaction (ns, $p = 0.072$) "$F_{(2, 42)} = 2.8$" Pre-CS and 1 h CS (****, $p < 10^{-5}$) "$F_{(1, 42)} = 79.69$" Genotype effect (ns, $p = 0.79$) "$F_{(2, 42)} = 0.24$"	Tukey's multiple comparisons test 1 h CS 1. *Gad2*-Cre$^+$ vs. *Eif2a*$^{A/A}$*fTg*$^+$ (ns, $p = 0.94$) 2. *Gad2*-Cre$^+$ vs. *Eif2α* cKI^{Gad2} (ns, $p = 0.14$) 3. *Eif2a*$^{A/A}$*fTg*$^+$ vs. *Eif2α* cKI^{Gad2} (ns, $p = 0.36$)
Extended Data Figure 6h 1. *Gad2*-Cre$^+$ (*n* = 7) 2. *Eif2a*$^{A/A}$*fTg*$^+$ (*n* = 6) 3. *Eif2α* cKI^{Gad2} (*n* = 8)	Two-way ANOVA (alpha 0.05) Interaction (*, $p = 0.018$) "$F_{(2, 36)} = 4.48$" Pre-CS and 24 h CS (****, $p < 10^{-5}$) "$F_{(1, 36)} = 124.4$" Genotype effect (**, $p = 4.4 \times 10^{-3}$) "$F_{(2, 36)} = 6.32$"	Tukey's multiple comparisons test 24 h CS 1. *Gad2*-Cre$^+$ vs. *Eif2a*$^{A/A}$*fTg*$^+$ (ns, $p = 0.94$) 2. *Gad2*-Cre$^+$ vs. *Eif2α* cKI^{Gad2} (**, $p = 1.3 \times 10^{-3}$) 3. *Eif2a*$^{A/A}$*fTg*$^+$ vs. *Eif2α* cKI^{Gad2} (***, $p = 8.1 \times 10^{-4}$)
Extended Data Figure 6i 1. *Gad2*-Cre$^+$ (*n* = 12) 2. *Eif2a*$^{A/A}$*fTg*$^+$(*n* = 12) 3. *Eif2α* cKI^{Gad2} (*n* = 11)	Two-way ANOVA (alpha 0.05) Interaction (ns, $p = 0.59$) "$F_{(2, 64)} = 0.52$" Outer and Inner zone (****, $p < 10^{-4}$) "$F_{(1, 64)} = 165.33$" Genotype effect (ns, $p = 0.99$) "$F_{(2, 64)} = 9.8 \times 10^{-12}$"	Tukey's multiple comparisons test Outer 1. *Gad2*-Cre$^+$ vs. *Eif2a*$^{A/A}$*fTg*$^+$ (ns, $p = 0.94$) 2. *Gad2*-Cre$^+$ vs. *Eif2α* cKI^{Gad2} (ns, $p = 0.75$) 3. *Eif2a*$^{A/A}$*fTg*$^+$ vs. *Eif2α* cKI^{Gad2} (ns, $p = 0.92$) Inner 1. *Gad2*-Cre$^+$ vs. *Eif2a*$^{A/A}$*fTg*$^+$ (ns, $p = 0.94$) 2. *Gad2*-Cre$^+$ vs. *Eif2α* cKI^{Gad2} (ns, $p = 0.75$)

		3. *Eif2a*$^{A/A}$*fTg*$^+$ vs. *Eif2α* cKI^{Gad2} (ns, $p = 0.92$)
Extended Data Figure 6k-m (E-LTP) 1. *Gad2*-Cre$^+$ • Baseline ($n = 8$) • 30 min ($n = 8$) • 180 min ($n = 8$) 2. *Eif2α* cKI^{Gad2} • Baseline ($n = 8$) • 30 min ($n = 8$) • 180 min ($n = 8$)	Two-way RM ANOVA Time × Genotype effect (***, $p = 8 \times 10^{-4}$) "$F_{(2, 28)} = 9.25$" Time (****, $p < 10^{-4}$) "$F_{(2, 28)} = 33.37$" Genotype effect (**, $p = 8.5 \times 10^{-3}$) "$F_{(1, 14)} = 9.34$" Two-way RM ANOVA Time × Genotype effect (**, $p = 0.0063$) "$F_{(2, 14)} = 7.43$" Time (****, $p < 10^{-4}$) "$F_{(2, 14)} = 44.18$" Genotype effect (*, $p = 0.0338$) "$F_{(1, 7)} = 6.9$"	Tukey's multiple comparisons tests *Gad2*-Cre$^+$ 1. Baseline vs. 30 min (**, $p = 4.2 \times 10^{-3}$) 2. Baseline vs. 180 min (ns, $p = 0.3688$) 3. 