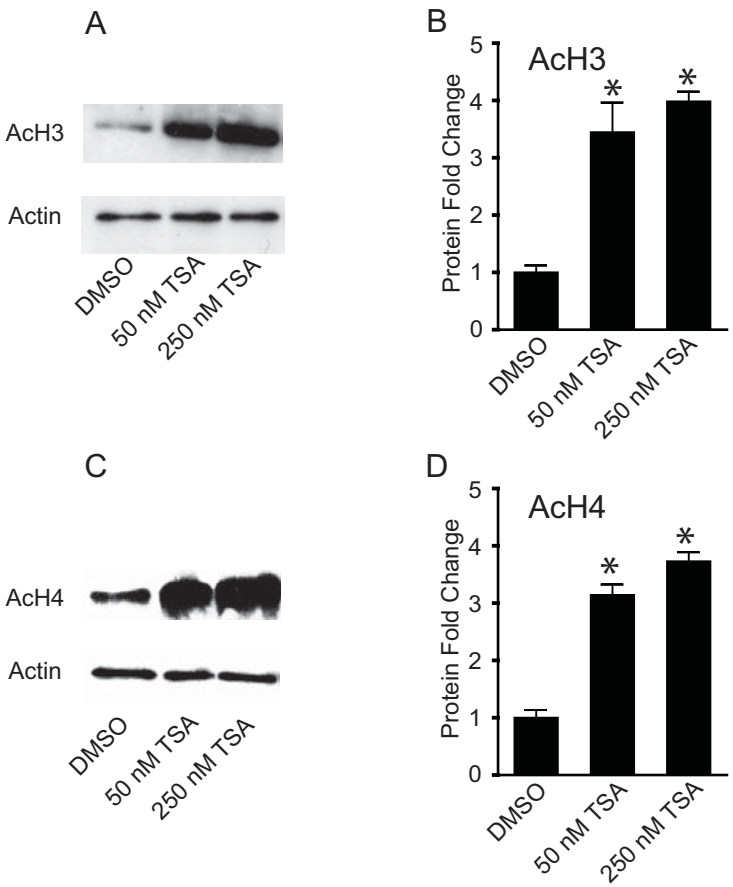
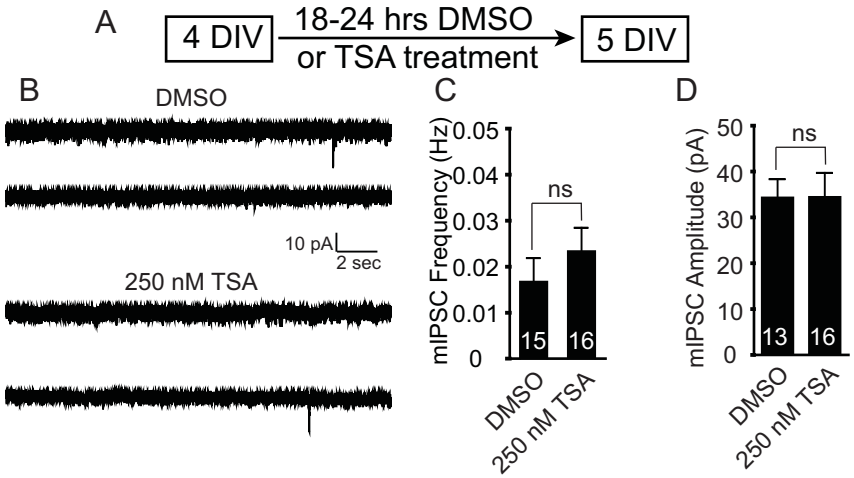
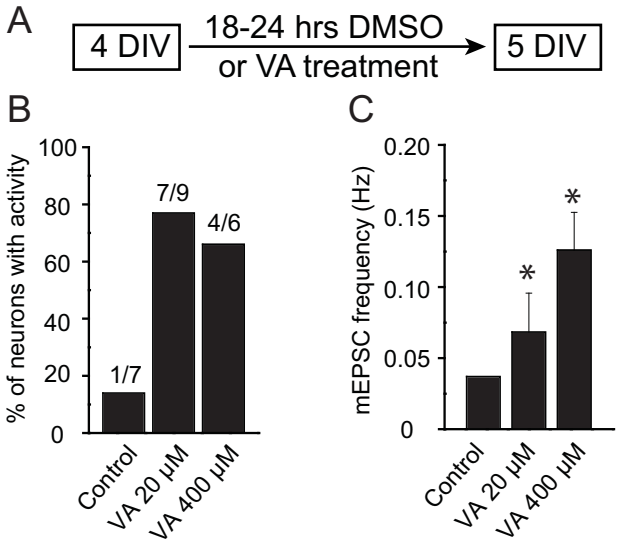


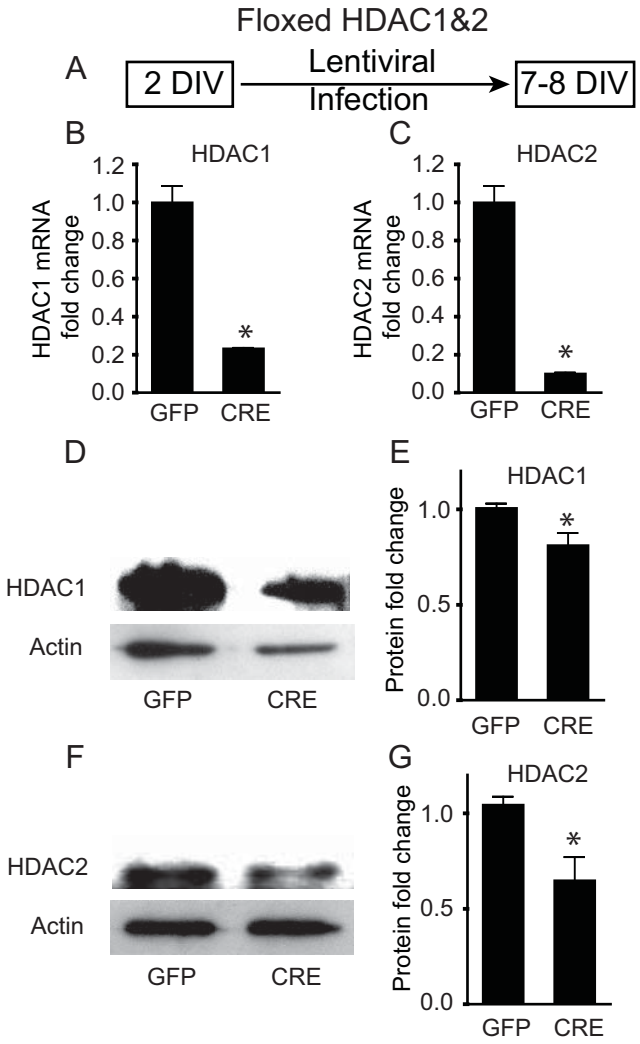
Supplementary Figure 1. Treatment of young hippocampal cultures (4 DIV) for 18-24 hours with TSA produces histone H3 and H4 hyperacetylation. A and C, Representative western blots of acetylated histone H3 (AcH3) and histone H4 (AcH4) levels following TSA treatment. Actin was used as the internal control to normalize protein levels. B and D, Bar graphs depicting AcH3 and AcH4 levels relative to actin were calculated using ImageJ software (n=3) (* $p < 0.05$ in this and all subsequent figures).



