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Corresponding Author:	Yun Li & Da-Ting Lin	# Main Figures:	3
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Reporting Checklist for Nature Neuroscience

This checklist is used to ensure good reporting standards and to improve the reproducibility of published results. For more information, please read Reporting Life Sciences Research.

Please note that in the event of publication, it is mandatory that authors include all relevant methodological and statistical information in the manuscript.

Statistics reporting, by figure

- Please specify the following information for each panel reporting quantitative data, and where each item is reported (section, e.g. Results, & paragraph number).
- Each figure legend should ideally contain an exact sample size (n) for each experimental group/condition, where n is an exact number and not a range, a clear definition of how n is defined (for example x cells from x slices from x animals from x litters, collected over x days), a description of the statistical test used, the results of the tests, any descriptive statistics and clearly defined error bars if applicable.
- For any experiments using custom statistics, please indicate the test used and stats obtained for each experiment.
- Each figure legend should include a statement of how many times the experiment shown was replicated in the lab; the details of sample collection should be sufficiently clear so that the replicability of the experiment is obvious to the reader.
- For experiments reported in the text but not in the figures, please use the paragraph number instead of the figure number.

Note: Mean and standard deviation are not appropriate on small samples, and plotting independent data points is usually more informative. When technical replicates are reported, error and significance measures reflect the experimental variability and not the variability of the biological process; it is misleading not to state this clearly.

		TEST USED		n			DESCRIPTIVE STATS (AVERAGE, VARIANCE)		P VALUE		DEGREES OF FREEDOM & F/t/z/R/ETC VALUE	
	FIGURE NUMBER	WHICH TEST?	SECTION & PARAGRAPH #	EXACT VALUE	DEFINED?	SECTION & PARAGRAPH #	REPORTED?	SECTION & PARAGRAPH #	EXACT VALUE	SECTION & PARAGRAPH #	VALUE	SECTION & PARAGRAPH #
example	1a	one-way ANOVA	Fig. legend	9, 9, 10, 15	mice from at least 3 litters/group	Methods para 8	error bars are mean +/- SEM	Fig. legend	p = 0.044	Fig. legend	F(3, 36) = 2.97	Fig. legend
example	results, para 6	unpaired t-test	Results para 6	15	slices from 10 mice	Results para 6	error bars are mean +/- SEM	Results para 6	p = 0.0006	Results para 6	t(28) = 2.808	Results para 6