30 min vs. 180 min (ns, $p = 0.099$) *Eif2α* cKI^{Gad2} 1. Baseline vs. 30 min (****, $p < 10^{-4}$) 2. Baseline vs. 180 min (****, $p < 10^{-4}$) 3. 30 min vs. 180 min (ns, $p > 0.99$) Sidak's multiple comparisons tests *Gad2*-Cre$^+$ vs. *Eif2α* cKI^{Gad2} 1. Baseline (ns, $p = 0.9937$) 2. 30 min (*, $p = 0.0177$); Extended Data Figure 6l 3. 180 min (***, $p = 5 \times 10^{-4}$); Extended Data Figure 6m
Extended Data Figure 6n-o (L-LTP) 1. *Gad2*-Cre$^+$ • Baseline ($n = 8$) • 30 min ($n = 8$) • 180 min ($n = 8$) 2. *Eif2α* cKI^{Gad2} • Baseline ($n = 8$) • 30 min ($n = 8$) • 180 min ($n = 7$)	Mixed-effects model (REML) Time × Genotype effect (ns, $p = 0.18$) "$F_{(2, 27)} = 1.81$" Time (****, $p < 10^{-4}$) "$F_{(2, 27)} = 17.83$" Genotype effect (ns, $p = 0.104$) "$F_{(1, 14)} = 3.03$" Mixed-effects model (REML) Time × Genotype effect (ns, $p = 0.2$) "$F_{(2, 13)} = 1.8$" Time (***, $p < 10^{-3}$) "$F_{(2, 14)} = 17.83$" Genotype effect (ns, $p = 0.13$) "$F_{(1, 7)} = 3.03$"	Tukey's multiple comparisons tests *Gad2*-Cre$^+$ 1. Baseline vs. 30 min (*, $p = 0.0205$) 2. Baseline vs. 180 min (ns, $p = 0.2037$) 3. 30 min vs. 180 min (ns, $p = 0.5096$) *Eif2α* cKI^{Gad2} 1. Baseline vs. 30 min (****, $p < 10^{-4}$) 2. Baseline vs. 180 min (**, $p = 3 \times 10^{-3}$) 3. 30 min vs. 180 min (ns, $p = 0.29$) Sidak's multiple comparisons tests *Gad2*-Cre$^+$ vs. *Eif2α* cKI^{Gad2} 1. Baseline (ns, $p > 0.99$) 2. 30 min (ns, $p = 0.13$) 3. 180 min (ns, $p = 0.29$); Extended Data Figure 6o
Extended Data Figure 6p 1. *Gad2*-Cre$^+$ ($n = 12$) 2. *Eif2α* cKI^{Gad2} ($n = 12$)	Linear regression 1. *Gad2*-Cre$^+$ ($R^2 = 0.84$) 2. *Eif2α* cKI^{Gad2} ($R^2 = 0.58$)	
Extended Data Figure 6q **1.** *Gad2*-Cre$^+$ ($n = 18$) **2.** *Eif2α* cKI^{Gad2} ($n = 16$)	Two-way ANOVA (alpha 0.05) Interaction (ns, $p = 0.84$) "$F_{(3, 128)} = 0.28$" Paired-pulse ratio (ns, $p = 0.065$) "$F_{(3, 128)} = 2.5$" Genotype effect (ns, $p = 0.22$) "$F_{(1, 128)} = 1.54$"	Sidak's multiple comparisons test Pulse interval 20 - 110 (ms) (ns, $p \geq 0.61$)
Extended Data Figure 7d 1. *Sst*-Cre$^+$ ($n = 18$) 2. *Eif2α* cKI^{Sst} ($n = 9$)	Unpaired t-test with Welch's correction, $t_{(10.11)} = 3.6$, **, $p = 4.8 \times 10^{-3}$	
