

Supplementary Fig. 1. Fyn(39-57) blocks the enhancement of NMDAR currents by recombinant Fyn kinase. (A) Fyn(39-57) inhibits (N=10) the increase of NMDAR currents by Fyn in acutely isolated rat CA1 neurons. Sample traces from cells with Fyn (1 U/ml) or Fyn plus Fyn(39-57) are shown at the beginning (t = 3min) and end of a recording (t = 26min). Both Fyn and Fyn(39-57) applied via the patch pipette. **(B)** For a series of recordings, the effects of various reagents on the Fyn-mediated increase in I_{NMDA} expressed as percent inhibition, are summarized. While Fyn(39-57) (N=10) blocked the effect of Fyn on NMDAR currents, scrambled_{i-pep} (N=7), Src (40-58) (N=6) and scrambled Src (40-58) (N=5) did not (all added to the patch pipette). In addition, Fyn(39-57) (N=4) did not inhibit the enhancement of NMDAR currents by Src. ** indicates $p < 0.01$, one-way ANOVA. Concentrations and amounts of reagents as described in the main manuscript.

Supplementary Fig. 2. The activation of VPAC receptors enhances NMDAR currents via Fyn and GluN2B in acutely isolated rat CA1 neurons. (A) VIP (1 nM; perfusion barrel) increased NMDAR currents in acutely hippocampal CA1 cells (N=5) and Ro25-6981 (500 nM) (N=6) blocked this potentiation. Sample traces from cells treated with VIP (N=6) or VIP plus Ro25-6981 (N=6) are shown at the beginning (t = 3min) and end of a recording (t = 26min). **(B)** Quantification of normalized I_{NMDA} recorded from neurons treated with VIP. The enhancement of I_{NMDA} by VIP (N=5) was prevented by Fyn(39-57) (patch pipette) (N=6) and Ro25-6981 (500 nM, bath and perfusion pipette (N=6), but not by scrambled_{i-pep} (25 $\mu\text{g/ml}$, N=5). ** indicates $p < 0.01$, one-way ANOVA.

Supplementary Fig. 3. Lack of PACAP38 effects on baseline fEPSPs. (A)

Application of PACAP does not affect baseline fEPSP slopes in rat hippocampal slices. Representative traces taken during baseline, 10 minutes after the start of PACAP application (1 nM, bath applied), as well as 25-35 and 50-60 minutes after washout of PACAP. Representative time-matched traces from a control untreated slice are also shown. Below, quantitative analysis from a series of similar recordings.

(B) Application of PACAP or SKF81297 (10 μ M, bath applied) does not alter paired-pulse facilitation of excitatory synaptic transmission. Field EPSPs were recorded following paired stimulation delivered at inter-stimulus interval of 40 ms. Paired responses were recorded before and during application of PACAP or SKF81297. The histograms show the outcome from a series of recordings. Results are presented as the amplitude of the second fEPSP expressed as a ratio of the first (paired-pulse ratio).

Controls (n=3), PCAP (n=4), SKF (n= 5)

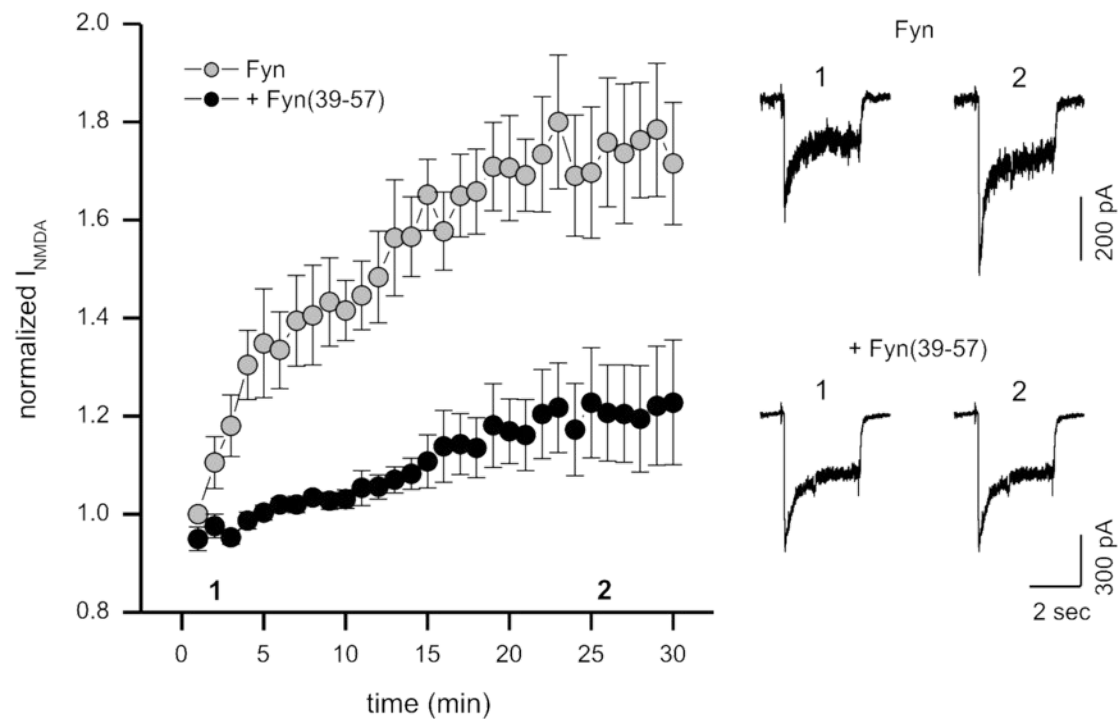
Supplementary Fig. 4. Mutation of GluNR2A subunit (GluNR2A^{Y1325F}) has no observed effect on Src and Fyn expression and their phosphorylation.

