Fast, Calibrated, Quantitative Functional MRI for Single Repeats Using Hyperoxia

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Introduction

Measurement of the cerebral metabolic rate of oxygen during functional tasks is a key step towards the clinical implementation of functional MRI. The use of increased fractions of inspired oxygen as a calibration step enables the modelling of relative changes in $CMRO_2$, as well as estimating the baseline cerebral blood volume. In this pilot study two subjects were imaged using a 5-slice, interleaved, gradient-echo EPI/Q2TIPS sequence while they performed a simple 2-level graded motor task followed by two short hyperoxic epochs delivered via a 2-tube nasal cannula. These data were then used to estimate the theoretical maximal BOLD signal (M) and thereby calculate the relative regional increase in $CMRO_2$ for each task. The hyperoxia BOLD data were then also used to produce baseline CBV maps. From the baseline CBV values and measured relative CBF changes, estimates of quantitative blood volume changes in the motor regions with activation were then calculated.

Theory & Methods

Analogous to the derivation of the hypercapnia-calibrated model[1], hyperoxia calibration makes use of the expression for BOLD signal change, as well as the expression for $R_2^*|_{dHb}$ derived by Boxerman *et al*[2]. The hyperoxia calibration model described by Chiarelli *et al*[3] is given by:

$$\frac{\Delta BOLD}{BOLD_0} = M\left(1-\left(\frac{CBF}{CBF_0}\right)^{\alpha}\left(\frac{[dHb]_v}{[dHb]_{v_0}}+\frac{CBF_0}{CBF}-1\right)^{\beta}\right) \qquad (1)$$

where $M = TE \cdot A \cdot CBV_0 \cdot [dHb]_{v_0}^{\beta}$. Additionally, CBV was calculated from the BOLD data during the hyperoxia epochs using the hyperoxia contrast method described by Bulte *et al*[4]. Images were acquired on a Siemens Trio 3T MRI scanner using a 12-channel head-coil. An interlaced BOLD/pulsed arterial spin-labelling (ASL) sequence was used to collect T_2^*-weighted EPI images and Q2TIPS[5] cerebral perfusion images. Changes in the blood relaxation times caused by the heightened oxygen were also taken into account[6]. The subjects were healthy normal volunteers who gave informed consent, in accordance with the ethics approval for the study. The total scan duration was 26 minutes, consisting of 6 minutes of *45 sec off/45 sec on* alternating bilateral finger tapping with blocks 1 and 3 at a rate of one tap cycle per 6 seconds and blocks 2 and 4 at a rate of one cycle per 3 seconds. This was followed by two 5-minute blocks of hyperoxia separated by 4 minutes of normal air breathing. Oxygen was administered via a 2-tube nasal cannula to ensure minimal invasiveness and discomfort for the subject. Subjects were instructed to breathe both in and out through the nose to enable sampling of end-tidal gases. Oxygen was delivered at a rate of 7 litres per minute, inducing an end tidal level of ~35%, equivalent to an inspired fraction of ~50%. Analysis was performed using the FMRIB Software Library (FSL) package[7].

Results & Discussion

Figs 1A and 1B shows the BOLD and perfusion changes induced in one subject for the low level motor stimulus (task 1), overlaid onto a high-resolution structural image. Next to this is the baseline cerebral blood volume map calculated from the BOLD data during the hyperoxia blocks showing absolute, quantitative values in ml of blood per 100g of tissue. The median BOLD signals and ASL changes from the motor activations at the two task levels are shown in Table 1. M in the motor areas was calculated to be 4.05% and 4.29% for subjects 1 and 2 respectively. The CBV values given here were calculated using the Grubb equation[8] ($CBV/CBV_0=(CBF/CBF_0)^{\alpha}$, with α=0.38) and the relative changes in $CMRO_2$ were calculated using equation (1).

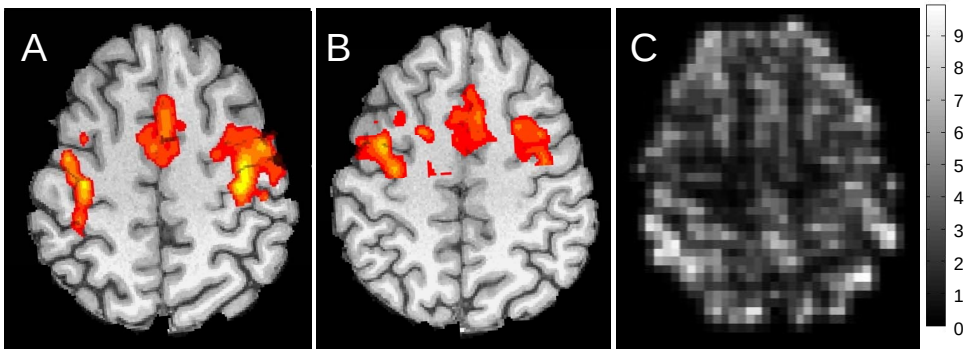

Fig. 1: Subject 1, (A) BOLD activation from low level motor task, (B) ASL activation from low level motor task, (C) baseline CBV map determined from hyperoxic BOLD contrast, scale is ml/100g.

Subject 1	BOLD	ΔCBF	CBV	$\Delta CMRO_2$	Subject 2	BOLD	ΔCBF	CBV	$\Delta CMRO_2$
Baseline	-	-	2.82	-	Baseline	-	-	4.92	-
Task 1	1.65%	+12.6%	2.95	+8.7%	Task 1	1.53%	+26.9%	5.39	+18.1%
Task 2	1.92%	+28.3%	3.10	+18.7%	Task 2	1.72%	+37.6%	5.55	+25.2%

Table 1: Results from the 2 levels of motor task in each subject, showing BOLD signal, percent change in ASL signal, absolute CBV in ml/100g under each condition and relative change in $CMRO_2$ in the left and right motor cortices and the SMA.

The range of values calculated for both the CBV and $\Delta CMRO_2$ for each subject are within credible limits, although quite different from each other. This is most likely reflecting the different demands placed on different subjects while performing the same task and is to be expected in single-repeat trials. The quality of the data can be clearly seen from the images which show very strong and clean activation in both the left and right motor cortices and the supplementary motor area (SMA), and a CBV map which shows significantly higher blood volume in the grey matter in comparison to the white matter at values within the expected range for such tissues.

Conclusions

The technique outlined here provides a clinically viable, calibrated method of obtaining the majority of significant metabolic information regarding a functional task in a relatively short amount of time, while being easy to administer, non-invasive and requiring a minimum of specialist hardware. Full validation of the technique would require comparison with PET imaging obtained from the same subject performing the same task on the same day. Such a method could potentially provide a significant amount of valuable information regarding the cerebral metabolism of a single subject and thus may be applicable for clinical use with patients.

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