Extended Data Figure 7e 1. *Sst*-Cre$^+$ ($n = 5$) 2. *Eif2α* cKI^{Sst} ($n = 9$)	Two-way ANOVA (alpha 0.05) Interaction (ns, $p = 0.2$) "$F_{(1, 24)} = 1.75$" Outer and Inner zone (****, $p < 10^{-5}$) "$F_{(1, 24)} = 146.3$" Genotype effect (ns, $p = 0.99$) "$F_{(1, 24)} = 7.1 \times 10^{-10}$"	Sidak's multiple comparisons test Outer 1. *Sst*-Cre$^+$ vs. eIF2α$^{A/A}$ cKI^{Sst} (ns, $p = 0.59$) Inner 1. *Sst*-Cre$^+$ vs. eIF2α$^{A/A}$ cKI^{Sst} (ns, $p = 0.59$)
Extended Data Figure 7g, h (L-LTP) 1. *Sst*-Cre$^+$ • Baseline ($n = 7$) • 30 min ($n = 7$) • 180 min ($n = 6$) 2. *Eif2α* cKI^{Sst} • Baseline ($n = 8$) • 30 min ($n = 8$) • 180 min ($n = 8$)	Mixed-effects model (REML) Time × Genotype effect (ns, $p = 0.0587$) "$F_{(2, 25)} = 3.182$" Time (****, $p < 10^{-4}$) "$F_{(2, 25)} = 35.28$" Genotype effect (ns, $p = 0.0654$) "$F_{(1, 13)} = 4.05$" Mixed-effects model (REML) Time × Genotype effect (*, $p = 0.0147$) "$F_{(2, 10)} = 6.628$" Time (****, $p < 10^{-4}$) "$F_{(2, 14)} = 23.62$" Genotype effect (*, $p = 0.0176$) "$F_{(1, 7)} = 9.531$"	Tukey's multiple comparisons tests *Sst*-Cre$^+$ 1. Baseline vs. 30 min (***, $p = 1 \times 10^{-3}$) 2. Baseline vs. 180 min (ns, $p = 0.2421$) 3. 30 min vs. 180 min (ns, $p = 0.0763$) *Eif2α* cKI^{Sst} 1. Baseline vs. 30 min (****, $p < 10^{-4}$) 2. Baseline vs. 180 min (***, $p = 2 \times 10^{-4}$) 3. 30 min vs. 180 min (*, $p = 0.0153$) Sidak's multiple comparisons tests *Sst*-Cre$^+$ vs. *Eif2α* cKI^{Sst} 1. Baseline (ns, $p = 0.9997$) 2. 30 min (**, $p = 0.0038$) 3. 180 min (*, $p = 0.0215$); Extended Data Figure 7h
Extended Data Figure 7j 1. *Sst*-Cre$^+$ ($n = 7$) 2. *Eif2α* cKI^{Sst} ($n = 8$)	Unpaired t test with Welch's correction Resting membrane potential $t_{(10.43)} = 0.86$, ns, $p = 0.41$	
Extended Data Figure 7k	Unpaired t test with Welch's correction	

1. *Sst*-Cre$^+$ ($n = 10$) 2. *Eif2α* cKI^{Sst} ($n = 10$)	Input resistance $t_{17.92}$ = 0.38, ns, $p = 0.71$	
Extended Data Figure 7l 1. *Sst*-Cre$^+$ ($n = 7$) 2. *Eif2α* cKI^{Sst} ($n = 8$)	Unpaired t test with Welch's correction F/I gain $t_{7.825}$ = 4.7, **, $p = 1.6 \times 10^{-3}$	
