Quantitative relationships of metabolic and vascular parameters in brain activation: a multi-modal fMRI study

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Introduction: Neural activation results in changes in various metabolic and vascular parameters, including cerebral blood volume (CBV), cerebral blood flow (CBF), oxygen extraction fraction (OEF), venous oxygenation (Y_v), and cerebral metabolic rate of oxygen ($CMRO_2$) [1]. While several fMRI techniques are available to selectively image these parameters and it is generally assumed that they all provide an indirect measure of the underlying neuronal activity, the precise relationships amongst these fMRI signals are not fully investigated. Therefore, direct comparison of these parameters can provide us with an in-depth understanding of brain physiology and can help us in evaluating different fMRI methodologies. In this abstract, we use three fMRI techniques, BOLD, ASL and VASO, to measure BOLD, CBF and CBV changes, respectively. In addition, the baseline Yv is also estimated using a recently developed technique, T2-Relaxation-Under-Spin-Tagging (TRUST) MRI [2]. Based on these measured physiological parameters, OEF and $CMRO_2$ were also estimated using a biophysical model [3]. The correlations between these parameters across subjects were evaluated.

Methods: Experiments were conducted on a 3T MR system (Tim Trio, Siemens) in a group of healthy volunteers (n=15). A single slice (5 mm) covering the calcarine fissure was chosen for the functional scans, FOV = 230mm × 230mm, matrix = 64 × 64, TR = 3000ms. For BOLD, TE = 30ms, Flip Angle = 70. For ASL, TE = 13ms, Inversion Time= 1500ms, Flip Angle = 90. For VASO, TE = 13ms, Inversion Time = 889ms, Flip Angle = 90. Each experiment consists of 30s of visual stimulation (blue-yellow flashing checkerboard, frequency = 4.17Hz) interleaved with 54s of fixation and repeated 3 times. 54s of extra fixation time was used before the first stimulation. TRUST MRI scan was used to measure the venous blood T2 in the sagittal sinus [2], which can be converted to venous oxygenation via a calibration curve. Since resting state Y_v is homogeneous throughout the brain [4], this value is used as $Y_{v,baseline}$ for the activated voxels in the calculation of OEF and $CMRO_2$.

In data processing, motion correction was performed using SPM. Activation detection was based on cross-correlation with a box-car function (|cc|>0.2, positive cc for BOLD and ASL data, negative cc for VASO data, voxel cluster size >3). Voxels that were activated in all three scans (overlapping voxels) were spatially averaged for signal amplitude. ΔCBF/CBF was calculated from the ASL data using a perfusion model. ΔCBV/CBV was calculated from the VASO data using an equation described in literature [5], assuming a $CBV_{baseline}$ based on $CBF_{baseline}$. Then the BOLD and CBV changes were first combined to calculate OEF changes [3], which, in turn, are combined with CBF changes to estimate $\Delta CMRO_2/CMRO_2$ [3]. All values are shown in percentage changes.

Results and Discussion: All three fMRI techniques showed clear activation maps in the occipital lobe. The numbers of overlapping voxels were 30.6±4.3 (mean±SEM, n=15). Across the subjects, there was a significant (p=0.015) correlation between BOLD signal changes and CBF signal changes (Fig. 1a). Fitting the points with a straight line passing the origin resulted in the ratio of 32:1, i.e. for every 32% of ΔCBF/CBF increase, a 1% of BOLD signal is expected (for our BOLD sequence of TE=30ms at 3T). Comparing BOLD signal with VASO signal, no significant relationship was observed, likely because ΔVASO/VASO is more closely related to ΔCBV rather than ΔCBV/CBV [5]. If we assume that baseline CBV follows an exponential relationship with baseline CBF [6], then ΔCBV/CBV can be calculated. Fig. 1b shows that ΔCBV/CBV is positively correlated (p=0.025) with BOLD. Similarly, a significant relationship (R^2=0.37, p=0.016) was found between ΔCBF/CBF and ΔCBV/CBV (Fig. 1c), giving a ratio of 2.4:1, i.e. for every 32% of ΔCBF/CBF increase, a 13% of ΔCBV/CBV increase will occur. Aside from these experimentally measured parameters, comparison was also made between the BOLD signal and metabolic parameters calculated from the model [3]. Figs. 2a and b show the correlation of BOLD with $\Delta Y_v/Y_v$ (p=0.0048) and ΔOEF/OEF (p=0.0012), respectively, suggesting that the BOLD signal is indeed a reflection of blood oxygenation changes, although its correlation with ΔYv is actually more significant (R^2=0.61, p=0.0006), i.e. more related to ΔY_v than $\Delta Y_v/Y_v$. However, it should be noted that the estimation of Yv and OEF used the BOLD data, therefore they are not completely independent measures. The CMRO2 change (15.3±4.5%) was found to be correlated with ΔCBF/CBF (Fig. 3), but not with BOLD or with ΔCBV/CBV. The slope between ΔCMRO2/CMRO2 and ΔCBF/CBF was 0.34, higher than PET literature but comparable to previous MRI reports [7]. In summary, our data suggest that there is a general correlation between different fMRI contrasts, and the related vascular and metabolic changes also appear to be correlated. However, if we consider CMRO2 to be the closest measure of the neuronal activity, CBF percentage change seems to be the most accurate fMRI contrast.

