Supplementary Figure Legends.

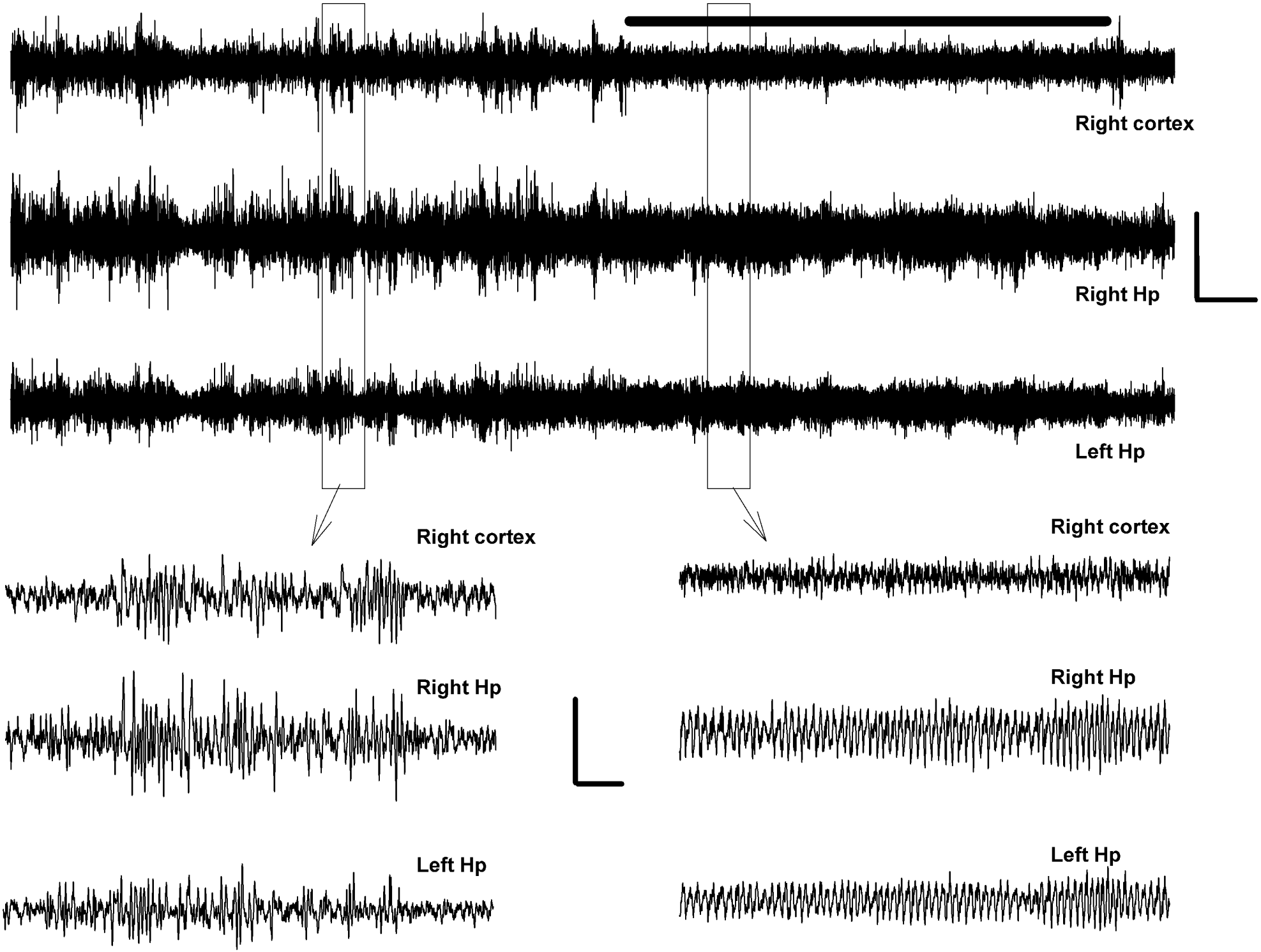
Supplementary Figure 1. EEG recordings show normal background in adult rats after ELS. A, Video EEG recording from typical control rat at P60+ during sleep/in-activity from right cortex, right hippocampus (hp) and left hippocampus. In top traces, fast, irregular, semi-synchronous activity often evolves to lower-amplitude, higher frequency cortical activity with synchronous 7 Hz bilateral hippocampal activity, indicated by the bar. Sections of each (rectangles) are expanded in the bottom traces to show the detail. B, Video EEG recording from typical ELS rat at P60+ during sleep/in-activity. Similar to A, evolution of waveforms is noted to 7 Hz bilateral synchronous hippocampal activity. No discharges or video consistent with seizures were recorded. A,B, Scale bar in top traces 1.5 mV for hp, 0.5 mV for cortex x 15 s. Scale bar in bottom traces1.5 mV for hp, 0.5 mV for cortex x 1 s.

