Concurrent fMRI Measurements with Optical Imaging Spectroscopy and Laser Doppler Flowmetry Measurements

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Introduction:

Variation in *f*MRI signals are based upon a confound of blood flow, volume and oxygenation. The purpose of the present study was to disambiguate these variables by investigating the relationship between these haemodynamic factors. Using the rodent barrel cortex as an experimental model, we performed simultaneous measurements of *f*MRI and Laser Doppler Flowmetry (LDF) or Optical Imaging Spectroscopy (OIS) following whisker stimulation or hypercapnic challenge. Flowmetry measures changes in flow while optical spectroscopy independently measures changes in volume and oxygen saturation. As well as BOLD measurements, MRI was used to estimate baseline blood volume fraction and normalised change in blood volume (CBV-MRI using a contrast agent) following whisker stimulation. The profile of baseline blood volume fraction was also used in the optical spectroscopy analysis to estimate the changes in blood volume in barrel cortex following activation and hypercapnic challenge. Thus, combined measurements from *f*MRI, CBV-MRI and optical imaging spectroscopy were used to examine the degree of concordance between the two imaging methods. Time series of the changes in blood flow and volume changes measured were compared. The resulting quantitative relationship between changes in blood flow and volume following experimental challenges is important in interpreting measurements of the BOLD signal as reflecting changes in metabolic activity (1).

Previously, data was input to a dynamic model of oxygen transport to tissue (2), which was used to separate the changes in blood volume and oxygenation in the arteriolar, venous and capillary compartments. These parameters were then input into a modified version of Yablonskiy-Haacke (3) biophysical model of the extravascular BOLD signal, but were found to under-estimate the measured signal. Therefore we introduced velocity nulling gradient pulses into the GE sequence to show the change in BOLD measurements as a function of increasing 'velocities' (4). The critical issue of the nulling was 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 Yablonkiy-Haacke model.

Methods:

MRI measurements were made at 3T in a small animal magnet facility (Magnex with MRRS console). Urethane anaesthetized animals were artificially ventilated and cannulated for monitoring arterial blood pressure and intravenous infusion. Both MRI measurements of the BOLD signal and CBV-MRI estimates of changes in cerebral blood volume (CBV) were obtained concurrently with either measurements of flow (10 animals) using a magnet compatible LDF probe (Perimed), or measurements of changes in blood volume and oxygenation using optical imaging spectroscopy (10 animals) with a MR compatible endoscope. A thinned skull cranial window was used for optical imaging localization of the barrel cortex and positioning of the LDF probe and endoscope. The 'probe' assembly incorporated a 2.0cm diameter surface coil fixed to the head around the cranial window (Fig 1). A 2% agar solution was used to avoid susceptibility artifacts. MRI measurements were obtained a using GE-EPI sequence (TE 15ms, TR 2s) at a voxel resolution of 470x470x2000µm. CBV-MRI data was collected after BOLD measurements following infusion of the contrast agent MION: AMI-227 (Guerbet: Sinerem. 10mgFe/kg ~200µmol Fe/kg).

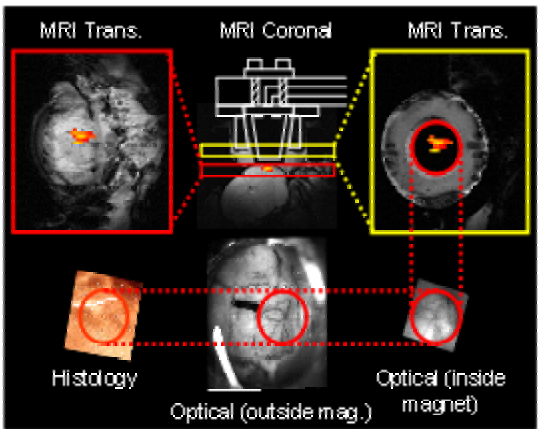

Fig 1. Concurrent MRI and optical measures of volume and saturation were conducted. fMRI activation maps were related to histological identification of the vasculature and cortical barrels. The BOLD signal was seen to originate around the barrels in the somatosensory cortex.

Summary of Results:

- Comparison of fMRI signals and histological results showed activation was located over the barrel cortex (Fig 1); The BOLD-fMRI signal contained a draining vein not present in the optical spectroscopy, so the spatial profiles are different. Profiles of CBV-MRI and volume from optical spectroscopy were similar.
- Baseline blood volume fractions (v_f) ranged from 8% in the superficial cortical layers to 4% in deeper layers. Maximum BOLD changes were greater in the superficial layers while changes in volume were greater in the deeper layers.
- Using v_f to parameterize optical spectroscopy data we found that the blood volume response measured by optical spectroscopy corresponded to the blood volume response measured by CBV-MRI in the superficial cortex.
- Measurements of CBF and CBV/Hbt showed a similar relationship to that reported by Grubb et al. (5). 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 *wind-kessel* model (6,7) incorporating delayed compliance.
- Intra-vascular effects accounted for 25 - 35% of the total BOLD signal.

Conclusions & Discussion:

Using *f*MRI as a calibration factor, the different imaging modalities were combined to increase understanding of the BOLD *f*MRI signal source. The concurrent flow, volume, oxygenation and BOLD data will be used to improve further the haemodynamic response models to enhance our understanding of the link between BOLD and neuronal activity. This work represents the basis for future investigations of the haemodynamics underlying *f*MRI signals. Present linking of fMRI and optical measures will be related to concurrent investigation involving optical measures and electrophysiology recording of neural activity. Together this will forge a link between the BOLD fMRI signal and neuronal activity; an essential precondition for correct interpretation of human BOLD data.

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