		TEST USED		n			DESCRIPTIVE STATS (AVERAGE, VARIANCE)		P VALUE		DEGREES OF FREEDOM & F/t/z/R/ETC VALUE	
	FIGURE NUMBER	WHICH TEST?	SECTION & PARAGRAPH #	EXACT VALUE	DEFINED?	SECTION & PARAGRAPH #	REPORTED?	SECTION & PARAGRAPH #	EXACT VALUE	SECTION & PARAGRAPH #	VALUE	SECTION & PARAGRAPH #
+ -	1a	Non-parametric Mann-Whitney U-test	Fig. Legend	22 (WT) 23 (TDP)	neurons from 3 mice/group	Fig. Legend	error bars are mean+/- SEM WT, 44.3 ± 2.3 pA; TDP, 35.0 ± 2.3 pA; WT, 9.8 ± 0.3 Hz; TDP, 6.8 ± 0.4 Hz	Fig. Legend	p = 0.0062 for amplitude p < 0.0001 for frequency	Fig. Legend	z(43) = 2.74 for amplitude, z(43) = 4.38 for frequency	Fig. Legend
+ -	1b	Non-parametric Mann-Whitney U-test	Fig. Legend	53, 58 (WT and TDP) and 40, 50 (WT and TDP, with PTX)	neurons from 6 mice/group (no PTX); neurons from 3 mice/group (with PTX)	Fig. Legend	error bars are mean+/- SEM	Fig. Legend	p < 0.0001 (for 600pA current injection without PTX) p = 0.242 (for 600pA current injection with PTX)	Fig. Legend	z(109) = 4.22 for no PTX; z(88) = 1.17 for with PTX	Fig. Legend and Supplementary Table 1
+ -	1c	Non-parametric Mann-Whitney U-test	Fig. Legend	18, 9, 9 (6-, 9-, 15-week YFP), 16, 9, 7 (6-, 9-, 15-week TDP/YFP)	images from 10, 5, 5 mice (6-, 9-, 15-week YFP and TDP/YFP mice)	Fig. Legend	error bars are mean+/- SEM	Fig. Legend	p = 0.0005 (6-week vs 9-week) p=0.0065 (9-week vs 15-week) p = 0.02 (6-week vs 15-week)	Fig. Legend	z(23) = 3.227 for 6-week vs 9-week TDP/YFP, z(14) =2.699 for 9-week vs 15-week TDP/YFP, z(21) =2.038 for 6-week vs 15-week TDP/YFP	Fig. Legend and Supplementary Table 3
+ -	1d	Non-parametric Mann-Whitney U-test	Fig. Legend	18, 42, 54 (6-, 9-, 15-weeks WT) 42, 36, 72 (6-, 9-, 15-weeks TDP)	both sides of 9, 21, 27 slices from 3,4,3, mice across 6-, 9-, 15-weeks WT mice; both sides of 21, 18, 36 slices from 4, 3, 6 across 6-, 9-, 15-weeks TDP mice	Fig. Legend	error bars are mean+/- SEM	Fig. Legend	p < 0.0001(6-week vs 9-week) p < 0.0001(9-week vs 15-week) p < 0.0001(6-week vs 15-week)	Fig. Legend	z(76) = 4.591 for 6-week vs 9-week TDP, z(106) =8.404 for 9-week vs 15-week TDP, z(112) =8.879 for 6-week vs 15-week TDP	Fig. Legend and Supplementary Table 4
+ -	2a	Non-parametric Mann-Whitney U-test	Fig. Legend	23 (Ctrl), 20 (TDP)	neurons from 3 mice/group	Fig. Legend	error bars are mean+/- SEM Ctrl, -61.3 ± 0.8 mV; TDP, -54.7 ± 1.5 mV Ctrl, 29.3 ± 4.3 Hz; TDP, 42.0 ± 3.4 Hz;	Fig. Legend	p = 0.039 for Resting Membrane Potential, p = 0.023 for AP firing frequency	Fig. Legend	z(41) = 2.06 for Resting Membrane Potential, z(41) = 2.27 for AP firing frequency	Fig. Legend
+ -	2b	Non-parametric Mann-Whitney U-test	Fig. Legend	34 (Ctrl), 29 (TDP)	neurons from 3 mice/group	Fig. Legend	error bars are mean+/- SEM Ctrl, -68.2 ± 1.0 mV; TDP, -71.8 ± 0.7 mV Ctrl, 21.3 ± 3.7 Hz; TDP, 8.5 ± 2.2 Hz	Fig. Legend	p = 0.0043 for Resting Membrane Potential, p = 0.0080 for AP firing frequency	Fig. Legend	z(61) = 2.82 for Resting Membrane Potential, z(61) = 2.53 for AP firing frequency	Fig. Legend

