Supplementary Material

Supplementary Video 1: GLD IS only dog at 10 weeks of age

Supplementary Video 2: GLD 2Wk-High at 116 weeks of age

Supplementary Video 3: GLD 2Wk-Low at 27 weeks of age

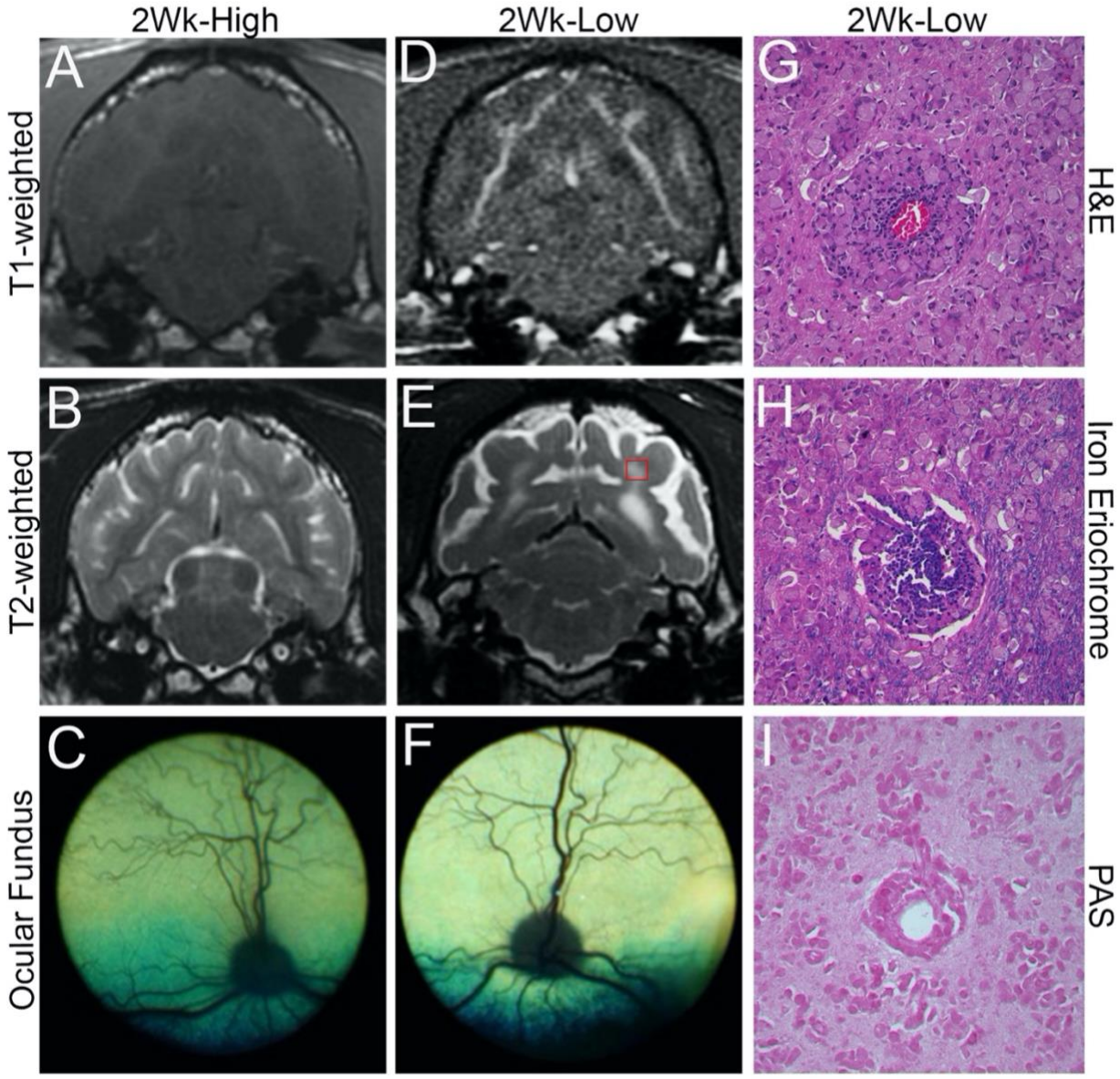
Supplemental Figure 1: Evaluation of visual deficits by MRI and ophthalmic examination.

Supplemental Figure 2: Cerebrospinal fluid total protein concentration.

