

Supporting Information

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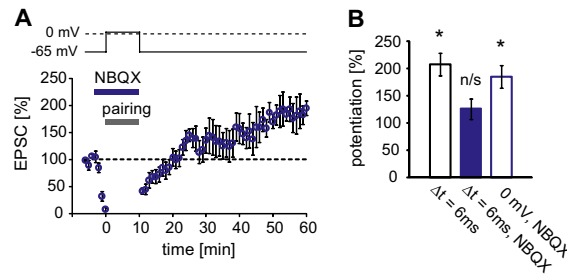


Fig. S1. Rescue of LTP in NBQX by somatic depolarization. (A) LTP could be induced in the presence of 1 μ M NBQX if the cell was voltage clamped to the reversal potential of synaptic currents during pairing ($n = 6$). During baseline and washout, holding potential was -65 mV. To improve space clamp, a Cs^+ -based intracellular solution was used consisting of 135 mM Cesium methanesulfonate, 10 mM HEPES, 4 mM $MgCl_2$, 4 mM Na_2-ATP , 0.4 mM $Na-GTP$, 10 mM Na-phosphocreatine, and 5 mM glutathione. LTP was induced when NBQX wash-in reached steady state by pairing 120 single EPSCs evoked at 0.2 Hz (equivalent to the spike-timing protocol) with constant postsynaptic depolarization to the synaptic reversal potential (0 V at the stimulated synapses, +8 to +12 mV at the soma). NBQX washout was started after completion of the LTP protocol. (B) Although NBQX blocked the induction of t-LTP in the current clamp, it did not prevent LTP induction in the voltage clamp at the reversal potential. Potentiation of the postsynaptic response relative to baseline in a time window of 50–60 min after onset of pairing is plotted for three experimental conditions.

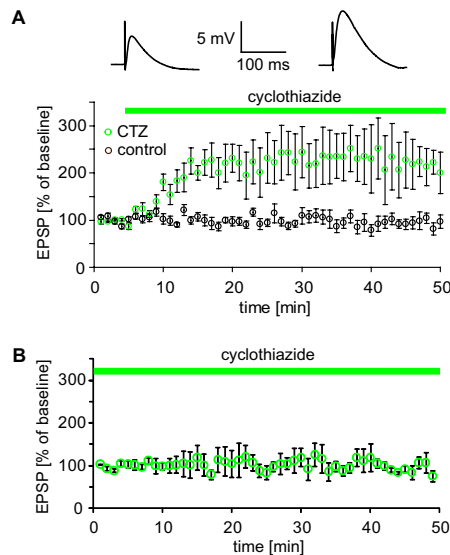


Fig. S2. Wash-in of cyclothiazide (CTZ). (A) Time course of EPSP amplitude in control condition (black, $n = 7$) and during wash-in of 100 μ M CTZ (green, $n = 5$). Bath application of CTZ increases EPSP amplitude. Example traces show EPSPs before and 30 min after CTZ application. (B) Without pairing, the presence of CTZ did not induce plasticity ($n = 4$).

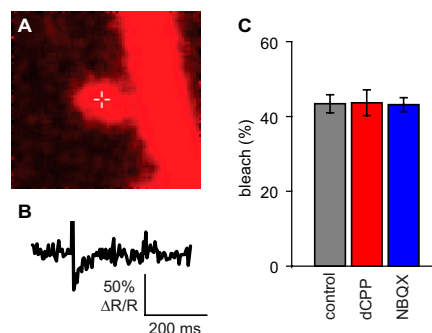


Fig. S3. Assessing local laser intensity by bleaching of fluorescent dye. (A) To ensure equal stimulation strength in different experiments, we directed a laser pulse to the center of a spine and monitored the amount of bleaching of the red fluorophore (Alexa Fluor 594) before each set of calcium measurements. (B) Fluorescence recovery after photobleaching (FRAP) of the red fluorophore in spine shown in A. (C) Alexa Fluor 594 bleaching was similar under different pharmacological conditions, indicating identical stimulation strength ($n = 18, 9,$ and 18).