+ -	2c	Non-parametric Mann-Whitney U-test	Fig. Legend	39 (Ctrl), 41 (TDP)	neurons from 3 mice/group	Fig. Legend	error bars are mean+/- SEM Ctrl, 22.1 ± 2.0 Hz; TDP, 32.9 ± 2.3 Hz Ctrl, 34.3 ± 2.3 pA; TDP, 40.1 ± 2.5 pA	Fig. Legend	p = 0.0014 (frequency) p = 0.1556 (amplitude)	Fig. Legend	z(78) = 3.2 (frequency) z(78) = 1.42 (amplitude)	Fig. Legend
+ -	2d	Non-parametric Mann-Whitney U-test	Fig. Legend	24 (Ctrl), 28 (TDP)	neurons from 3 mice/group	Fig. Legend	error bars are mean+/- SEM Ctrl, -66.1 ± 1.0 mV; TDP, -62.3 ± 1.1 mV Ctrl, 74.6 ± 7.3 Hz; TDP, 107.0 ± 10.9 Hz	Fig. Legend	p = 0.031 for Resting Membrane Potential, p = 0.0372 for AP firing frequency	Fig. Legend	z(50) = 2.36 for Resting Membrane Potential, z(50) = 2.08 for AP firing frequency	Fig. Legend
+ -	2e	Wilcoxon Signed Rank Test	Fig. Legend	15 (Chr2) 20 (eNpHR3.0)	neurons from 3 mice/group	Fig. Legend	error bars are mean+/- SEM ChR2: 0.93 ± 0.04 eNpHR3.0: 1.22 ± 0.11	Fig. Legend	p = 0.0215 (Chr2) p = 0.0016 (eNpHR3.0)	Fig. Legend	z(14) = 2.26 (ChR2) z(19) = 3.16 (eNpHR3.0)	Fig. Legend
+ -	3a	one-way ANOVA and post-hoc Tukey Test	Fig. Legend	From Group1 to 4: 25, 26, 27, 28	neurons from 3 mice/group	Fig. Legend	error bars are mean+/- SEM Group 1, DTR::SstCre + Saline, 21.10 ± 0.44 Hz; Group 2, DTR::SstCre + DT, 22.34 ± 0.53 Hz; Group 3, TDP::DTR::SstCre + Saline, 15.19 ± 0.68 Hz; Group 4, TDP::DTR::SstCre + DT, 18.65 ± 0.71 Hz	Fig. Legend	p < 0.00001(ANOVA) p < 0.00001 (Group 1 vs 3), p = 0.0005 (Group 3 vs 4), p = 0.0002 (Group 2 vs 4), p = 0.026 (Group 1 vs 4), p = 0.50 (Group 1 vs 2) p < 0.00001 (Group 2 vs 3)	Fig. Legend	F(3, 102) = 26.7	Fig. Legend
+ -	3b	Brown and Forsythe Test and post-hoc Games-Howell test	Fig. Legend	From Group1 to 4: 15, 18, 12, 10	neurons from 3 WT, 4 DTR/Sst, 4 TDP, 3 TDP/DTR/Sst mice	Fig. Legend	error bars are mean+/- SEM Group 1, WT + DT, 15.5 ± 2.3 Hz; Group 2, DTR::SstCre + DT, 13.5 ± 3.9 Hz; Group 3, TDP + DT, 35.7 ± 6.2 Hz; Group 4, TDP::DTR::SstCre + DT, 8.7 ± 4.4 Hz	Fig. Legend	p = 0.0015 (BF test) p = 0.038(WT vs TDP), p =0.01 (TDP vs TDP/DTR/Sst), p = 0.85 (DTR/Sst vs TDP/DTR/Sst), p = 0.54 (WT vs TDP/DTR/Sst), p = 0.97 (WT vs DTR/Sst) p = 0.03 (DTR/Sst vs TDP)	Fig. Legend	F(3, 44) = 6.34	Fig. Legend

+ -	3c	Brown and Forsythe Test and post-hoc Games-Howell test	Fig. Legend	From Group1 to 4: 180, 120, 143, 195	neurons from 3 WT, TDP, and TDP/DTR/Sst mice, 2 DTR/Sst mice	Fig. Legend	error bars are mean+/- SEM Group1, WT + DT, 21.54 ± 0.59; Group 2, DTR::SstCre + DT, 21.05 ± 0.75; Group 3, TDP + DT, 19.44 ± 0.54; Group 4, TDP::DTR::SstCre + DT, 21.95 ± 0.62	Fig. Legend	p =0.026 (BF test) p = 0.043 (WT vs TDP), p = 0.013 (TDP vs TDP/DTR/Sst), p = 0.79 (DTR/Sst vs TDP/DTR/Sst), p = 0.96 (WT vs TDP/DTR/Sst), p = 0.96 (WT vs DTR/Sst) p = 0.3 (DTR/Sst vs TDP)	Fig. Legend	F(3, 584) = 3.10	Fig. Legend
+ -	3d	Non-parametric Mann-Whitney U-test	Fig. Legend	From Group1 to 4: 24, 24, 36, 42	both sides of 12 slices from 4 WT, 12 slices from 4 DTR/Sst, 18 slices from 6 TDP, 21 slices from 7 TDP/DTR/Sst mice	Fig. Legend	error bars are mean+/- SEM Group 1, WT + DT and Group 2, DTR::SstCre + DT, 0; Group 3, TDP + DT, 25.9 ± 3.5; Group 4, TDP::DTR::SstCre + DT, 10.7 ± 1.7	Fig. Legend	p = 0.0002 (TDP vs TDP/DTR/Sst)	Fig. Legend	z(76) = 3.7085 for TDP vs TDP/DTR/Sst	Fig. Legend
+ -	3e	Brown and Forsythe Test and post-hoc Games-Howell test	Fig. Legend	From Group1 to 4: 18, 16, 24, 24	both sides of 9 slices from 3 WT, 8 slices from 3 DTR/Sst, 12 slices from 4TDP, 12 slices from 4 TDP/DTR/Sst mice	Fig. Legend	error bars are mean+/- SEM Group 1, WT + DT, 1358.9 ± 32.6; Group 2, DTR::SstCre + DT, 1220.2 ± 41.3; Group 3, TDP + DT, 960.1 ± 68.9; Group 4, TDP::DTR::SstCre + DT, 1257.1 ± 48.1	Fig. Legend	p =2.36x10e-6 (BF test) p = 0.000056 (WT vs TDP), p = 0.0054 (TDP vs TDP/DTR/Sst), p = 0.94 (DTR/Sst vs TDP/DTR/Sst), p = 0.31 (WT vs TDP/DTR/Sst), p = 0.06 (WT vs DTR/Sst) p = 0.013 (DTR/Sst vs TDP)	Fig. Legend	F(3, 62) = 12.15	Fig. Legend
+ -	s1a	Non-parametric Mann-Whitney U-test	Fig. Legend	11,11	neurons from 3 mice/group	Fig. Legend	error bars are mean+/- SEM WT, 5.1 ± 0.3 nA; TDP, 3.1 ± 0.4 nA	Fig. Legend	p = 0.0007	Fig. Legend	z(20) = 2.6	Fig. Legend
+ -	s1b	Unpaired t-test	Fig. Legend	45 (YFP), 42(TDP::YFP)	neurons from 4 mice/group	Fig. Legend	error bars are mean+/- SEM TDP::YFP, 79.5 ± 6.0% of YFP control	Fig. Legend	p = 0.0326	Fig. Legend	t(85) = 2.173	Fig. Legend
+ -	s1c	Non-parametric Mann-Whitney U-test	Fig. Legend	24 (WT), 20(TDP)	neurons from 3 mice/group	Fig. Legend	error bars are mean+/- SEM WT, 11.3 ± 0.7 pA; TDP, 11.5 ± 0.9 pA WT, 5.6 ± 0.5 Hz; TDP, 5.9 ± 1.1 Hz	Fig. Legend	p = 0.99 (amplitude) p = 0.47 (frequency)	Fig. Legend	z(42) = 0.01 (amplitude) z(42) = 0.72 (freqeuncy)	Fig. Legend