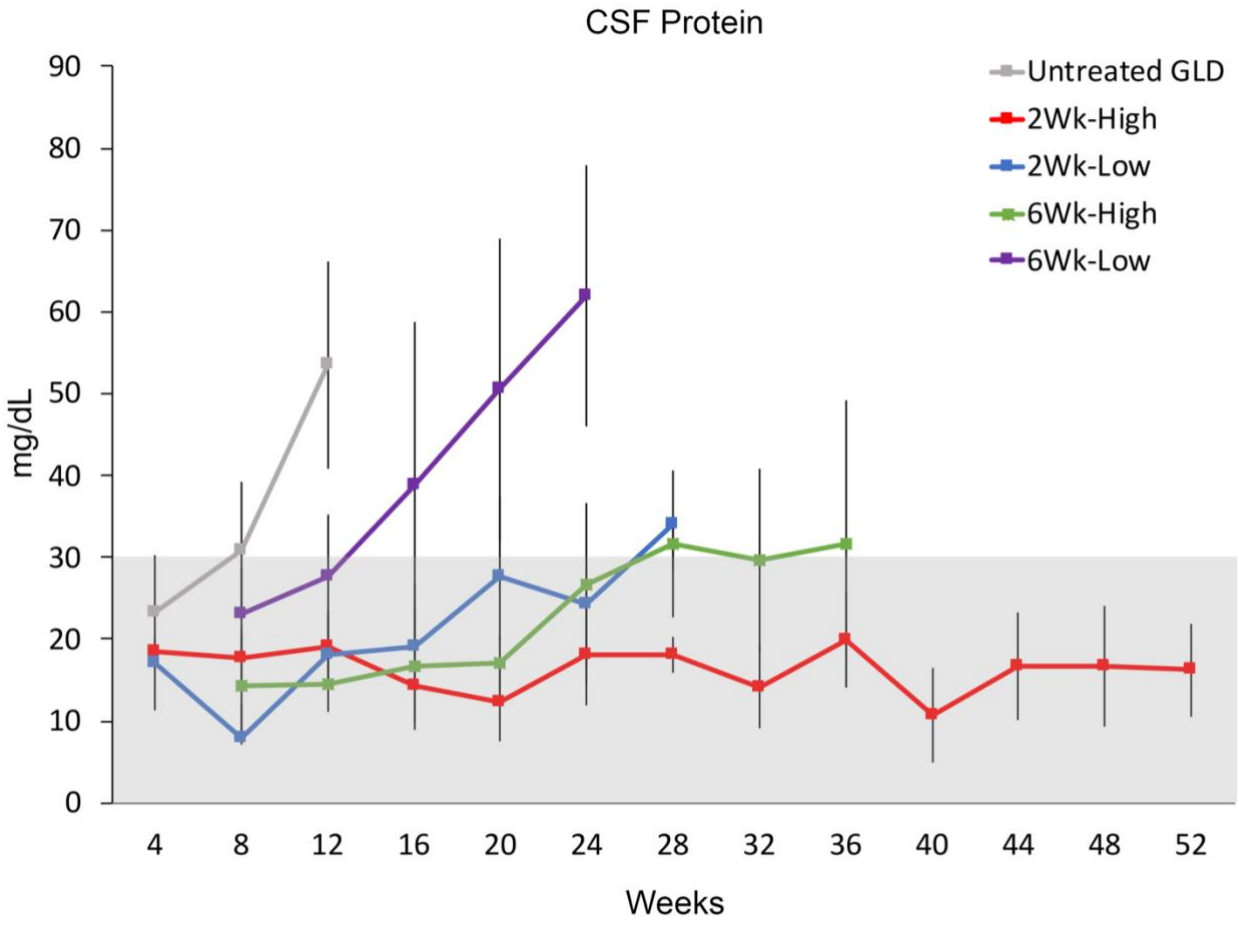
Supplemental Figure 3: Brainstem auditory evoked response (BAER) testing.

Supplemental Figure 4. GALC immunohistochemical staining of the CNS.

