Learning rules for spike timing-dependent plasticity depend on dendritic synapse location

Johannes J. Letzkus, Björn M. Kampa* and Greg J. Stuart#

Supplementary Figures 1 to 5.
Supplementary Fig. 1. Computer simulations of the influence of dendritic synapse location on somatic EPSP rise time.

A) Model morphology with colour-coded location of synaptic inputs (left). Somatic (centre) and dendritic (right) EPSP voltage waveforms for the different synaptic locations. B) Somatic EPSP peak plotted against distance of the synapse from the soma. Note the strong correlation of synaptic distance and somatic amplitude. C) The EPSP rise time at the soma for different synaptic distances in the model (colour coded circles with linear fit) overlaps with visualised layer 2/3 to layer 5 connections (filled squares). Simulations used the same model as Fig. 8.

Supplementary Fig. 2. Synapses from layer 2/3 pyramidal neurons impinge onto the apical dendritic domain of layer 5 pyramidal neurons.

A) The experimental set-up (left) consisted of a paired somatic recording between synaptically connected layer 2/3 (grey pipette) and layer 5 (blue pipette) pyramidal neurons combined with a dendritic recording (red pipette; 429 ± 13 µm from the soma). In this configuration a presynaptic AP (grey) elicited a uEPSP which was recorded both in the dendrite (red) and the soma (blue). B) uEPSPs in the dendrite had a significantly faster rise time than at the soma (left, p<0.001, n=16). In addition, their amplitude was greater in the apical dendrite (right, p<0.01, n=16). Together, these data suggest that layer 2/3 synapses are located on the apical dendrite of layer 5 neurons.
Supplementary Fig. 3. $I_h$ normalises uEPSP half-width, but does not compromise the relationship between rise time and synapse location.

A) In control uEPSP half-width does not correlate with rise time ($r=0.10$, $p>0.05$, $n=82$). B) Upon block of $I_h$ by ZD7288 (50 $\mu$M) a clear correlation between uEPSP half-width and rise time is observed ($r=0.75$, $p<0.001$, $n=34$), as expected for passive filtering of uEPSPs located at different distances from the soma. In this situation rise time can be used as a measure of the electrotonic distance of the synapse from the soma. C) uEPSP rise time in control and ZD7288 are strongly correlated ($r=0.79$, $p<0.001$, $n=34$), indicating that rise time in control is a good indicator of synapse location despite the impact of $I_h$ on EPSP time course. D) Example uEPSP in control and after application of ZD7288 (averages of 100 sweeps). Note the marked increase in half-width and amplitude.

Supplementary Fig. 4. 100 $\mu$M NiCl$_2$ does not block NMDA responses in layer 5 pyramidal neurons.

NMDA (100 $\mu$M) was applied by brief (5 to 10 ms) pressure ejection from a patch pipette at proximal dendritic locations. After a baseline period of 10 minutes, 100 $\mu$M NiCl$_2$ was bath-applied (red bar) for 15 minutes and then washed out. NiCl$_2$ had no effect on NMDA response amplitude ($p>0.05$, $n=4$). Top traces are average NMDA responses of all experiments before, during and after application of NiCl$_2$. 
Supplementary Fig. 5. Calculation of NMDA receptor-dependent synaptic plasticity.

Plot of the relationship between normalised, integrated NMDA receptor conductance (NMDA activation) and STDP (see Experimental Procedures). High levels of NMDA receptor activation (>80%) lead to LTP (STDP >100%), moderate levels (<80%) lead to LTD (STDP <100%) and low levels (<55%) cause no change in synaptic weight. Circles indicate the threshold for induction of LTD and LTP.
Supplementary Fig. 4 Letzkus et al.
Supplementary Fig. 5 Letzkus et al.