SUPPLEMENTARY METHODS

Miniature EPSC's were detected using the Mini Analysis program (Synaptosoft, Decatur, GA) with a threshold set at three times the root mean square of membrane current noise. Cells showing a negative correlation between mEPSC amplitude and rise time were excluded from this analysis. The first 300 events with rise time $\leq$ 3 ms were used to estimate the cell's mEPSC amplitude distribution and the mean of the first 50 non-overlapping miniature currents was taken as the average mEPSC for that cell. The results are restricted to those cases in which at least two cells/hemisphere/rat were recorded. Scaling factors are given by the ratio between the amplitudes of averaged mEPSCs from opposing hemispheres. Scaled cumulative distributions are derived from multiplying the amplitude of each independent mEPSC by a single constant scaling factor given by the ratio of averaged amplitudes.

Supplementary Figure 1 (Related to Figure 1). Two independent layer IV->II/III pathway procedures

(A) Stimulus-recording configuration: a pyramidal cell was recorded in layer II/III, while two stimulating electrodes (inter-electrode distance ~900 μm) were placed in the underlying. (B) Regular spiking in the pyramidal cell was tested with a series of 5-10 current pulses (800 msec, from -300 pA to 300 pA). (C) The two stimulated pathways were judged independent if the responses add linearly (top panel), and by the absence of paired pulse interactions (bottom two panels). (D-E) Pairing induced input-specific LTP. (D) Pairing protocol: Vm was alternated between 0 mV and -80mV and one input was stimulated 100 msec after the depolarization onset. (E) Example showing the time course of the EPSP changes in the paired pathway (filled circles), in the non-paired pathway (open circles), as well as changes in paired pulse ratio (PPR: dots at the bottom) and the RC value used to evaluate the stability of Rm. (F) Average of ten consecutive responses recorded before (black) and 30 min after pairing (red) evoked by stimulation of the paired pathway (top), the non-paired pathway (middle), and evoked by: hyperpolarizing current pulses (bottom). The insets show the initial slopes at an expanded timescale. (G-I) Simultaneous induction of LTP and LTD in the same cell. (G) The protocol is similar as in D except that Vm alternates between 0 mV and -40 mV and both inputs are paired: one with 0 mV (filled circles), the other one to -40 mV (open circles). Conventions in (H,I) are the same as in (E,F) except that the open circles now depict the results of pairing with -40 mV.