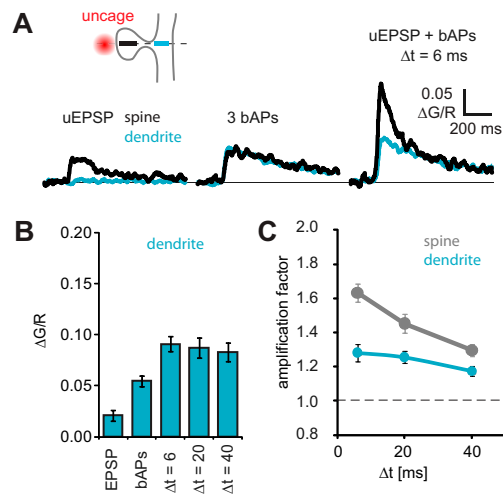


Fig. 54. Dendritic calcium transients during pairing stimulation. (A) Spine and dendritic Ca^{2+} transients in response to uncaging alone, bAPs alone, and uncaging paired with bAPs ($\Delta t = 6$ ms). Dendritic Ca^{2+} was measured close to the base of the spine. (B) Peak dendritic Ca^{2+} amplitudes in response to uncaging alone, bAPs alone, or uncaging paired with bAPs ($\Delta t = 6, 20,$ and 40 ms; $n = 16$). (C) Spine and dendritic Ca^{2+} transient amplitudes for different spike timings normalized by the linear sum ($n = 16$). In the dendrite close to the stimulated spine, both the degree of Ca^{2+} amplification and the dependence on timing were strongly reduced.

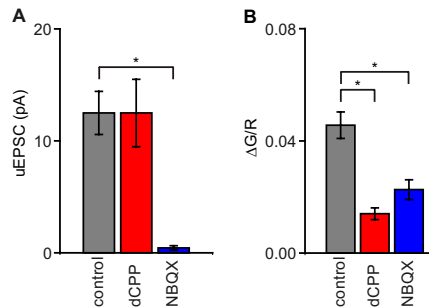


Fig. 55. Effect of glutamate receptor blockers on uncaging-evoked postsynaptic currents and calcium signals. (A) Blocking NMDARs with dCPP ($20 \mu\text{M}$) did not significantly affect uEPSCs. Blocking AMPARs with NBQX ($10 \mu\text{M}$) strongly reduced uEPSCs ($n = 18, 9,$ and 18). (B) Blocking NMDARs with dCPP ($20 \mu\text{M}$) or AMPARs with NBQX ($10 \mu\text{M}$) significantly depressed uncaging-evoked spine calcium signals ($n = 18, 9,$ and 18). $*P < 0.05$.

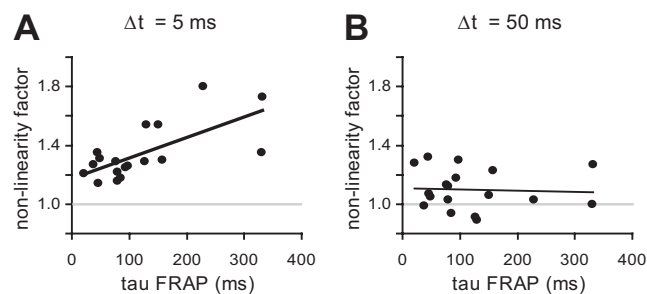


Fig. 56. Correlation between calcium nonlinearity and diffusional coupling of spines in organotypic slice cultures. Spines on oblique dendrites of CA1 pyramidal cells were stimulated by two-photon uncaging of MNI-glutamate and FRAP time constants were measured. (A) At $\Delta t = 5$ ms, the amount of Ca^{2+} signal amplification was correlated with FRAP time constants ($R = 0.681, P = 0.001, n = 18$). (B) At $\Delta t = 50$ ms, no correlation was observed ($R = 0.056, P = 0.823, n = 18$).