Supplementary Table S1. Detailed Analysis of GluR1 Decay Kinetics			
		Deactivation	
Condition	τ_{fast} (ms)	τ_{slow} (ms)	A_{slow} (%)
GluR1 alone (n = 11)	0.82 ± 0.05	N/A	N/A
GluR1 + γ–2 (n = 15)	1.41 ± 0.10 ##	5.12 ± 1.02	26.96 ± 8.62
GluR1 + γ–3 (n = 9)	1.77 ± 0.10 ##	4.08 ± 0.72	18.36 ± 12.26
GluR1 + γ–4 (n = 8)	2.09 ± 0.16 ### ***	4.70 ± 0.53	29.02 ± 6.33
GluR1 + γ–8 (n = 8)	1.72 ± 0.15 ##	6.24 ± 0.77	18.16 ± 3.13
		Desensitization	
Condition	τ_{fast} (ms)	τ_{slow} (ms)	A_{slow} (%)
GluR1 alone (n = 14)	2.49 ± 0.14	4.63 ± 0.52	36.70 ± 3.78
GluR1 + γ–2 (n = 12)	2.46 ± 0.16	8.33 ± 0.76 #	33.12 ± 3.85
GluR1 + γ–3 (n = 9)	3.20 ± 0.24	9.38 ± 1.22 ##	37.86 ± 5.94
GluR1 + γ–4 (n = 8)	4.07 ± 0.56 # *	6.98 ± 0.82	60.22 ± 7.81 *
GluR1 + γ–8 (n = 13)	2.78 ± 0.22	8.13 ± 0.44 ##	58.84 ± 3.23 ## ***

Supplementary Table S1. Detailed Analysis of GluR1 Decay Kinetics

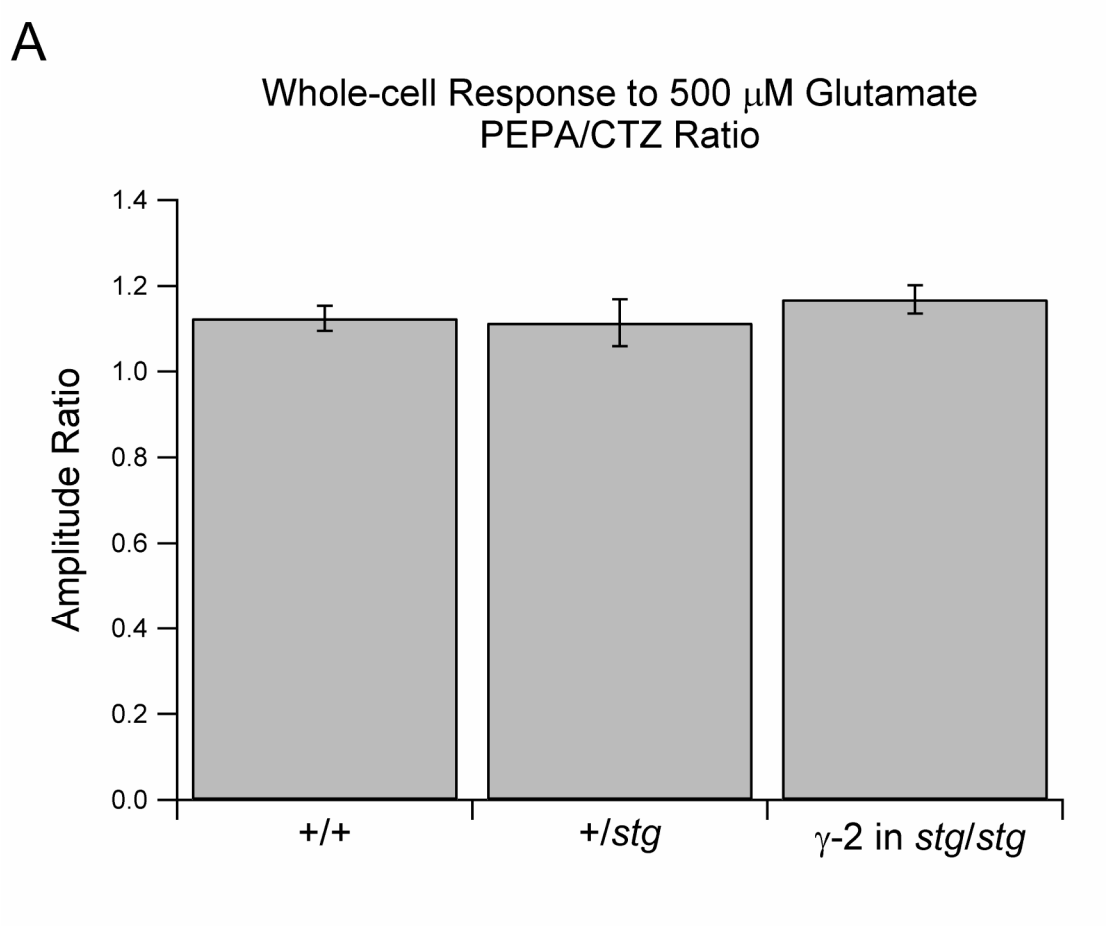
τ_{fast}, τ_{slow} and A_{slow} are, respectively, the time constants of the fast and slow components of decay and the relative amplitude of the slow component of decay obtained by fitting the average current from individual patches with a double exponential function, as described in the Experimental Procedures. The measurements are shown as mean ± SEM. Symbols indicate significant difference with respect to either GluR1 alone (# $p<0.003$, ## $p<0.001$, ### $p<0.0001$) or TARP γ-2 (* $p<0.005$, ** $p<0.001$, *** $p<0.0001$, Wilcoxon test with alpha adjusted for multiple comparisons).

