Estimation of Relative Oxidative Metabolic Changes during Motor Activity using Graded Hypercapnic Calibration at 4 Tesla

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Introduction

Large relative changes in cerebral blood flow (ΔrCBF=ΔCBF/CBF), cerebral blood volume (ΔrCBV=ΔCBV/CBV), and the rate of cerebral glucose metabolism are well-correlated with changes in neural activity. Relative changes in the rate of oxygen metabolism ($\Delta rCMRO_2 = \Delta CMRO_2/CMRO_2$) also appear to accompany changes in neural activity, although quantitative estimates of these changes have varied widely from negligible to substantial increases during various types of physiological stimulation. A complex relationship appears to exist between the hemodynamic variables, ΔrCBF and ΔrCBV, and their metabolic counterpart, $\Delta rCMRO_2$, the result of which is the relative change in venous blood oxygenation (ΔrY=ΔY/(1-Y)) that causes the increase in the blood oxygenation level dependent (BOLD) signal in T2- and T2*-weighted fMRI.

In low concentrations, carbon dioxide (CO_2) is a harmless but effective vasodilator, yet presumably causes no increase in $rCMRO_2$. As such, it allows ΔrCBF to be calibrated with relative changes in the BOLD signal (ΔrBOLD=ΔBOLD/BOLD). In this study, we calibrated ΔrBOLD with ΔrCBF during graded hypercapnia in human subjects and, using a theoretical model (1,2) relating these hemodynamic and metabolic variables, estimated the $\Delta rCMRO_2$ during a sequential finger movement exercise.

Theory

The theoretical model used in this study has been described in detail elsewhere (2) and is described briefly here. A mathematical relationship between ΔrCBV and ΔrCBF has been established in monkeys during hypercapnia (3). However, this relationship relates ΔrCBF to changes in *total* CBV rather than *venous* CBV, the latter of which contributes to ΔrBOLD. In our model, we used the equation $\Delta rCBV_{bold} = (0.15)\Delta rCBF$ (4) to estimate venous or BOLD-related ΔrCBV from ΔrCBF. Changes in ΔR_2^* can be expressed, to a first-order approximation, as $\Delta R_2^* = -(\Delta rBOLD)(1/TE) = -\alpha^*\{\Delta rY - \beta'\Delta rCBV_{bold}\}$, where α* and β' are constants. Finally, changes in $rCMRO_2$ can be calculated by Fick's principle, rewritten as $\Delta rCMRO_2 = (\Delta rCBF + 1)(1 - \Delta rY) - 1$. $\Delta rCMRO_2$ is set to zero in this formula when calculating changes occurring during hypercapnia.

Methods

Four normal subjects (two men and two women) were studied in a Siemens 4 Tesla magnet with a homogeneous head coil. A single axial slice which contained the hand area of the primary motor cortex was selected for the experiment based on anatomical landmarks.

Functional magnetic resonance EPI images weighted for BOLD contrast (TE = 0.03 s, TR = 1.5 s, flip angle = 90°) and for perfusion using the FAIR technique (TI = 1.4 s, TE = 0.016 s, TR = 1.5 s, flip angle = 90°, slice-selective inversion slab thickness = 1.5 cm) were acquired in an interleaved manner during the hypercapnia and motor experiments. The image FOV of 21 x 21 cm^2 with 0.5-cm slice thickness was acquired in a 64 x 64 matrix.

In the hypercapnia experiments, following a 1.5-minute control period during which subjects breathed normal air, hypercapnia was induced by breathing gas mixtures of 3, 4, 5, and 6% carbon dioxide for two 3-minute epochs followed by 3-minute control periods. The motor activation paradigm consisted of sequential finger movement of the dominant hand, paced at one movement every 0.5 s by red LEDs flashing at 2 Hz.

Functional images were zero-filled to a 128 x 128 matrix size, smoothed with a gaussian filter, and corrected pixel-by-pixel for linear drift. A gray matter mask was created for each subject's data by appropriately thresholding the subject's T1-weighted EPI anatomical image. This served as the region of interest (ROI) for analysis of the hypercapnia images. A map of active pixels ($p < 0.01$) in the primary motor area was created by performing a logical "or" of the BOLD and FAIR motor activation maps and limiting pixels to the gray matter with the gray matter mask.

Results

Relative BOLD and CBF changes were calculated for each subject and plotted together (see Fig. 1). Using linear least squares regression, the two-parameter model equation was fit to the pooled hypercapnia data. The optimal value of the β' parameter was obtained by constraining β' between 0 and 1 so as to be consistent with the physiological extremes of either no relative CBV contribution to the BOLD signal or complete contribution. The α* parameter was allowed to vary freely. The best fit was obtained with β' = 1 and α* = 5.87 ± 0.30 ($R^2 = 0.64$, see fitted curve in Fig. 1), although this was only marginally better than the linear fit with β' = 0 ($R^2 = 0.62$).

The intersubject mean ΔrCBF and ΔrBOLD during 2-Hz sequential finger movement were 38 ±10% and 2 ± 0.4%, respectively. The intersubject $\Delta rCMRO_2$ was calculated as 14 ± 3% based on the intersubject mean ΔrCBF and ΔrBOLD and intersubject estimates of α* and β'.

ΔrBOLD vs. ΔrCBF during Graded Hypercapnia and Sequential Finger Movement

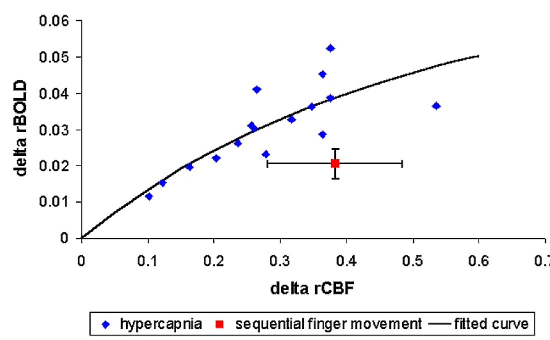

Fig. 1

Discussion

The estimated value of α* (5.87 ± 0.30 s^{-1}) obtained at 4 T is larger than that obtained at 1.5 T (4.23 s^{-1}) with a similar model (2). This parameter modulates the contribution of the venous oxygenation and volume changes to the BOLD signal changes and is expected to increase with increasing field strength. Further investigation of the field strength dependence of the model parameters and the validity of this biophysical model at various field strengths needs to be made.

The obtained value of the mean $\Delta rCMRO_2$ of approximately 14% supports the notion of considerable relative changes in oxygen consumption during motor activity. Furthermore, the ratio of ΔrCBF to $\Delta rCMRO_2$ of approximately 2.7:1 in motor cortex is similar to a measured ratio of 2:1 in the visual cortex obtained by functional MRI (5).

References

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