Concurrent fMRI measurements with optical imaging spectroscopy and LDF measurments

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Introduction:

The BOLD signal is a confound of intravascular and extra vascular effects. This has been shown by Monte Carlo Simulations and analytic modeling. Experimentally it has been shown that gradient echo (GE) sequences containing velocity nulling pulses greatly reduce the magnitude of the BOLD signal at low field strengths (1.5-3T) by eliminating the intravascular contribution. We describe here the initial experiments in which we investigate the relative contribution of the intravascular and extravascular contributions in an animal model. Measurements from optical imaging spectroscopy (OIS), laser Doppler flowmetry (LDF) concurrently with magnetic resonance imaging (MRI) were used to investigate the hemodynamic response to neural activation in rat barrel cortex. The data was input to a dynamic model of oxygen transport to tissue (1) which was used to determine the changes in blood volume and oxygenation in the arteriolar, venous and capillary compartments. These parameters were then input to a version of Yablonskiy-Haacke (2)biophysical model of the extravascular BOLD signal (modified to include arteriolar, venous and capillary compartments) and the predictions compared with the measured BOLD signals.

Methods:

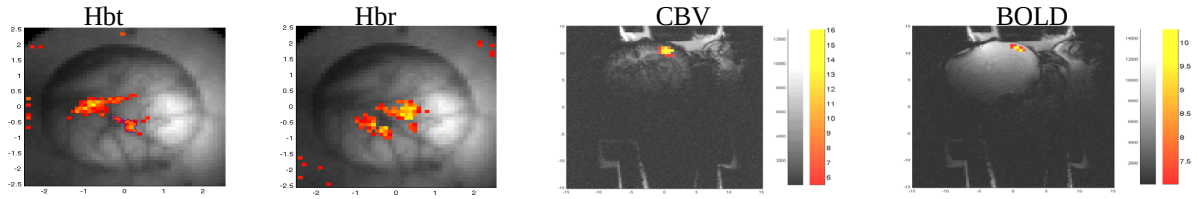
The MRI measurements were made at 3T in a small animal magnet facility (Magnex with MRRS console). Animal were anaesthetised with urethane, artificially ventilated and cannulated for arterial blood pressure monitoring and intravenous infusion. Both MRI measurements of the BOLD signal and cbv-MRI estimates of changes in blood volume (CBV) were obtained concurrently with either measurements of CBF (8 animals) using a magnet compatible LDF probe (Perimed), or measurements of changes in blood volume and oxygenation using optical imaging spectroscopy (4 animals) with a MR endoscope. A thinned skull cranial window was used for optical imaging localisation of the barrel cortex and positioning of the LDF probe and endoscope. The 'probe' assembly incorporated a 1.5cm diameter surface coil was affixed to the head around the cranial window. A 1% agar solution was used to avoid susceptibility artefacts. MRI measurements were obtained a using GE-EPI sequence (TE 15ms TR 2s) at a voxel resolution of 470x470x2000µm. Of necessity, cbv-MRI data was collected after BOLD measurements following infusion of the contrast agent AMI-227 (Guerbet: Sinerem. 10mgFe/kg ~200µmol Fe/kg).

Summary of Results:

1) OIS measurements of Hbt (blood volume) changes and simultaneous cbv-MRI measurements of CBV changes from the activated region of cortex were almost identical in magnitude and time series.
2) LDF measurements of CBF and CBV/Hbt measures were found to follow a similar relationship to that reported by Grubb et al. (1974). The function linking the dynamics of flow to volume changes was identified as a second order non-linear extension of Mandeville's version of the *windvessel* model (3) incorporating delayed compliance.
3) Baseline blood volume fractions in cortex ranged from 4-8% at the periphery. Changes in CBV were greater in the deeper layers of cortex.
4) The measured BOLD and Hbt and saturation (from the OIS data) were used to estimate the scaling term $M = TE.A.CBV_o[Hbr]_{vo}^{\beta}$ and the value of the exponent β used in the MGH biophysical model of the BOLD signal (4). The values of M and β calculated from the hypercapnia data from the same region of cortex did not quite match the activation data. We obtained values of 0.25 for M and 1.3 for β for activation data. With β clamped at 1.3, the value of M was 0.19 and 0.25 for the 5 and 10% $FiCO_2$ respectively.
5) The predicted extravascular contribution was 25-50% of the measured BOLD signal depending on the selection of baseline blood volume fraction.

Conclusions-Discussion:

This project is ongoing. The next stage of research is to introduce velocity nulling gradient pulses into the sequence and plot the change in BOLD measurements as a function of increasing 'velocities' as did Boxerman (5). The critical issue is whether the decrease in magnitude of the BOLD signal asymptotes at the value predicted from the OIS, LDF and CBV data input to the modified Yablonskiy-Haacke model.



Optical imaging spectroscopy maps showing Hbt and Hbr changes collected concurrently with BOLD and cbv-MRI data

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