

(A) Representative I_{sAHP} traces elicited by brief depolarization (80ms, 50mV) of CA3 pyramidal neurons in WT mice. Example I_{sAHP} is shown during control period (black) and after kainate receptor-mediated inhibition (red). (B) Representative I_{sAHP} traces in $GluK4^{-/-}/GluK5^{-/-}$ mice before (black) and after (red) inhibition with 50nM kainate. Calibration 50pA, 2s (C) Grouped data from all recordings in which 50nM kainate was applied to inhibit I_{sAHP} . (D) I_{sAHP} inhibition in WT (black) and $GluK4^{-/-}/GluK5^{-/-}$ mice (grey) produced by several concentrations of kainic acid.

Supplemental

Figure S1 Generation of $GluK4$ knockout mouse.

(A) Schematic representation of the *Grik4* gene and targeting construct. Following homologous recombination two loxP sites were inserted into intronic regions flanking exon 14 (Ex 14), along with a loxP flanked neo cassette in the adjacent intronic region. (EV=EcoRV, K=Kpn1, DT=Diphtheria toxin) (B i & ii) Southern blot analysis of targeted clones using two probes external to the targeting at 5' and 3' regions of the gene. Positive clones were identified by the presence of ~9kb band (5' probe) and ~7.5kb band (3' probe). (C) PCR analysis of exon deletion following Cre-mediated recombination of loxP sites. (D) $GluK4$ transcript is absent in $GluK4^{-/-}$ mice. RT-PCR failed to amplify any product using primers spanning exon 14 in $GluK4^{-/-}$ mice (top panel). Amplification of $GluK2$ gene was used as a positive control for the RT reaction (bottom panel) (E) Immunoblot analysis of hippocampal homogenates from $GluK4$ and $GluK4/GluK5$ knockout mice. Protein homogenates were immunoprecipitated with α - $GluK2$ followed by immunoblotting with α - $GluK4$. 125kDa band is absent in samples from $GluK4^{-/-}$ and $GluK4^{-/-}/GluK5^{-/-}$ mice. This band corresponds to the predicted size of the $GluK4$ receptor subunit protein. (F) Nissl stained coronal sections from WT and $GluK4^{-/-}/GluK5^{-/-}$ mice. There are no gross anatomical differences between the two genotypes. Calibration: 1 mm