Comparison of Cerebral Blood Flow using Arterial Spin Labeling and Phase Contrast Angiography under hyperoxia and hypercarbia.

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Introduction: Cerebral blood flow (CBF) is highly sensitive to changes in inhaled gas concentrations, in particular CO_2 and O_2. The use of hyperoxia as a treatment for stoke patients is currently under investigation[1]. CBF decreases of 10-15% in healthy subjects breathing 100% oxygen have been previously demonstrated using phase contrast angiographic (PCA) MRI [2] and along with CBF increases of 20-30% when breathing 5% carbon dioxide[3]. Previous groups using ASL have shown perfusion changes with CO_2 but have been unable to replicate the perfusion changes with oxygen[4]. This study directly compares CBF results using both ASL and PCA under both hyperoxic and hypercarbic conditions.

Methods: Four healthy subjects 2 male and 2 female (aged 24-29) underwent MRI imaging performed at Salford Royal Hospital (Salford, UK) using a 3.0T Philips Achieva system, a SENSE Head Coil (Philips Medical Systems BV, the Netherlands).
Gas delivery: Gases were delivered by a Mapleson A closed anesthetic gas circuit via a mouthpiece. The subjects were given each of the following gasses each for approximately 15 minutes in a random order with a 2 min gap between gas change over to imaging: 100% O_2, medical air and carbogen gas (95% O_2 5% CO_2) each delivered at a flow rate of 15 l/min.
Imaging protocol: consisted ASL sequence followed by a PCA acquisition under each gas. ASL imaging used STAR labeling and EPI collection (20 slices; 1mm slice gap; TR: 3000ms; TE: 21ms; FOV: 224 x 224 mm; Voxel size: 3.5mm x 3.5mm; Slice thickness: 5mm; Matrix size: 64 x 64, Label thickness: 150mm; 10mm label gap; 20 dynamic scans) collected at 4 inversion times: 800ms, 1200ms, 1600ms and 2000ms. PCA acquisition was collected using sagittal 2D cine phase-contrast images. ECG cardiac gating was used to cover the entire cardiac cycle. 16 phase images were calculated over the cardiac cycle from 256 acquisitions. The imaging parameters were as follows: TE 4.43 msec; TR dependant on heart rate ranging between 7.4 – 14.1 msec; flip angle 10°; number of averages 3; matrix 256 x 256; pixel size 1.17 x 1.17 mm; slice thickness 6 mm; and velocity encoding 200 cm/s.) For each subject a 2D PCA slice was collected at a level of skull base containing both internal carotid arteries and basilar artery.
Image analysis: PCA results were analysed using Q flow software (Philips, the Netherlands) CBF was calculated from the sum of the average flow over the cardiac cycle in each vessel producing a flow result in ml/s. ASL images were analysed using in-house code written in MATLAB (Mathworks, USA), assuming a single blood compartment model [5]. M_0 and T1 maps were calculated by fitting the control data at the four inversion times to a recovery curve. Masks of grey matter and white matter were created based on T1, and a global value for M_0 was calculated. Control and labeled images were subtracted and first a three-parameter fit for bolus width (tau), arrival time (tA) and CBF was performed on whole brain data. Then tau was fixed and a 2 parameter fit for tA and CBF was performed on a voxel by voxel basis, producing CBF and tA maps. Perfusion was calculated independently for grey and white matter with units ml/100ml/min. To allow for the effect of 100% O2 on the T1 of blood a published value of 1932ms was used for perfusion calculations using both O2 and carbogen, and a value of 1660 ms when using air [6]. Results were compared using paired t test with significance set at p< 0.05 trend p<0.1.

Results: In each subject CBF values were higher during carbogen inhalation compared to medical air with both PCA and ASL measurements (fig 1B-C). Although O2 CBF was not significantly different from medical air using both PCA and ASL (fig 1D), during 100% O2 inhalation the difference between label and control signal (ΔM) for each inversion time was significantly decreased during oxygen inhalation compared to medical air and increased during CO_2 inhalation (fig 1A). There was also a trend to increased bolus arrival time during O_2 compared to medical air (see table).

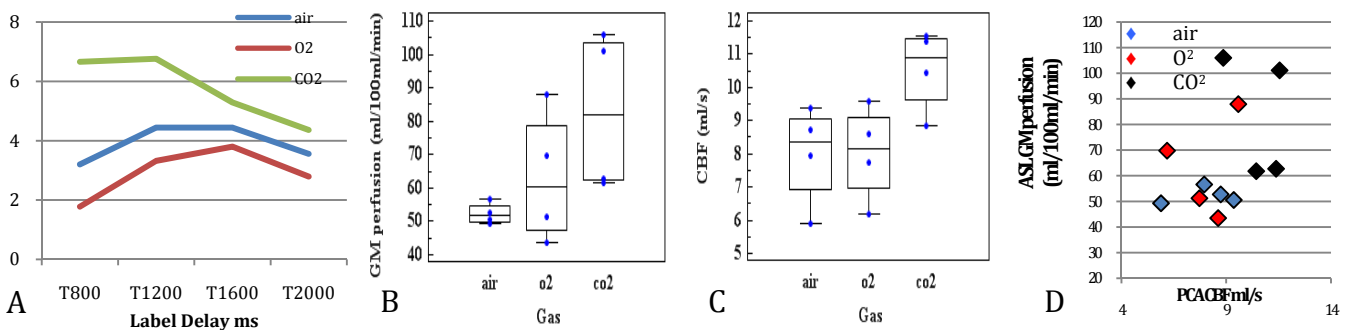|	Units	Medical air	SD	O_2	SD	Difference from air (p)	CO_2	SD	Difference from air (p)
PCA	CBF (ml/s)	8.0	1.5	8.0	1.4	0.95	10.6	1.2	0.02
ASL	GM CBF (ml/100ml/min)	52.3	3.2	63.1	20.0	0.32	82.9	25.0	0.08
tA	(ms)	661	124.	750	114	0.09	552	36.4	0.27
ΔM		4.2	0.9	3.4	0.8	>0.01	4.8	1.2	0.05

Figure 1 A: Example of ΔM values during different gases from a single subject. B: ASL grey matter perfusion results under each gas. C: PCA CBF results for each gas. D: Comparison of ASL grey matter perfusion to PCA CBF results.

Discussion: The ability to quantify CBF changes during hyperoxia has importance for investigating the use of hyperoxic treatments for example in stroke patients, and also for the use of hyperoxia in calibrated fMRI [7]. This study has shown STAR ASL is able to detect changes in CBF during CO_2 compared to medical air with equal precision to PCA CBF measurements. ASL imaging also demonstrated reductions in ΔM and an increase in arrival time during hyperoxia, although no change in CBF, in agreement with PCA measurements.

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