Supplementary Table S2. Detailed Analysis of mEPSC Decay Kinetics			
Condition	τ_{fast} (ms)	τ_{slow} (ms)	A_{slow} (%)
+/+ (n = 22)	1.21 ± 0.05	9.91 ± 0.58	19.22 ± 1.04
+/*stg* (n = 28)	1.02 ± 0.04 $^{\#}$	9.97 ± 0.74	14.80 ± 1.08 $^{\#}$
γ–2 in *stg*/*stg* (n = 40)	1.56 ± 0.05 $^{\#\#}$	13.25 ± 0.52 $^{\#\#}$	25.76 ± 0.80 $^{\#\#\#}$
γ–3 in *stg*/*stg* (n = 25)	1.30 ± 0.05 *	11.41 ± 0.61	20.27 ± 0.74 **
γ–4 in *stg*/*stg* (n = 18)	2.87 ± 0.90 **	20.62 ± 1.32 **	43.04 ± 2.23 **
γ–8 in *stg*/*stg* (n = 14)	1.69 ± 0.11	17.21 ± 4.88	15.76 ± 1.67 **

Supplementary Table S2. Detailed Analysis of mEPSC Decay Kinetics

τ_{fast}, τ_{slow} and A_{slow} are, respectively, the time constants of the fast and slow components of mEPSC decay and the relative amplitude of the slow component of mEPSC decay obtained by fitting the average mEPSC from individual neurons with a double exponential function, as described in the Experimental Procedures. The measurements are shown as mean ± SEM. Symbols indicate significant difference with respect to either +/+ ($^{\#}$ $p<0.05$, $^{\#\#}$ $p<0.001$, $^{\#\#\#}$ $p<0.0001$) or TARP γ-2 (* $p<0.001$, ** $p<0.0001$, Wilcoxon test with alpha adjusted for multiple comparisons).

Supplementary Figure S1.



Supplementary Figure S1. Dependence of AMPAR Properties on TARP Expression Level Does Not Reflect Changes in Surface Expression of AMPAR Splice Variants