Hippocampal tissue lysate prepared from wild and mutated mice was subject to WB or IP. (A) is an example of WB showing the expression of Src and the phosphorylation (pSrcY416) between WT and GluNR2AY1325F mice, (B) data normalized to total Src are summarized from 3 tests, (C) showed the phosphorylation of Fyn (pFyn^{Y420}) by WB with pSrcY416 antibody, following IP with antibody against Fyn, (D) results normalized to immunoprecipitated Fyn and quantified from 3 experiments. There are no statistically significant difference between WT and the mutation for either Src or Fyn, and the phosphorylation as well.

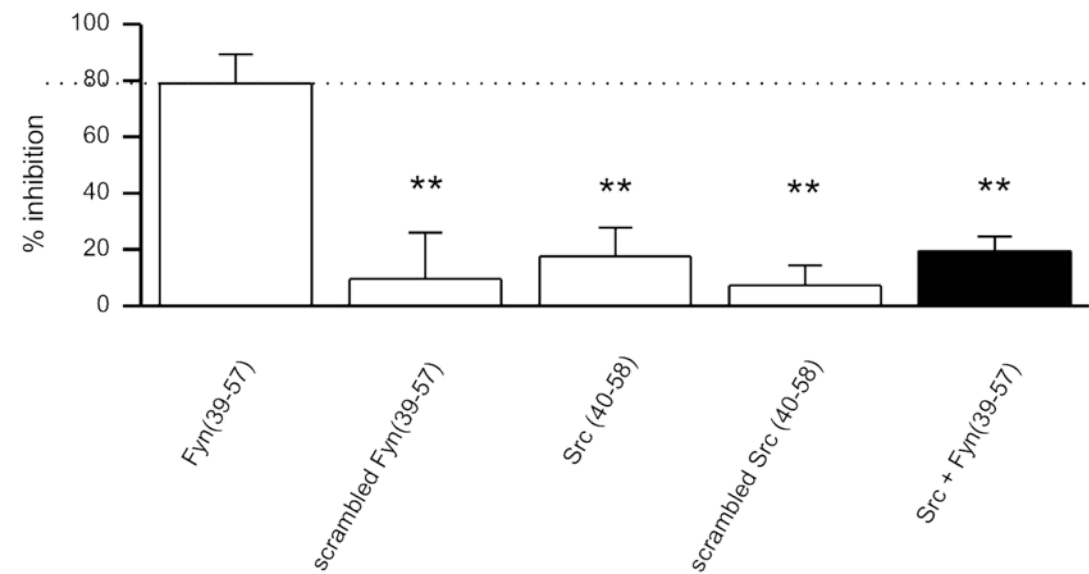
Supplemental Fig. 5. Mutation of NR2B subunit (NR2B^{Y1472F}) has no observed effect on Src and Fyn expression and their phosphorylation. (A) and (B) show Src expression and phosphorylation at tyrosine residual 416, (C and D) show Fyn expression and phosphorylation at tyrosine residual 420 (pFynY420) by IP with Fyn antibody followed by WB using antibody of pSrcY416. No statistically significant difference was found between WT and the mutation mice for both Src and Fyn expression, as well as their phosphorylation.