Extended Data Figure 7o 1. *Sst*-Cre$^+$ (Saline) ($n = 7$) 2. *Sst*-Cre$^+$ (CNO) ($n = 8$) 3. *Eif2α* cKI^{Sst} (Saline) ($n = 6$) 4. *Eif2α* cKI^{Sst} (CNO) ($n = 8$)	Two-way ANOVA (alpha 0.05) Interaction (*, $p = 0.029$) "$F_{(3, 50)} = 3.25$" 24 h CS Saline/CNO (****, $p < 10^{-4}$) "$F_{(1, 50)}$ = 282.9" Genotype effect (**, $p = 8.2 \times 10^{-3}$) "$F_{(3, 50)} = 4.38$"	Sidak's multiple comparisons test 24 h 1. *Sst*-Cre$^+$ (Saline) vs. *Sst*-Cre$^+$ (CNO) (ns, $p >$ 0.99) 2. *Sst*-Cre$^+$ (Saline) vs. eIF2α$^{A/A}$ cKI^{Sst} (Saline) (*, p = 0.012) 3. eIF2α$^{A/A}$ cKI^{Sst} (Saline) vs. eIF2α$^{A/A}$ cKI^{Sst} (CNO) (ns, $p = 0.99$) 4. *Sst*-Cre$^+$ (CNO) vs. eIF2α$^{A/A}$ cKI^{Sst} (CNO) (*, p = 0.0272)
Extended Data Figure 8c 1. *Pvalb*-Cre$^+$ ($n = 7$) 2. *Eif2α* cKI^{Pvalb} ($n = 7$)	Unpaired t test with Welch's correction p-eIF2α/t-eIF2α ratio $t_{11.86}$ = 3.5, **, $p = 4.5 \times 10^{-3}$	
Extended Data Figure 8d 1. *Pvalb*-Cre$^+$ ($n = 9$) 2. *Eif2α* cKI^{Pvalb} ($n = 10$)	Two-way ANOVA (alpha 0.05) Interaction (ns, $p = 0.21$) "$F_{(1, 34)} = 1.62$" Naive and 24 h (****, $p < 10^{-4}$) "$F_{(1, 34)} = 163.0$" Genotype effect (ns, $p = 0.36$) "$F_{(1, 34)} = 0.85$"	Sidak's multiple comparisons test 24 h 1. *Pvalb*-Cre$^+$ vs. *Eif2α* cKI^{Pvalb} (ns, $p = 0.96$)
Extended Data Figure 8e 1. *Pvalb*-Cre$^+$ ($n = 9$) 2. *Eif2α* cKI^{Pvalb} ($n = 9$)	Two-way ANOVA (alpha 0.05) Interaction (ns, $p = 0.49$) "$F_{(1, 32)} = 0.50$" Pre-CS and 24 h CS (****, $p < 10^{-4}$) "$F_{(1, 32)} = 100.5$" Genotype effect (ns, $p = 0.73$) "$F_{(1, 32)} = 0.124$"	Tukey's multiple comparisons test 24 h 1. *Pvalb*-Cre$^+$ vs. *Eif2α* cKI^{Pvalb} (ns, $p = 0.99$)
Extended Data Figure 8f 1. *Pvalb*-Cre$^+$ ($n = 9$) 2. *Eif2α* cKI^{Pvalb} ($n = 9$)	Two-way ANOVA (alpha 0.05) Interaction (ns, $p = 0.75$) "$F_{(1, 32)} = 0.1$" Outer and Inner zone (***, $p < 10^{-3}$) "$F_{(1, 32)} = 96$" Genotype effect (ns, $p > 0.99$) "$F_{(1, 32)} = 6.6 \times 10^{-12}$"	Tukey's multiple comparisons test Outer/Inner 1. *Pvalb*-Cre$^+$ vs. eIF2α$^{A/A}$ cKI^{Pvalb} (ns, $p = 0.97$)
Extended Data Figure 8h 1. *Pvalb*-Cre$^+$ ($n = 15$) 2. *Eif2α* cKI^{Pvalb} ($n = 8$)	Unpaired t test with Welch's correction Puromycin incorporation $t_{10.67}$ = 5.85, ***, $p = 1 \times 10^{-4}$	
