Efficient measurement of resting and elevated absolute $CMRO_2$ and their within session repeatability in the human brain using calibrated FMRI

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Target audience: Researchers and clinicians interested in a quantitative FMRI measure of cerebral oxygen metabolism.

Purpose: We aim to (i) quantify stimulus-induced changes in regional absolute $CMRO_2$ (ii) determine the viability of a shortened acquisition time for absolute $CMRO_2$ quantification and (iii) assess the within-session repeatability of absolute $CMRO_2$ measurement. Calibrated FMRI techniques providing absolute $CMRO_2$ quantification have recently been reported[1,2]. Using a BOLD signal model[1-3], simultaneous CBF and BOLD measures performed during hypercapnia and hyperoxia enable estimation of cerebral venous oxygen saturation (S_vO_2) and in turn absolute $CMRO_2$. To become clinically useful, the technique must be quick, sensitive enough to detect disease or treatment induced changes in absolute $CMRO_2$ and repeatable. Here we use a calibrated FMRI approach, exploiting rapid transitions to hypercapnia and hyperoxia facilitated by end-tidal forcing[4], to measure regional absolute $CMRO_2$. This was performed at rest and during a continuous visual and motor task for the duration of the entire scan to simulate a disease/treatment-like condition in which $CMRO_2$ is elevated. The data from each scan were split in half to determine the viability of a rapid (half-duration) acquisition.

Methods: 7 healthy volunteers (age 34.7±3.8; 1 female) were scanned at 3T (GE HDx). A functional localizer (5.5min) was performed allowing regions of significantly active voxels in the visual and motor cortices (fVC and fMC, respectively) to be defined. Two absolute $CMRO_2$ acquisitions (each 18min) were performed in randomised order (i) at rest with the participant fixating on a cross hair and (ii) during a combined visual (flashing checkerboard) and motor (finger tapping) task that continued without rest for the whole 18mins of the scan. Simultaneous BOLD and CBF data were acquired with a dual gradient-echo, spiral readout, PICORE QUIPSSII acquisition; TR/TE1/TE2=2.2s/3ms/29ms TI1/TI2 = 700/1600ms, 20cm tag thickness. End-tidal forcing[4] was used for independent control of end-tidal O_2 and CO_2 ($P_{ET}CO_2$ and $P_{ET}CO_2$) (Fig. 1). From the dual-echo data and a BOLD model[5] estimates of S_vO_2 and $CMRO_2$ were produced using a Bayesian parameter estimation routine. To determine within session repeatability the data were analysed for the entire 18min acquisition and then, after splitting and each 9min half was analysed separately (Fig1). Intra-class correlation (ICC) indicated the repeatability of $CMRO_2$ estimates between halves I and II. The ability to detect stimulus-induced changes in $CMRO_2$ was examined for the VC and MC functional regions of interest.

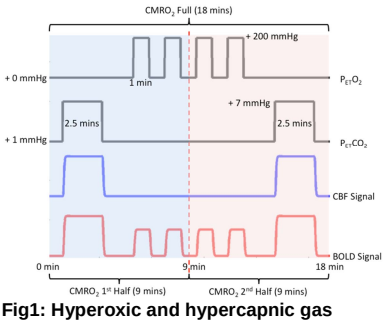

Fig1: Hyperoxic and hypercapnic gas challenges with schematic CBF and BOLD time-series showing the full experiment with splitting into half I and half II.

Results:

Table 1: Summary CBF, S_vO_2 and $CMRO_2$ for both halves of the data and the full analysis.
Grey matter (GM), functional visual and motor cortex (fVC and fMC). Mean±SD given.
* indicates p<0.05 for one-tailed test for task > rest $CMRO_2$

		CBF (mL/100g/min)		S_vO_2		$CMRO_2$ (µmol/100g/min)	
		rest	*task*	*rest*	*task*	*rest*	*Task*
GM	half I	50±5	53±5	0.58±0.03	0.61±0.02	165±27	160±15
	half II	50±4	53±5	0.57±0.05	0.61±0.03	168±28	160±20
	entire	50±5	53±5	0.58±0.06	0.64±0.05	167±38	151±23
fVC	half I	61±12	84±20	0.60±0.02	0.61±0.04	197±42	254±64*
	half II	61±12	84±20	0.58±0.02	0.61±0.04	199±40	258±65*
	entire	61±11	84±20	0.59±0.03	0.64±0.06	199±46	238±63*
fMC	half I	45±19	61±10	0.63±0.07	0.64±0.06	123±29	172±37*
	half II	44±18	61±10	0.60±0.04	0.64±0.09	135±43	172±41
	entire	44±19	61±10	0.63±0.08	0.68±0.10	122±30	153±42*

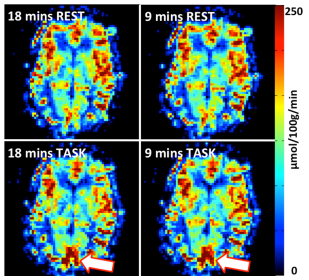

Fig2: $CMRO_2$ maps for single subject showing increased metabolism in VC for task

Table 2: Intra-class correlation (fMC value driven by one subject)

	GM	fVC	fMC
Rest	0.93	0.97	0.69
Task	0.94	0.88	0.24

Discussion: Tasks increased absolute $CMRO_2$ by 20%($p<0.05$) in VC and 25%($p<0.05$) in MC using the full 18min of data. Fig2 shows the regional increase in VC for a single subject after 9 and 18mins (indicated by white arrows) with no appreciable difference in image quality between the two. Significant differences are maintained between rest and task conditions for the split half data in all but one case (fMC half II, poor fitting in one subject). CBF and S_vO_2 values agree well with those established in PET literature[6] and intra-class correlation showed high repeatability (Table2) of absolute $CMRO_2$ estimates between the two halves of the experiment.

Conclusion: The absolute $CMRO_2$ measurement is sensitive to sustained task-induced increases in oxygen consumption, indicating promise for clinical or pharmacological applications in which $CMRO_2$ is altered. Furthermore resting and task-elevated absolute $CMRO_2$ measurement is repeatable within session and the measurement can be gained in 9mins without compromising the sensitivity of the technique to detect changes in oxygen metabolism.

References: 1. Bulte et al . NeuroImage. 2012; 60: 582; 2. Gauthier et al. NeuroImage. 2012; 60:1212; 3. Davis et al. PNAS. 1998, 95:1834;
4. Wise et al. JCBFM. 2007, 27:1521-1532; 5. Wise et al. Proc ISMRM 2012, 2908; 6. Leenders et al. Brain. 1990, 113:27-47