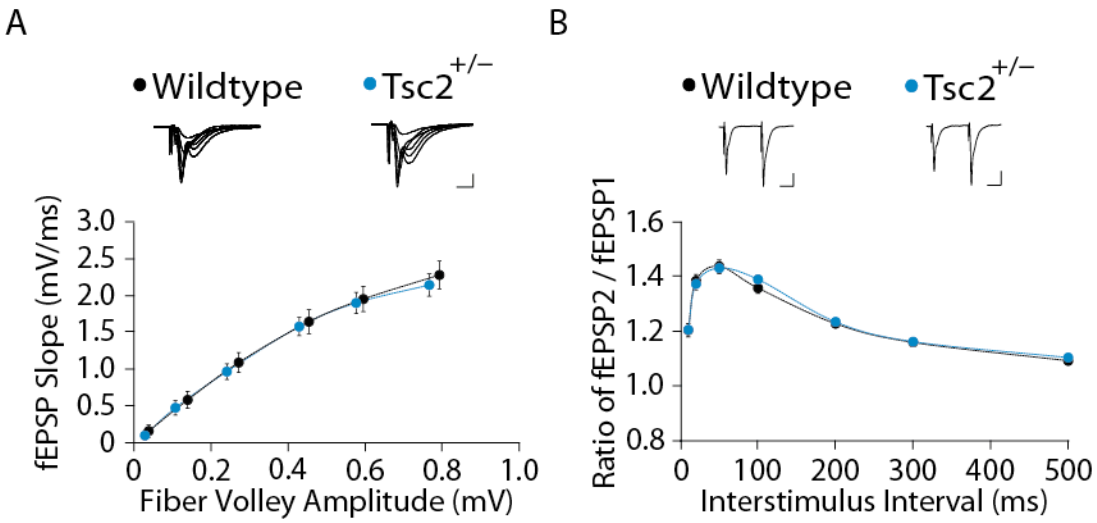
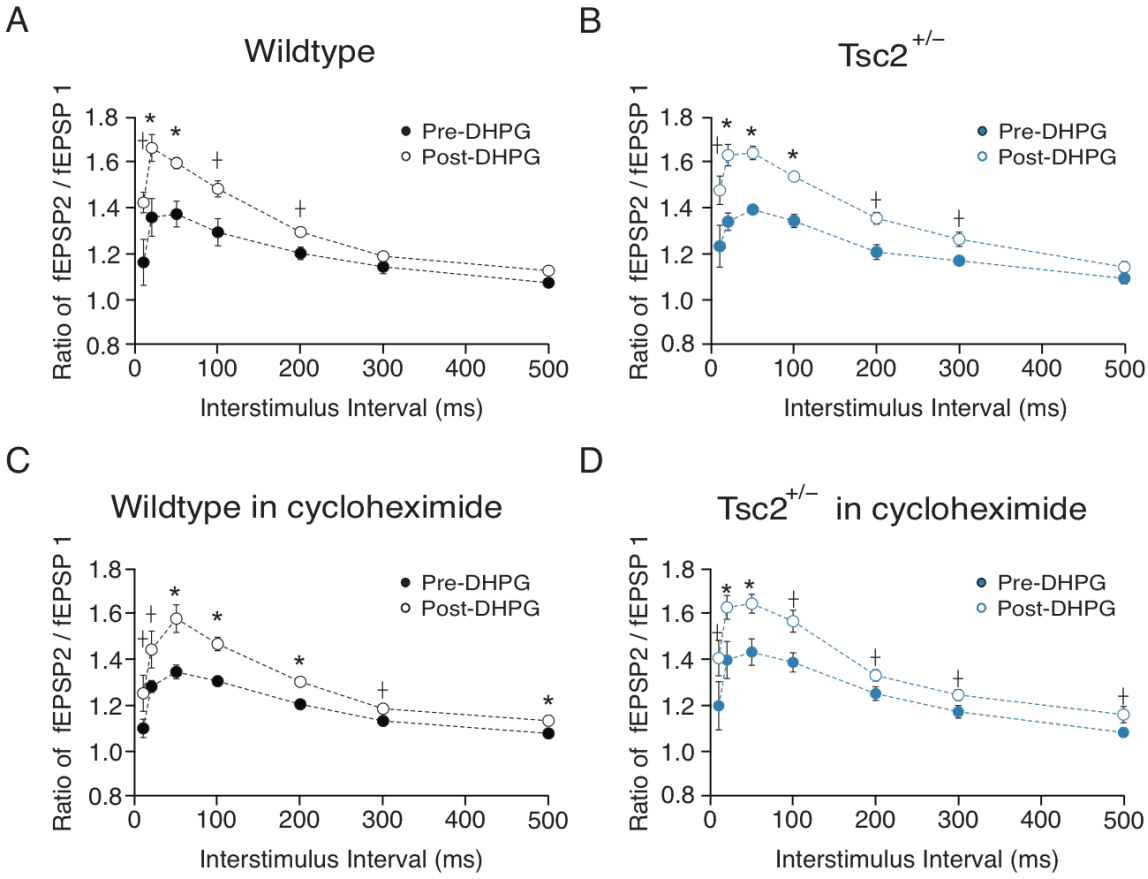
