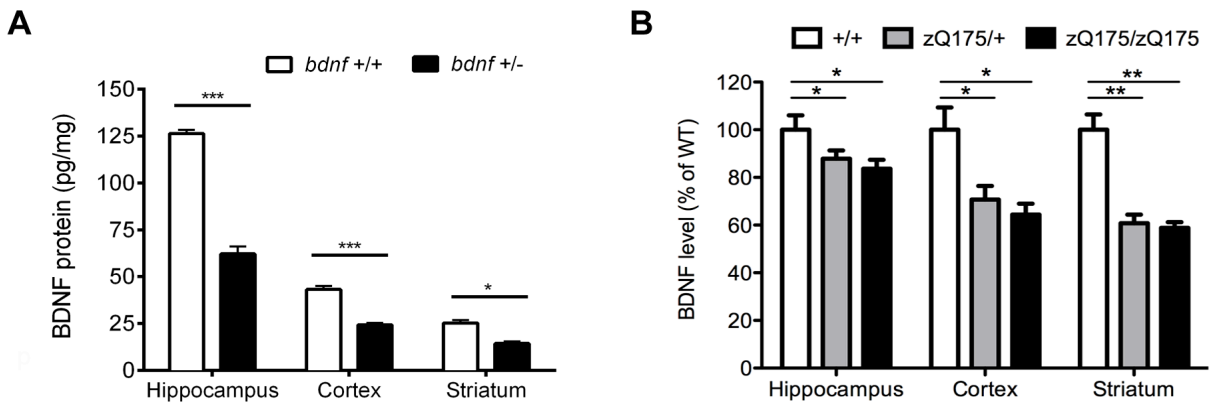
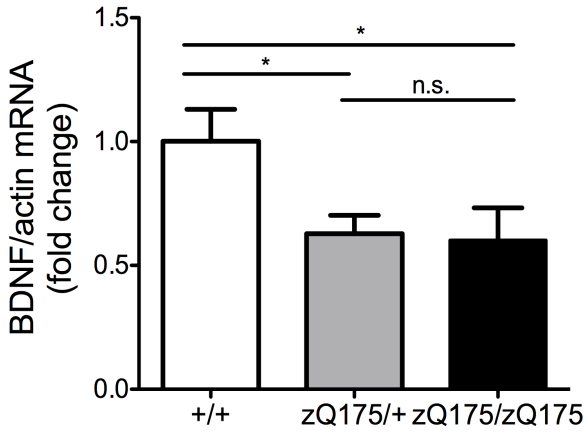
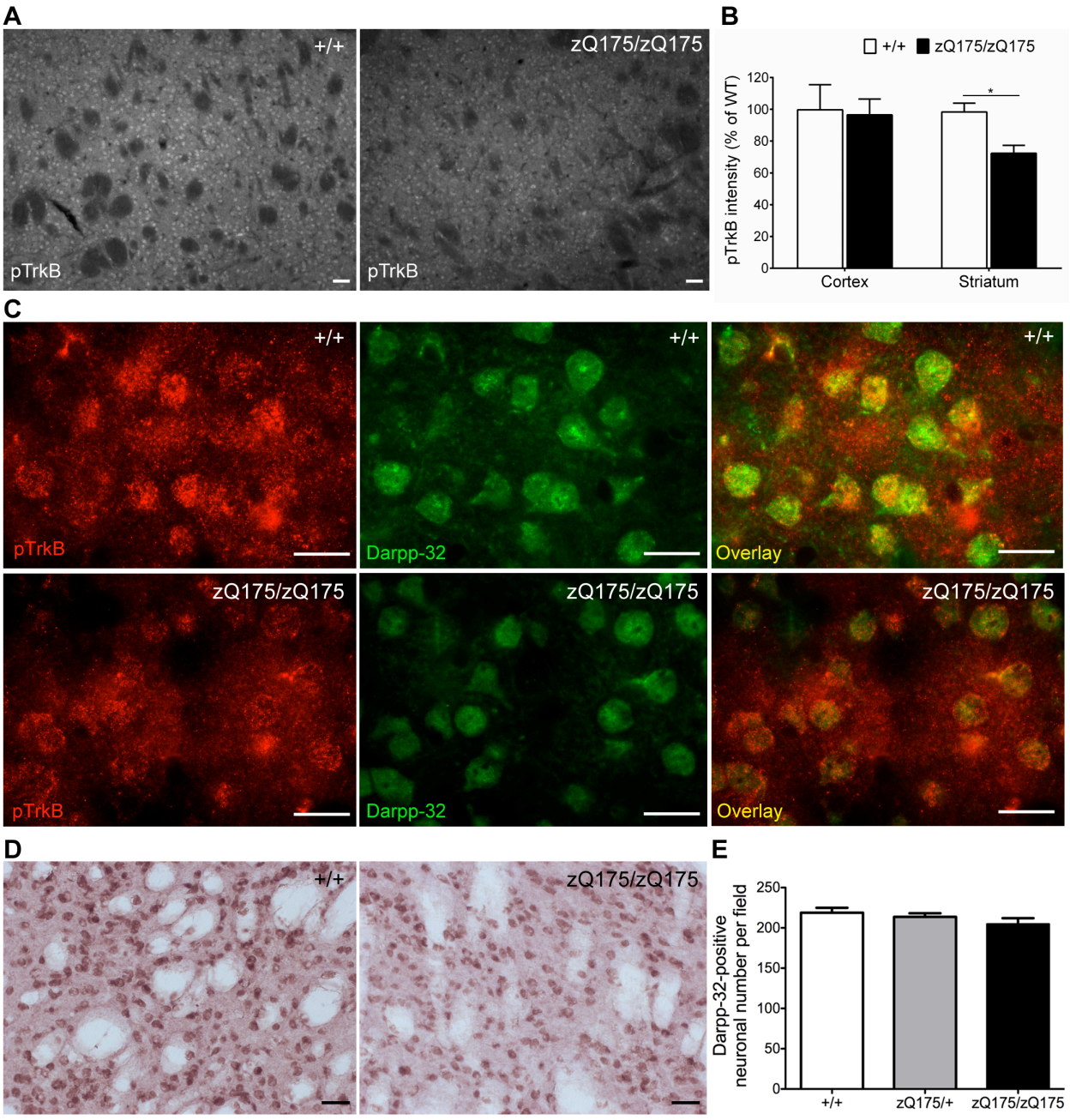


