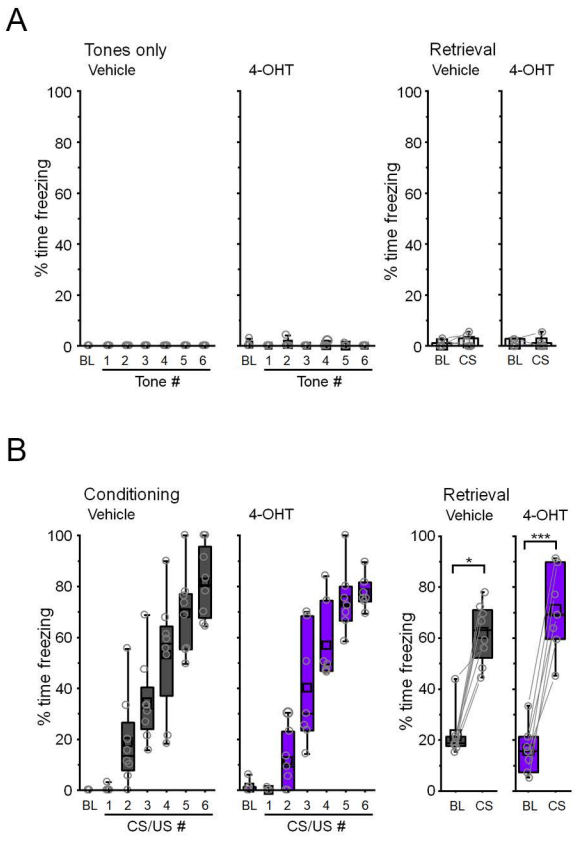
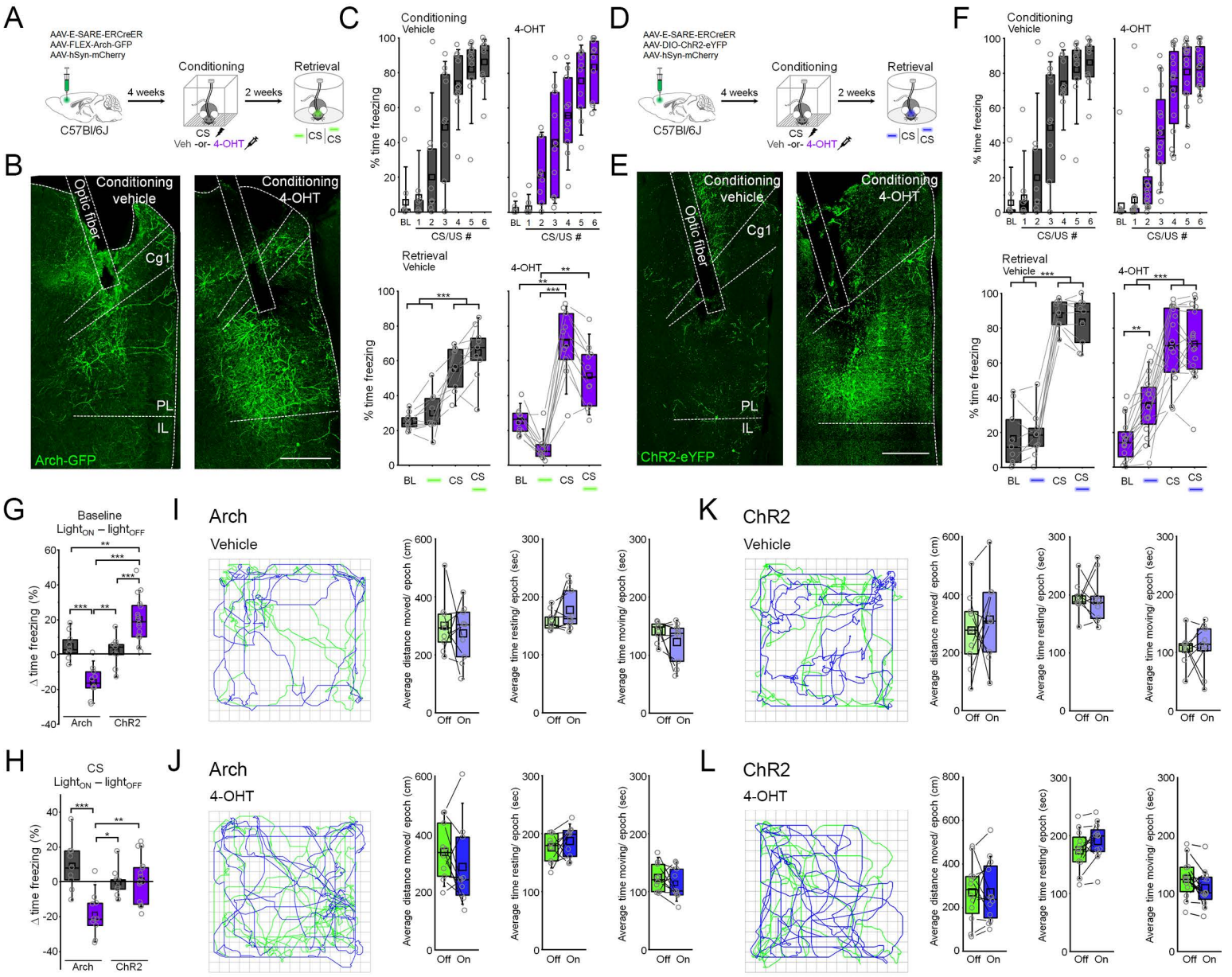
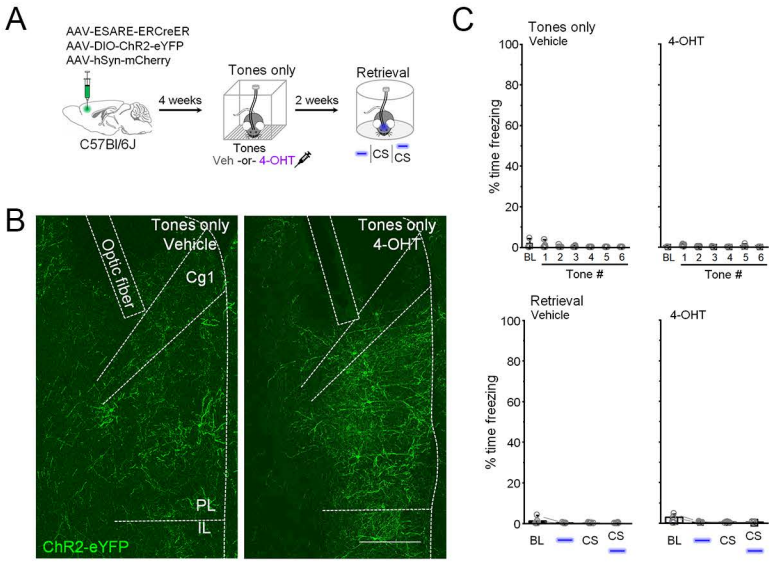


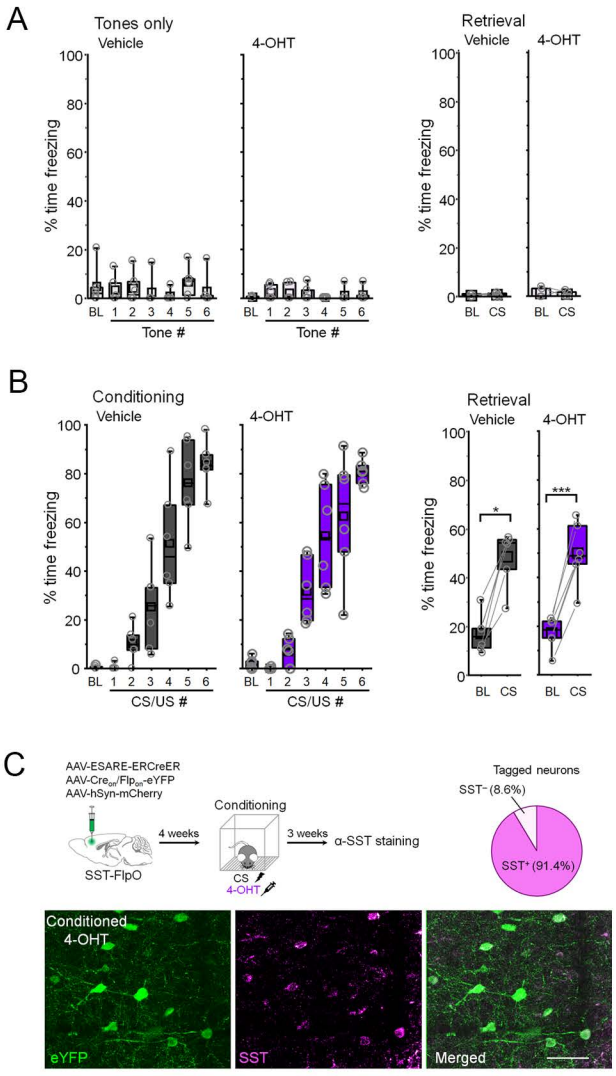
Supplemental Figure 1 - related to Figure 1. Freezing during training and retrieval for mice in Fig 1. (A) Freezing during conditioning and retrieval for mice exposed to tones only. Vehicle retrieval: W = 3, p = 0.58, Wilcoxon signed rank test, n = 8 mice. 4-OHT retrieval: W = 5, p = 1, Wilcoxon signed ranked test, n = 7 mice. **(B)** Freezing during CS-US pairing and CS-evoked retrieval for conditioned mice. Vehicle retrieval: W = 0, p = 0.014, Wilcoxon signed rank test, n = 8 mice. 4-OHT retrieval: t_6 = -11.4, p = 2.68 x 10^{-5}, paired t-test, n = 7 mice. Experiment was performed in 3 different cohorts and pooled together. * p < 0.05, *** p < 0.001 by Wilcoxon signed rank (**B**: vehicle) and paired t-test (**B**: 4-OHT).



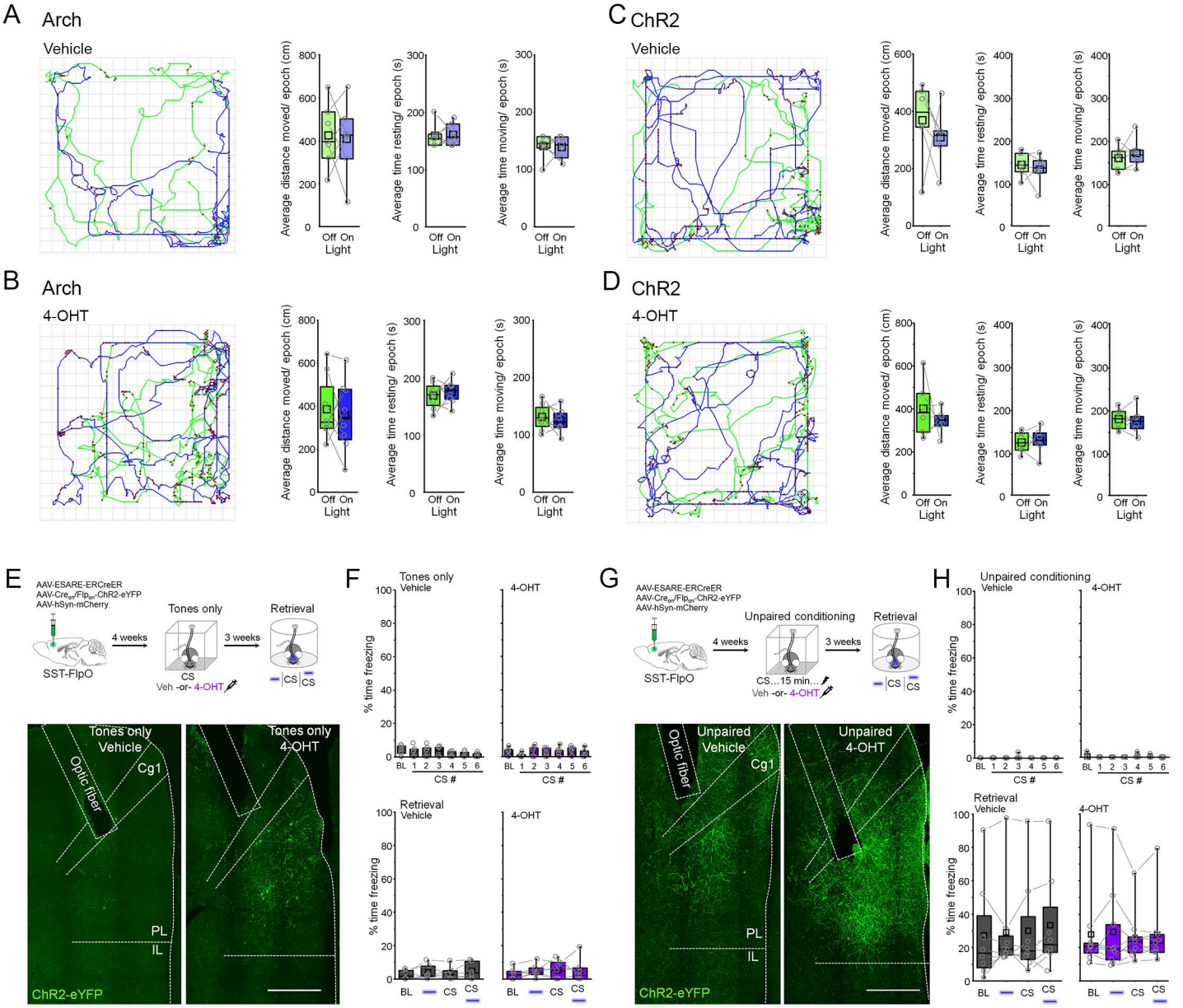
Supplementary Figure 2 - related to Figure 1. Prefrontal neurons activated by fear learning mediate conditioned freezing. (A) For *in vivo* optogenetic silencing of fear learning-related neurons, wildtype mice received bilateral infusions of a cocktail of vectors encoding E-SARE-ERCreER, Cre-dependent Arch, and hSyn-mCherry and were implanted with optic ferrules aimed at PL. Mice were subjected to CS-US pairing and immediately injected with vehicle (Veh) or 4-hydroxytamoxifen (4-OHT). Freezing was quantified two weeks later in a neutral context in response to independent and combined presentation of light and CS trials. **(B)** Representative histological images of Arch expression and optic fiber placement. Scale = 500 µm. Cg1 = cingulate area 1. PL = prelimbic cortex. IL = infralimbic cortex. **(C)** Modulation of freezing by light (532 nm, constant, 