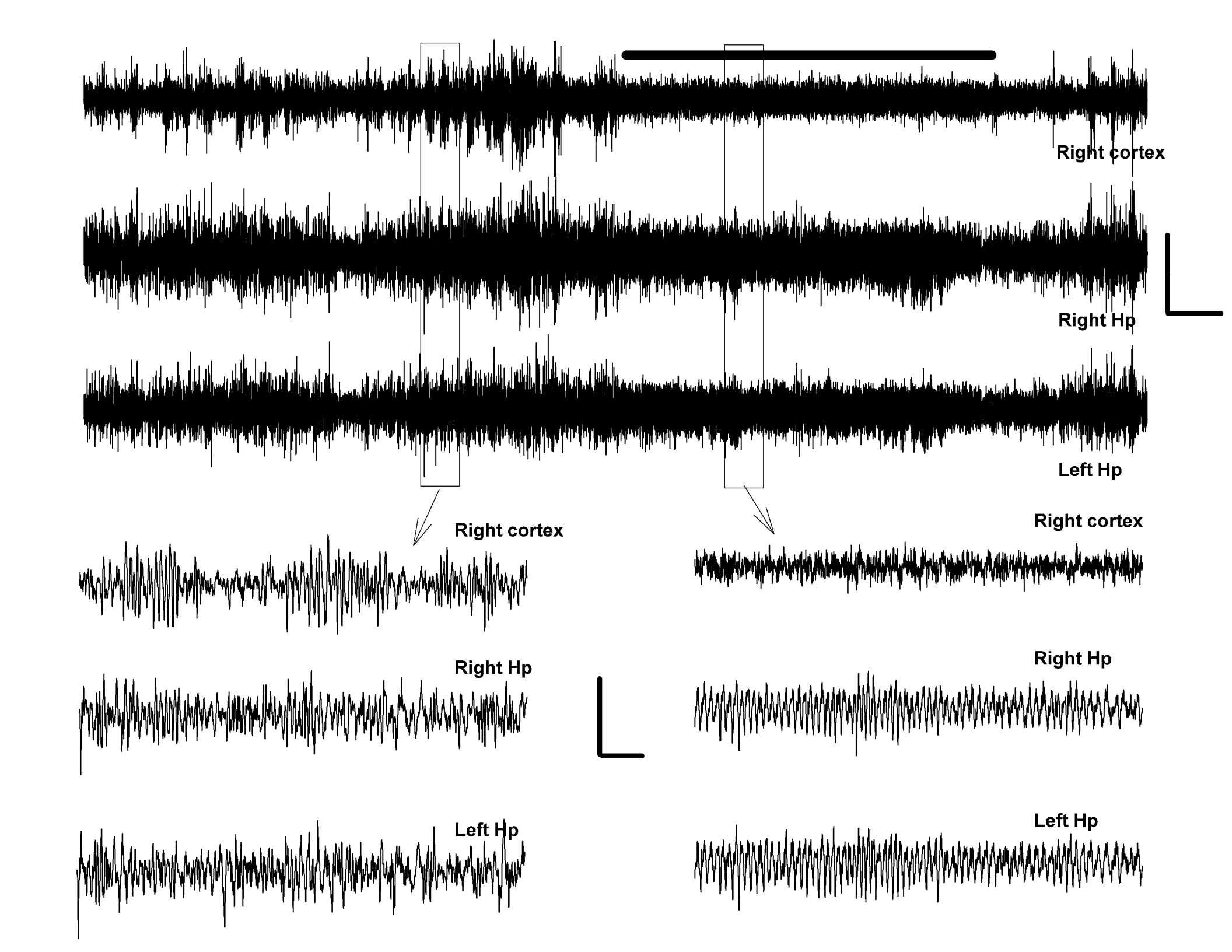
Supplementary Figure 2. Phospho Peptide Block and immunoprecipitation. A, To validate our phospho FMRP antibody we pre-absorbed the 6058 antibody with the immunogenic peptide prior to western blotting. This eliminates antigenicity of 6058 for the protein band around 75 kDa. B, Immunoprecipitaion of FMRP (7G1-1) followed by re-blot with 7G1-1 (showing a single band with only higher species (>200kDa) as seen by others(Hou et al., 2006)) and 6058 (showing a single band around 75 kDa) further demonstrated specificity of 6058 for FMRP and preservation of FMRP phosphorylation following immunoprecipitation by 7G1-1.