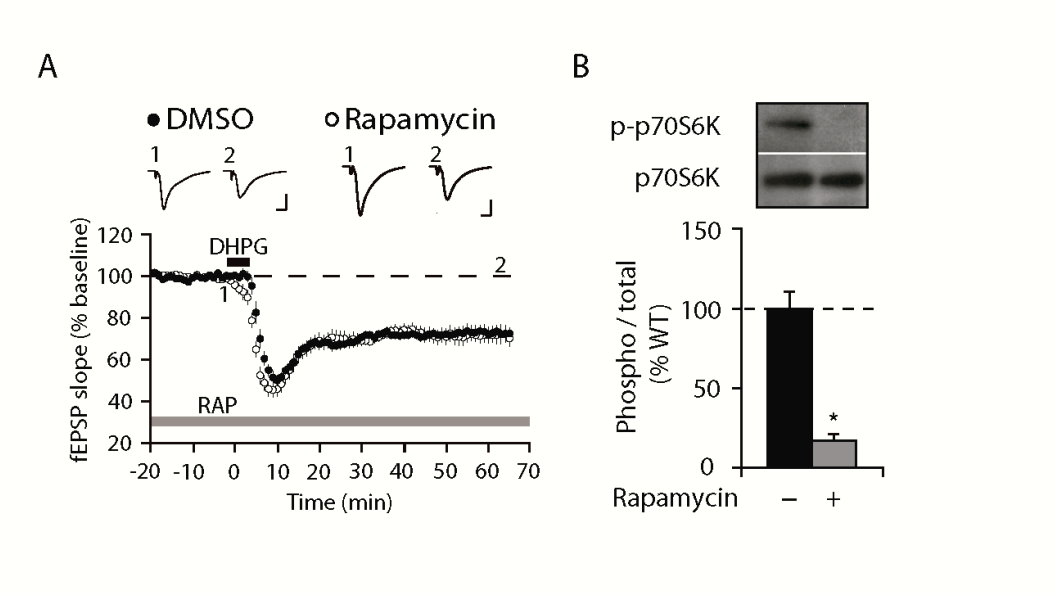