References: [1] Davis et al. PNAS 95:1834, (1998); [2] Lu ISMRM abstract, submitted (2007); [3] Lu, et al. JCBFM, 24:764, (2004); [4] Fox et al. PNAS 83: 1140, (1986); [5] Lu, et al. MRM 50:263, (2003); [6] Grubb, et al. Stroke, 5: 630, (1974); [7] Mandeville, et al. MRM 42: 944 (1999).

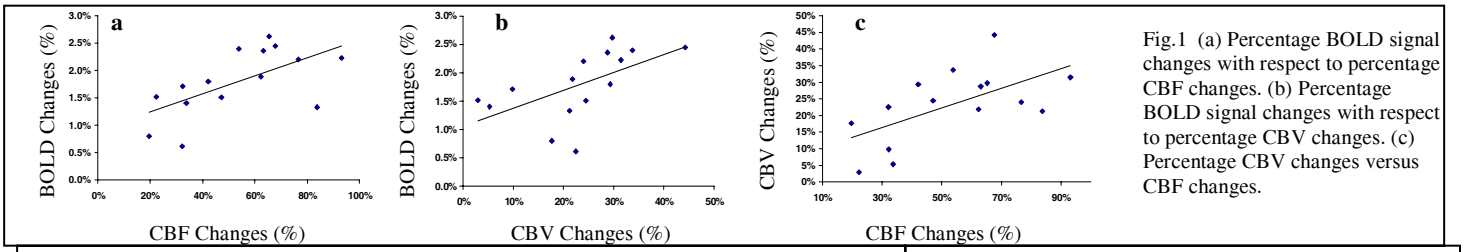

Fig.1 (a) Percentage BOLD signal changes with respect to percentage CBF changes. (b) Percentage BOLD signal changes with respect to percentage CBV changes. (c) Percentage CBV changes versus CBF changes.

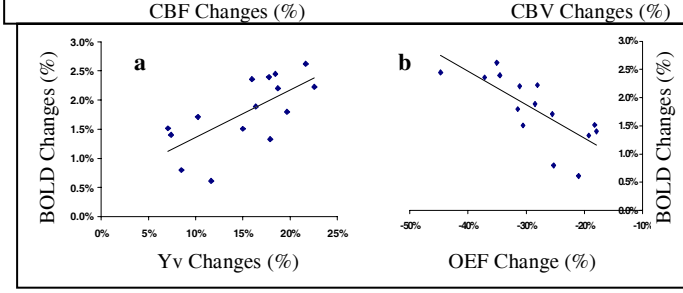

Fig. 2 (a) Percentage BOLD signal changes with respect to percentage Yv changes. (b) Percentage BOLD signal changes with respect to percentage OEF changes.

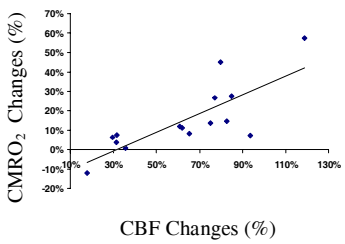

Fig.3 Percentage $CMRO_2$ changes versus percentage CBF changes.