20 s epochs) and CS trials in vehicle (gray) and 4-OHT (purple) injected mice. Vehicle: $F_{(1,8)} = 408.43$, $p = 3.75 \times 10^{-8}$, 1-way repeated measures ANOVA, n = 9 mice. 4-OHT: $\chi^2 = 27.84$ (3), $p = 3.92 \times 10^{-6}$, Friedman ANOVA, n = 10 mice. Experiments were performed in 3 different cohorts and pooled together. **(D)** For *in vivo* optogenetic activation of fear learning-related neurons, wildtype mice received bilateral infusions of a cocktail of vectors encoding E-SARE-ERCreER, Cre-dependent ChR2, and hSyn-mCherry and were implanted with optic ferrules aimed at PL. Behavior was conducted in a manner identical to **(A)**. **(E)** Representative histological images of ChR2 expression and optic fiber placement. Scale = 500 µm. **(F)** Modulation of freezing by light (473 nm, 5 ms pulses, 20 Hz, 20 s epochs) and CS trials in vehicle (gray) and 4-OHT (purple) injected mice. Vehicle: $F_{(1,8)} = 269$, $p = 1.91 \times 10^{-7}$, 1-way repeated measures ANOVA, n = 9 mice. 4-OHT: $F_{(1,15)} = 197$, $p = 4.99 \times 10^{-10}$, 1-way repeated measures ANOVA, n = 16 mice. Experiments were performed in 4 different cohorts and pooled together. **(G)** Change in freezing induced by photostimulation during the baseline period in **(C)** and **(F)**. Effect of photostimulation ($Light_{on}$- $Light_{off}$): $F_{(1,40)} = 37.2$, $p = 3.56 \times 10^{-7}$, interaction between opsin and light, 2-way ANOVA. **(H)** Change in freezing induced by photostimulation during CS trials in **(C)** and **(F)**. Effect of photostimulation ($Light_{on}$- $Light_{off}$): $F_{(1,40)} = 14.4$, $p = 4.8 \times 10^{-4}$, interaction between opsin and light, 2-way ANOVA. **(I-J)** Locomotion was tested in wildtype mice from **(A)** in a 20-minute open field test during light-on