**Supplemental Figure 1: Normal basal synaptic function in Tsc2$^{+/-}$ mice.**

**(A)** Basal synaptic transmission (plotted as fEPSP amplitude against presynaptic fiber volley amplitude) does not differ between genotypes. Scales bars equal 0.5 mV, 5 ms. Error bars represent SEM. (**B)** Paired pulse facilitation is normal across several inter-stimulus intervals (20, 30, 50, 100, 200, 300, 500 ms) in *Tsc2*$^{+/-}$ mice. Scale bars equal 0.5 mV, 20 ms for representative field potential traces. Error bars represent SEM.

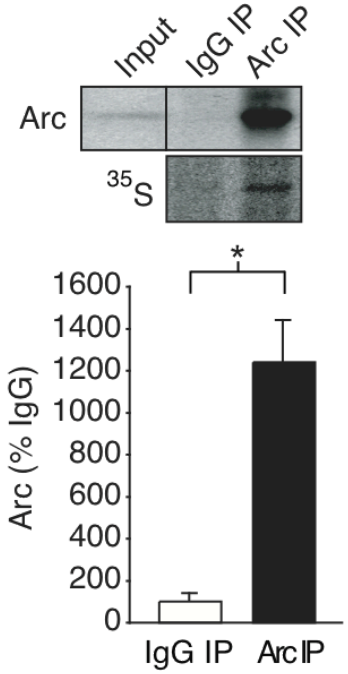



**Supplemental Figure 2: Presynaptic component of DHPG-induced LTD.**
Pairs of stimulation at several different inter-stimulus intervals were delivered during the baseline period and 60 minutes post DHPG application in slices either pretreated with CHX or control ACSF. **(A,B)** DHPG significantly increased paired pulse facilitation (PPF) in slices from both wildtype **(A)** and *Tsc2*$^{+/-}$ mice **(B)** across many inter-stimulus intervals (WT, n = 5 animals totaling 9 slices; *Tsc2*$^{+/-}$, n = 5 animals totaling 9 slices; *p < 0.01, $^{\dagger}$p < 0.05). **(C,D)** The enhancement of PPF by DHPG is not affected by the protein synthesis inhibitor cycloheximide (WT, n = 7 animals totaling 11 slices; *Tsc2*$^{+/-}$, n = 6 animals totaling 7 slices; *p < 0.01, $^{\dagger}$p < 0.05). There was no difference in paired pulse ratio between wildtype and *Tsc2*$^{+/-}$ mice at baseline, post DHPG, or post DHPG + CHX. Error bars represent SEM.




**Supplemental Figure 3: The effect of rapamycin treatment on mGuR-LTD in WT slices**

**(A)** Pretreatment of slices from WT mice with rapamycin (RAP, 20 nM, gray bar) has no effect on DHPG-induced LTD in hippocampal slices from WT animals (DMSO: 73.2 ± 3.3%, n = 7 animals totaling 12 slices; RAP: 71.9 ± 4.1%, n = 7 animals totaling 12 slices; p = 0.807). Representative field potential traces (average of 10 sweeps) were taken at times indicated by numerals. Scale bars equal 0.5 mV, 5 ms. Error bars represent SEM. **(B)** Rapamycin treatment robustly downregulates mTORC1 activity. Recovered hippocampal slices were incubated ± 20 nM rapamycin for 1 hour, then homogenized and processed for SDS PAGE. mTORC1 activity was assessed by measuring the phosphorylation of p70S6K (at Thr389), the direct substrate of mTORC1. Western blotting confirms that rapamycin robustly reduces p70S6K activation (control 100 ± 9%, rapamycin 15 ± 4%, *p = 0.0001; n = 13 animals). Error bars represent SEM.




**Supplemental Figure 4. Enrichment of Arc in immunoprecipitates.**

To ensure the specificity of Arc IPs, lysates from metabolically labeled hippocampal slices were incubated with either mouse monocloncal anti-Arc or non-immune mouse IgG, and IP experiments performed as described in Methods. Immunoblot analysis reveals that Arc is significantly enriched in anti-Arc IPs versus IgG IPs from the same lysates (t-test IgG vs. Arc *p = 0.002; n = 5 animals). Additionally, autoradiographs confirm the absence of $^{35}$S-incorporated protein in the IgG IP. Error bars represent SEM.