Cortical Recovery Following Gene Therapy in a Canine Model of Achromatopsia

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Purpose

To measure the cortical response to visual stimulation in dogs with hereditary loss of retinal cone function using rod- and cone-directed stimuli.

Methods

Subjects: Two normal dogs (CNGB3-null mutant carriers), 5 achromatopsia-affected dogs (CNGB3 mutants with S- and L/M-cone dysfunctions), and 2 CNGB3 mutants treated at 1.5 and 3 months of age (recovered L/M-cone function demonstrated by ERG) were studied using fMRI.

Gene therapy: Prior to imaging, the treated animals received unilateral recombinant adeno-associated virus (rAAV) subretinal injections containing human CNGB3 cDNA. An L/M specific promoter was used.

Methodology: Rod- and L/M cone-directed stimuli were developed using the silent substitution method, determined with respect to published spectral sensitivity properties of the canine L/M-cone, S-cone, and rod opsins.

Results

Following transformation of functional data to a canine digital atlas, functional activation was observed bilaterally within the primary visual cortex. Supra-threshold response volume was measured within a pre-defined V1/V2 ROI.

Example of an achromatopsia-affected canine:

Figure 4. Cortical responses were greater for low luminance (top) than high luminance (bottom), combining across rod- and cone-directed stimuli.

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Commercial interest

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