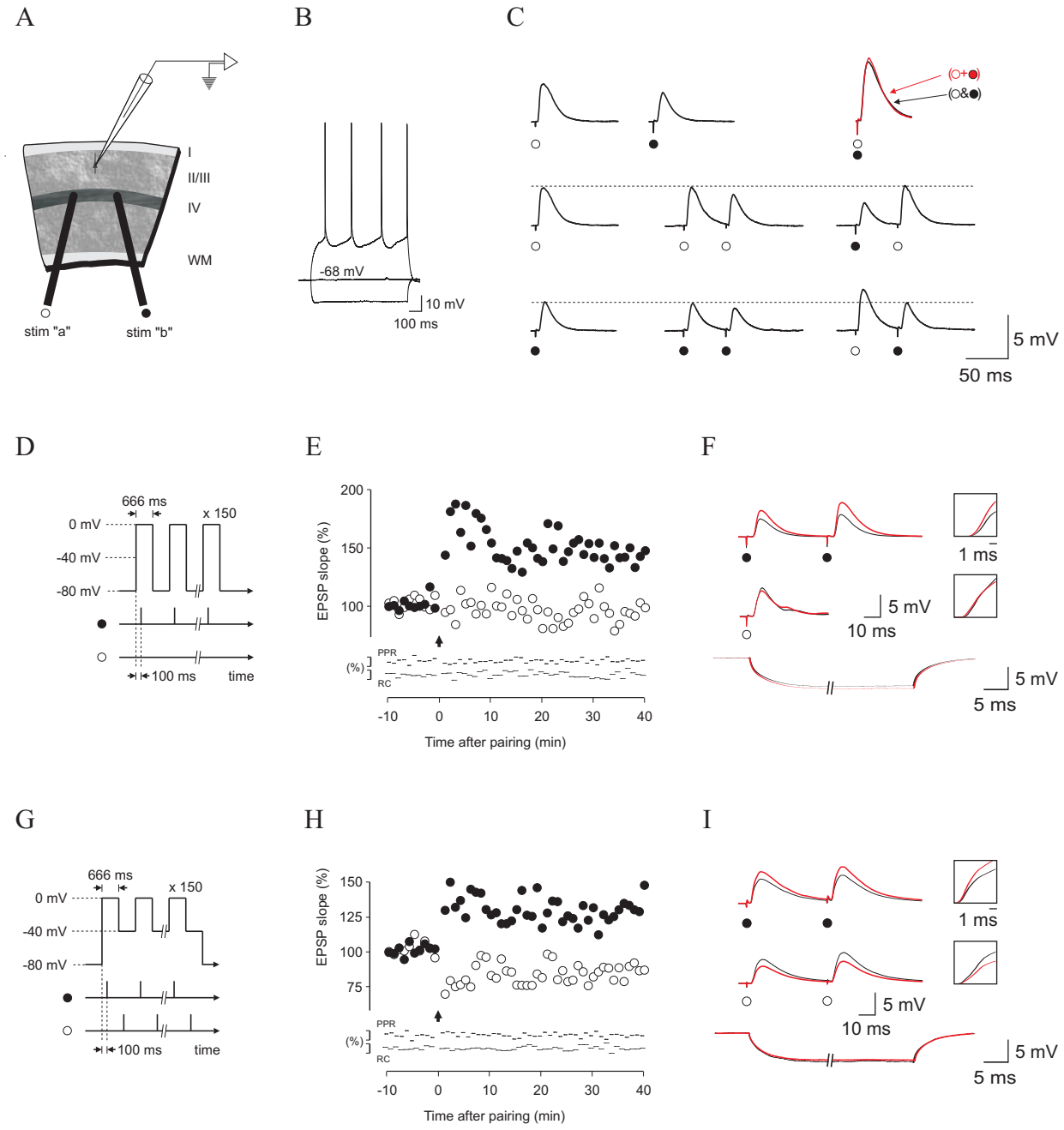
Supplementary Figure 2 (Related to Figure 1). Adrenergic suppression of LTP and LTD of putative EPSCs. Pharmachologically isolated IPSC's (in 25 μM CNQX + 100 μM APV) are prominent at 0 mV (A), and reverse at hyperpolarized potentials (B). Currents in B were normalized with respect to currents evoked with a V_h = -20 mV. Putative isolated EPSCs were identified as those cases in which there was no outward synaptic current at 0 mV (C). Dual pathway experiments show that putative isolated, small-amplitude, EPSCs (recorded at -70mV) exhibit paired induced LTP (filled circles) and LTD (open circles) (D), suppression of LTP by 5 μM methoxamine (E), and suppression of LTP by 10 μM isoproterenol (F). On the bottom of the graphs (D-F) are plotted the changes (in % of per-pairing baseline) in Im. Rm and Rs. Example traces for experiments D-F are shown in G-I, and are average of 10 consecutive responses

recorded before (thin line) and 30 min after pairing at the indicated Vm. The number of experiments is indicated in parentheses.