and light-off periods (473 nm, 5 ms pulses, 20 Hz). Light on/off epochs were 5 minutes long and were presented in a counterbalanced fashion. Experiments were performed in 3 different cohorts and pooled together. **(I)** Example activity plot and quantification of locomotor parameters for vehicle mice (n = 9 mice). Distance moved: $t_8 = -0.587$, $p = 0.57$, paired t-test. Time resting: $t_8 = 0.13$, $p = 0.90$, paired t-test. Time moving: $t_8 = -0.129$, $p = 0.90$, paired t-test. **(J)** Example activity plot and quantification of locomotor parameters for 4-OHT mice (n = 10 mice). Distance moved: $t_{11} = 0.012$, $p = 0.99$, paired t-test. Time resting: $t_{11} = -1.92$, $p = 0.081$, paired t-test. Time moving: $t_{11} = 1.92$, $p = 0.081$, paired t-test. **(K-L)** Locomotion was tested in wildtype mice from **(D)** in a 20-minute open field test during light-on and light-off periods (532 nm, solid light). Light on/off epochs were 5 minutes long and were presented in a counterbalanced fashion. Experiments were performed in 4 different cohorts and pooled together. **(K)** Example activity plot and quantification of locomotor parameters for vehicle mice (n = 9 mice). Distance moved: $t_8 = 0.55$, $p = 0.59$, paired t-test. Time resting: W = 12, $p = 0.24$, Wilcoxon signed rank test, n = 9 mice. Time moving: W = 33, $p = 0.24$, Wilcoxon signed rank test, n = 9 mice. **(N)** Example activity plot and quantification of locomotor parameters for 4-OHT mice (n = 12 mice). Distance moved: $t_9 = 1.33$, $p = 0.21$, paired t-test. Time resting: $t_9 = -0.956$, $p = 0.36$, paired t-test. Time moving: $t_9 = 0.96$, $p = 0.36$, paired t-test. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, Tukey's post-hoc test (**C:** vehicle, **F, G, H**) or Dunn's post-hoc test (**C:** 4-OHT).



