# Neurovascular Coupling in the Human Visual and Motor Cortices

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## Introduction

Recent advances in the investigation of neurovascular coupling have embraced graded functional activation as a means to disentangle the biophysical and physiological factors complicating the interpretation of fMRI data [1,2]. Investigation based on the hypercapnia-normalized method for estimating aerobic metabolism ($CMR_{O2}$) [1,2] has yielded evidence of a linear relationship between baseline-normalized changes in $CMR_{O2}$ and CBF, and has supported the notion that the CBF:$CMR_{O2}$ coupling ratio is not 1:1, but instead is substantially greater, with fMRI-based estimates ranging between 2:1 and 5:1 [3,4]. In this study, we simultaneously acquire graded-stimulation BOLD and CBF data from three distinct brain regions—the visual cortex, the primary motor cortex, and the supplementary motor area (SMA). We use an intra-session $CO_2$ challenge to calibrate the BOLD signal in each area, and we observe unique coupling estimates within the three regions. This work represents the first simultaneous study of neurovascular coupling in multiple regions of the brain. The understanding achieved in this work may have significant impact, both for the clinical understanding of metabolic disorders, and for appropriate physiological interpretation of blood oxygenation level dependent (BOLD) fMRI studies.

## Experimental

Interlaced BOLD and pulsed arterial spin-labelling images were acquired on a Siemens 3 Tesla Trio MRI scanner, used with an 8-channel head radio-frequency receiver coil. BOLD measurements had TR/TE=4.5s/32ms, and perfusion experiments (Q2TIPS) had TR/TE=4.5s/23ms and TI=1.4s. 10 subjects were studied (8 male, 2 female) with a randomized 45 s on/off block-design paradigm containing blocks of visual or motor stimulation, with three graded levels of each stimulus type. The visual stimulus was an oscillating non-isoluminant square checkerboard stimulus of variable white/black contrast intensity at 8 Hz. The motor stimulus was variable-rate bilateral finger apposition, timed to a flashing cue. Each level of stimulation intensity was repeated four times. After completion of all metabolic-activation tasks, 4 % $CO_2$ was delivered in two 5-minute blocks, to effectively calibrate the BOLD and CBF measurements for calculation of $CMR_{O2}$. Five oblique slices were planned through the primary visual, primary motor, and supplementary motor areas, using a functional localizer experiment to identify the regions (Figure 1). BOLD and perfusion data were analyzed using the FSL package [5], incorporating motion correction (MCFLIRT), brain extraction (BET), and a GLM-based estimation of activation intensity. Temporal sinc-interpolation was applied to perfusion images prior to pairwise subtraction of control and tag. Averaged BOLD and perfusion estimates were interrogated within a single region of interest (ROI), defined by the overlap of thresholded BOLD and perfusion activation images, further constrained by an anatomical image.

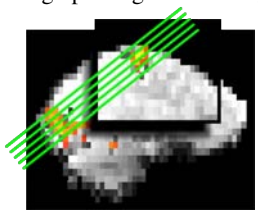

**Figure 1.** Oblique slices prescribed through motor and visual regions based on functional localizer

## Results

Visual and motor stimuli were delivered within a single scanning session, along with a 4% $CO_2$ challenge. The hypercapnia calibration constant ($M$) [1] was calculated for the primary motor, primary visual, and supplementary motor areas to be 4.5, 8, and 7.5, respectively. Figure 2 displays relative $CMR_{O2}$ calculated within each of the three areas, plotted against relative change in CBF. We find the CBF:$CMR_{O2}$ coupling ratio to be ~4:1 in the motor cortex, ~3:1 in the visual cortex, and ~2.5:1 in the SMA.

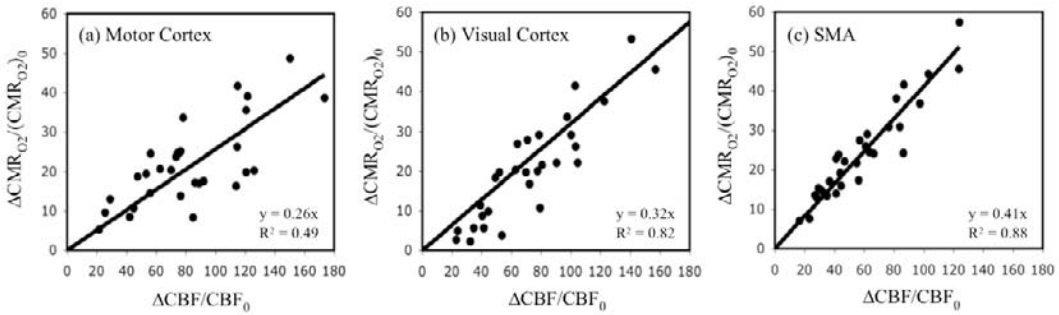


**Figure 2.** Relative changes in $CMR_{O2}$ and CBF during stimulation of the (a) primary motor area, (b) primary visual area, and (c) SMA. The $CMR_{O2}$–CBF coupling slope and the linear correlation coefficient, as determined from a linear fit to the data from each region, are supplied.

## Discussion and Conclusions

We present the first simultaneous investigation of neurovascular coupling in the visual and motor cortices using the hypercapnia-normalized method of $CMR_{O2}$ estimation. Observed CBF:$CMR_{O2}$ coupling estimates (~4:1, ~3:1, ~2.5:1) correspond well to the established range of values in the literature, and show a significant difference between the three cortical regions. The value we determined in the motor cortex fits more closely with values obtained from PET measurements than any published graded fMRI values to date.

$CMR_{O2}$–CBF coupling in the SMA is substantially tighter than coupling in the primary motor cortex, a trend that persists using a range of thresholding methods to obtain the ROI. Part of the difference in the linearity of coupling may be attributed to the difference in estimated calibration ($M$) values between the regions, although the raw BOLD–CBF data also reflects a tighter coupling pattern in the SMA. Furthermore, data within the SMA appear more tightly coupled than data in the visual cortex, where a comparable $M$ value is used. Since larger $M$ values independently generate greater linearity in the $CMR_{O2}$ vs. CBF plot, our *low* values of $M$ calculated in this study (especially in the motor cortex) give us enhanced confidence in the quality of our experimental data. The low $M$ value may stem from the use of a 4% $CO_2$ calibration challenge, which induces less stress in a majority of subjects than the typical 5% $CO_2$ challenge. Ultimately, our results suggest that there exist large-scale regional differences in the human metabolic machinery.

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