SUPPLEMENTARY MATERIALS

Table S1. Study design

Mice (age of treatment)	Control/SD (genotype)	Treatment with AAV9
Neonates (1-2 day) (denoted as 'n' in manuscript)	Control (+/+ or +/-)	HexB (n=5)
		LacZ (n=5)
	SD (-/-)	HexB (n=5)
		LacZ (n=5)
Adults (6 weeks) (denoted as 'a' in manuscript)	Control (+/+ or +/-)	HexB (n=5)
		LacZ (n=5)
	SD (-/-)	HexB (n=5)
		LacZ (n=5)

Table S2. Statistical comparisons of control groups that are merged within figures.

Data/Related Figure	Comparison	P value	Test
Total distance travelled/ Figure 1b	at Wk 14 a Control-LacZ (n=5) a Control-HexB (n=5) n Control-LacZ (n=4) n Control-HexB (n=5)	P = 0.7290	one way ANOVA
	at Wk 15 a Control-LacZ (n=5) a Control-HexB (n=5) n Control-LacZ (n=4) n Control-HexB (n=5)	P = 0.7177	one way ANOVA
	at Wk 16 a Control-HexB (n=5) n Control-LacZ (n=5) n Control-HexB (n=4)	P = 0.2498	one way ANOVA
	at Wk 21 a Control-HexB (n=2) vs n Control-HexB (n=5)	P = 0.8723	two tailed T-test
	at Wk 30 n Control-HexB (n=5)	1 group no intragroup comparison	none
Vacuolization / Figure 2b	a Control-LacZ (n=5) a Control-HexB (n=5) n Control-LacZ (n=5) n Control-HexB (n=5)		one way ANOVA
	in CB Md/Po	p = 0.9257 p = 0.4182	

	Mid CX/Hp Thy/HY/Sep OA	p = 0.8900 p = 0.5847 p = 0.9328 p = 0.5472	
G_{M2} ganglioside proportions/ Figure 2d	a Control-LacZ (n=5) a Control-HexB (n=5) n Control-LacZ (n=5) n Control-HexB (n=5)	p = 0.0913	one way ANOVA
Serum hex activity/ Figure 3a	At wk: 10, 12-14, final a Control-LacZ vs n Control-LacZ a Control-HexB vs n Control-HexB a Control-LacZ and n Control-LacZ vs a Control-HexB a Control-LacZ and n Control-LacZ vs n Control-HexB	 p > 0.05 at all times points p > 0.05 at all time points *p value ≤ 0.05 at all time points (see Fig. S2a) *p value ≤ 0.05 at all time points (see Fig. S2a)	two tailed t-tests
Brain hex activity/ Figure 3b	a Control-LacZ vs n Control-LacZ a Control-HexB vs n Control-HexB	p > 0.05 *p value = 0.0117 (see Fig. S2b)	Two tailed T-test
Vector copy number in brain/ Figure 5	male vs female	a Control = 0.3192 M (n=14), F (n=6) n Control = 0.7340 M (n=8), F (n=12) a Control-HexB =0.7870 M (n=6), F (n=4) a Control-LacZ = 0.1026 M (n=8), F (n=2) n Control-HexB = 0.4203 M (n=3), F (n=7) n Control-LacZ = 0.3241 M (n=5), F (n=5)	two tailed T-test
Vector copy number in liver/ Figure 5	male vs female	a Control = 0.4215 M (n=14), F (n=6) n Control = 0.3524 M (n=8), F (n=12) a Control-HexB =0.5390 M (n=6), F (n=4) a Control-LacZ = 0.4323 M (n=8), F (n=2) n Control-HexB = 0.2740 M (n=3), F (n=7) n Control-LacZ = 0.4650 M (n=5), F (n=5)	two tailed T-test

Figures

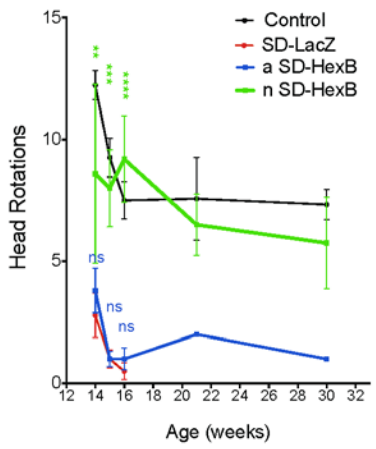

Figure S1 Head rotations. Mice were videotaped in an open field at 3-5 time points post rAAV9 administration, and head rotations were analyzed using ANY-maze software. Plotted values are average number of head rotations ± SEM. **** p<0.0001; ***p<0.001; **p<0.01; ns- not significant.