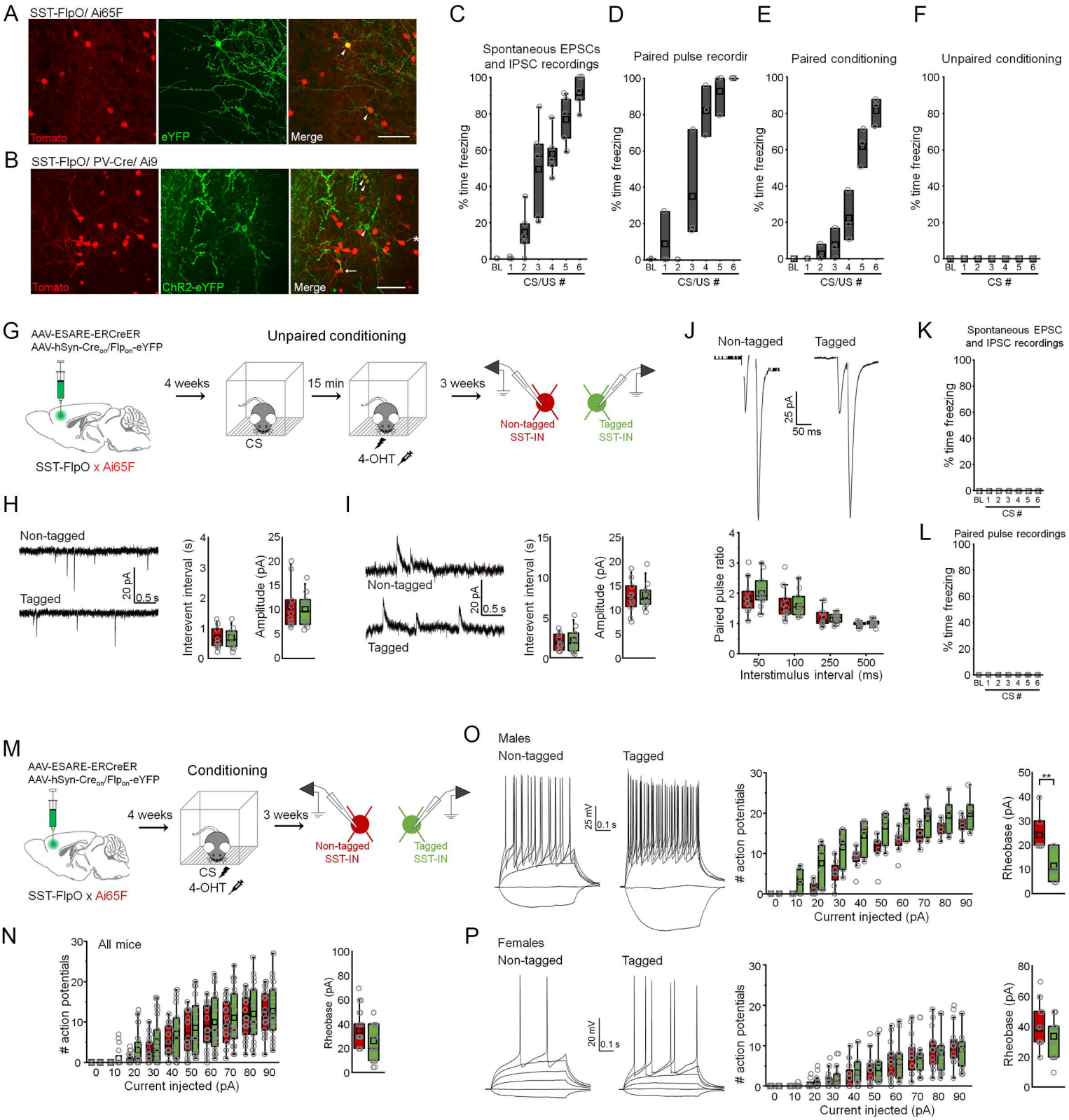
Supplemental Figure 3 – related to Figure 1. No effect of photostimulation of neurons tagged during tones only training. (A) For *in vivo* optogenetic activation of neurons tagged during tones only training, wildtype mice received bilateral infusions into prelimbic cortex of a cocktail of vectors encoding E-SARE-ERCreER, Cre-dependent ChR2, and hSyn-mCherry and were implanted with optic ferrules aimed at PL. Mice were presented with 6 auditory tones and immediately injected with vehicle (veh) or 4-hydroxytamoxifen (4-OHT). Freezing was quantified two weeks later in a neutral context while testing the independent and combined effect of light and tone presentation. **(B)** Representative histological images of ChR2 expression and optic fiber placement. Scale = 500 µm. Cg1 = cingulate area 1, PL = prelimbic, IL = infralimbic. **(C)** Quantification of freezing during photoexcitation (473 nm, 5 ms pulses, 20 Hz, 20 s epochs) and CS presentation in vehicle (gray, n = 7 mice) and 4-OHT (purple, n = 6 mice) mice. Retrieval vehicle: $\chi^2 = 0.214$ (3), p = 0.98, Friedman ANOVA. Retrieval 4-OHT: $\chi^2 = 0.65$ (3), p = 0.88, Friedman ANOVA. Experiment was performed in 2 different cohorts and pooled together.