Supplemental Figure 1. Quantification of total BDNF protein level by ELISA. (A) The sensitivity and accuracy of BDNF ELISA (Promega) to measure the level of total BDNF in different brain region is validated using tissues from 5-month-old *bdnf* +/- mice and wild type littermates. (B) Total BDNF level from the hippocampus, the cortex, and the striatum of zQ175 mice are all decreased significantly compared to wild type littermates at the age of 12 months.

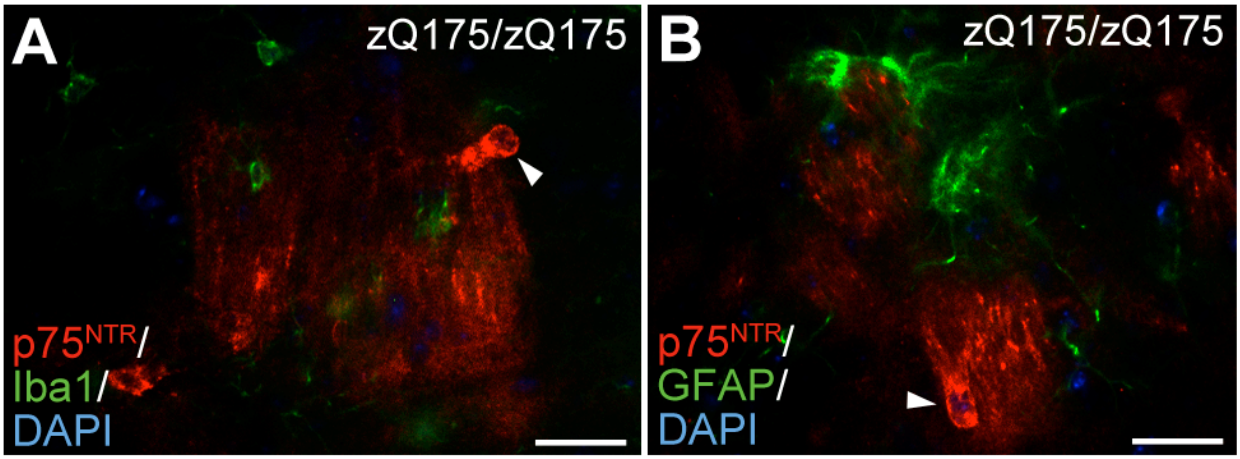


Supplemental Figure 2. Reduced BDNF transcription in the cortex of 12-month-old zQ175 mice by quantitative PCR analysis. Total *bdnf* mRNA from the cortices of zQ175 mice decreases significantly at the age of 12 months compared with wild type, as measured by real-time quantitative RT-PCR. All samples were normalized to β-actin mRNA level and results are mean±S.E.M. relative to wild type (N=3 of each genotype *P<0.05, two-way ANOVA followed by Bonferroni's post-test).

