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Supplemental Information

RNAi-Based GluN3A Silencing Prevents and Reverses Disease Phenotypes Induced by Mutant huntingtin

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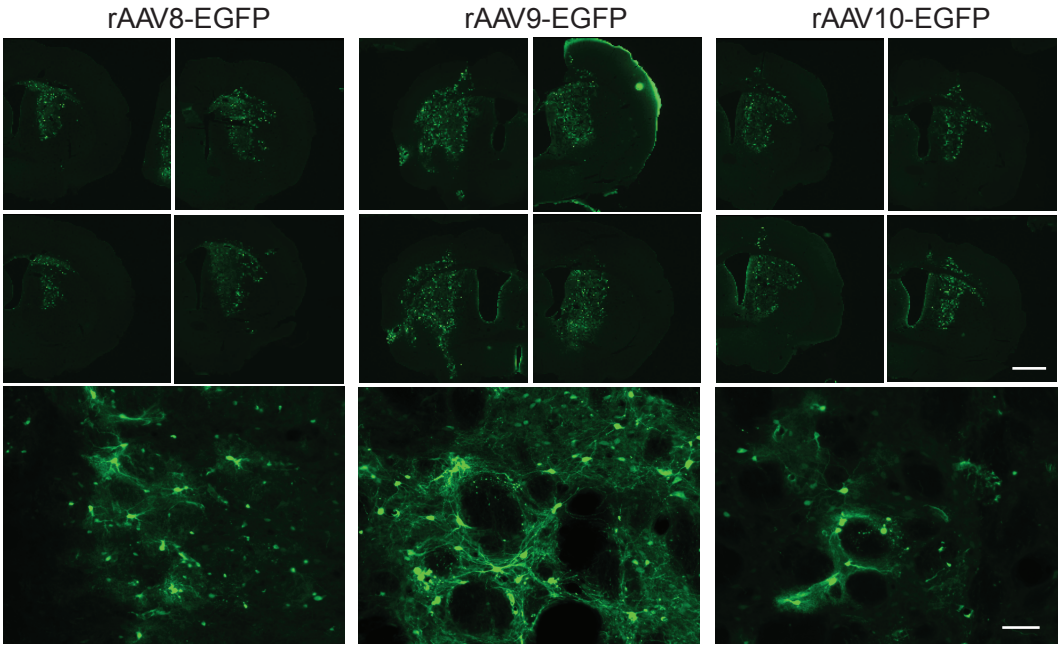
A

Viral vector	Titer (viral genomes/mL)	Injection volume (µL)	Dose (viral genomes)
rAAV8-CMV-EGFP	2.35 x10^{12}	1.6	3.76x10^{9}
rAAV9-CMV-EGFP	2.50 x10^{12}	1.5	3.75x10^{9}
rAAV10-CMV-EGFP	2.50 x10^{12}	1.5	3.75x10^{9}

B



C

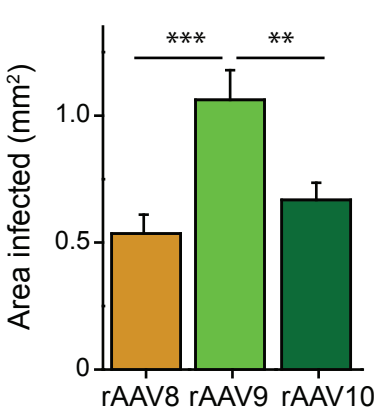


Figure S1. Comparison of transduced striatal area between rAAV serotypes upon a single striatal injection
(A) Titers and volumes of injection for rAAVs used in serotype comparison. (B) Photomicrographs of coronal sections from mice bilaterally injected into the striatum with rAAV8-, rAAV9-, or rAAV10-EGFP, and sacrificed 2 weeks later. Scale bar: 1mm and 100 µm. (C) Quantification of striatal area displaying GFP fluorescence in series of mosaic images separated 240 µm. Data are mean ± S.E.M. (n=3 animals per serotype; ** $P < 0.01$, *** $P < 0.001$, one-way ANOVA followed by Bonferroni multiple comparison test).

