HIGH RESOLUTION BOLD FMRI OF THE HUMAN RETINA OF OXYGEN AND CARBOGEN INHALATION

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INTRODUCTION Very high resolution MRI of the retina in animal models has been reported. Anatomical laminar resolution [1, 2], relaxation and diffusion time constants [3], and blood flow MRI [4], BOLD fMRI of physiological [1] and visual stimuli [5] have been reported in animal models. Similar applications in the human retina remain challenging because the eye is near air-tissue interface, high spatial resolution is needed to image the thin retina, gradients are less powerful on the clinical MRI scanners than those on the animal scanners, and there is potential eye movement.

In this study, we explored the feasibility of performing BOLD fMRI associated with oxygen and carbogen (5%CO_2, 95% O_2) challenge in normal human retina. BOLD fMRI utilized an Inversion-Recovery, PRinciples of Echo Shifting using a Train of Observations (IR-PRESTO) pulse sequence. Inversion recovery contrast was used to suppress vitreous signal to minimize partial volume effect. PRESTO was used to achieve high spatiotemporal resolution to minimize image distortion and signal drop out in the region of high magnetic susceptibility of the eye. Stable eye fixation on a target with cued eye blinks was utilized to avoid eye movement.

METHODS Experiments were performed on 5 normal human volunteers with 2 or 3 repeated measurements made on each subject. Subjects were asked to blink if needed immediately after the data readout train (which generated distinct sounds as cue) but otherwise fixated on a target during MRI. MRI studies were performed on a 3T Philips Achieva. A custom-made surface coil of 7 cm in diameter was used. fMRI scans utilized a 2D IR-PRESTO sequence with repetition cycle between inversion pulses of 4s and inversion delay of 1.3s. Inversion recovery procedure was applied to suppress the otherwise bright vitreous signal. The chemical shift direction of fat was set posterior to avoid fat signal overlap on the retina signal. Other MRI parameters were: TRTE/FA=17ms/11ms/10º, readout bandwidth=6.4 kHz, FOV=100x100 mm, matrix size=64x50, and spatial resolution of 1.6x2x4.0mm^3. The higher resolution direction was placed along the anterior-posterior direction. The paradigm was three inhalation epochs of 30 s air and 30 s O2 or carbogen, followed by another 30 s of air. Image corregistration was performed as needed. fMRI time courses were obtained from an ROI of the posterior retina (as shown in Figure 1B). Percent changes were tabulated at 80% of maximum fMRI signal changes.

RESULTS BOLD fMRI time-series images of the retina were free of movement artifacts. Time-series movies of the MR images showed no gross motion (4% of images were discarded). **Figure 1** shows a BOLD fMRI color activation map overlaid on the T2*-weighted image and the corresponding time course associated with O_2 challenge. BOLD percent change during O_2 inhalation was 5.2±1.5% (±SD, N=5) relative to air in the posterior retina ROI. Similarly, **Figure 2** shows a BOLD fMRI color activation map and the corresponding time course associated with carbogen challenge from one subject. BOLD percent change during carbogen inhalation was 5.2±1.3% (±SD, N=5). The group-averaged percent changes from carbogen challenge were not statistically different from those from oxygen challenge (P>0.05).

Figure 3 shows a reproducibility test of BOLD fMRI maps (carbogen challenge) from 3 repeated trials from the same subject in the same setting. BOLD percent changes were 6.2±1.2%, 4.9±0.9%, and 4.4±1.0% in the ROI of the posterior retina, the standard deviations were those across pixels within the ROI. The activation patterns in the retina were reasonably reproducible.

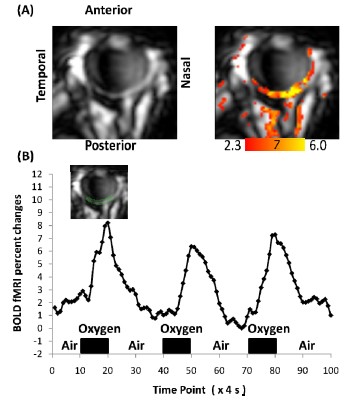

Figure 1. BOLD fMRI of O_2 inhalation. Color indicates Z score.

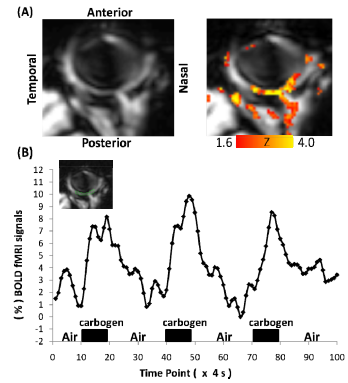

Figure 2. BOLD fMRI of carbogen.

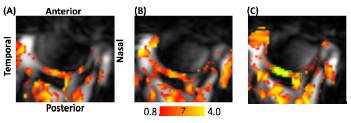

Figure 3. Reproducibility of BOLD fMRI (carbogen inhalation) of three repeated trials in the same subject.

DISCUSSION BOLD increase in the retina/choroid complex during oxygen challenge was larger than those of brain (3.3% at 3T [6]). This is likely because the retina has a higher vascular density than the brain, and thus the larger percent changes. In addition, it is worth pointing out that hyperoxia has vasoconstrictive effect on the retinal vessels but not on choroidal vessels, and hyperoxia is known to markedly decrease retinal blood flow by 30-60% relative to air inhalation [7] compared to a 10% reduction in brain blood flow under hyperoxia [8]. The net effect observed in our study is a positive BOLD increase, suggesting that the increased oxygen delivery per se from oxygen inhalation dominates. The results are consistent with a BOLD fMRI study of oxygen challenge reported in the rat retina [1].

BOLD percent change to carbogen challenge was not statistically different from oxygen challenge, contrary to prediction based on brain data. There are three possible explanations. First, while 5% CO_2 has significant vasodilatory effect on retinal vessels, it has little vasodilatory effect on choroid vessel [9], and the choroid is expected to dominate the BOLD responses because of its high vascular density [9]. Second, the BOLD signal may have been nearly saturated with room air, further vasodilation of the retinal vessels with carbogen and the already small arteriovenous oxygen difference in the choroid at baseline [7] would not further increase BOLD responses. Third, BOLD fMRI may not have sufficient sensitivity to detect the small BOLD differences between oxygen and carbogen inhalation. The next logical step is to explore laminar specific BOLD fMRI responses, as has been shown in animal model (1).

CONCLUSION This study demonstrates, for the first time, an innovative MRI application to detect BOLD fMRI signal changes associated with oxygen and carbogen challenges in the unanesthetized human retina. Clinical scanners have sufficient SNR, gradient strength, and stability to perform retinal BOLD fMRI. Eye movement can be managed with stable eye fixation and synchronized blinks. With improvements in spatiotemporal resolution, BOLD fMRI can be a valuable tool to study the human retina because it provides depth resolution, large field of view and potentially quantitative data.

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