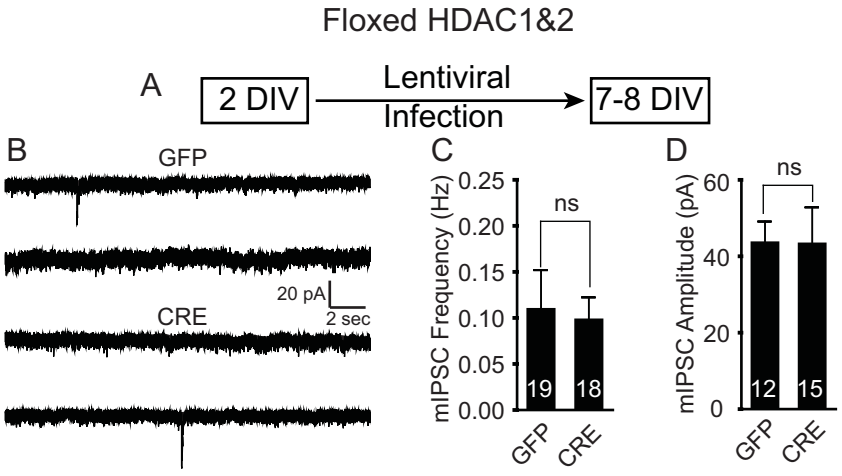
Supplementary Figure 2. Treatment of young hippocampal cultures (4 DIV) for 18-24 hours with TSA does not effect spontaneous inhibitory neurotransmission. A, Schematic timeline of the experiment. B, Representative recordings of miniature inhibitory events (mIPSCs) in DMSO and TSA treated neurons recorded in the presence of 1 μM tetrodotoxin, 50 μM AP5, and 10 μM CNQX. C, Bar graph reveals no change of mIPSC frequency following TSA treatment. D, Bar graph of mIPSC amplitude reveals no statistical difference following TSA treatment.