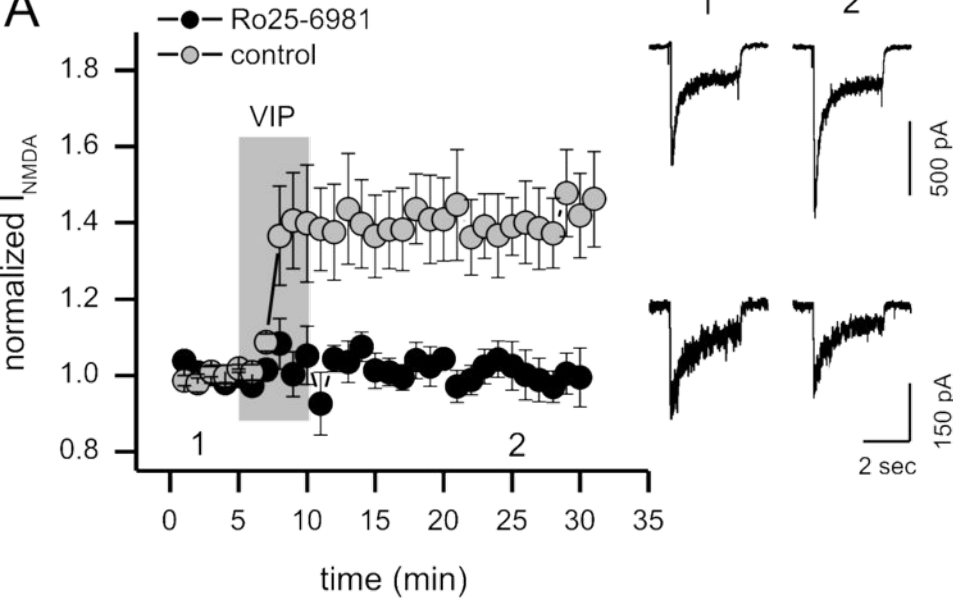
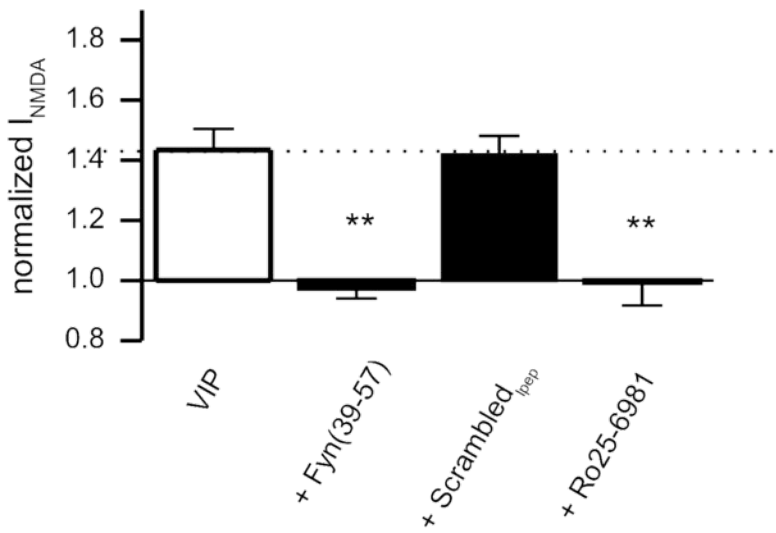
recombinant Fyn

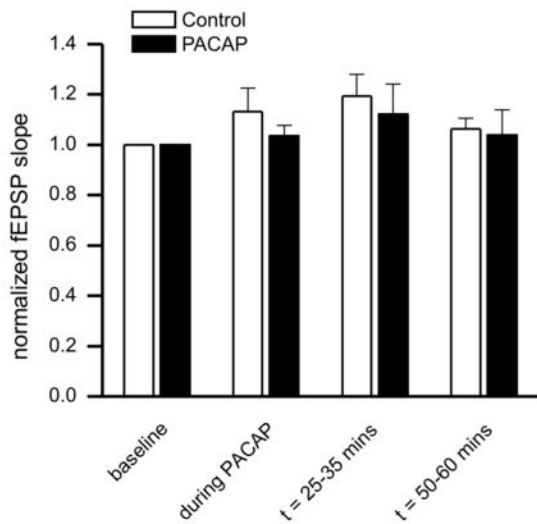
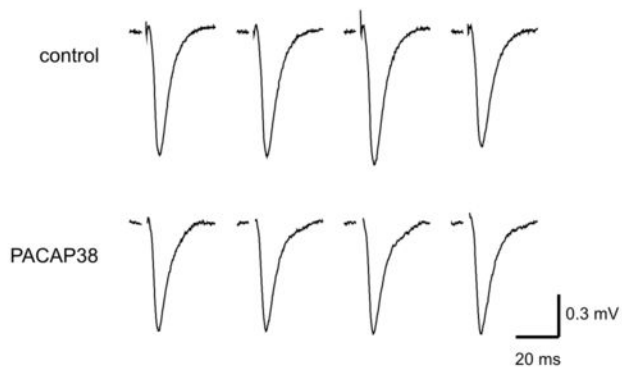
A



B



A**B**

A**B**