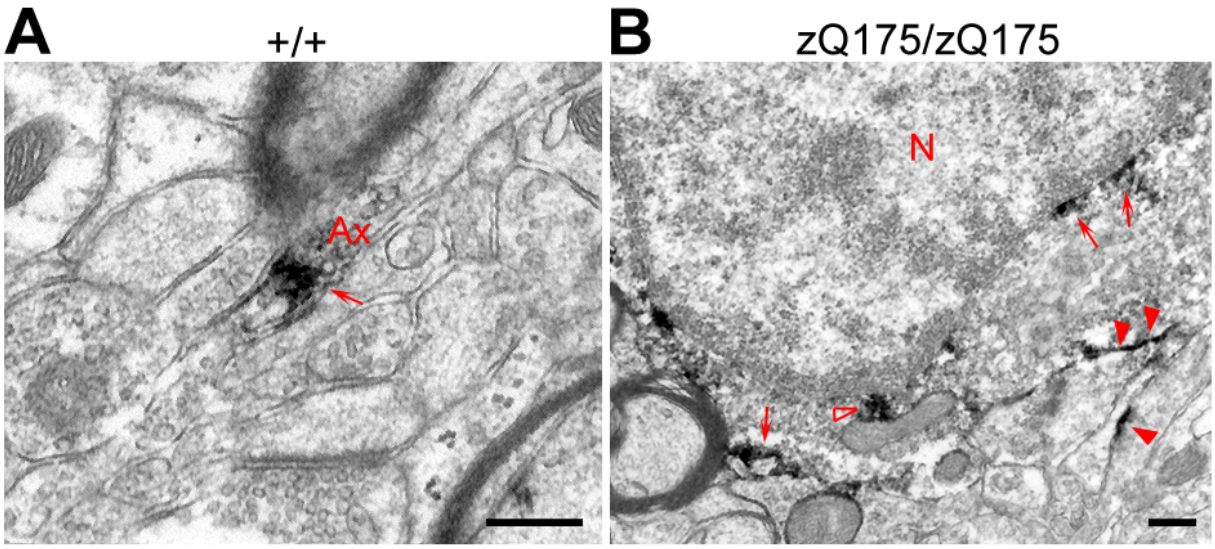


Supplemental Figure 3. Reduction of TrkB phosphorylation in medium spiny neurons. (A) Immunofluorescence detection of phosphorylated TrkB in the striatum of wild type (left panel) and zQ175 homozygous mice (right panel) at 12 months of age. The immunofluorescent intensity of pTrkB is decreased in the zQ175/zQ175 striatum, but not the cortex, as quantified in (B). (C) Double labeling of pTrkB and Darpp-32 (to detect medium spiny neurons) reveals that pTrkB signal is reduced in the cell bodies of medium spiny neurons of zQ175 homozygous mice compared to wild type. (D) Staining of Darpp-32-labeled medium spiny neurons in the caudate

putamen of wild type (left panel) and zQ175 homozygous mice (right panel) at the age of 12 months by immunohistochemistry. (E) Quantification of the number of Darpp-32 labeled cell bodies per field. The ~2% and ~7% decrease in Darpp-32-labeled neuronal number per field of zQ175 heterozygous and homozygous mice respectively does not reach statistical significance. Scale bar, 50µm (A), 20µm (C), 40µm (D).



Supplemental Figure 4. $p75^{NTR}$ is not upregulated in microglia or astrocytes in the striatum of zQ175 homozygous animals at 12 months of age. Double immunofluorescence microscopy indicates that $p75^{NTR}$ does not co-localize with Iba1 (microglial marker) (A) or GFAP (astrocyte marker) (B) in the zQ175 HD striatum at 12 months. Scale bar, 20µm.



