Differential BOLD and Blood Flow Response During and Immediately After Transient Carotid Occlusion

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Target Audience: Physiologists and clinicians interested in the retina and its blood flow autoregulation

Purpose: The retinal and choroidal blood flows (BF) supplying the retina are regulated differently. Postocclusion reactive hyperemia describes the BF overshoot immediately after a transient arterial occlusion. Reactive hyperemia has been attributed to metabolic local control in various tissues [1], where metabolic local control describes the matching of BF to local metabolic demands. This study used BOLD and laser-based BF techniques to investigate postocclusion reactive hyperemia in the retinal and choroidal circulations during and after transient retinal ischemia induced by carotid artery occlusion in rats.

Method: Long-Evans rats were used for MRI (N=14) and combined laser speckle imaging and laser Doppler flowmetry (N=13). The rats were anesthetized with urethane (~1g/kg), mechanically ventilated and paralyzed with pancuronium bromide. Their femoral arterial BP was continuously monitored. The left common carotid artery was exposed. A custom-made reversible occlusive device was wrapped around the artery to reversibly occlude the artery for 1 min from outside the scanner. For each rat, 2~3 trials of transient occlusion were collected. A 15-min break was given between consecutive trials.

MRI was performed on an 11.7 T Bruker Biospec. A surface coil (ID = 1 cm) was used to image the left eye. BOLD fMRI of a single axial slice bisecting the optic nerve head was acquired using 4-segment EPI with TR/TE = 1500/12 ms, resolution = 51×51×800 μm. The retinal BOLD signals were extracted as described elsewhere [2]. The extracted BOLD time courses were detrended and normalized to their baseline period.

The custom-made LSI system was used to measure the retinal BF (RBF) [3]. ROIs were manually drawn to avoid visible retinal vessels in the LSI images. The mean value of the pixels in the ROIs of each image was reported. To simultaneously measure the anterior choroidal BF (ChBF), a LDF probe was place to slightly touch the sclera posterior to the ciliary body from the dorsal side using a micromanipulator [4].

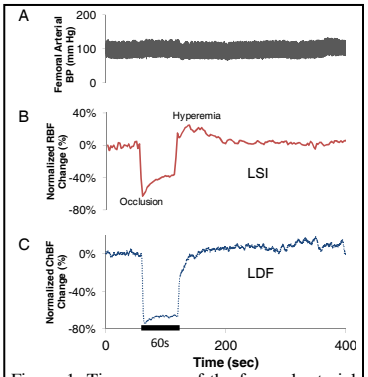

Figure 1. Time course of the femoral arterial BP (A), normalized RBF (B) measured by LSI and normalized ChBF (C) measured by LDF during a typical trial.

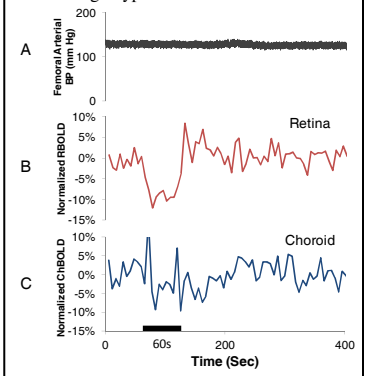

Figure 2. A blood pressure (BP) time course (A), and a normalized RBOLD (B) and ChBOLD (C) time courses during a MRI typical trial.

Results: *Figure 1* shows the time courses of BP, RBF and ChBF from a typical trial. The BP was stable during the entire trial. At the start of the occlusion, RBF and ChBF dropped sharply. RBF gradually returned toward baseline but ChBF did not. Then, after release of the occlusion, RBF overshot but ChBF did not. The BOLD data (*Figure 2*) showed similar trends as BF data albeit at lower SNR.

During occlusion, the mean ChBF reduction was larger than RBF reduction (*Figure 3A*). By contrast, the mean ChBOLD reduction was smaller than RBOLD reduction (*Figure 3B*). During the reactive hyperemia, the accumulated ChBF and ChBOLD (areas under the curve) were not significantly different from 0 but the accumulated RBF and RBOLD increased significantly (*Figure 3C and 3D*), indicating that hyperemia was present in the retinal but not the choroidal circulation.

Discussion & Conclusion: The difference in the RBF and ChBF recovery towards baseline during the occlusion is likely due to differences in BF autoregulatory ranges. However, because it was not possible to measure blood pressure in the ophthalmic artery during the occlusion, the lower limits of retinal and choroidal autoregulation could not be determined.

During the occlusion, the marked differences between retinal and choroidal responses measured by BF and BOLD fMRI can be explained by the differences in BF. ChBF is about 7 times RBF (RBF is similar to brain BF) [2]. As a result, the arterial-venous oxygen tension difference in the choroidal circulation is small (only 3%), whereas that of the retinal circulation is larger (38%) and similar to the brain [5]. The larger oxygen reserve may explain the small ChBOLD reduction in spite of the large BF drop.

Immediately after release of the occlusion, a reactive hyperemia was observed in the retinal circulation, consistent with metabolic local control. Reactive hyperemia was not detected in the choroid circulation, consistent with results in cats and rabbits [1], suggesting that the choroidal circulation is not under metabolic local control. Other studies have found that the choroid does not respond to flicker stimulation or hyperoxia [6], again suggesting that metabolic local control does not play a role in the ChBF regulation.

In summary, we report differential BOLD and BF responses in the retinal and choroidal circulations during and immediately after transient carotid occlusion. Reactive hyperemia was detected in the retina but not in the choroid, suggesting that the retinal circulation is under metabolic local control but the choroid is not. These findings provide novel insights in the hemodynamic regulation of the retinal and the choroidal circulations.

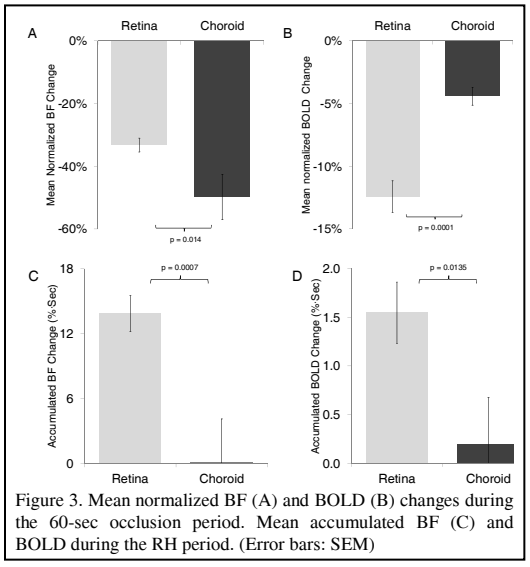

Figure 3. Mean normalized BF (A) and BOLD (B) changes during the 60-sec occlusion period. Mean accumulated BF (C) and BOLD during the RH period. (Error bars: SEM)

[1] Kiel, The Ocular Circulation, 2010; [2] Li et al. Exp. Eye Res. 2012 101:90-96; [3] Cheng H. et al. SPIE 2009.7163:716304; [4] Kawarai et al. Eur. J. Pharm. 1998. 363(1):35-40; [5] Nickla et al. Prog. Retin. Eye Res. 2010 29(2):144-168; [6] Riva et al. IOVS 1994 35:608-618