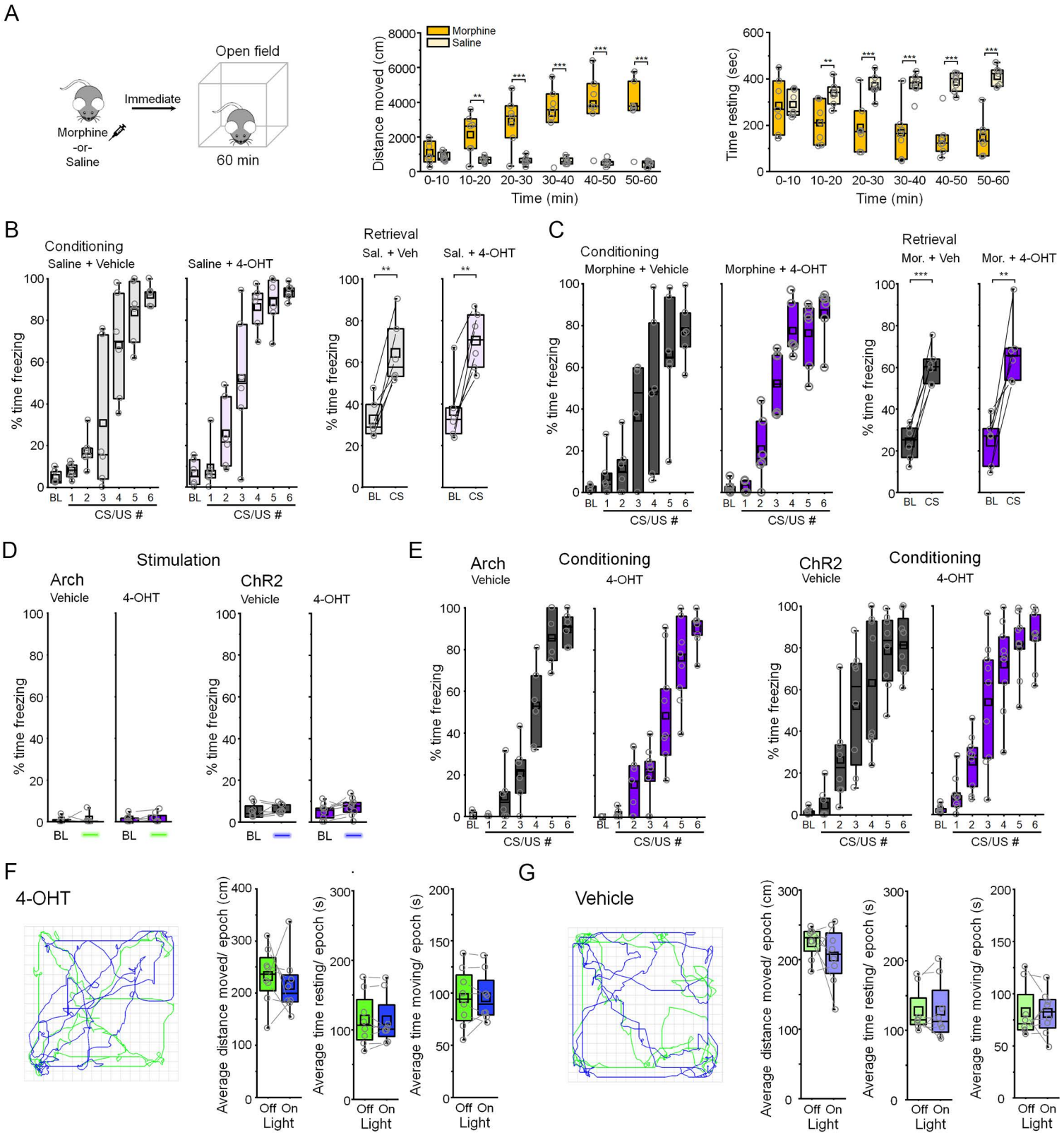
Supplemental Figure 4 – related to Figure 2. Quantification of freezing during training and retrieval and confirmation of intersectional tagging for SST-FlpO mice in Fig 2. (A) Freezing during tone presentation and retrieval for mice exposed to tones only. Vehicle retrieval: W = 3, p = 0.36, Wilcoxon signed rank test, n = 6 mice. 4-OHT retrieval: W = 4, p = 0.79, Wilcoxon signed ranked test, n = 6 mice. **(B)** Freezing during CS-US pairing and CS-evoked retrieval for conditioned mice. Vehicle retrieval: W = 0, p = 0.036, Wilcoxon signed rank test, n = 6 mice. 4-OHT retrieval: t_5 = -9.95, p = 1.75 x 10^{-4}, paired t-test, n = 6 mice. Experiment was performed in 4 different cohorts and pooled together. **(C)** For a random subset of 4-OHT-injected conditioned mice (n = 4) from Fig. 2, tissue was stained against somatostatin (SST). The percent of tagged neurons positive for SST was quantified and reported as an average across all mice. Scale = 100 µm. Experiment was performed in 2 different cohorts and pooled together. * $p < 0.05$, *** $p < 0.001$ by Wilcoxon signed rank (**B**: vehicle) and paired t-test (**B**: 4-OHT).