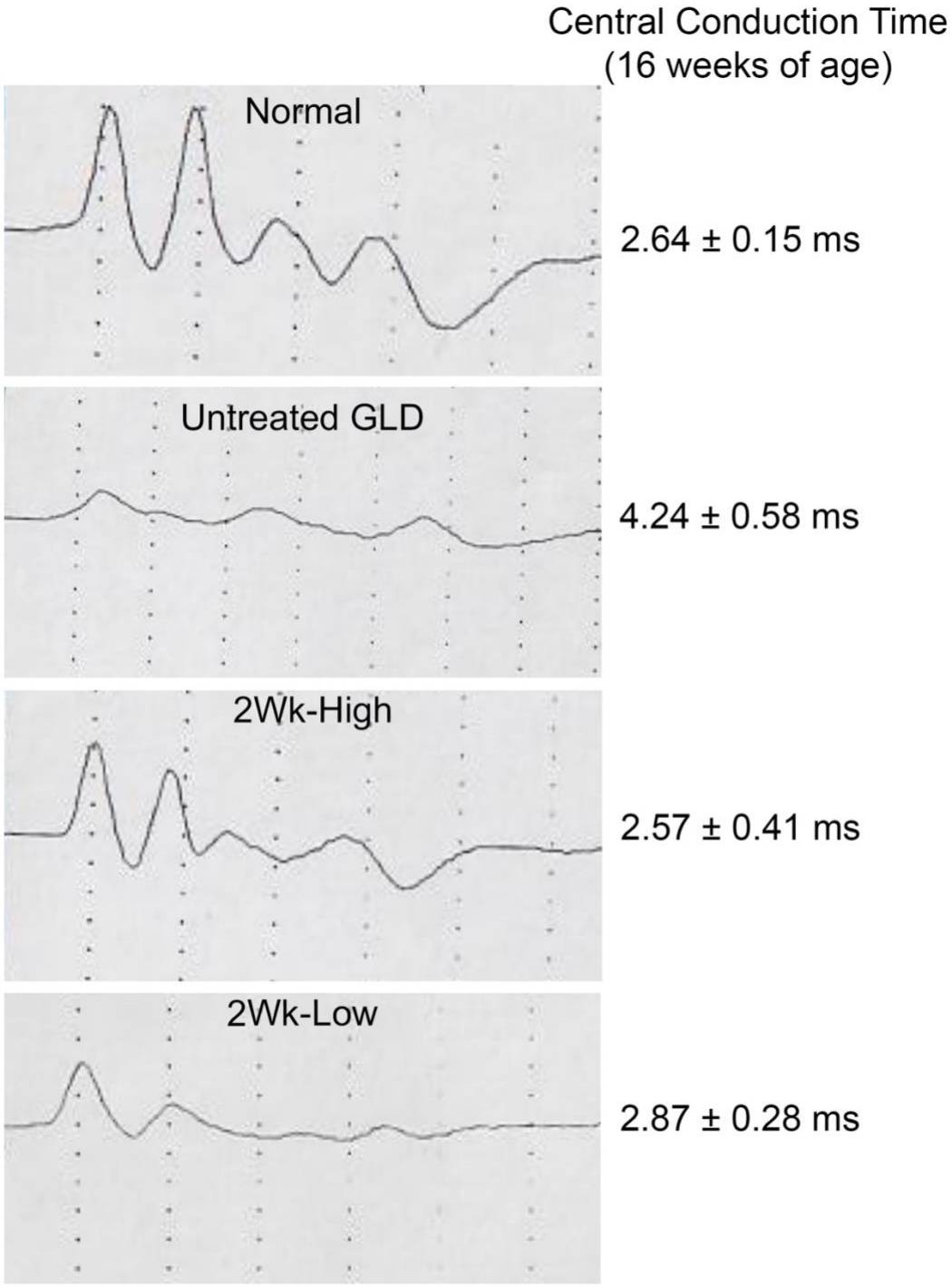
Supplemental Figure 5. Hematoxylin and Eosin (H&E) staining of dorsal root ganglion (DRG).



