Effect of Occlusion Durations on Postocclusion Reactive Hyperemia in Rat Retina

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Target Audience: Basic and translational researchers of the retina.

Background: Postocclusion reactive hyperemia, in which blood flow (BF) overshoots baseline after a brief arterial occlusion, has been used to distinguish metabolic local control from other local control mechanisms [1]. Reactive hyperemia after different occlusion durations has been studied in the heart, brain, intestine and stomach [see references below]. In these organs, reactive hyperemia reaches its maximum response after 1.5 to 5 mins of occlusion. In the retina, postocclusion reactive hyperemia and the effect of occlusion duration has not yet been explored. This study used BOLD and laser-speckle BF measurements to investigate retinal reactive hyperemia after graded occlusion durations and gain insight into retinal blood flow regulation.

Method: Long-Evans rats were used for BOLD fMRI (N=14) and laser speckle imaging (LSI, N=13) studies. The rats were anesthetized with urethane (~1 g/kg), mechanically ventilated and paralyzed with pancuronium bromide. Their femoral arterial blood pressure (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 from outside the scanner. For each rat, 2~3 trials were collected for each occlusion duration of 6 (LSI only), 15, 30, 60 and 90 seconds. A 10~15-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.

A 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.

Results: *Figure 1* shows the mean normalized RBF and retinal BOLD (RBOLD) time courses for different occlusion durations. The red rectangle indicates the postocclusion reactive hyperemia periods where the accumulated RBF and RBOLD were calculated. *Figure 1C and 1D* show the mean accumulated RBF and RBOLD changes (areas under the curve) during the reactive hyperemia period for different occlusion durations. The mean accumulated RBF change increased with the occlusion duration and reached maximum with 30-sec occlusion. Further increases in the occlusion duration did not increase the accumulated RBF changes during the hyperemia period. The accumulated BOLD showed the similar trend.

Discussion & Conclusions: The accumulated RBF and BOLD during the reactive hyperemia period increased with occlusion duration, consistent with other reactive hyperemia studies in dog heart [4, 5], dog intestine [6], dog stomach [7], cat skeletal muscle [8], rabbit kidney [9], human skin [10], rat limb [11], and rat brain [12]. This finding suggests that BF autoregulation in the retinal circulation is under metabolic local control.

However, reactive hyperemia in the retina circulation reached its maximum response after only 30–sec occlusion. By contrast, in the aforementioned organs and tissue, reactive hyperemia still had not reached its maximum response until 1.5 to 5 min occlusion. For example, in the intestine and kidney, reactive hyperemia did not reach their maximum responses even after 5-min occlusion. Because our experiment used incomplete ischemia rather than the complete ischemia used in the above-mentioned studies, it strongly suggests that the retinal circulation has a comparatively smaller capacity for postocclusion reactive hyperemia.

In summary, our findings indicate that the retinal circulation is under metabolic control but it has a relatively small capacity for reactive hyperemia compared to many organs reported previously. This study provides further support to the notion that retinal BF is regulated differently compared to other organs. To our knowledge, this is the first study of the effects of occlusion duration on the reactive hyperemia in the retina, providing novel insights into retinal metabolic autoregulation and hemodynamic reserve.

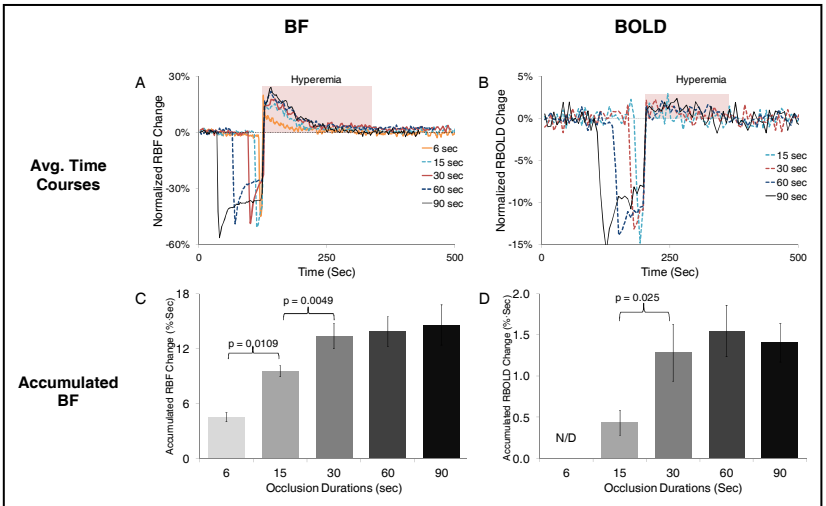

Figure 1. The mean RBF (A) and RBOLD (B) time courses with various carotid occlusion durations were plotted, where the red rectangle areas are the reactive hyperemia period. The accumulated RBF (C) and RBOLD (D) during the reactive hyperemia period were plotted.

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