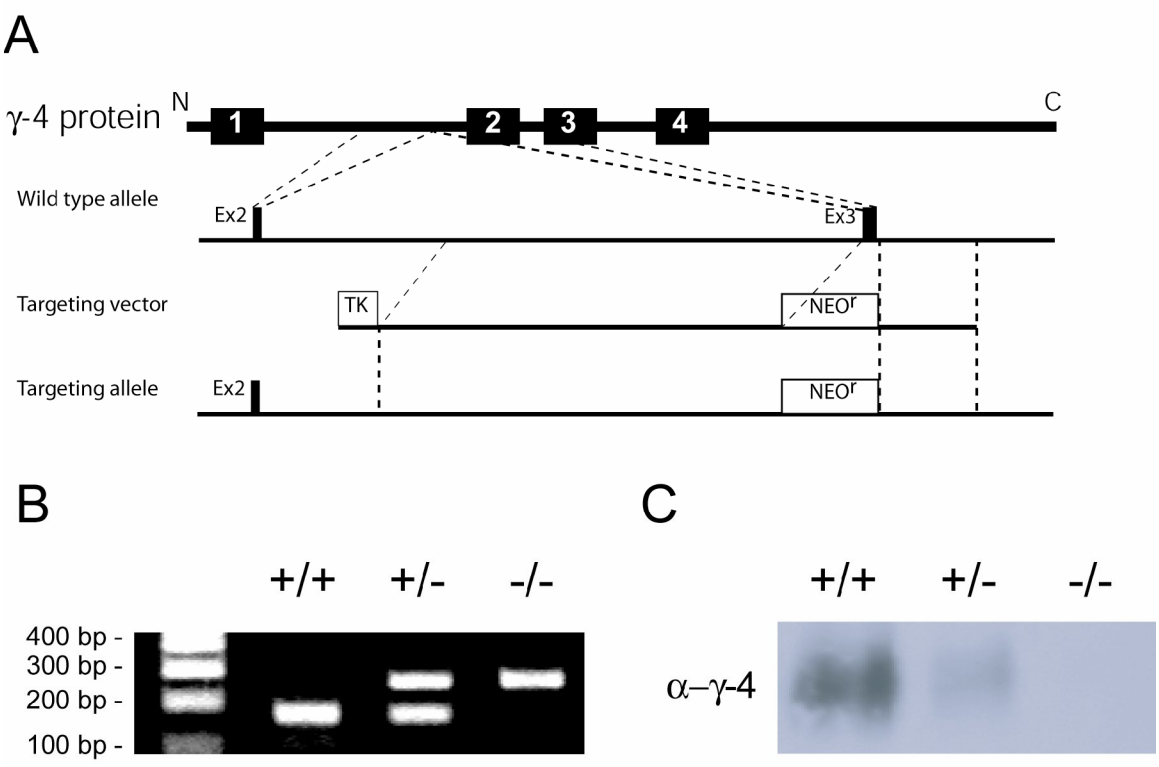
(A) Whole-cell responses to 500 μM Glutamate were first recorded in the presence of 100 μM CTZ and then in the presence of 100 μM PEPA in cultured granule neurons. A ratio of current amplitudes was calculated to assay the relative contributions of AMPARs containing flip and flop isoforms. No difference was observed across the three conditions tested (Kruskal-Wallis Rank Sum Test, +/+, n = 10; +/*stg*, n = 10; γ-2 in *stg*/*stg*, n = 10, n.s.).

Supplementary Table S3. Analysis of Kainate Dose-Response Relationship			
Condition	I_{max} (pA)	EC_{50} (μM)	n_H
+/+ (n = 12)	267.51 ± 19.13	36.91 ± 1.56	1.46 ± 0.05
+/*stg* (n = 12)	191.73 ± 8.33 $^{\#\#}$	42.16 ± 1.51 $^{\#}$	1.48 ± 0.02
γ–2 in *stg*/*stg* (n = 8)	417.83 ± 52.21 $^{\#}$	27.69 ± 0.76 $^{\#\#\#}$	1.53 ± 0.04
γ–3 in *stg*/*stg* (n = 12)	341.35 ± 35.81	37.12 ± 0.86 **	1.59 ± 0.02
γ–4 in *stg*/*stg* (n = 12)	251.35 ± 32.06	8.46 ± 0.89 **	1.26 ± 0.04 *
γ–8 in *stg*/*stg* (n = 7)	387.48 ± 79.35	25.28 ± 2.11	1.39 ± 0.06

Supplementary Table S3. Analysis of Kainate Dose-Response Relationship

I_{max}, EC_{50}, and n_H are, respectively, the maximum current evoked by local application of 3 mM kainate, the concentration at which the kainate-evoked current is half-maximal, and the Hill coefficient. The latter two values were obtained from a best fit of the data with the logistic equation. The measurements are shown as mean ± SEM. Symbols indicate significant difference with respect to either +/+ ($^{\#}$ $p < 0.03$, $^{\#\#}$ $p < 0.002$, $^{\#\#\#}$ $p < 0.001$) or TARP γ-2 (* $p < 0.002$, ** $p < 0.0001$, Wilcoxon test with alpha adjusted for multiple comparisons).