+ -	s1d	Non-parametric Mann-Whitney U-test	Fig. Legend	53,40 (WT, with and without PTX) and 58,50 (TDP with and without PTX)	neurons from 6 mice/group without PTX neurons from 3 mice/group with PTX	Fig. Legend	error bars are mean+/- SEM	Fig. Legend	p < 0.0001 (WT, 600pA current injection) p = 0.0024 (TDP, 600pA current injection)	Fig. Legend	z(91) = 5.23 (WT) z(106) = 3.02 (TDP)	Fig. Legend
+ -	s1e	Non-parametric Mann-Whitney U-test	Fig. Legend	25 (WT), 29 (TDP)	neurons from 3 mice/group	Fig. Legend	error bars are mean+/- SEM WT, -62.5 ± 1.6 mV; TDP, -61.6 ± 1.0 mV (RMP) WT, -40 ± 0.9 mV; TDP, -41.6 ± 1.3 mV (AP threshold) WT, 92.6 ± 5.0 MΩ; TDP, 92.1 ± 4.7 MΩ (input resistance)	Fig. Legend	p = 0.65 (RMP) p = 0.53 (threshold) p = 0.96 (Rin)	Fig. Legend	z(52) = 0.39 (RMP) z(52) = 0.66 (threshold) z(52) = 0.05 (Rin)	Fig. Legend
+ -	s2a	Log-rank (Mantel-Cox) Test	Fig. Legend	22 (male), 11(female)	mice from male vs female TDP	Fig. Legend	N/A	Fig. Legend	p < 0.0001	Fig. Legend	Df=1, Chi square = 28.12	Fig. Legend
+ -	s2b	Non-parametric Mann-Whitney U-test	Fig. Legend	101 (YFP), 92 (TDP::YFP)	neurons from 4 mice/group	Fig. Legend	error bars are mean+/- SEM TDP::YFP, 68.3 ± 3.2 % of YFP control	Fig. Legend	p < 0.0001	Fig. Legend	z(191) = 5.69	Fig. Legend
+ -	s2c	Unpaired t-test	Fig. Legend	21 (WT), 20 (TDP)	neurons from 3 mice/group	Fig. Legend	error bars are mean+/- SEM	Fig. Legend	p = 0.0317	Fig. Legend	t(39) = 2.228	Fig. Legend
+ -	s3e	Non-parametric Mann-Whitney U-test	Fig. Legend	36 (YFP), 25 (TDP::YFP)	slices from 5 mice/ group	Fig. Legend	error bars are mean+/- SEM YFP, 3348 ± 107.6 mm–3; TDP::YFP, 2048 ± 170.2 mm–3	Fig. Legend	p < 0.0001	Fig. Legend	z(59) = 4.8532	Fig. Legend
+ -	s4a	Non-parametric Mann-Whitney U-test	Fig. Legend	30 (WT), 31 (TDP)	neurons from 3 mice/group	Fig. Legend	error bars are mean+/- SEM WT, 24.2 ± 1.9 Hz; TDP, 25.5.8 ± 1.8 Hz; WT, 32.7 ± 1.9 pA; TDP, 37.0 ± 2.0 pA	Fig. Legend	p = 0.5485 (frequency) p = 0.1141 (amplitude)	Fig. Legend	z(59) = 0.6 (frequency) z(59) = 1.58 (amplitude)	Fig. Legend
+ -	s4b	Non-parametric Mann-Whitney U-test	Fig. Legend	29 (Ctrl), 28 (TDP)	neurons from 3 mice/group	Fig. Legend	error bars are mean+/- SEM Ctrl, -68.4 ± 0.8 mV; TDP, -68.9 ± 0.8 mV Ctrl, 94.0 ± 21.6 Hz; TDP, 84.9 ± 14.4 Hz	Fig. Legend	p = 0.32 (RMP) p = 0.68 (AP frequency)	Fig. Legend	z(55) = 0.47 (RMP) z(55) = 0.42 (AP frequency)	Fig. Legend
+ -	s4c	Unpaired t-test	Fig. Legend	16 (WT), 16 (TDP)	counts from each side of 8 slices, from 4 mice/group	Fig. Legend	error bars are mean+/- SEM	Fig. Legend	p = 0.5197	Fig. Legend	t(30) = 0.651	Fig. Legend