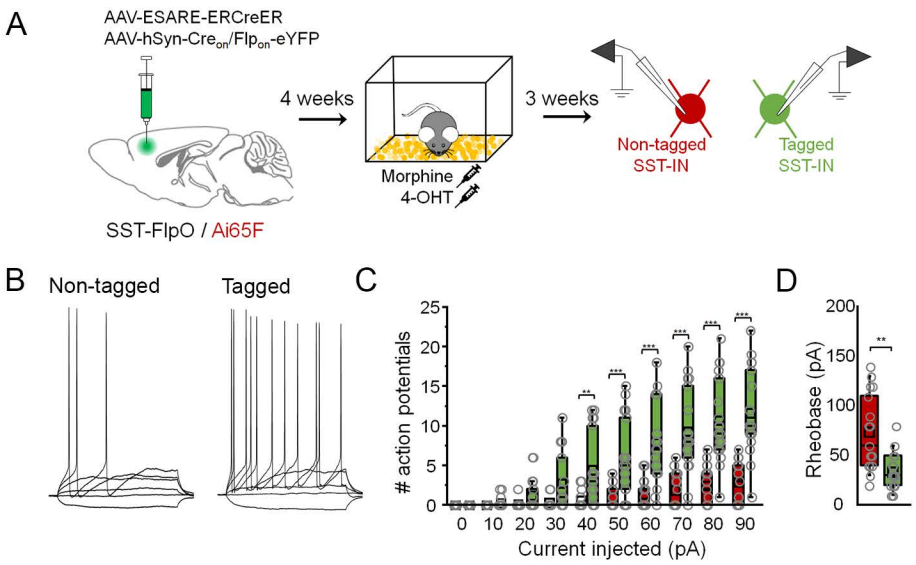
Supplemental Figure 5 – related to Figure 3. Locomotor measures for mice in Fig.3 and no effect of photostimulation of SST-INs tagged during tones only or unpaired training. (A-D) SST-FlpO transgenic mice received bilateral infusions into prelimbic cortex of a cocktail containing vectors encoding E-SARE-ERCreER, Cre- and Flp-dependent Arch, and hSyn-mCherry. Four weeks later, mice were subjected to CS-US pairing and then immediately injected with vehicle (veh) or 4-hydroxytamoxifen (4-OHT). **(A-B)** Three weeks after conditioning, locomotion was tested in a 20-minute open field test during light-on and light-off periods (532 nm, constant). Light on/off epochs were 5 minutes long and were presented in a counterbalanced fashion. Experiments were performed in 2 different cohorts and pooled together. **(A)** Example activity plot and quantification of locomotor parameters for vehicle mice (n = 7 mice). Distance moved: $t_6 = 0.209$, p = 0.841, paired t-test. Time resting: W = 13, p = 0.932, n = 7 mice, Wilcoxon signed rank test. Time moving: W = 15, p = 0.932, n = 7 mice, Wilcoxon signed rank test. **(B)** Example activity plot and quantification of locomotor parameters for 4-OHT mice (n = 8 mice). Distance moved: $t_7 = 0.472$, p = 0.65, paired t-test. Time resting: $t_7 = -0.762$, p = 0.47, paired t-test. Time moving: $t_7 = 0.763$, p = 0.47, paired t-test. **(C-D)** SST-FlpO transgenic mice received bilateral infusions into prelimbic cortex of a cocktail containing vectors encoding E-SARE-ERCreER, Cre- and Flp-dependent ChR2, and hSyn-mCherry. Four weeks later, mice were subjected to CS-US pairing and then immediately injected with vehicle (veh) or 4-hydroxytamoxifen (4-OHT). After three weeks, locomotion was tested in a 20-minute open field test during light-on and light-off periods (473 nm, 10 ms pulses, 20 Hz). Light on/off epochs were 5 minutes long and were presented in a counterbalanced fashion. **(C)** Example activity plot and quantification of locomotor parameters for vehicle mice (n = 6 mice). Distance moved: $t_5 = 0.724$, p = 0.50, paired t-test. Time resting: $t_5 = 0.795$, p = 0.46, paired t-test. Time moving: $t_5 = -0.793$, p = 0.46, paired t-test. **(D)** Example activity plot and quantification of locomotor parameters for 4-OHT mice (n = 6 mice). Distance moved: $t_5 = 0.822$, p = 0.45, paired t-test. Time resting: $t_5 = -0.247$, p = 0.81, paired t-test. Time moving: $t_5 = 0.247$, p = 0.81, paired t-test. Experiments were performed in 2 different cohorts and pooled together. **(E)** For *in vivo* optogenetic activation of SST-INs activated by tones only experience, SST-FlpO transgenic mice received bilateral infusions into prelimbic cortex of a cocktail of vectors encoding E-SARE-ERCreER, Cre- and Flp-dependent ChR2, and hSyn-mCherry and were implanted with optic ferrules aimed at PL. Mice were exposed to 6 auditory tones and immediately injected with vehicle (veh) or 4-hydroxytamoxifen (4-OHT). Freezing was quantified two weeks later in a neutral context while testing the independent and combined effect of light and tone presentation. Scale = 500 μM**. (F)** Modulation of freezing by photoexcitation (473 nm, 5 ms pulses, 20 Hz, 20 s epochs) and tone presentation in vehicle (gray) and 4-OHT (purple) injected mice. Vehicle retrieval: $F_{(3,15)} = 0.712$, p = 0.56, 1-way repeated measures ANOVA, n = 6 mice. 4-OHT retrieval: $\chi^2 = 2.61$ (3), p = 0.46, Friedman ANOVA, n = 7 mice. Experiment was performed in 2 different cohorts and pooled together. **(G)** For *in vivo* optogenetic activation of SST-INs activated by unpaired conditioning, SST-FlpO transgenic mice underwent surgery as described in (**E**). After 4 weeks, mice underwent unpaired conditioning followed immediately by injections of vehicle (veh) or 4-hydroxytamoxifen (4-OHT). Freezing was quantified two weeks later in a neutral context while testing the independent and combined effect of light and CS presentation. Scale = 500 μm. **(H)** Quantification of freezing during photoexcitation (473 nm, 5 ms pulses, 20 Hz, 20 s epochs) and CS presentation in vehicle (gray) and 4-OHT (purple) injected mice. Vehicle retrieval: $\chi^2 = 1.99$ (3), p = 0.58, Friedman ANOVA, n = 8 mice. 4-OHT retrieval: $\chi^2 = 1.4$ (3), p = 0.71, Friedman ANOVA, n = 9 mice. Experiment was performed in 3 different cohorts and pooled together.