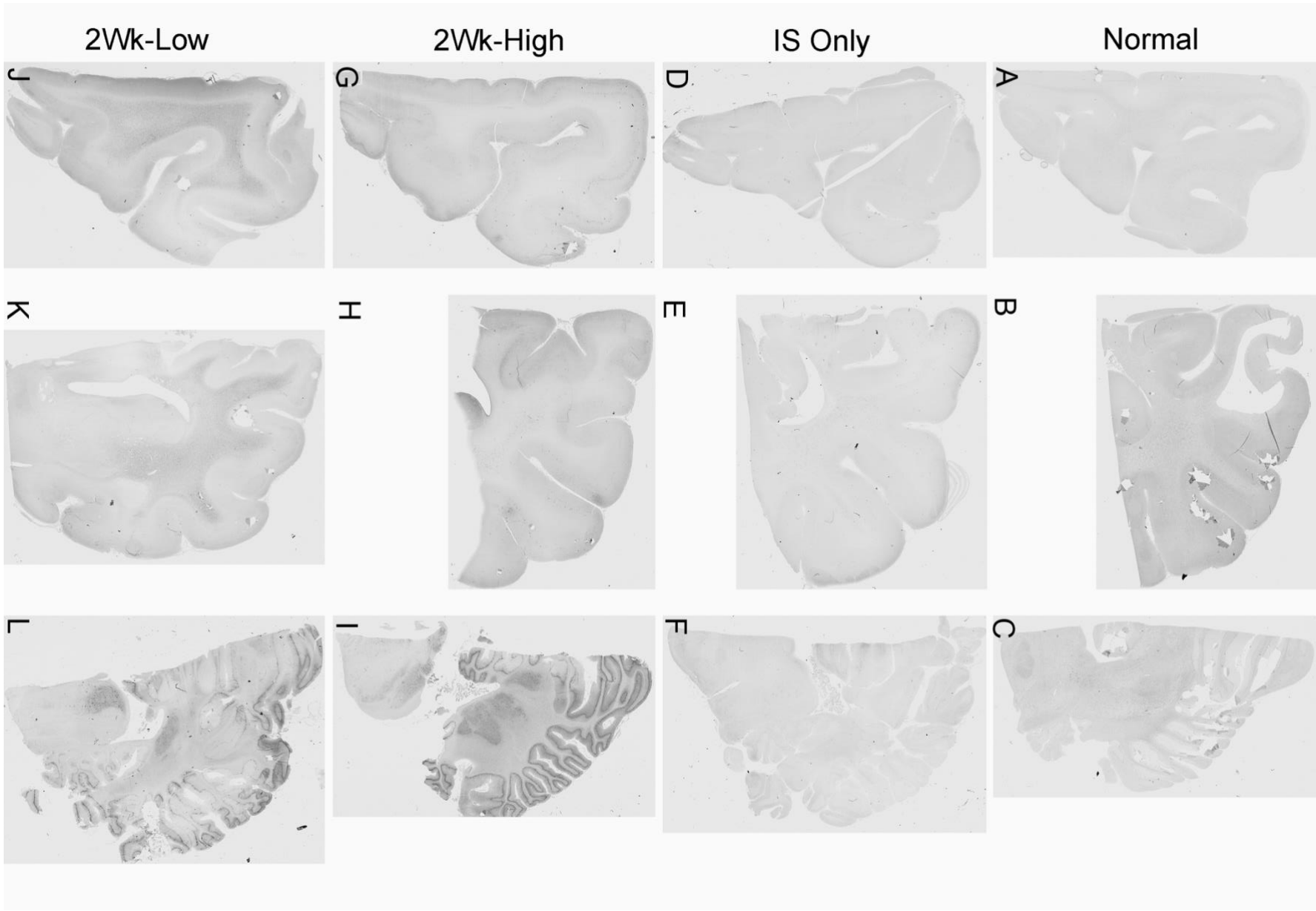
Supplemental Figure 1. Evaluation of visual deficits by MRI and ophthalmic examination. A) T1-weighted MRI of 2Wk-High dog shows no white matter enhancement in contrast to D) 2Wk-Low dog demonstrating contrast enhancement in the optic radiations. B) T2-weighted MRI of a 2Wk-High dog showing normal white matter signal intensity and sulcal width compared to E) 2Wk-Low dog showing hyperintensity of the white matter and wide sulci. Ophthalmic exam revealed structurally normal fundus in both C) 2Wk-High and F) 2Wk-Low dogs. 2Wk-Low histochemical stains taken from the location of red box shown in panel E: G) H&E stain of the occipital radiation showing perivascular cuffing and infiltration of lymphocytes. H) Iron eriochrome stain of the occipital radiation showing loss of myelin. I) Periodic acid-Schiff staining of the occipital radiation showing accumulation of storage granules.