+ -	s4d	Unpaired t-test	Fig. Legend	24 (WT), 24 (TDP)	counts from each side of 12 slices, from 4 mice/group	Fig. Legend	error bars are mean+/- SEM	Fig. Legend	p = 0.393	Fig. Legend	t(46) = 0.863	Fig. Legend
+ -	s5a	Unpaired t-test	Fig. Legend	24 (Ctrl), 22 (TDP)	counts from 12 slices, from 4 mice each group	Fig. Legend	error bars are mean+/- SEM TDP, 83.1 ± 3.2% of age matched Ctrl	Fig. Legend	p = 0.0003	Fig. Legend	t(44) = 3.961	Fig. Legend
+ -	s5b	Unpaired t-test	Fig. Legend	23 (Ctrl), 24 (TDP)	counts from 12 slices, from 4 mice each group	Fig. Legend	error bars are mean+/- SEM TDP, 109.5 ± 2.5% of age matched Ctrl	Fig. Legend	p = 0.013	Fig. Legend	t(45) = 2.586	Fig. Legend
+ -	s6b	Wilcoxon matched-pairs signed rank test	Fig. Legend	14 (ChR2), 20 (eNpHR3.0)	neurons from 3 mice/group	Fig. Legend	error bars are mean+/- SEM ChR2 light off, 1.0 ± 0.3 Hz; light on, 1.5 ± 0.3 Hz eNpHR3.0 light off, 2.8 ± 0.6 Hz; light on, 2.0 ± 0.5 Hz	Fig. Legend	p = 0.004 for ChR2 p < 0.0001 for eNpHR3.0	Fig. Legend	z(13) = 2.72 (ChR2) z(19) = 3.91 (eNpHR3.0)	Fig. Legend
+ -	s6c	paired T-TEST Wilcoxon Signed Rank Test (for normalized ratio)	Fig. Legend	14 (Chr2) 18 (eNpHR3.0)	neurons from 3 mice/group	Fig. Legend	error bars are mean+/- SEM ChR2 light off, 1.80 ± 0.44 Hz; light on, 2.20 ± 0.47 Hz, eNpHR3.0 light off, 6.07 ± 0.98 Hz; light on, 4.09 ± 0.81 Hz ChR2 Ratio of "light on" over "light off", 1.58 ± 0.24 eNpHR3.0 Ratio of "light on" over "light off", 0.65 ± 0.09	Fig. Legend	paired T-TEST P = 0.0039 (Chr2) P = 0.0016 (eNpHR3.0) Wilcoxon Signed Rank Test p = 0.0064 (Chr2) p = 0.0020 (eNpHR3.0)	Fig. Legend	paired T-TEST t(13)=3.45 (Chr2) t(17)= 3.75 (eNpHR3.0) Wilcoxon Signed Rank Test z(13) = 2.57 (Chr2) z(17) = 3.1 (eNpHR3.0)	Fig. Legend
+ -	s6d	paired T-TEST (Chr2) Wilcoxon Signed Rank Test (eNpHR3.0)	Fig. Legend	15 (Chr2), 20 (eNpHR3.0)	neurons from 3 mice/group	Fig. Legend	error bars are mean+/- SEM ChR2 light off, 1.34 ± 0.21 pC S–1; light on, 1.24 ± 0.18 pC S–1 eNpHR3.0 light off, 1.07 ± 0.13 pC S–1; light on, 1.30 ± 0.21 pC S–1	Fig. Legend	P = 0.019 (Chr2) p = 0.001 (eNpHR3.0)	Fig. Legend	t(14)= 2.64 (Chr2) z(19) = 3.09 (eNpHR3.0)	Fig. Legend
+ -	s6e	Wilcoxon matched-pairs signed rank test	Fig. Legend	21 (ChR2), 22 (eNpHR3.0)	neurons from 3 mice/group	Fig. Legend	error bars are mean+/- SEM ChR2 light off, 3.6 ± 0.5 Hz; light on, 0.5 ± 0.3 Hz, eNpHR3.0 (light off, 1.4 ± 0.4 Hz; light on, 2.5 ± 0.4	Fig. Legend	p < 0.0001 ChR2 p = 0.0005 eNpHR3.0	Fig. Legend	z(20) = 4.01 (ChR2) z(21) = 3.24 (eNpHR3.0)	Fig. Legend