A
SST-FlpO/ Ai65F
Tomato
eYFP
Merge
B
SST-FlpO/ PV-Cre/ Ai9
Tomato
ChR2-eYFP
Merge
C
Spontaneous EPSCs and IPSC recordings
% time freezing
CS/US #
D
Paired pulse recordir
E
Paired conditioning
F
Unpaired conditioning
CS #
G
AAV-ESARE-ERCreER
AAV-hSyn-Cre$_{on}$/Flp$_{on}$-eYFP
SST-FlpO x Ai65F
4 weeks
CS
15 min
4-OHT
3 weeks
Non-tagged SST-IN
Tagged SST-IN
Unpaired conditioning
H
Non-tagged
Tagged
20 pA
0.5 s
Interevent interval (s)
Amplitude (pA)
I
J
Non-tagged
Tagged
25 pA
50 ms
Paired pulse ratio
Interstimulus interval (ms)
K
Spontaneous EPSC and IPSC recordings
L
Paired pulse recordings
M
AAV-ESARE-ERCreER
AAV-hSyn-Cre$_{on}$/Flp$_{on}$-eYFP
SST-FlpO x Ai65F
4 weeks
CS
4-OHT
3 weeks
Non-tagged SST-IN
Tagged SST-IN
Conditioning
N
All mice
action potentials
Current injected (pA)
Rheobase (pA)
O
Males
Non-tagged
Tagged
25 mV
0.1 s
action potentials
Current injected (pA)
Rheobase (pA)
**
P
Females
Non-tagged
Tagged
20 mV
0.1 s
action potentials
Current injected (pA)
Rheobase (pA)

Supplemental Figure 6 – related to Figure 4. Additional freezing measures and electrophysiological analysis of tagged versus nontagged neurons after unpaired or paired fear conditioning. (A) Discrimination of tagged (eYFP+, tdTomato+) from non-tagged (tdTomato+) SST-INs following intersectional labeling as described in Fig. 4A. Scale = 100 µm. **(B)** Discrimination of tagged SST-INs (ChR2-eYFP$^+$; arrow heads), PV-INs (tdTomato$^+$; putative PV-IN denoted with arrow) and tagged PNs (tdTomato$^+$; putative tagged PN denoted with asterisk) following intersectional labeling as described in Fig. 4E. **(C)** Freezing during CS/US pairings for mice used for spontaneous EPSC and IPSC recordings in Fig. 4. **(D)** Freezing during CS/US pairings for mice used for paired pulse recordings in Fig. 4. **(E)** Freezing during CS/US pairings for mice used to record light-elicited responses from tagged SST-INs onto neighboring PV-INs, tagged PNs, and non-tagged PNs in Fig. 4. **(F)** Freezing during CS presentations (training in unpaired mice) for mice used to record light-elicited responses from tagged SST-INs onto neighboring PV-INs, tagged PNs, and non-tagged PNs in Fig. 4. **(G-L)** No differences in synaptic properties between tagged and nontagged SST-INs following unpaired conditioning. **(G)** SST-FlpO/ Ai65F double transgenic mice received prelimbic infusions of a cocktail of vectors encoding E-SARE-ERCreER, as well as Cre- and Flp-dependent eYFP. Mice were subjected to unpaired conditioning and immediately injected with 4-hydroxytamoxifen (4-OHT). Three weeks later, recordings were obtained from eYFP+/ tdTomato+ (tagged) and eYFP-/ tdTomato+ (non-tagged) SST-INs. **(H)** Spontaneous excitatory postsynaptic currents (EPSCs) were recorded from tagged (n = 10 cells) and non-tagged SST-INs (n = 10 cells) in the same slices (n = 4 slices from 4 mice). Interevent interval: t_{18} = -0.062, p = 0.95, two-sided unpaired t-test. Amplitude: U = 51, p = 0.97, Mann-Whitney U-test. **(I)** Spontaneous inhibitory postsynaptic currents (IPSCs) were recorded from tagged (n = 10 cells) and non-tagged SST-INs (n = 10 cells) in the same slices (n = 4 slices from 4 mice). Interevent interval: t_{18} = -0.269, p = 0.79, two-sided unpaired t-test. Amplitude: t_{18} = -0.243, p = 0.81, two-sided unpaired t-test. **(J)** EPSC recordings from non-tagged (n = 10 cells) and tagged SST-INs (n = 11 cells) in the same slices (n = 3 slices in 3 mice) during paired pulse stimulation. Paired pulse ratio: $F_{(3,27)}$ = 0.545, p = 0.66, 2-way repeated measures ANOVA. **(K)** Freezing during CS presentation (training) for unpaired mice used for spontaneous EPSC and IPSC recordings. **(L)** Freezing during CS presentation (training) for unpaired mice used for paired pulse recordings. Experiment was performed in mice from 2 different litters and pooled together. **(M-O)** Higher excitability of tagged relative to nontagged SST-INs in male mice following paired conditioning. **(M)** SST-FlpO/ Ai65F double transgenic mice received prelimbic infusions of a cocktail of vectors encoding E-SARE-ERCreER, as well as Cre- and Flp-dependent eYFP. Mice were subjected to CS-US pairing and were immediately injected with 4-hydroxytamoxifen (4-OHT). Three weeks later, recordings were obtained from eYFP+/ tdTomato+ (tagged) and eYFP-/ tdTomato+ (non-tagged) SST-INs. **(N)** Input-output curves and rheobase quantification for tagged (n = 21 cells) and non-tagged (n = 23 cells) SST-INs in the same slices of male and female mice (n = 6 slices from 6 mice). Input-output: $F_{(9,180)}$ = 1.79, p = 0.072, 2-way repeated measures ANOVA. Rheobase: U = 306.5, p = 0.12, Mann-Whitney U-test. **(O)** Representative spike trains (-20 pA and +10-40 pA current injections), input-output curves, and rheobase quantification for tagged (n = 7 cells) and non-tagged (n = 7 cells) SST-INs in the same slices of male mice (n = 3 slices from 3 mice). Input-output: $F_{(9,36)}$ = 1.81, p = 0.10, 2-way repeated measures ANOVA. Rheobase: U = 44, p = 0.0090, Mann-Whitney U-test. **(P)** Representative spike trains (-20 pA and +10-40 pA current injections), input-output curves, and rheobase quantification for tagged (n = 14 cells) and non-tagged (n = 16 cells) SST-INs in the same slices of female mice (n = 3 slices from 3 mice). Input-output: $F_{(9,99)}$ = 0.522, p = 0.86, 2-way repeated measures ANOVA. Rheobase: U = 126, p = 0.56, Mann-Whitney U-test. ** p < 0.01 by Mann-Whitney U-test (**O**: rheobase). Experiments were performed in mice from 2 different litters and pooled together.