Supplementary Figure S2.



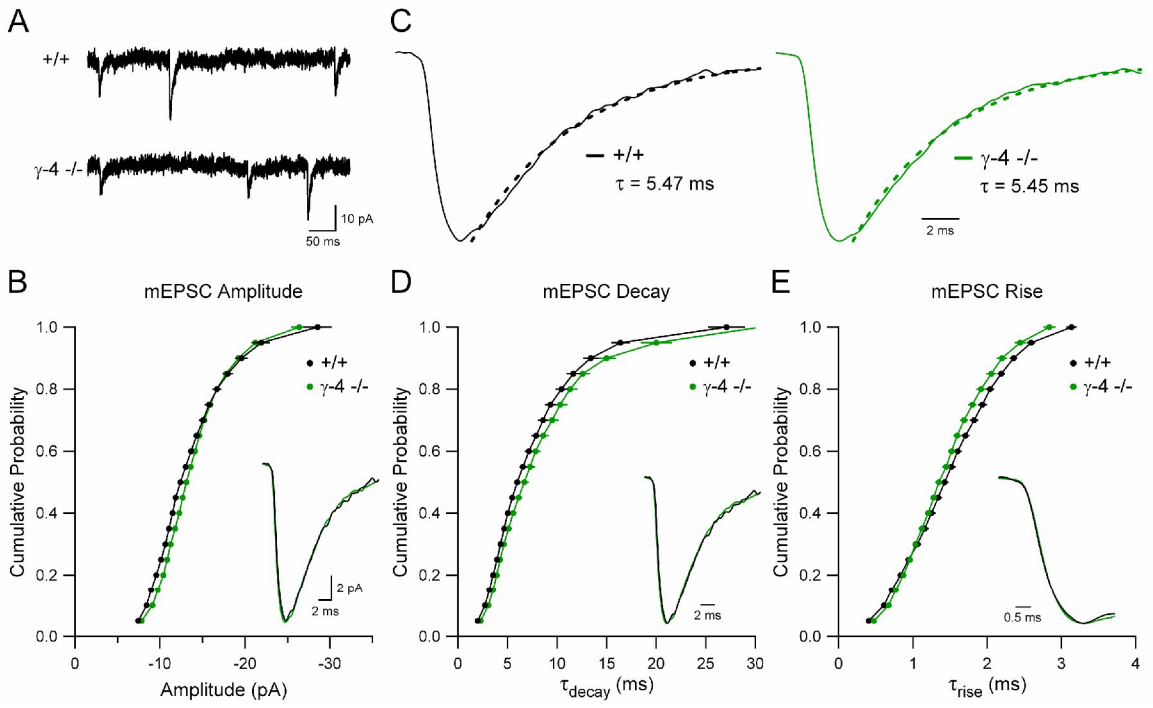
Supplementary Figure S2. Generation of TARP γ-4 Knockout Mice

(A) Schematic representation of γ-4 protein, genomic locus, targeting vector and targeted allele. Homologous recombination removes DNA that encodes first extracellular domain and the second and third transmembrane domains. Ex: exon; TK: thymidine kinase gene, a negative selection marker; NEO^r: neomycin resistance gene, a positive selection marker.

(B) PCR reaction used to genotype γ-4 -/- mice. Primers designed to amplify the wild type allele produce the lower band in +/+ and +/- mice, while primers designed to amplify the mutant allele produce the upper band in +/- and -/- mice.

(C) Western blot analysis of brain extracts immunoprecipitated with a γ-4-selective antibody demonstrates absence of γ-4 protein in -/- mice.

Supplementary Figure S3.



Supplementary Figure S3. Normal Synaptic AMPAR Function in Striatum of Juvenile TARP γ-4 Knockout Mice

(A) Sample records demonstrate that quantal synaptic AMPAR transmission is normal in MSNs in the striatum of juvenile (P14-P16) γ-4 -/- mice.