Representative figures

1. Are any representative images shown (including Western blots and immunohistochemistry/staining) in the paper?

   If so, what figure(s)?

Yes.
Main figures: Fig. 1c, 1d; Fig. 3c, 3d, 3e.
Supplementary figures: Fig. S1b; Fig. S2b; Fig. S3c, S3d; Fig. S4c, 4d; Fig. S5a, S5b; Fig. S8

2. For each representative image, is there a clear statement of how many times this experiment was successfully repeated and a discussion of any limitations in repeatability?

   If so, where is this reported (section, paragraph #)?

Yes.
n of cells (or slices) and mice are presented in their corresponding figure legends.

Statistics and general methods

1. Is there a justification of the sample size?

   If so, how was it justified?

   Where (section, paragraph #)?

   Even if no sample size calculation was performed, authors should report why the sample size is adequate to measure their effect size.

Yes. Our estimates of animal use for electrophysiological recordings (n>= 10 neurons from 3-4 animals per group), and for immunostaining (n>=8 slices from 3-7 animals) are based on past experience and those presented in the literature.
In Methods, subsection with heading "sample size, randomization and blinding statement".

2. Are statistical tests justified as appropriate for every figure?

   Where (section, paragraph #)?

Yes. In Methods, subsection 8 with heading "statistical analysis".

   a. If there is a section summarizing the statistical methods in the methods, is the statistical test for each experiment clearly defined?

Yes. A subsection of statistical methods was summarized in Methods, and statistical test for each experiment was clearly defined in corresponding figure legend.

   b. Do the data meet the assumptions of the specific statistical test you chose (e.g. normality for a parametric test)?

      Where is this described (section, paragraph #)?

Yes. For two-group comparison, D'Agostino & Pearson omnibus test was used for normality test and the variances were calculated with Prism5.0 analysis function. If both groups having normal distribution and equal variance, unpaired t-test was used. Otherwise non-parametric Mann-Whitney U-test was used. For multiple groups comparison, Jarque-Bera test was used for normality test, and Levene's test was used for variance test. If all groups having normal distribution and equal variance,One-way ANOVA with Tukey test was used, otherwise Brown and Forsythe Test with Games-Howell test was used.
In Methods, subsection with heading "statistical analysis".

   c. Is there any estimate of variance within each group of data?

      Is the variance similar between groups that are being statistically compared?

      Where is this described (section, paragraph #)?