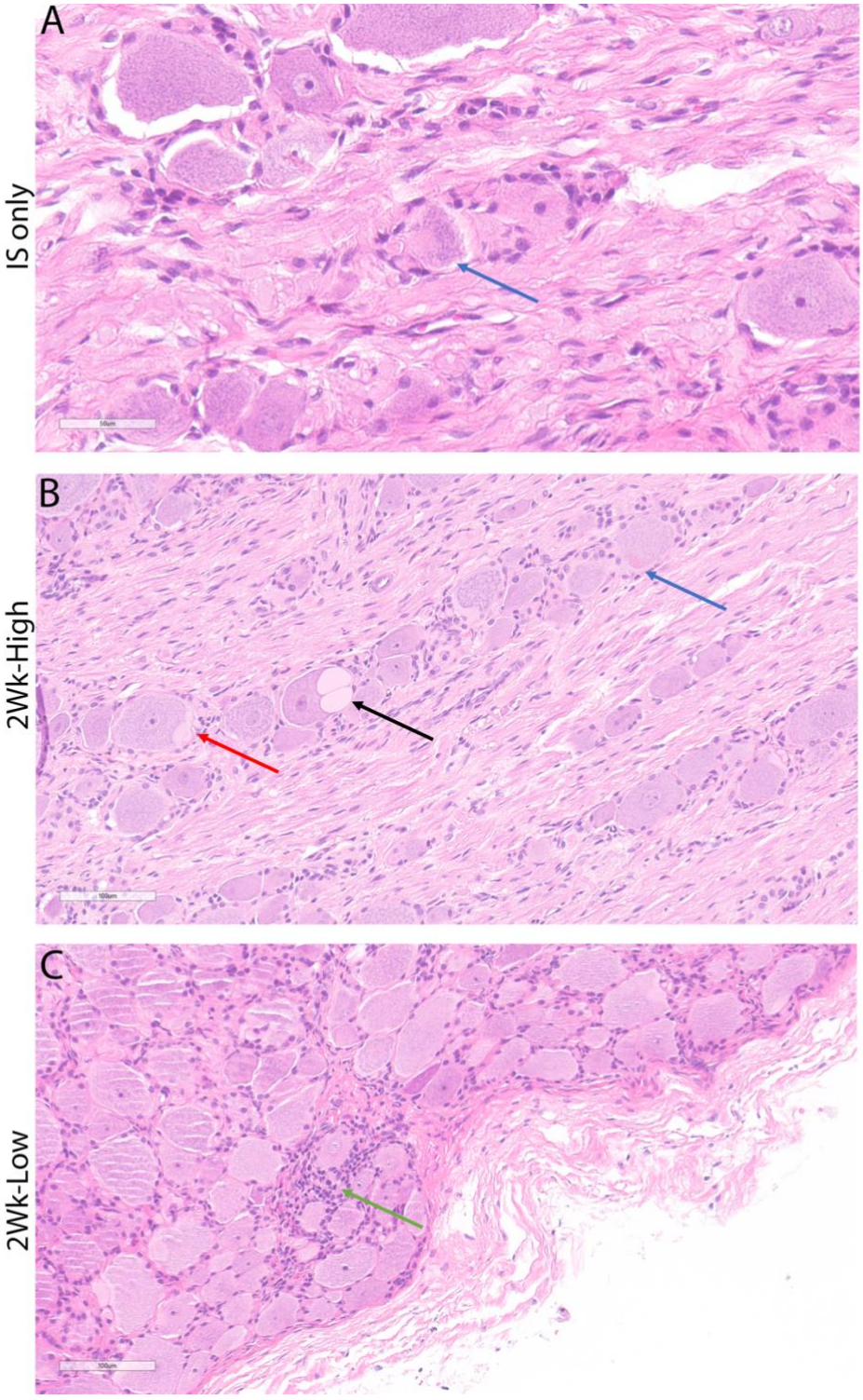
Supplemental Figure 2. Cerebrospinal fluid total protein concentration. Protein quantified by colorimetric analysis every 4 weeks up to 52 weeks of age. Gray shading indicates normal reference range for canine samples collected at the cisterna magna (< 30mg/dL). GLD (n=4, gray), 2Wk-High (n=10 ≤ 16 weeks of age; n=6 > 16 weeks of age, red), 2Wk-Low (n=4 ≤ 16 weeks of age; n=3 > 16 weeks of age, blue), 6Wk-High (n=4 ≤ 16 weeks of age; n=3 > 16 weeks of age, green) and 6Wk-Low (n=4, purple).



Supplemental Figure 3. Brainstem auditory evoked response (BAER) testing. BAER was performed every 8 weeks in untreated GLD, normal, and AAV-treated dogs. A representative time point of 16 weeks of age is shown. Central conduction time is defined as the latency in ms between Peak I (the first peak) and Peak V (the last peak). 2Wk = treated at 2 weeks of age, High = high dose 1E14 vg, Low = low dose 2e13 vg.


2Wk-Low
2Wk-High
IS Only
Normal
J
G
D
A
K
H
E
B
L
I
F
C

Supplemental Figure 4. GALC immunohistochemical staining of the CNS. Immunohistochemical staining with GALC antibody demonstrates GALC expression in dogs at the level of the frontal lobe, internal capsule, and cerebellum. Normal dogs (A-C), Is only dogs (D-F), 2Wk-High (G-I), 2Wk-Low (J-L). 2Wk = treated at 2 weeks of age, High = high dose 1E14 vg, Low = low dose 2e13 vg.



Supplemental Figure 5. Hematoxylin and Eosin (H&E) staining of dorsal root ganglion (DRG). Blue arrows show cytoplasmic eosinophilic granular material. Red arrows show neuronal cytoplasm swelling and loss of Nissl substance. Black arrows show neuronal cytoplasmic vacuolation. Green arrows indicated possible inflammatory cell infiltrates.