Extended Data Figure 9a-c (E-LTP) 1. *Pvalb*-Cre$^+$ • Baseline ($n = 7$) • 30 min ($n = 7$) • 180 min ($n = 7$) 2. *Eif2α* cKI^{Pvalb} • Baseline ($n = 7$) • 30 min ($n = 7$) • 180 min ($n = 7$)	Two-way RM ANOVA (alpha 0.05) Time × Genotype effect (ns, $p = 0.849$) "$F_{(2, 24)}$ = 0.1648" Time (****, $p < 10^{-4}$) "$F_{(2, 24)} = 19.43$" Genotype effect (ns, $p = 0.2078$) "$F_{(1, 12)} = 1.772$" Two-way RM ANOVA Time × Genotype effect (ns, $p = 0.8097$) "$F_{(2, 12)}$ = 0.2149" Time (***, $p = 4 \times 10^{-4}$) "$F_{(2, 12)} = 15.76$" Genotype effect (ns, $p = 0.2155$) "$F_{(1, 6)} = 1.917$"	Tukey's multiple comparisons tests *Pvalb*-Cre$^+$ 1. Baseline vs. 30 min (**, $p = 0.0073$) 2. Baseline vs. 180 min (ns, $p = 0.5663$) 3. 30 min vs. 180 min (***, $p = 6 \times 10^{-4}$) *Eif2α* cKI^{Pvalb} 1. Baseline vs. 30 min (**, $p = 4.2 \times 10^{-3}$) 2. Baseline vs. 180 min (ns, $p = 0.9687$) 3. 30 min vs. 180 min (**, $p = 2.3 \times 10^{-3}$) Sidak's multiple comparisons test *Pvalb*-Cre$^+$ vs *Eif2α* cKI^{Pvalb} 1. Baseline (ns, $p = 0.8988$) 2. 30 min (ns, $p = 7689$); Extended Data Figure 9b 3. 180 min (ns, $p = 0.3844$); Extended Data Figure 9c
Extended Data Figure 9d, e (L-LTP) 1. *Pvalb*-Cre$^+$ • Baseline ($n = 8$) • 30 min ($n = 8$) • 180 min ($n = 6$) 2. *Eif2α* cKI^{Pvalb} • Baseline ($n = 8$) • 30 min ($n = 8$) • 180 min ($n = 5$)	Mixed-effects model (REML) Time × Genotype effect (*, $p = 0.0373$) "$F_{(2, 23)}$ = 3.806" Time (****, $p < 10^{-4}$) "$F_{(2, 23)} = 35.85$" Genotype effect (*, $p = 0.0439$) "$F_{(1, 14)} = 4.904$"	Tukey's multiple comparisons tests *Pvalb*-Cre$^+$ 1. Baseline vs. 30 min (****, $p < 10^{-4}$) 2. Baseline vs. 180 min (**, $p = 2.4 \times 10^{-3}$) 3. 30 min vs. 180 min (*, $p = 0.0124$) *Eif2α* cKI^{Pvalb} 1. Baseline vs. 30 min (**, $p = 1.2 \times 10^{-3}$) 2. Baseline vs. 180 min (**, $p = 4.1 \times 10^{-3}$) 3. 30 min vs. 180 min (ns, $p = 9976$) Unpaired t-test with Welch's correction *Pvalb*-Cre$^+$ vs *Eif2α* cKI^{Pvalb} 180 min ($t_{7.542}$ = 0.6136, ns, $p = 0.5575$); Extended Data Figure 9e

Extended Data Figure 9h 1. *Pvalb*-Cre$^+$ (n = 13) 2. *Eif2α* cKI^{Pvalb} (n = 11)	Kolmogorov–Smirnov test for inter-event intervals of mEPSCs (ns, p = 0.68) Kolmogorov-Smirnov D = 0.071	
Extended Data Figure 9h (Inset) 1. *Pvalb*-Cre$^+$ (n = 13) 2. *Eif2α* cKI^{Pvalb} (n = 11)	Unpaired t test with Welch's correction mEPSC Frequency $t_{(15.41)}$ = 0.84, ns, p = 0.41	