Supplementary Figure 3. EIF4B activation is unchanged following ELS. Total EIF4B (ELS: 130.37 ± 19.51, n = 10; control: 100.00 ± 16.75, n = 7, P= N.S.) and phosphorylated EIF4B (ELS: 83.06 ± 16.30, n = 11; control: 100.00 ± 17.12, n = 7, P= N.S.) are unchanged following ELS.

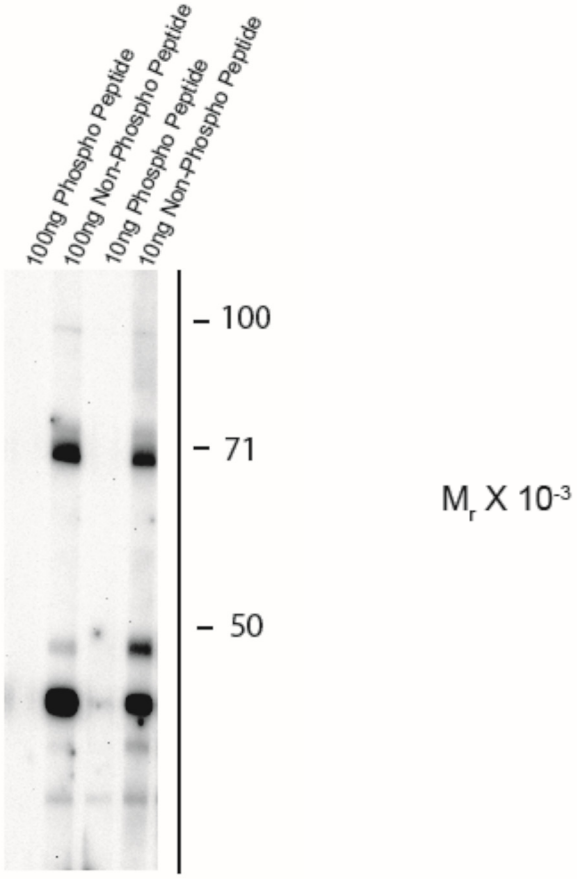
Supplementary Figure 4. PSD95 is enriched in synaptosomal fractions and excluded from cytosolic fractions. To validate our subfractionation technique we demonstrate that PSD95 is exclusively present in our synaptosomal fractions and absent in our cytosolic fractions.

Supplementary Figure 5. Mechanisms involved in enhanced mLTD. In the naïve state (upper half of figure), PP2A and S6K regulate the ability of FMRP to inhibit local protein translation. Basally, FMRP is typically phosphorylated, which stalls ribosomal protein translation. Upon activation of mGluRs, PP2A (itself activated by mGluR activation) dephosphorylates FMRP to initiate translation. Subsequently, S6K (also activated by mGluR activation) re-phosphorylates FMRP, reinstating the "brake" on translation and ultimately limiting mLTD expression. Our data indicate that the FMRP/PP2A/S6K "brake"on protein translation/mLTD may function in both the synaptosomal compartment (P2) and the cytosolic compartment (S2). Block of PP2A that results in increased mLTD is not fully consistent with prior models (Bassell and Warren, 2008), requiring an additional modulatory step possibly downstream of protein translation. Following ELS (lower half of figure), selective reduction of PP2A and FMRP in the cytosolic (S2) compartment directly mediates increased mLTD. Basal loss of FRMP from S2 results in leaky translation and increase of STEP. STEP accumulates in P2 (not shown), increasing the amount of STEP available for activation and to mediate enhanced mLTD expression. Loss of PP2A from the cytosolic pool responsible for the downstream regulation of mLTD is consistent with a lack of further modulation of mLTD following ELS by PP2A blockade. This loss of PP2A from S2 could be mediated by co-relocalization with FMRP. An alternative explanation is the brake on translation is initially removed by mGluR triggered synaptic degradation of FMRP; the brake is reapplied by the dynamic replenishment of the synaptic pool of FMRP/PP2A/S6K complex from the cytosolic pool. Loss of the cytosolic pool following ELS results in loss of the available brake to mediate increased mLTD. Heuristic diagram based on previous model (Osterweil et al., 2010).