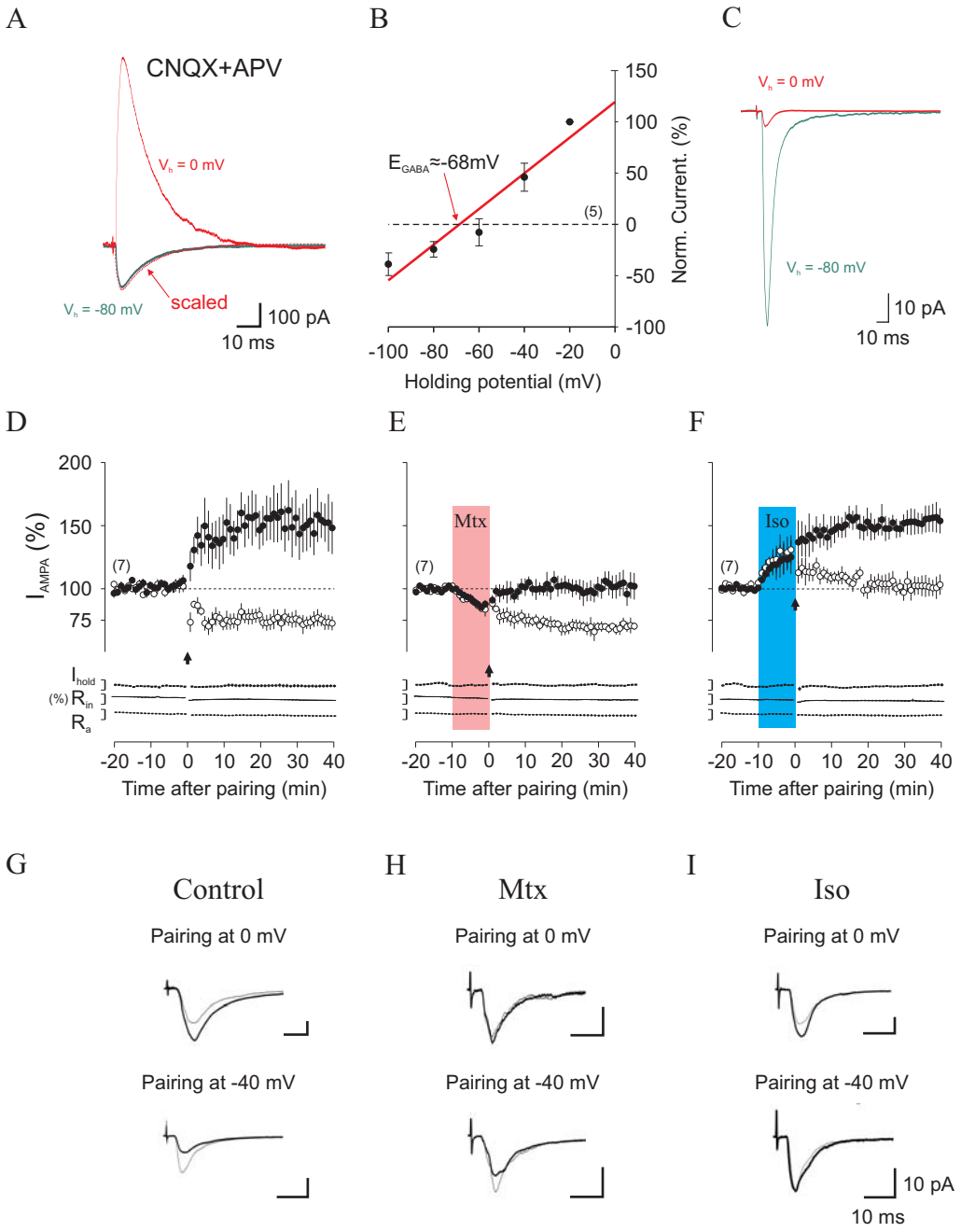
Supplementary Figure 3 (Related to Figure 3). Acute adrenergic modulation of fast glutamatergic transmission

(A) A 10 min application of 10 μM Isoproterenol (Iso: blue box) produced a rapid and reversible increase in the AMPAR- (open circles) and NMDAR- (filled circles) mediated synaptic currents, and no significant changes in Im or Rm. AMPAR- mediated currents were quantified as the peak of the response recorded at -80 mV (inward), whereas NMDAR- mediated current were quantified as the current value at 150 msec of the responses recorded +40 mV (outward). (B) Example of AMPAR- and NMDAR-responses recorded before (black lines), at the end of the isoproterenol application (blue lines) and 15 min after wash out of the drug (grey line). (C,D) Similarly, isoproterenol transiently increased the magnitude of pharmacologically isolated NMDAR currents recorded at + 40 mV in the presence of 25 μM CNQX and 100 μM PTX. Traces in (D) are averages of ten consecutive responses recorded before (black) during (blue) and 15 min after wash out (grey) of 10 μM isoproterenol. (E,F) Bath application of 5 μM Methoxamine for 10 min (mtx: red box in E) produced a reversible decrease in the AMPAR- (open circles) and NMDAR- (filled circles) mediated synaptic currents. Conventions as in (A,B). Similarly, methoxamine transiently reduce the pharmacologically isolated NMDAR-mediated responses currents (G,H). Conventions as in (C,D). (I-L) The voltage-dependence of the NMDAR-mediated currents is not affected by bath application of isoproterenol or methoxamine. (I) I-V plot of the peak amplitude response of pharmachologically isolated NMDAR-responses recorded at different holding potentials, and evoked in control ACSF (black circles), or in the presence of isoproterenol (blue circles: 10 μM, 7-12 min) or methoxamine (red circles: 5 μM, 7-12 minutes). In each experiment the NMDAR-currents were normalized to the values recorded at +20mV. There was no statistical differences between the three conditions at any voltage (two-way ANOVA: $F[6, 178]= 0.047$, $p>0.999$). (J-L) Example experiments showing responses (average of 3-4 traces) evoked at +40mV, 20mV, 0mV, -20mV and -40mV, and recorded either in control ACSF (J), or in the presence of isoproterenol (K) or methoxamine (L).

SupplementalFigures1



SupplementalFigures2



Supplemental Text and Figures