Extended Data Figure 9i 1. *Pvalb*-Cre$^+$ (n = 13) 2. *Eif2α* cKI^{Pvalb} (n = 11)	Kolmogorov–Smirnov test for Amplitude of mEPSCs (****, $p < 10^{-4}$) Kolmogorov-Smirnov D = 0.415	
Extended Data Figure 9i (Inset) 1. *Pvalb*-Cre$^+$ (n = 13) 2. *Eif2α* cKI^{Pvalb} (n = 11)	Unpaired t test with Welch's correction mEPSC Amplitude $t_{(20.34)}$ = 3.35, **, $p = 3.1 \times 10^{-3}$	
Extended Data Figure 9k 1. *Pvalb*-Cre$^+$ (n = 10) 2. *Eif2α* cKI^{Pvalb} (n = 10)	Kolmogorov–Smirnov test for inter-event intervals of mIPSCs (ns, p = 0.54) Kolmogorov-Smirnov D = 0.080	
Extended Data Figure 9k (Inset) 1. *Pvalb*-Cre$^+$ (n = 10) 2. *Eif2α* cKI^{Pvalb} (n = 10)	Unpaired t test with Welch's correction mIPSC Frequency $t_{(17.83)}$ = 0.52, ns, p = 0.61	
Extended Data Figure 9l 1. *Pvalb*-Cre$^+$ (n = 10) 2. *Eif2α* cKI^{Pvalb} (n = 10)	Kolmogorov–Smirnov test for Amplitude of mIPSCs (ns, p = 0.54) Kolmogorov-Smirnov D = 0.265	
Extended Data Figure 9l (Inset) 1. *Pvalb*-Cre$^+$ (n = 10) 2. *Eif2α* cKI^{Pvalb} (n = 10)	Unpaired t test with Welch's correction mIPSC Amplitude $t_{(13.70)}$ = 2.04, ns, p = 0.061	
Extended Data Figure 9n 1. *Pvalb*-Cre$^+$ (n = 10) 2. *Eif2α* cKI^{Pvalb} (n = 10)	Unpaired t-test with Welch's correction Resting membrane potential $t_{(17.55)}$ = 0.79, ns, p = 0.44	
Extended Data Figure 9o 1. *Pvalb*-Cre$^+$ (n = 10) 2. *Eif2α* cKI^{Pvalb} (n = 10)	Unpaired t test with Welch's correction Input resistance $t_{(17.92)}$ = 0.38, ns, p = 0.71	
Extended Data Figure 9p 1. *Pvalb*-Cre$^+$ (n = 10) 2. *Eif2α* cKI^{Pvalb} (n = 10)	Unpaired t test with Welch's correction F/I gain $t_{(18)}$ = 1.72, ns, p = 0.10	
Extended Data Figure 10d-f 1. *Sst*-Cre$^+$ wTBS (n = 6) 2. *Sst*-Cre$^+$ wTBS+TBS (n = 8) 3. *Eif2α* cKI^{Sst} wTBS (n = 7) 4. *Eif2α* cKI^{Sst} wTBS+TBS (n = 7)	One-way ANOVA 20-30 min post induction fEPSP slope (****, $p = 5.9 \times 10^{-5}$) "$F_{(3, 24)}$ = 11.85"	Tukey's multiple comparisons test 20-30 min post induction fEPSP slope 1. *Sst*-Cre$^+$ wTBS vs. *Sst*-Cre$^+$ wTBS+TBS (*, p = 0.049) 2. *Sst*-Cre$^+$ wTBS vs. Eif2α cKI^{Sst} wTBS (ns, p = 0.85) 3. *Sst*-Cre$^+$ wTBS vs. Eif2α cKI^{Sst} wTBS+TBS (****, p = 9 × 10-5) 4. *Sst*-Cre$^+$ wTBS+TBS vs. Eif2α cKI^{Sst} wTBS (ns, p = 0.21) 5. *Sst*-Cre$^+$ wTBS+TBS vs. Eif2α cKI^{Sst} wTBS+TBS (*, p = 0.038) 6. Eif2α cKI^{Sst} wTBS vs. Eif2α cKI^{Sst} wTBS+TBS (***, p = 4.2 × 10-4)