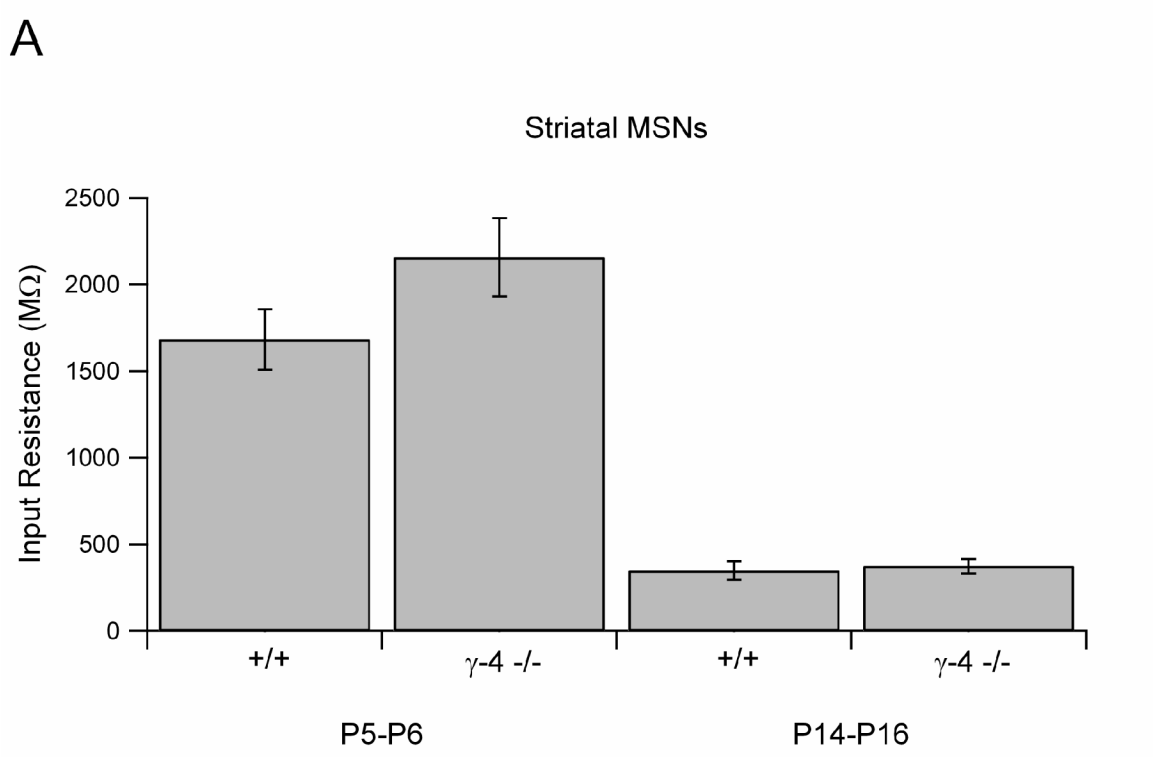
(B) mEPSC amplitude is normal in juvenile γ-4 -/- mice (Kolmogorov-Smirnov test, +/+: n = 21 vs. γ-4 -/-: n = 25; n.s.). Cumulative distributions are displayed as mean ± SEM, and representative averaged mEPSCs are aligned to the peak and superimposed (inset).

(C) Representative averaged mEPSCs are normalized to the peak (solid lines), and the decay phase is fit with a single exponential function (broken lines). The corresponding decay time constant values are displayed.

(D) mEPSC decay is normal in juvenile γ-4 -/- mice (Kolmogorov-Smirnov test, n.s.). Cumulative distributions are displayed as mean ± SEM, and the representative averaged mEPSCs from (C) are aligned to the peak and superimposed (inset).

(E) mEPSC rise is normal in juvenile γ-4 -/- mice (Kolmogorov-Smirnov test, n.s.). Cumulative distributions are displayed as mean ± SEM, and the representative averaged mEPSCs from (C) are aligned to the 10% rise point and superimposed (inset).

Supplementary Figure S4.



Supplementary Figure S4. Input Resistance of Striatal MSNs Decreases During Development

(A) In parallel with a slowing of mEPSC decay from P5-P6 to P14-P16, the input resistance of MSNs decreased in both wild type and γ-4 -/- mice (Wilcoxon test, $p < 0.0001$).