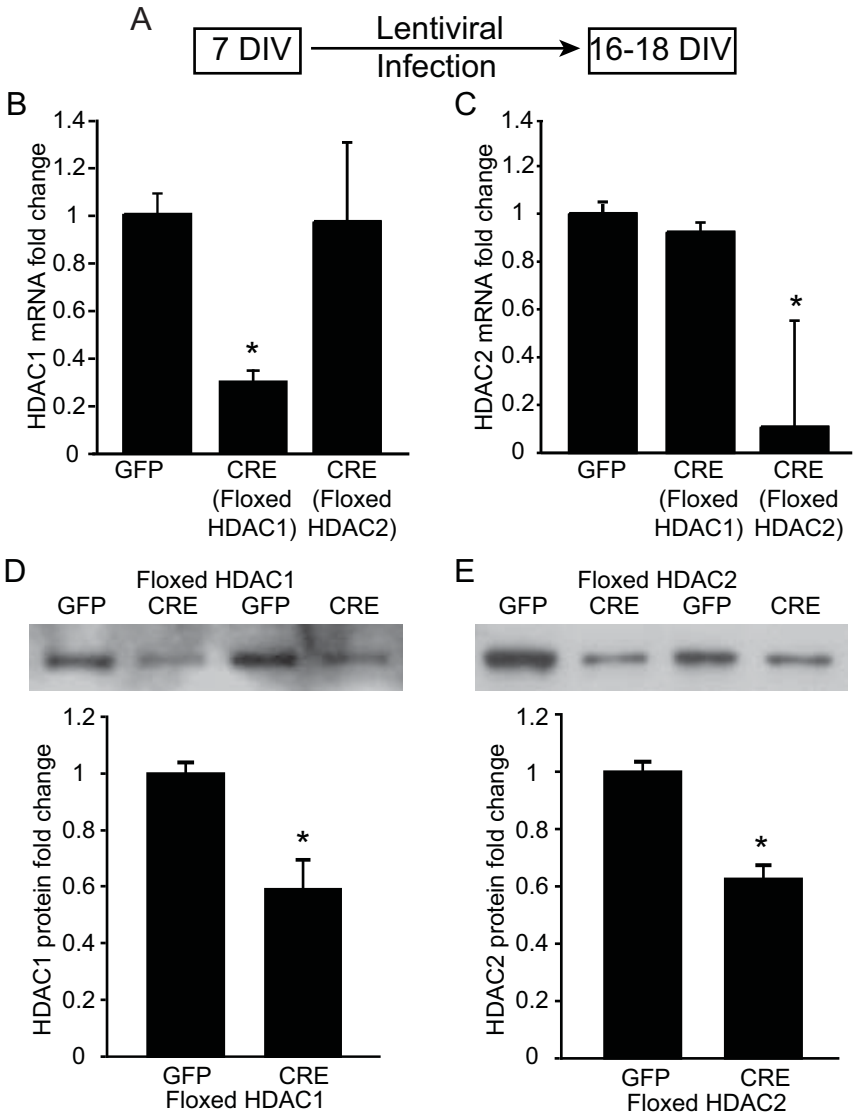
Supplementary Figure 3. Valproic acid (VA) mimics the effect of TSA on spontaneous excitatory neurotransmission in 5 DIV cultured hippocampal neurons. A, Timeline of experiment. B, Percentages of young hippocampal neurons (5 DIV) showing mEPSC activity during 15 minute recordings at -70 mV following 18-24 hour treatment with 20 or 400 µM Valproic acid. mEPSCs were recorded in the presence of 1 µM tetrodotoxin and 50 µM picrotoxin. The number on top of the bars denotes the number of neurons with activity over the total number of recorded neruons. C, Average mEPSC frequency of the active cells shown in panel A reveals a significant increase in mEPSC frequency following VA treatment (* $p < 0.05$).



