SUPPLEMENTARY METHODS

Hippocampal slice preparation

3 – 32 day-old Wistar rats were used for experiments. Rats older than 8 days were anaesthetized with isoflurane prior to decapitation. The brain was removed and placed in an ice-cold solution containing (in mM): 140 cholineCl, 2.5 KCl, 0.5 CaCl$_2$, 7 MgCl$_2$, 25 NaHCO$_3$, 1.25 NaH$_2$PO$_4$, 1.3 ascorbic acid, 7 dextrose. Transverse hippocampal slices (300 µm thick) were cut (Slicer HR 2, Sigmann Elektronik) in the same ice-cold solution and they were subsequently stored in artificial cerebrospinal fluid (ACSF) containing (in mM): 124 NaCl, 3 KCl, 2 CaCl$_2$, 2 MgCl$_2$, 26 NaHCO$_3$, 1.25 NaH$_2$PO$_4$, 0.5 ascorbic acid, 3 myo-inositol, 4 D,L-lactic acid, and 10 D-glucose at 25º C. Slices were allowed to recover for a minimum of 1.5 hours, and then a single slice was transferred to the recording chamber. All ACSF solutions were continuously bubbled with 95% O$_2$ and 5% CO$_2$(pH ~7.4)

EPSC measurements

AMPA EPSCs were measured as mean amplitude during a 1 ms time window around the negative peak between 3 and 8 ms after the stimulation artifact. NMDA EPSCs were measured as the mean amplitude at 50 – 80 ms after the stimulation artifact, or, for the paired-pulse experiments, as the peak amplitude (a 2 ms time window around the peak). For the composite AMPA-NMDA EPSCs in zero magnesium solution the AMPA component was measured as the initial slope (least-square linear regression from 20 to 80% of the rising phase).
**Stimulation and LTP induction**

Stimulation started 2 – 5 minutes after establishing the whole-cell configuration (for the experiments in which peptide inhibitors were included in the pipette a waiting time of up to eight minutes was used). Sometimes recordings were made from more than one cell per slice. If so the stimulation pipette was always put in a new position before the new recording began.

In the pairing experiments, the pairing protocol consisted of 60 stimuli at 1 Hz paired with depolarization to –10 mV and 1 Hz was also used as test frequency. The fact that no potentiation was observed in nearly two thirds of the experiments is likely explained by wash-out, which may occur quickly in these rather small cells.

**Data analysis**

For the data presented in **Fig. 6a**, failures were visually identified and averaged across each experiment. No deflection from the baseline level was detected in these averaged failure sweeps, indicating that no synaptic current was present. When the failure frequency exceeded 50%, the estimation of failure frequency and EPSC size was based on 40 (instead of 20) sweeps to reduce statistical noise. For the data presented in **Fig. 7b**, an amplitude histogram was generated for all sweeps, and the standard deviation for the positive side of the zero amplitude peak was calculated. The failure threshold was then set to 1.96 standard deviations at the negative side of the peak. Summary graphs were generated by normalizing each individual experiment to the first six sweeps, binning the data in intervals of six sweeps and then averaging the binned data across experiments. PPR for a series of paired responses was calculated as the mean of the 2\textsuperscript{nd} EPSC amplitude over the mean of the 1\textsuperscript{st} EPSC amplitude. Since the 2\textsuperscript{nd} NMDA EPSC was evoked on the decaying phase of the 1\textsuperscript{st} one, its amplitude was subtracted by what
remained of the 1st one at the time of measurement (obtained from NMDA EPSCs evoked by single volley stimulations). Coefficient of variation (CV; standard deviation / mean) was calculated for the last twenty AMPA EPSCs and the subsequent NMDA EPSCs in experiments which did not contain any failures. Data are expressed as means ± SEM. Statistical significance for paired and independent samples was determined using Student’s t test.

**Chemicals**

Chemicals were from Sigma-Aldrich except for D-2-amino-5-phosphono pentanoate (D-AP5), L-AP5, LY341495 and QX-314 from Tocris Neuramin, FK-506 that was obtained from Calbiochem and PKI (6-22) amide from Biomol.