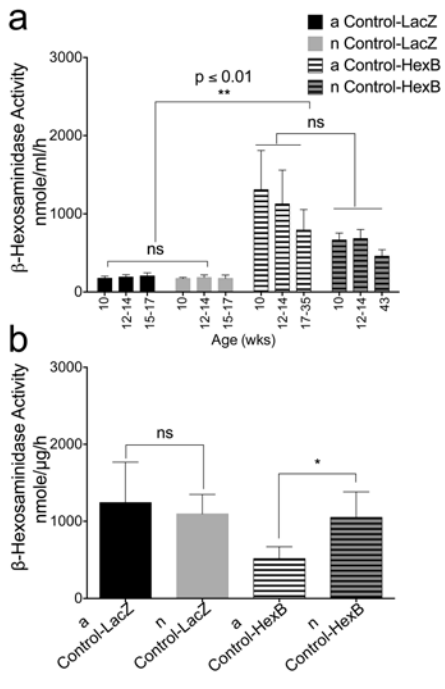

Figure S2 β-hexosaminidase activity levels in control groups. Total β-hexosaminidase activity was determined using 4-MUG as a substrate. Bars represent the average activity + SEM. **(a)** Sera were collected at 10, 12-14, and 15-43 wks (just before death). Control animals injected with HexB had significantly more activity than normal LacZ-injected mice. Therefore only LacZ-injected mice were included in Fig.3 of the manuscript as controls. (b) brains were collected at death. The significant difference between the HexB-injected adults and neonates reflects the different genotypic composition of these two groups (*Hexb*$^{+/+}$ vs *Hexb*$^{+/-}$). ** indicates p<0.01, *indicates p<0.05, ns- not significant.

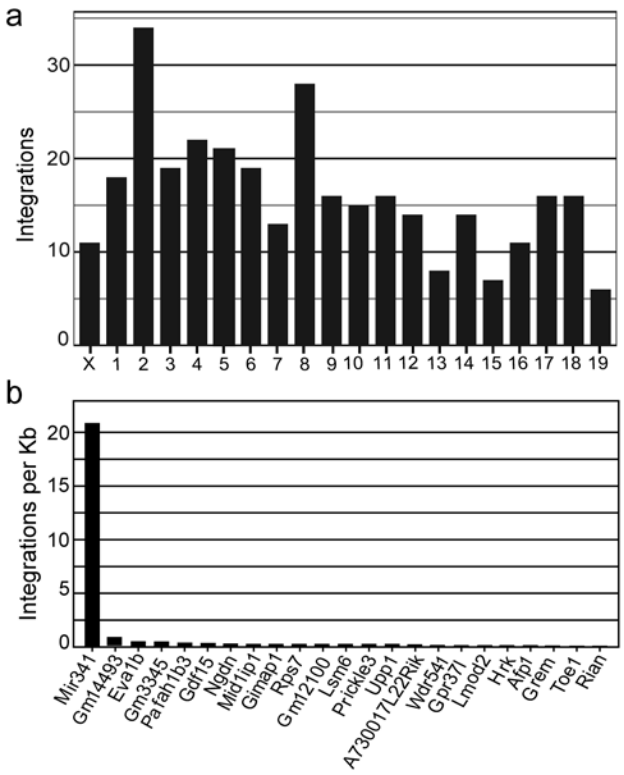

Figure. S3 AAV9 Integration Sites. (a) Integrations per chromosome. (b) Genes with largest number of integrations per kb of DNA.

Video S1. Comparison of the activity of neonatally-treated mice. A SD mouse treated with AAV9-HexB as a neonate (female), an AAV9-LacZ-treated SD mouse (front), and a normal control (*HexB*$^{+/-}$ male) treated neonatally with AAV9-HexB were place in an open field at 16 wks. The LacZ-treated SD mouse at the front of the field exhibits tremors, little movement and does not splay its rear limbs on the tail suspension test. The SD mouse treated as a neonate with AAV9-HexB is on the left side at the beginning of the video.

Video S2. Comparison of the activity of adult-treated mice. A SD mouse treated with AAV9-HexB as an adult, an AAV9-LacZ-treated SD mouse (front), and a normal control (*Hexb*$^{+/-}$) treated with AAV9-HexB as an adult were placed in an open field at 16 wks of age. The LacZ-treated SD mouse exhibits little movement and does not splay its rear limbs on a tail suspension

test. The SD mouse treated with AAV9-HexB as an adult is obviously slower than its normal counterpart; its body is very close to the ground compared to the normal mouse.