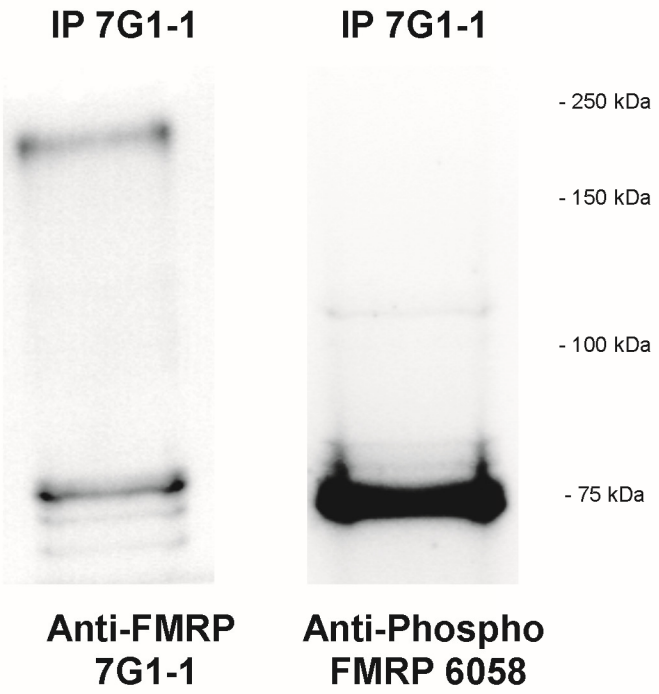

Right cortex
Right Hp
Left Hp
Right cortex
Right Hp
Left Hp
Right cortex
Right Hp
Left Hp


Right cortex
Right Hp
Left Hp
Right cortex
Right Hp
Left Hp
Right cortex
Right Hp
Left Hp