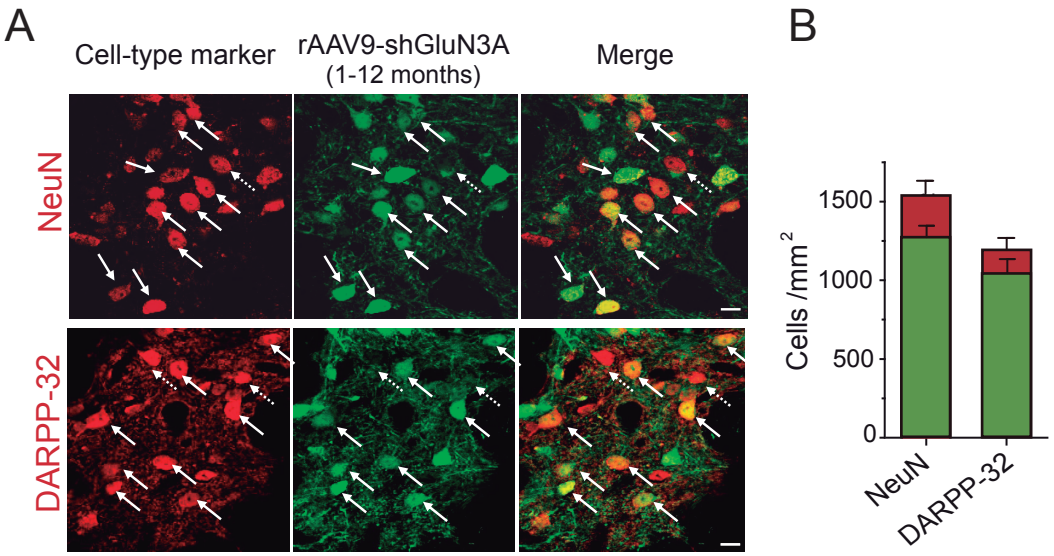


Figure S2. Long-lasting transduction of striatal neurons by rAAV9-shGluN3A
(A) Single confocal images of representative striatal sections from a YAC128 mouse receiving rAAV9-shGluN3A at 1 month of age (green) and stained by immunohistochemistry for NeuN or DARPP-32 at 12 months (red). Solid arrows: examples of colocalization; dashed arrows: no colocalization. Scale bar: 10 µm.
(B) Quantification of number of striatal neurons transduced by rAAV9-shGluN3A. Data are mean ± S.E.M. (n= 3 mice, 2-3 striatal fields analysed and averaged per mice).

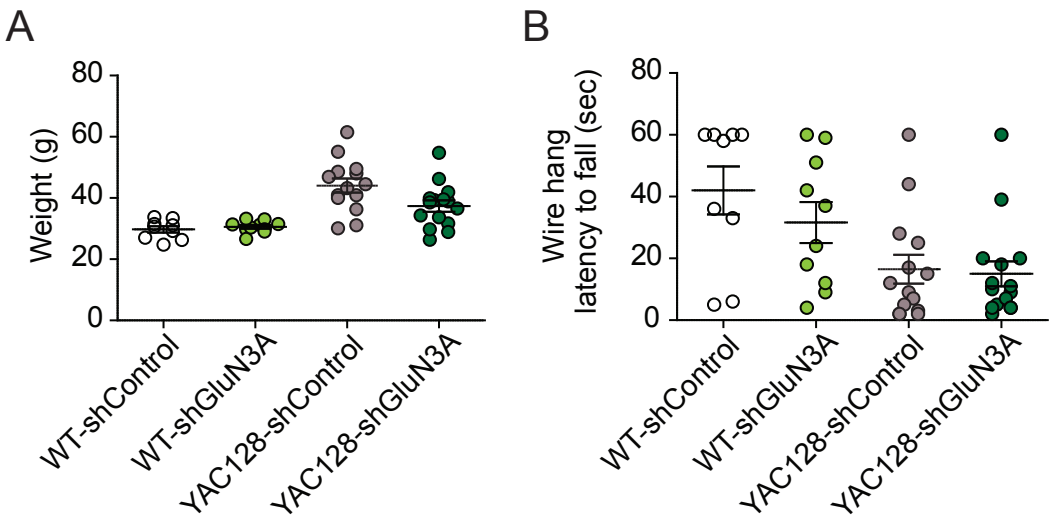


Figure S3. Body weight and muscular strength are not affected by rAAV9-shGluN3A intrastriatal injection.

(A) Body weight is increased in 10-12 month-old YAC128 mice compared to WT mice. Injection into the striatum of rAAV9-shGluN3A has no significant effect in body weight. Two-way ANOVA: genotype x shRNA interaction $F(1,44) = 3.95$, $P = 0.0530$; shRNA $F(1,44) = 2.37$, $P = 0.1305$; genotype $F(1,44) = 31.1$, $P < 0.0001$.

(B) Latency to fall from the wire. Two-way ANOVA: genotype x shRNA $F(1,44) = 0.635$, $P = 0.4298$; shRNA $F(1,44) = 1.14$, $P = 0.2924$; genotype $F(1,44) = 14.2$, $P = 0.0005$.