Supplemental Figure 5. Ultrastructural immunolabeling of p75^{NTR} in the striatum of wild type and zQ175 homozygous mice at 12 months of age. (A) In the striatum of wild type mice, p75^{NTR}-immunoreactivity (arrow) is primarily detected in axons (Ax) where it is affiliated with small synaptic vesicles (arrow). (B) In the striatum of zQ175/zQ175 mice, p75^{NTR}-immunoreactivity is detected in the cytoplasm of oligodendrocyte perikarya, where it is affiliated with the nuclear membrane (arrows), the plasma membrane (closed arrowheads) and near mitochondria (open arrowhead). N=nucleus. Scale bar, 250nm.

Supplemental Table 1.

Summary of prior studies of BDNF levels in genetic mouse models of HD

HD model	Animal model	Age	Brain region	BDNF content	Method	Change	Reference
Full-length Transgenic Mice	YAC72	9m	Cortex	mRNA	qPCR	↓	24
			Cortex	protein	ELISA	↓	
		3m	Cortex	mRNA	RT-PCR	↓	9
		16m	Cortex	protein	ELISA	→	15
			Striatum	protein	ELISA	↑	
	YAC128	16m	Cortex	mRNA	ISH	→	21
			Cortex	protein	WB	→	
			Striatum	protein	WB	↓	
	BACHD	8m	Striatum	protein	WB	↓	17
		6m	Cortex	mRNA	qPCR	↓	8
		2,4,6 m	Cortex	mRNA	qPCR	↓	4
		6m	Cortex	protein	ELISA	↓	
			Striatum	protein	ELISA	↓	
		6-8m	Cortex	mRNA	qPCR	→	13
			Cortex	protein	WB	→	
			Striatum	protein	WB	→	
N-terminal Fragment Transgenic Mice	R6/2	12wk	Total brain	protein	ELISA	↓	22
		6,8,12wk	Cortex	mRNA	RT-PCR	↓	23
		13wk	Cortex	protein	ELISA	→	15
			Striatum	protein	ELISA	→	
		10wk	Cortex	mRNA	qPCR	↓	1
			Cortex	protein	WB	↓	
		13wk	Cortex	mRNA	qPCR	↓	6
			Cortex	protein	ELISA	↓	
			Striatum	mRNA	qPCR	↓	
			Striatum	protein	ELISA	↓	
	R6/1	5m	Cortex	protein	WB	→	19
			Striatum	protein	WB	↓	
		6m	Striatum	protein	ELISA	↓	3
		5m	Striatum	protein	ELISA	→	12
			Hippocampus	protein	ELISA	→	
			Cortex	protein	ELISA	↑	

			Striatum	mRNA	qPCR	↓	
			Hippocampus	mRNA	qPCR	↓	
			Cortex	mRNA	qPCR	↓	
	N171-82Q	4m	Cortex	mRNA	qPCR	↓	4
			Cortex	protein	ELISA	↓	
			Striatum	protein	ELISA	↓	
		4m	Cortex	protein	WB	↓	14
			Striatum	protein	WB	→*	
		3m	Cortex	protein	ELISA	↓	5
			Striatum	protein	ELISA	↓	
Knock-in Mice	Hdh 111/111	5m	Cortex	protein	ELISA	↓	7
			Striatum	protein	WB	↓	
		3m	Total brain	protein	ELISA	→*	2
		2m	Hippocampus	protein	WB	↓	11
	Hdh (CAG140)	2m	Hippocampus	protein	WB	↓	16
	zQ175	5-6m	Cortex	mRNA	qPCR	→	13
		12m	Hippocampus	protein	ELISA	→	18
			Cortex	protein	ELISA	→	
			Striatum	protein	ELISA	↓	
	HdhQ200	100 wk	Forebrain	mRNA	qPCR	↓	20
	HdhQ250	6,9,12m	Cortex	protein	ELISA	↓	10
			Striatum	protein	ELISA	↓	

Supplemental Table 1. Summary of part of the literatures regarding BDNF levels in different HD mouse models. m, months; wk, weeks; qPCR, quantitative polymerase chain reaction; RT-PCR, reverse-transcriptase-polymerase chain reaction; ELISA, enzyme-linked immunosorbent assay; WB, Western blot analysis; ISH, in-situ hybridization; ↓, decrease; →, no change; ↑, increase; *, slight but non-significant decrease.

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