Variance for each group of data was calculated with Prism5.0 analysis function or Levene's test.
For two-group comparison, if both groups having normal distribution and equal variance, unpaired t-test was used. Otherwise non-parametric Mann-Whitney U-test was used. For multiple groups comparison, if all groups having normal distribution and equal variance,One-way ANOVA with Tukey test was used, otherwise Brown and Forsythe Test with Games-Howell test was used. In Methods, subsection 8 with heading "statistical analysis".

d. Are tests specified as one- or two-sided?	All tests are two-sided.
e. Are there adjustments for multiple comparisons?	For comparison between multiple groups, one-way ANOVA or Brown and Forsythe Test were used with post-hoc Tukey test or Dunnett test.
3. Are criteria for excluding data points reported? Was this criterion established prior to data collection? Where is this described (section, paragraph #)?	We did not exclude any data point.
4. Define the method of randomization used to assign subjects (or samples) to the experimental groups and to collect and process data. If no randomization was used, state so. Where does this appear (section, paragraph #)?	Mice were randomly allocated to treatment condition and all data were randomly collected. In Methods, subsection with heading "sample size, randomization and blinding statement".
5. Is a statement of the extent to which investigator knew the group allocation during the experiment and in assessing outcome included? If no blinding was done, state so. Where (section, paragraph #)?	Initial electrophysiological recordings (i.e., mIPSCs), Ubiquitin stainings, NeuN immunostainings, and VGAT immunostainings were performed in a blinded manner. All other data were collected and analyzed without the investigator blinded to genotype and treatment conditions. In Methods, subsection with heading "sample size, randomization and blinding statement".
6. For experiments in live vertebrates, is a statement of compliance with ethical guidelines/regulations included? Where (section, paragraph #)?	Yes, in Methods, subsection 1 with heading "Mice".
7. Is the species of the animals used reported? Where (section, paragraph #)?	Yes, in Methods, subsection 1 with heading "Mice".
8. Is the strain of the animals (including background strains of KO/ transgenic animals used) reported? Where (section, paragraph #)?	Yes, in Methods, subsection 1 with heading "Mice".
9. Is the sex of the animals/subjects used reported? Where (section, paragraph #)?	Yes, in Methods, subsection 1 with heading "Mice".
10. Is the age of the animals/subjects reported? Where (section, paragraph #)?	Yes, in Results and Figure Legends accordingly.
11. For animals housed in a vivarium, is the light/dark cycle reported? Where (section, paragraph #)?	No. mice were group housed in regular cages. Light/dark cycle is 12/12 hours.
12. For animals housed in a vivarium, is the housing group (i.e. number of animals per cage) reported? Where (section, paragraph #)?	N/A

13. For behavioral experiments, is the time of day reported (e.g. light or dark cycle)?

    Where (section, paragraph #)?

N/A

14. Is the previous history of the animals/subjects (e.g. prior drug administration, surgery, behavioral testing) reported?

    Where (section, paragraph #)?

N/A

    a. If multiple behavioral tests were conducted in the same group of animals, is this reported?

       Where (section, paragraph #)?

N/A

15. If any animals/subjects were excluded from analysis, is this reported?

    Where (section, paragraph #)?

None animals were excluded from analysis.

    a. How were the criteria for exclusion defined?

       Where is this described (section, paragraph #)?

N/A

    b. Specify reasons for any discrepancy between the number of animals at the beginning and end of the study.

       Where is this described (section, paragraph #)?

N/A

Reagents

1. Have antibodies been validated for use in the system under study (assay and species)?

Yes, antibodies used in this manuscript have been widely used and commercial available.

    a. Is antibody catalog number given?

       Where does this appear (section, paragraph #)?

Yes. In Methods, subsection 5 with heading "immunostaining".

    b. Where were the validation data reported (citation, supplementary information, Antibodypedia)?

       Where does this appear (section, paragraph #)?

Antibodies used in this manuscript are all commercial available and have been widely used in literature. We have included citations for antibodies.

2. Cell line identity

    a. Are any cell lines used in this paper listed in the database of commonly misidentified cell lines maintained by ICLAC and NCBI Biosample?

       Where (section, paragraph #)?

N/A

    b. If yes, include in the Methods section a scientific justification of their use--indicate here in which section and paragraph the justification can be found.

N/A

c. For each cell line, include in the Methods section a statement that specifies:
- the source of the cell lines
- have the cell lines been authenticated? If so, by which method?
- have the cell lines been tested for mycoplasma contamination?

Where (section, paragraph #)?

N/A

Data deposition

Data deposition in a public repository is mandatory for:

a. Protein, DNA and RNA sequences
b. Macromolecular structures
c. Crystallographic data for small molecules
d. Microarray data

Deposition is strongly recommended for many other datasets for which structured public repositories exist; more details on our data policy are available here. We encourage the provision of other source data in supplementary information or in unstructured repositories such as Figshare and Dryad.

We encourage publication of Data Descriptors (see Scientific Data) to maximize data reuse.

1. Are accession codes for deposit dates provided?

   Where (section, paragraph #)?

