Supplemental Methods

TABLE S1. Case cohort characteristics, including HC, SZ, and distinguish SZ on medication (N=11) and off-medication (N=10)

	N	Sex (F/M)	Age	SD	PMI	SD	RIN	SD
Healthy controls	21	3F/18M	57.4	13.4	19.4	6.14	7.7	1.83
Schizophrenia	21	9F/12M	52.8	12.8	17.7	8.34	7.0	2.03

Management of Hippocampal Dissection

The tissue was dissected according to a standard protocol which included removing the hippocampus whole bilaterally from the fresh brain, embedding it longitudinally into a mold and cutting blocks at 5 mm intervals. Alternate blocks were either frozen immediately in a mixture of dry ice and isopentane (1:1, v : v) or fixed in 4% paraformaldehyde and in Golgi stain until further use. Four samples, each 300 um thick, were cryostat sectioned from a frozen block from the anterior hippocampus using a Thermo Scientific Cryostat Microtome at -20°C, then stored at -80°C. Nissl staining of 14 mm sections adjacent to the samples was used to determine orientation. The 300 um sections were dissected by hand into samples enriched for the subfields CA1 and CA3 as previously described [22]. Frozen samples were pulverized in PBS buffer containing 1% triton, protease inhibitors and phosphatase inhibitors. Protein concentration of the homogenate was determined using the BCA assay (Pierce). A cohort of high tissue quality hippocampal cases with CA1 and CA3 enriched regions was created including schizophrenia (N=21) [including N=10 cases on antipsychotic medication at death (SZ-ON) and N=11 schizophrenia cases off antipsychotic

medication at death (SZ-OFF)] and age, sex, race and PMI and RIN-matched healthy control (HC) cases (n=21) (Table S1) [21]. Off medication at death was confirmed by the negative plasma antipsychotic drug levels at autopsy and confirmed by family history of no recent medication use or pharmacy records whenever available.

Blotting of Tissue Proteins

Primary antibodies were obtained as follows: GluN1 and GluN2B antibodies from R&D Systems; GAD67 antibody from Abcam; PSD95 antibody from Cell Signaling Technology; and GluN2A, p-CREB and B-tublin antibodies from Millipore. Western blot experiments were performed by the scientists blind to case diagnosis. 20ug of tissue protein was mixed with 2-mercaptoethnal and 5x loading buffer and resolved in duplicate on a 7.5 to 12% SDS-PAGE gel. Gels were transferred to nitrocellulose membrane, blocked for one hour at room temperature, then incubated overnight at 4° Celsius with GluN1 (1:1k), PSD95(1:5k), GluN2A(1:1k), GluN2B(1:1k), GAD67(1:5k), p-CREB (1:1k) or B-tublin (1:10K). After washing, blots were incubated with secondary antibody (1:10k, anti-mouse IgG for GluN1 and B-tublin, anti-rabbit IgG for PSD95, GluN2A, GluN2B, p-CREB and GAD67) for one hour. Immunoreactive proteins were detected via enhanced chemiluminescence using Fuji film. Images of immunoreactive bands were captured using Color Video Camera, and the intensities were analyzed by densitometry using Scion image software with the scientists blind to case diagnosis. The measurements of immunoreactivity for each protein of interest were normalized to B-tublin in each sample. All determinations were performed in duplicate and averaged for the final value; coefficient of variation, 0.05 for CA3 proteins.