Fig. S1. Incubation of hippocampal slices with NMDA receptor (NMDAR) antagonist does not affect synaptic efficacy. Organotypic hippocampal slices from the same rat were incubated without drug, with 100 μM D-APV, with 100 μM 7-Cl-kynurenate, or with 3 μM Ro 25-6981 for 20–30 h (n = 11 slices per condition). Miniature excitatory postsynaptic currents (mEPSC) were recorded from two CA1 neurons per slice. (A) Example traces. (B) Average mEPSC frequency, and (C) average mEPSC amplitude were calculated. Error bars, SEM.
**Fig. S2.** Time-dependent blockade of NMDARs by MK-801. The ratio of NMDAR EPSC over AMPAR EPSC (N/A ratio) in CA1 neurons was plotted against the time period the organotypic hippocampal slices were exposed to 30 μM MK-801. N/A ratios were normalized to the N/A ratio without MK-801 incubation.

**Fig. S3.** Acute blockade of GluN2B does not affect Aβ-mediated synaptic depression of AMPAR currents. Paired whole-cell recordings were used to determine the ratio of EPSC from APP-CT100-infected CA1 neurons over EPSC from uninfected counterpart, before and 10–15 min after wash-in of GluN2B antagonist Ro 25-6981 (3 μM). Individual pairs in gray, average denoted in black. Error bars, SEM.

**Fig. S4.** Oligomeric Aβ-mediated synaptic depression is blocked by tyrosine phosphatase inhibitor. Dot-plot of paired EPSC recordings, average denoted in red. Incubation with 5 μM bpv(phen) blocked synaptic AMPAR depression in APP-CT100–expressing cells.