N/A

Computer code/software

Any custom algorithm/software that is central to the methods must be supplied by the authors in a usable and readable form for readers at the time of publication. However, referees may ask for this information at any time during the review process.

1. Identify all custom software or scripts that were required to conduct the study and where in the procedures each was used.

We used Axograph X and Igor Pro (Wavemetrics) for electrophysiological analysis. We used ImageJ software for most image analysis, and a custom script in MATLAB to analysis VGAT puncta density presented in Fig. 3d.

2. If computer code was used to generate results that are central to the paper's conclusions, include a statement in the Methods section under "**Code availability**" to indicate whether and how the code can be accessed. Include version information as necessary and any restrictions on availability.

Custom script in MATLAB, which was used for VGAT puncta density analysis, is available upon request.

Human subjects

1. Which IRB approved the protocol?

   Where is this stated (section, paragraph #)?

N/A

2. Is demographic information on all subjects provided?

   Where (section, paragraph #)?

   N/A

3. Is the number of human subjects, their age and sex clearly defined?

   Where (section, paragraph #)?

   N/A

4. Are the inclusion and exclusion criteria (if any) clearly specified?

   Where (section, paragraph #)?

   N/A

5. How well were the groups matched?

   Where is this information described (section, paragraph #)?

   N/A

6. Is a statement included confirming that informed consent was obtained from all subjects?

   Where (section, paragraph #)?

   N/A

7. For publication of patient photos, is a statement included confirming that consent to publish was obtained?

   Where (section, paragraph #)?

   N/A

fMRI studies

For papers reporting functional imaging (fMRI) results please ensure that these minimal reporting guidelines are met and that all this information is clearly provided in the methods:

1. Were any subjects scanned but then rejected for the analysis after the data was collected?

   N/A

   a. If yes, is the number rejected and reasons for rejection described?

      Where (section, paragraph #)?

      N/A

2. Is the number of blocks, trials or experimental units per session and/or subjects specified?

   Where (section, paragraph #)?

   N/A

3. Is the length of each trial and interval between trials specified?

   N/A

4. Is a blocked, event-related, or mixed design being used? If applicable, please specify the block length or how the event-related or mixed design was optimized.

   N/A

5. Is the task design clearly described?

   Where (section, paragraph #)?

   N/A

6. How was behavioral performance measured?	N/A
7. Is an ANOVA or factorial design being used?	N/A
8. For data acquisition, is a whole brain scan used? If not, state area of acquisition.	N/A
a. How was this region determined?	N/A
9. Is the field strength (in Tesla) of the MRI system stated?	N/A
a. Is the pulse sequence type (gradient/spin echo, EPI/spiral) stated?	N/A
b. Are the field-of-view, matrix size, slice thickness, and TE/TR/ flip angle clearly stated?	N/A
10. Are the software and specific parameters (model/functions, smoothing kernel size if applicable, etc.) used for data processing and pre-processing clearly stated?	N/A
11. Is the coordinate space for the anatomical/functional imaging data clearly defined as subject/native space or standardized stereotaxic space, e.g., original Talairach, MNI305, ICBM152, etc? Where (section, paragraph #)?	N/A
12. If there was data normalization/standardization to a specific space template, are the type of transformation (linear vs. nonlinear) used and image types being transformed clearly described? Where (section, paragraph #)?	N/A
13. How were anatomical locations determined, e.g., via an automated labeling algorithm (AAL), standardized coordinate database (Talairach daemon), probabilistic atlases, etc.?	N/A
14. Were any additional regressors (behavioral covariates, motion etc) used?	N/A
15. Is the contrast construction clearly defined?	N/A
16. Is a mixed/random effects or fixed inference used?	N/A
a. If fixed effects inference used, is this justified?	N/A
17. Were repeated measures used (multiple measurements per subject)?	N/A
a. If so, are the method to account for within subject correlation and the assumptions made about variance clearly stated?	N/A

18. If the threshold used for inference and visualization in figures varies, is this clearly stated?	N/A
19. Are statistical inferences corrected for multiple comparisons?	N/A
a. If not, is this labeled as uncorrected?	N/A
20. Are the results based on an ROI (region of interest) analysis?	N/A
a. If so, is the rationale clearly described?	N/A
b. How were the ROI's defined (functional vs anatomical localization)?	N/A
21. Is there correction for multiple comparisons within each voxel?	N/A
22. For cluster-wise significance, is the cluster-defining threshold and the corrected significance level defined?	N/A

Additional comments

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