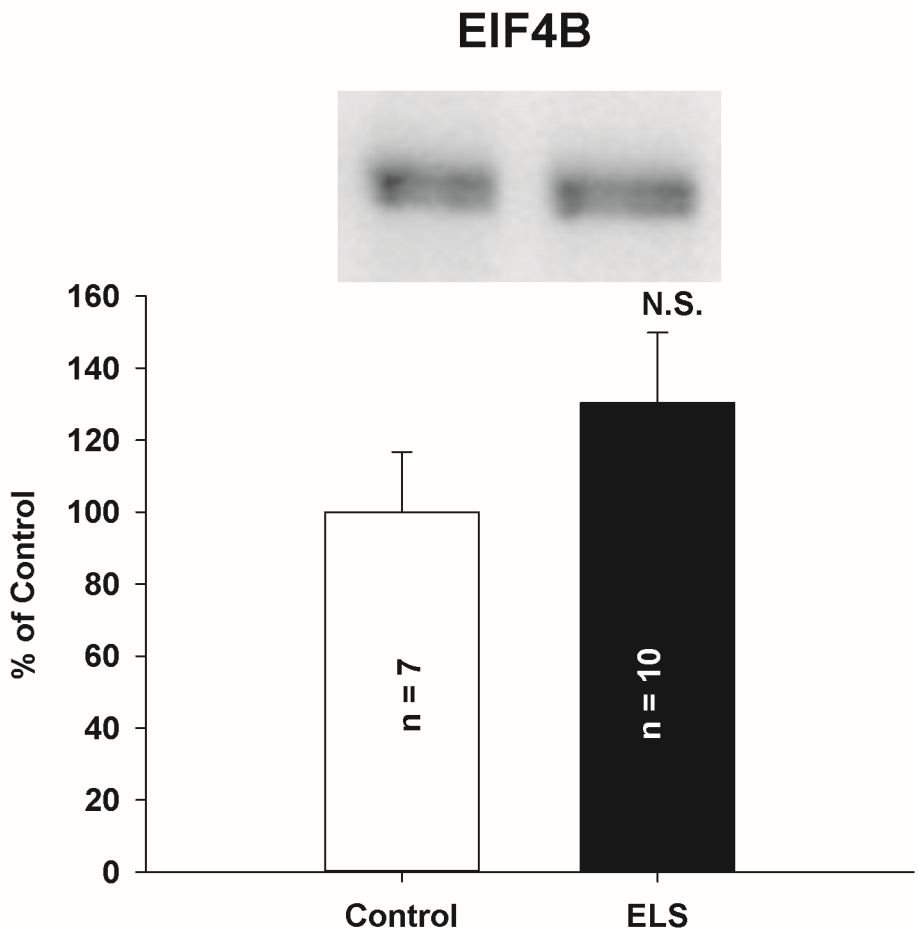
A


100ng Phospho Peptide
100ng Non-Phospho Peptide
10ng Phospho Peptide
10ng Non-Phospho Peptide
– 100
– 71
– 50
M_r X 10^{-3}

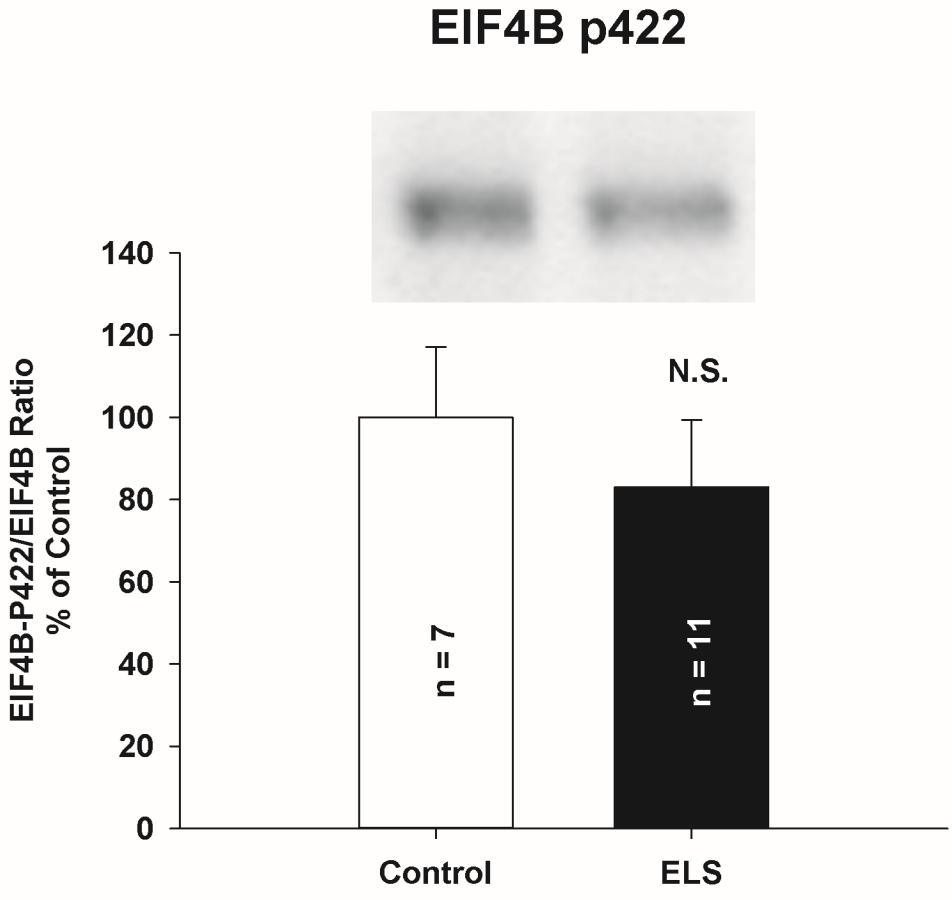
B


IP 7G1-1
IP 7G1-1
- 250 kDa
- 150 kDa
- 100 kDa
- 75 kDa
Anti-FMRP 7G1-1
Anti-Phospho FMRP 6058

