Low contrast visual stimuli yield differential volumes of functional MRI activation in affected and unaffected eyes following recovery from optic neuritis

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Background: Optic neuritis (ON) is inflammatory demyelination in the optic nerve and is a common early manifestation of multiple sclerosis (MS). It presents as monocular blurred vision or blindness progressing over days and recovering over months. Degree of ultimate recovery from ON is variable, and residual deficits become more apparent when testing affected eyes with low contrast (gray-on-white) eye charts.[1] Factors contributing to differential recovery from ON are unknown but may include cortical reorganization in addition to local remyelination.[2] Functional MRI (fMRI) may be useful to investigate cortical reorganization following ON.

Methods: Six patients with relapsing-remitting multiple sclerosis who experienced a single remote episode of unilateral optic neuritis underwent fMRI with visual stimulation. At least six months were required to have passed since onset of symptoms, allowing time for recovery to have reached a plateau.[3] Visual stimuli consisted of a radial checkerboard pattern inverting at a frequency of 15Hz, with a green fixation dot in the center of the stimulus. The pattern was presented at three different contrast levels (100%, 2.5%, 1.25%, Figure 1) individually displayed in sequence by video screen to fill the monocular visual field. Affected and unaffected eyes were stimulated independently. Activation maps were created based on the differences in activation between 100% stimulus and each of the low contrast stimuli. Volumes of cortical activation were measured at the T>3.5 level using AFNI software.[4] Clinical measures of visual acuity on a low contrast letter chart and optical coherence tomography (OCT) were collected as part of the same study visit.

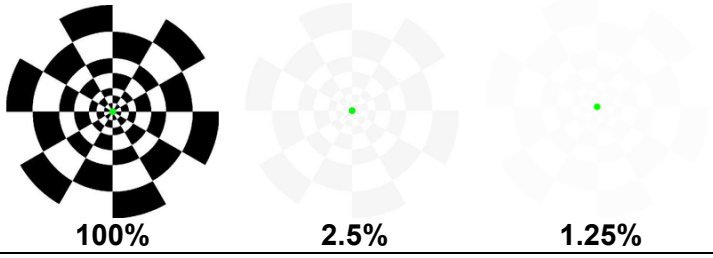

Figure 1: Visual fMRI stimulus as presented at 100%, 2.5%, and 1.25% contrast.

Results: Differences in volume of activation were more apparent between affected and unaffected eyes when using the lowest contrast (1.25%) stimulus (mean difference unaffected-affected eyes=3543.8mm3; 95%CI=-411.0-inf, p=0.065) compared to the 2.5% stimulus (mean difference unaffected-affected eyes=1037.8mm3; 95%CI=-574.8-inf, p=0.126)(Figure 2). Volume of activation using 1.25% stimulus may be related to both low contrast letter acuity (r=0.20, p=0.350) and retinal nerve fiber layer thickness (r=0.49, p=0.178, Figure 3). Enrollment of additional patients is ongoing.

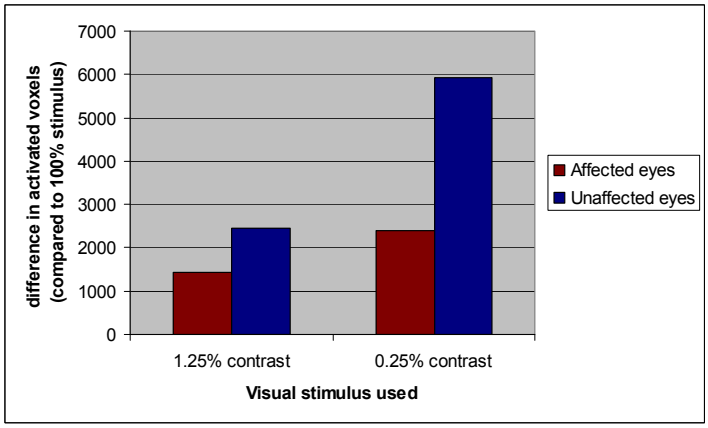

Figure 2: Differential change in volume of activation in affected vs. unaffected eyes when using low-contrast stimuli.

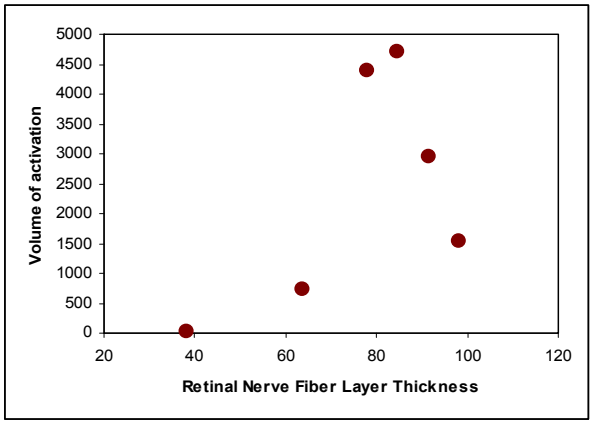

Figure 3: Relationship between volume of activation (1.25% relative to 100% stimulus) and retinal nerve fiber layer thickness measured by OCT.

Conclusion: Low contrast visual stimuli yield differential volumes of functional MRI activation in affected and unaffected eyes following recovery from optic neuritis. These preliminary results suggest low contrast visual fMRI may be sensitive to detect changes following ON. Variable contrast visual fMRI may augment findings detected on both clinical and anatomic evaluations for testing, treatment, and rehabilitation strategies.

References: **1.** Balcer LJ, Baier ML, Cohen JA, et al. Contrast letter acuity as a visual component for the multiple sclerosis functional composite. Neurology. 2003; 61:1367-1373. **2.** Toosy AT, Hickman SJ, Miszkiel KA, et al. Adaptive cortical plasticity in higher visual areas after acute optic neuritis. Ann Neurol. 2005; 57:622-633. **3.** Costello F, Hodge W, Pan YI, Eggenberger E, Coupland S, Kardon RH. Tracking retinal nerve fiber layer loss after optic neuritis: A prospective study using optical coherence tomography. Mult Scler. 2008;14:893-905. **4.** Cox RW. AFNI: Software for analysis and visualization of functional magnetic resonance neuroimages. Comput Biomed Res. 1996; 29:162-173.