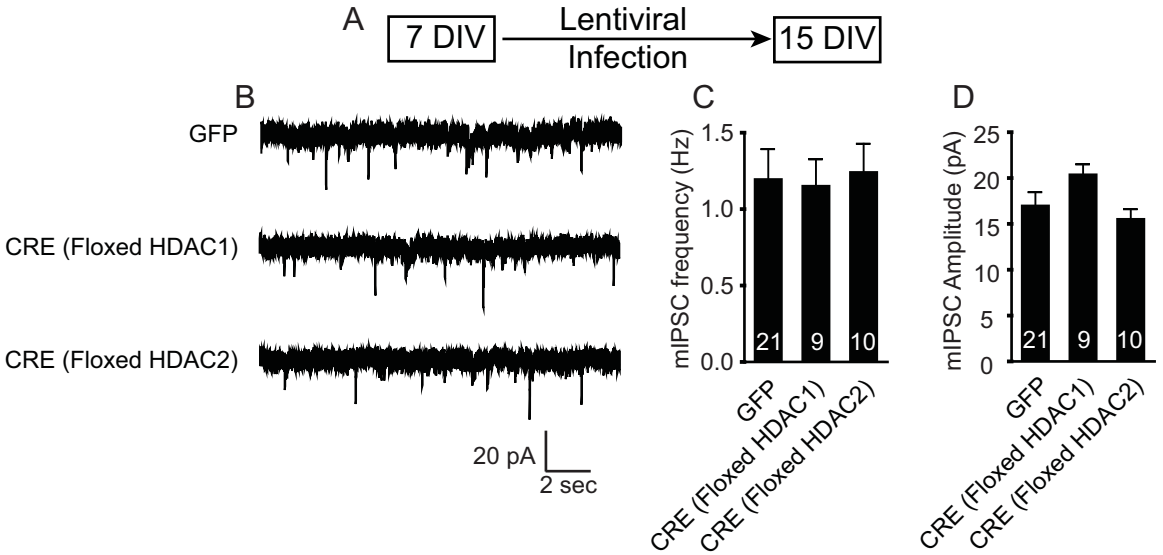
Supplementary Figure 4. CRE expression in floxed HDAC1&2 young hippocampal neurons significantly knocks down expression of HDAC1 and HDAC2. A, Schematic timeline of the experiment. B and C, Quantification of HDAC1 and HDAC2 mRNA in CRE infected cultures compared to GFP infected cultures using Q-PCR. Data were normalized against GAPDH control. D and F, Representative western blots of HDAC1, HDAC2 and actin. E and G, Fold change of HDAC1 and HDAC2 protein levels in CRE infected cultures compared to GFP infected cultures. Data were normalized against actin (* $p < 0.05$). Both the Q-PCR and westerns were done using two independent cultures.



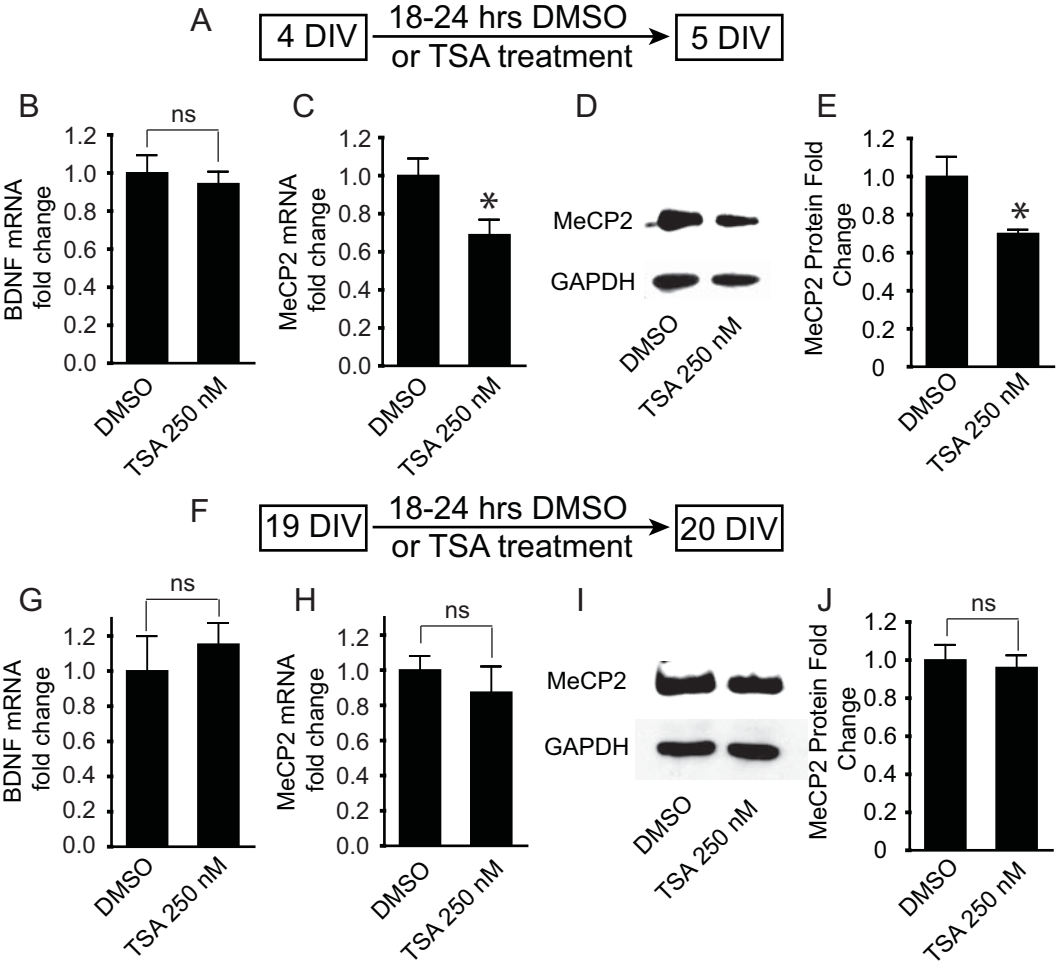
Supplementary Figure 5. HDAC1&2 deletion does not affect spontaneous inhibitory neurotransmission in young hippocampal neurons (7-8 DIV). A, Schematic of the experimental timeline. B, Representative recording of miniature inhibitory events in GFP and CRE infected neurons recorded in the presence of 1 μM tetrodotoxin, 50 μM AP5, and 10 μM CNQX. Cells were infected on 2 DIV and recordings were made on 7-8 DIV. C, The mIPSC frequency is not significantly altered following HDAC1&2 deletion. D, Bar graph of mIPSC amplitude also shows no statistical difference.



Supplementary Figure 6. Lentiviral infection of CRE in floxed HDAC1 or floxed HDAC2 mature hippocampal neurons significantly knocks down expression of HDAC1 and HDAC2. A, Schematic timeline of the experiment. B and C, Fold change in HDAC1 and HDAC2 mRNA with respect to cultures infected with GFP virus. The data were