Assessment of Retinal and Choroidal Vascular Reactivity in Humans with Arterial Spin Labeling Perfusion Imaging

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Introduction: There is a growing interest in the area of retinal and choroidal blood flow and vascular reactivity since it can be quantified non-invasively and therefore can be readily used to provide in-sight of the physiology of the retinal vasculature. The three major causes of irreversible vision loss, age-related macular degeneration, diabetic retinopathy and glaucoma, are characterized by a vascular dysfunction element in their patho-physiology [1,2]. The feasibility of measurement of the total blood flow to the retina with an optimized arterial spin labeling MRI method has been described previously [3]. In the current study, we hypothesized that the ASL perfusion imaging can be used to measure the changes in flow to the combined retinal and choroidal system induced by hypercarbic and hyperoxic stimuli in the human. Changes in rat retinal flow in response to hypercarbic/hyperoxic stimuli have been reported [4].

Methods: 9 clinically normal subjects (age:34±7yrs) were recruited (4 males, 5 females). The study consisted of one visit. The subjects breathed via a sequential gas delivery breathing circuit. End-tidal PCO_2 ($P_{ET}CO_2$) and PO_2 ($P_{ET}O_2$) were controlled using an automatic gas sequencer (Respiract™, TRI, Toronto, Canada) [5]. $P_{ET}CO_2$ was increased to target 45mmHg from the baseline at ($P_{ET}CO_2$=40mmHg and $P_{ET}O_2$=100mmHg). $P_{ET}O_2$ was then increased to target 300 mmHg, and 500 mmHg while keeping $P_{ET}CO_2$ constant at a 45mmHg. Before the MRI, a similar rebreathing protocol was also performed while the subjects were supine and an assessment of the intra-ocular pressure (IOP) in either the left or right eye was made. Blood pressure, pulse rate and respiration rate were monitored throughout both studies. Studies were performed on an HD 3.0 Tesla MR system (GE Healthcare Technologies) with an 8-channel array head coil. A background suppressed PCASL (BS-PCASL) sequence [6] was used for blood flow imaging (figure 1). An approximately axial image slice passing through the optic nerve heads was prescribed graphically based on the localizer image. Images were acquired using a 2D half Fourier single shot fast spin echo SSFSE sequence. Imaging parameters were FOV=24cm, Matrix=96×96, Band width=20.83, TR/TE=8000/36.5ms, post labeling delay=1.25s, slice thickness=10mm, axial labeling slab 5cm below the slice, and number of label and control pairs 20. Tissue T_1 and M_0 reference images were also obtained during imaging. All image data were reconstructed offline. A rectangular region of interest 1-1.25 cm in length along the retina centered on the fovea was defined. Retinal blood flow was quantified using a modified single compartment model [7]. The change in blood T_1 with increased levels of hyperoxia could confound the vascular reactivity measurements with MRI. Reduction of blood T_1 as a result of increased PO_2 was modeled according to in-vitro results reported in [8].

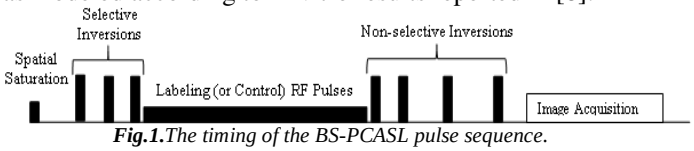

Fig.1.*The timing of the BS-PCASL pulse sequence.*

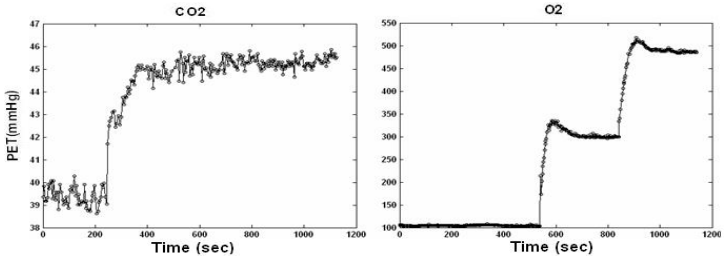

Figure.2.*Time course of $P_{ET}CO_2$ (left) and $P_{ET}O_2$ (right) for a single subject.*

Results: All the targeted end tidal values were achieved with minimal group variability (p<0.0001), (one subject, figure 2). The measured total blood flow increased significantly from 1.55±0.17μL/mm2/min at the baseline to 1.96±0.18μL/mm2/min during hypercarbia. With increasing $P_{ET}O_2$, retinal blood flow didn't change significantly relative to the hypercarbia condition but remained significantly elevated relative to the baseline (fig 3 & 4). There were no significant changes in systolic, diastolic or mean blood pressure, heart rate or IOP (as a result ocular perfusion pressure) during all 4 breathing conditions.

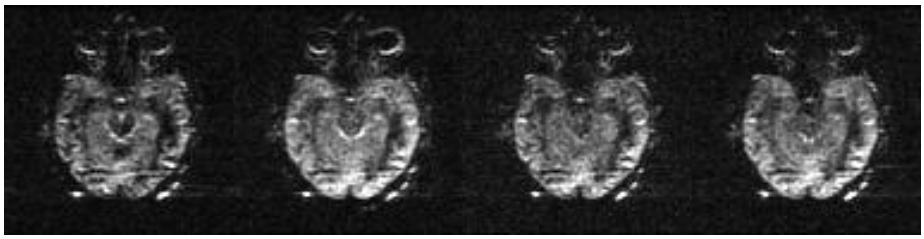

Figure.3. *From left to right, ASL perfusion weighted images at baseline, hypercarbia/ normoxia, hypercarbia/ hyperoxia 300 and hypercarbia/hyperoxia 500 for one subject.*

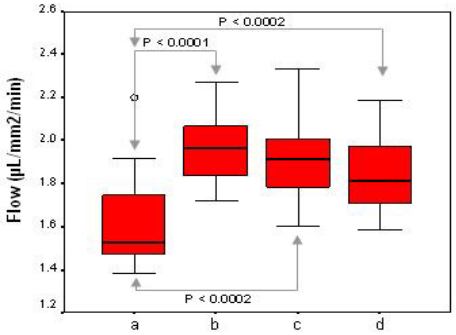

Figure.4.*The group mean blood flow values in response to normocarbia/normoxia (a), hypercarbia/normoxia (b) hypercarbia/hyperoxia 300 (c) and hypercarbia/hyperoxia 500 (d)*

Conclusion: Since hyperoxia reduces retinal blood flow but not choroidal flow, provoking vascular reactivity in response to hypercarbic and hyperoxic stimuli and comparing the responses to the results from optical measurements [9] suggests that the detected ASL signal is predominantly weighted by choroidal blood flow changes. Our results indicate that a CO_2 provocation challenge in combination with the ASL-MR perfusion imaging may be a promising approach to investigate choroidal vascular reactivity under normal and disease states.

References: [1] Schmetterer et al., Diabetologia 1999[2] Ciulla TA, Acta Ophthalmol Scand. 2001 [3] Maleki et al, ISMRM 2008 [4] Li et al, IOVS 2008 [5] Slessarev et al., J Physiol. 2007 [6] Dai et al, MRM 2008 [7] Buxton et al, MRM 1998[8] d'Othée et al., Acad Radiol 2003 [9] kisilevsky et al. 2008 Microvasc Res