A
Open field
Immediate
Morphine
-or-
Saline
60 min
Morphine
Saline
Distance moved (cm)
Time (min)
Time resting (sec)
0-10
10-20
20-30
30-40
40-50
50-60
B
Conditioning
Saline + Vehicle
Saline + 4-OHT
Retrieval
Sal. + Veh
Sal. + 4-OHT
% time freezing
CS/US #
BL
CS
C
Conditioning
Morphine + Vehicle
Morphine + 4-OHT
Retrieval
Mor. + Veh
Mor. + 4-OHT
D
Stimulation
Arch
ChR2
Vehicle
4-OHT
E
Arch
ChR2
Conditioning
F
4-OHT
Average distance moved/ epoch (cm)
Average time resting/ epoch (s)
Average time moving/ epoch (s)
Off On
Light
G
Vehicle

Supplemental Figure 7 – related to Figure 5. Additional locomotor and freezing measures for mice that received both morphine and fear conditioning. (A) To obtain a behavioral readout of acute morphine effects, wildtype mice received IP injections of 10 mg/kg morphine in saline or saline alone and were immediately submitted to an open field test for 60 minutes. Quantification of locomotor parameters was conducted for morphine (n = 7 mice) and saline mice (n = 7 mice) in the open field immediately after morphine or saline injections. Distance moved: $F_{(5,30)} = 28.3$, $p = 1.68 \times 10^{-10}$, interaction between drug group and time, 2-way repeated measures ANOVA. Time resting: $F_{(5,30)} = 19.4$, $p = 1.35 \times 10^{-8}$, interaction between drug group and time, 2-way repeated measures ANOVA. Experiment was performed in 1 cohort of mice. **, $p < 0.01$; ***, $p < 0.001$ by Tukey's post-hoc test. **(B-C)** Freezing during conditioning and retrieval for mice in Fig. 5B-F. **(B)** Freezing during conditioning and memory retrieval for mice injected with saline. Saline vehicle retrieval: $t_5 = -5.94$, $p = 0.002$, paired t-test, n = 6 mice. Saline 4-OHT retrieval: $t_5 = -5.94$, $p = 0.002$, paired t-test, n = 6 mice. **(C)** Freezing during conditioning and memory retrieval for mice injected with morphine. Morphine vehicle retrieval: $t_5 = -9.35$, $p = 2.36 \times 10^{-4}$, paired t-test, n = 6 mice. Morphine 4-OHT retrieval: $t_5 = -5.4$, $p = 0.003$, paired t-test, n = 6 mice. Experiment was performed in 2 different cohorts and pooled together. **(D-E)** Freezing during pre-training photostimulation test and during fear conditioning for mice in Fig. 5G-I. **(D)** Freezing during the pre-training photostimulation test. Arch vehicle: W = 5, p = 1, Wilcoxon signed rank test. Arch 4-OHT: W = 3, p = 0.62, Wilcoxon signed rank test. ChR2 vehicle: $t_7 = -0.788$, $p = 0.46$, paired t-test. ChR2 4-OHT: $t_8 = -1.74$, $p = 0.12$, paired t-test **(E)** Freezing during fear conditioning for morphine-treated mice. **(F-G**) Photostimulation of morphine-activated SST-INs does not affect general locomotion. SST-FlpO transgenic mice received bilateral prelimbic infusions of a cocktail containing vectors encoding E-SARE-ERCreER, Cre- and Flp-dependent ChR2, and hSyn-mCherry. Four weeks later, mice were injected with morphine (10 mg/kg) followed 10 hours later by injections of vehicle (veh) or 4-hydroxytamonifen (4-OHT). After three weeks, locomotion was tested in a 20-minute open field test during light-on and light-off periods (473 nm, 10 ms pulses, 20 Hz). Light on/off epochs were 5 minutes long and were presented in a counterbalanced fashion. **(F)** Example activity plot and quantification of locomotor parameters for vehicle mice (n = 8 mice). Distance moved: $t_7 = 1.14$, $p = 0.29$, paired t-test. Time resting: W = 18, p = 1, Wilcoxon signed rank test. Time moving: W = 18, p = 1, Wilcoxon signed rank test. **(G)** Example activity plot and quantification of locomotor parameters for 4-OHT mice (n = 8 mice). Distance moved: $t_7 = 0.639$, $p = 0.54$, paired t-test. Time resting: W = 16, p = 0.83, Wilcoxon signed rank test. Time moving: $t_7 = -0.159$, $p = 0.88$, paired t-test. Experiments were performed in 2 different cohorts and pooled together. ** $p < 0.01$, ** $p < 0.01$, *** $p < 0.001$ by Tukey's post-hoc (**A**) or paired t-test (**B-C**).



Supplemental Figure 8 – related to Figure 8. Comparison of intrinsic excitability between tagged and non-tagged SST-INs after morphine administration. (A) SST-FlpO/ Ai65F double transgenic mice received prelimbic infusions of a cocktail of vectors encoding E-SARE-ERCreER, as well as Cre- and Flp-dependent eYFP. Mice were subjected to IP injections of 10 mg/kg morphine and were injected with 4-hydroxytamoxifen (4-OHT) 10 hours later. Three weeks later, recordings were obtained from eYFP+/ tdTomato+ (tagged) and eYFP-/ tdTomato+ (non-tagged) SST-INs. **(B)** Representative spike trains (-20 pA and +10-40 pA current injections), input-output curves, and rheobase quantification for tagged (n = 19 cells) and non-tagged (n = 17 cells) SST-INs in the same slices of male and female mice (n = 6 slices from 6 mice). **(C)** Input-output: $F_{(9,144)} = 36.3$, $p = 7.72 \times 10^{-33}$, interaction between cell type and current injected, 2-way repeated measures ANOVA. **(D)** Rheobase: $U = 268$, $p = 6.71 \times 10^{-4}$, Mann-Whitney U-test. ** $p < 0.01$, *** $p < 0.001$ by Tukey's post-hoc test in **(C)** or Mann-Whitney U-test in **(D)**. Experiments were performed in mice from 2 different cohorts and pooled together.