normalized to GAPDH. D, Representative western blots of HDAC1 and the fold change of HDAC1 protein levels with respect to GFP infected cultures. Actin was used for normalization as a loading control. E, Representative western blots of HDAC2 and the fold change of HDAC2 protein levels with respect to GFP infected cultures. Actin was used for normalization as a loading control (* $p < 0.05$, n=2).



Supplementary Figure 7. HDAC1 or HDAC2 deletion does not affect spontaneous inhibitory neurotransmission in mature hippocampal neurons. A, Scheme of the experimental timeline. B, Representative recording of miniature inhibitory events in GFP and CRE infected neurons recorded in the presence of 1 μM tetrodotoxin, 50 μM AP5, and 10 μM CNQX. Cells were infected on 7 DIV and were recorded on 15 DIV. C, The mIPSC frequency is not altered upon deletion of either HDAC1 or HDAC2 in mature neurons. D, Bar graph of mIPSC amplitude reveals no statistical change following the loss of HDAC1 or HDAC2 in mature neurons.



Supplementary Figure 8: Effect of TSA treatment on BDNF mRNA and MeCP2 mRNA and protein expression in young and mature hippocampal cultures
A and F, Timeline of the experiment. B and G, Treatment of young as well as mature hippocampal cultures with 250 nM TSA does not change BDNF mRNA expression as shown by quantitative real-time PCR. C-E and H-J, Treatment of young hippocampal cultures with 250 nM TSA significantly decreases both mRNA as well as protein levels of MeCP2 (* $p < 0.05$, n=3) whereas the similar treatment does not affect both the mRNA as well as protein levels of MeCP2 in mature cultures.