Using dual calibrated FMRI to detect CBF related changes in OEF during hyperventilation

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Target Audience: Researchers and clinicians interested in a quantitative measure of absolute cerebral oxygen metabolism.

Purpose: Dual calibrated FMRI (dcFMRI)[1-3] is an extension of the calibrated BOLD methodology[4,5], capable of producing regional measurements of oxygen extraction fraction (OEF) across the brain. This is performed by measuring venous oxygen saturation (S_vO_2) and assuming arterial blood is fully oxygenated (OEF = 1- S_vO_2). Regional measurements of OEF are desirable in both a clinical and research setting to assess compensatory responses due to alterations in cerebral blood flow (CBF). In order to maintain acceptable oxygen levels within brain tissue, reductions in CBF can lead to increases in OEF. Severe reductions in CBF can occur in cases of vascular dysfunction and stroke[6] where mismatches in OEF may mean sufficient levels of oxygen are not maintained leading to cell death. Here a hypocapnic challenge was used to demonstrate the sensitivity of the dcFMRI technique to detect increases in OEF associated with reductions in CBF. Hypocapnia causes vasoconstriction that is known to globally lower CBF[7] and is therefore expected to cause increases in OEF in the healthy brain[8]. Hypocapnia occurs when arterial partial pressure of CO_2 (P_aCO_2) in blood is lower than normal and can be induced by hyperventilation.

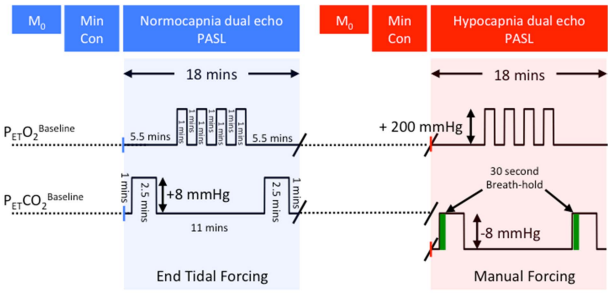

Figure 1: Schematic detailing the normocapnic and hypocapnic respiratory manipulations used to alter CBF and S_vO_2.

Methods: 6 normal healthy participants (aged 24-40; mean age 33.5±5.7; 1 female) were scanned using a 3T GE HDx MRI system (GE Healthcare, Milwaukee WI). Scan sessions lasted ~1 hour and consisted of two interleaved hypercapnic-hyperoxic dcFMRI protocols (18 mins each). The first dcFMRI protocol was performed at a normocapnic baseline allowing measurements of S_vO_2 at baseline CBF. The second dcFMRI protocol was performed using a hypocapnic baseline, providing a new low flow baseline from which changes in S_vO_2 could be detected **Fig1**. During the baseline condition scan the participant was told to rest with eyes open. In order to achieve a hypocapnic baseline of $P_{ET}CO_2^{base}$- 8 mmHg, an end-tidal CO_2 (ET CO_2) feedback task was used. The participant's $P_{ET}CO_2$ was displayed on a screen along with a target $P_{Et}CO_2$ shown alongside. To decrease the measured $P_{ET}CO_2$, participants voluntarily hyperventilated and used breath-holds to aid recovery back to normocapnic baseline. Blocks of hyperoxia were manually delivered during periods of hypocapnia, **Fig1**(Red). During these respiratory manipulations CBF and BOLD time-series were acquired using a dual-echo PASL acquisition and estimates of S_vO_2 were made by fitting mean grey matter (GM) ROI time-series and voxel-wise time-series data with a BOLD signal model (for further detail on dcFMRI acquisition and quantification see **Ref**[3]).

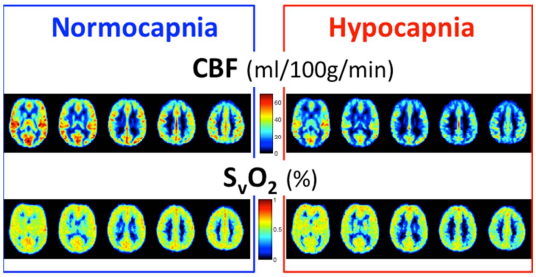

Figure 2: Group averaged (N=6), whole brain CBF and S_vO_2 maps acquired at normocapnia (left) and hypocapnia (right) using dcFMRI

	CBF (ml/100g/min)	S_vO_2 (%)
Normocapnia	46.3 ± 6.7	0.57 ± 0.15
Hypocapnia	35.5 ± 5.2	0.44 ± 0.03

Table 1: Group averaged (N=6) comparison of CBF and S_vO_2 measured during normocapnia and hypocapnia in global GM ROI's.

Results & Discussion: All participants successfully used mild voluntary hyperventilation to reach and maintain hypocapnic baseline. The mean group $P_{ET}CO_2$ for normocapnic baseline was 43.7±1.9 mmHg and hypocapnic baseline was 35.1±2.6 mmHg. ROI analysis of GM yielded estimates of CBF and S_vO_2, **Table1**. Significant decreases ($p<0.05$) between normo and hypocapnia were found for both parameters and the magnitude of decrease agreed well with literature[9,10]. In **Fig2**, whole brain reductions in both parameters due to hypocapnia can be seen. However as dcFMRI uses ASL to measure CBF the measures are currently limited to GM.

Conclusion: The data shows a clear trend in CBF and S_vO_2 and demonstrates the sensitivity of the dual calibrated FMRI protocol to detect changes in OEF. This suggests that the technique is appropriate for research and clinical application to vascular dysfunction in which flow and metabolism may be impaired.

References: 1. Bulte et al. NeuroImage. 2012,60: 582; **2. Gauthier et al.** NeuroImage. 2012,60:1212; **3. Wise et al.** Neuroimage. 2013,83:135; **4. Davis et al.** PNAS. 1998,95:1834; **5. Chiarelli et al.** NeuroImage. 2007,37:808; **6. Yamachui et al.** JNNP. 1996,61:18; **7. Kety&Schmidt.** JCI. 1946,25:107; **8. Gjedde et al.** JCBFM. 2005,25:1183; **9. Ito et al.** JCBFM. 2003,23:665; **10. Chen&Pike.** JCBFM. 2010,30:1094.