CORTICAL RESPONSES TO ROD- AND CONE-ISOLATING FLICKER IN A CANINE MODEL OF ACHROMATOPSIA

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Purpose

To measure the cortical response in area V1 to visual stimulation in a dog with hereditary retinal cone loss of function using rod- and cone-isolating visual stimuli.

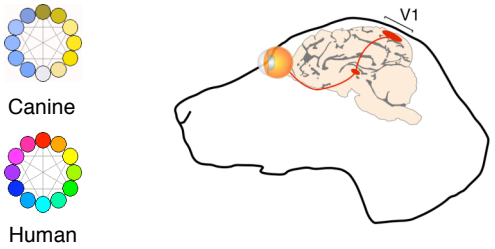

Figure 1. Canine and human color perception (left), and localization of the canine primary visual cortex (V1, right).

Methods

Subject: An 8 month old achromatopsia-affected (color blind) mutant canine (*CNGB3*-mutation with S- and L/M-cone dysfunctions) was studied using blood-oxygen-level dependent (BOLD) functional magnetic resonance imaging (fMRI).

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

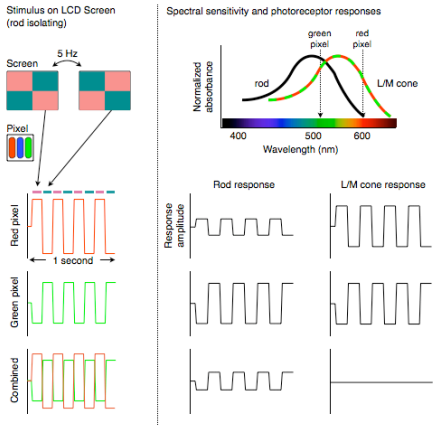

Figure 2. The silent substitution method for rod isolation.

Visual stimuli: Visual stimulation was a 4-quadrant checkerboard, 5 Hz flicker presented for 30 seconds, alternating with a gray screen. Scanning was conducted with low (0.41 cd/m^2) and high (1194 cd/m^2) average luminance stimuli. These levels correspond to scotopic and photopic luminance respectively.

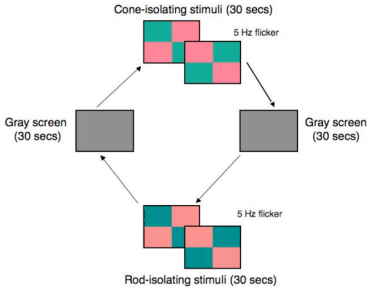

Figure 3. The stimulus presentation.

fMRI scans: Cortical responses were gathered using a 3 Tesla scanner, 3 mm isotropic voxels, at TR of 3 seconds for a total of 60 minutes of scanning. The animal was sedated with Ketamine and Valium, supported with positive pressure ventilation with 100% O_2

Results

Following transformation of functional data to standardized canine digital atlas, functional activation was observed bilaterally within the primary visual cortex.

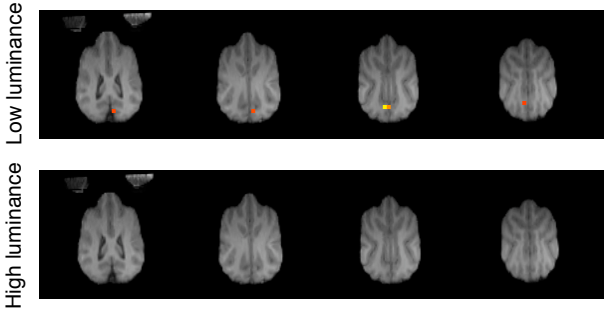

Figure 4. Cortical responses were greater for low luminance (top) than high luminance (bottom) stimulus.

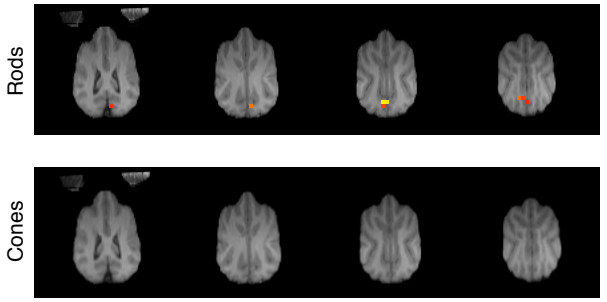

Figure 5. Within the low luminance condition, cortical responses were only present for the rod-isolating stimulus (top). No cortical response was observed for the cone-isolating stimulus (bottom).

Conclusions

Rod specific cortical responses can be identified and studied in a canine model.

In a *CNGB3*-mutant canine, cortical responses to a cone-isolating stimulus are absent.

Ongoing work is examining the cortical responses to this stimulation paradigm in control animals and in *CNGB3*-mutants following adeno-associated virus (AAV) gene therapy that restores L/M-cone function.

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