A


EIF4B
160
140
120
100
80
60
40
20
0
% of Control
N.S.
n = 7
n = 10
Control
ELS

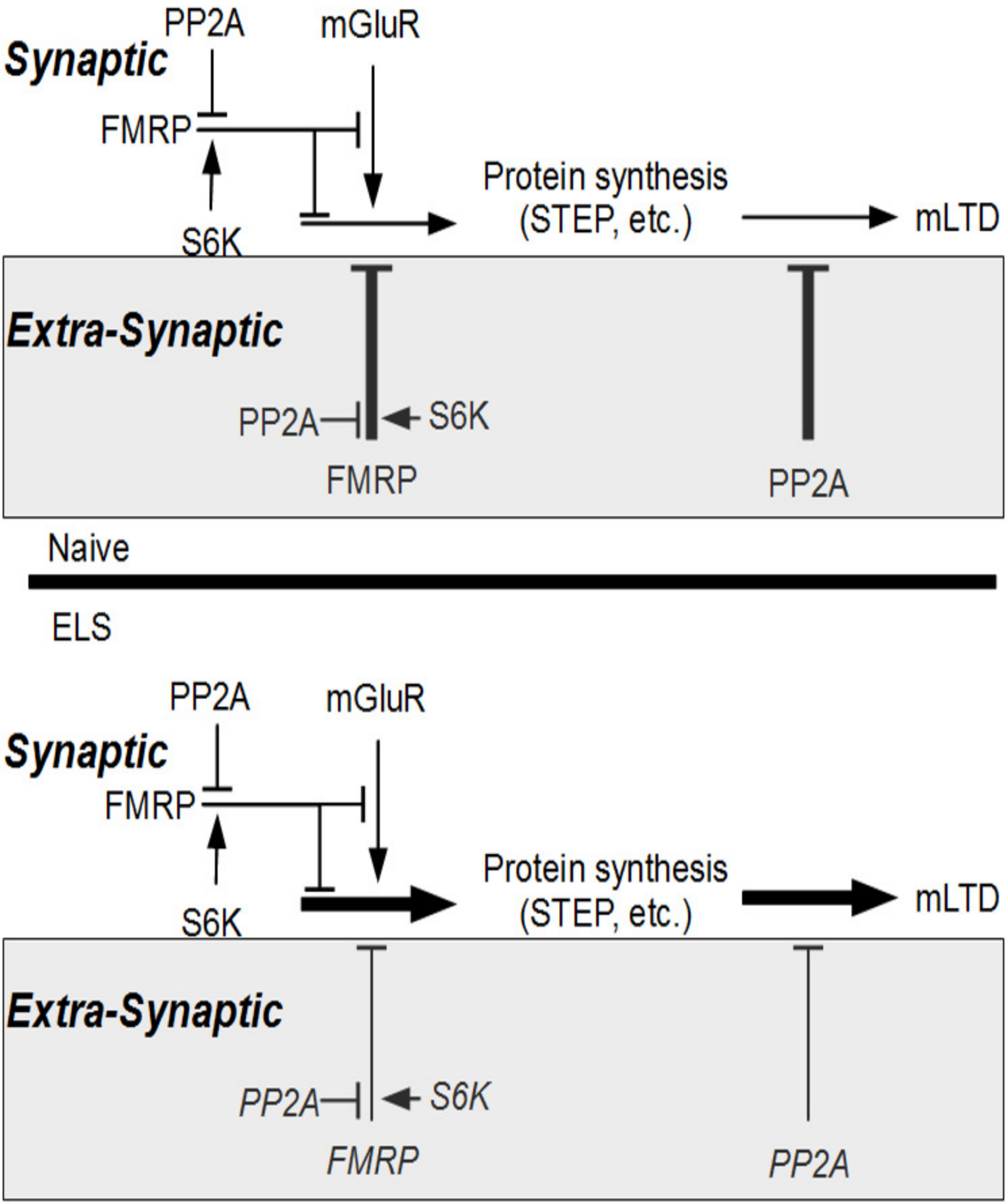
B


EIF4B p422
140
120
100
80
60
40
20
0
EIF4B-P422/EIF4B Ratio
% of Control
N.S.
n = 7
n = 11
Control
ELS

PSD 95
S2 P2 comparison

S2 S2 P2P2 S2 S2 P2P2 S2 S2 P2P2

Sample 1 **Sample 2** **Sample 3**


PP2A
mGluR
Synaptic
FMRP
S6K
Protein synthesis
(STEP, etc.)
mLTD
Extra-Synaptic
PP2A
S6K
FMRP
PP2A
Naive
ELS
PP2A
mGluR
Synaptic
FMRP
S6K
Protein synthesis
(STEP, etc.)
mLTD
Extra-Synaptic
PP2A
S6K
FMRP
PP2A