Measurement of Activation-induced Changes of Cerebral Blood Flow Using Concurrent Arterial Spin Labelling and Laser Doppler Flowmetry

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Introduction

Monitoring the dynamic changes in cerebral blood flow (CBF) is critical for understanding the haemodynamic and metabolic processes during brain activity [1]. Arterial spin labelling (ASL) MRI allows spatially-resolved non-invasive measurement of dynamic CBF (δCBF) employing arterial water as an endogenous contrast agent. However, it has several confounds caused by its coarse temporal resolution (typically one ASL image every 2 seconds or more) and its sensitivity to parameters (such as inversion efficiency and transit time) that may change dynamically, as a result of the CBF changes. Laser Doppler Flowmetry (LDF) [2,3] detects relative δCBF via the Doppler shift of laser scattering from moving red blood cells, at high temporal resolution. However, it does not provide absolute values of CBF and its spatial resolution is coarse (~2mm^2). The concurrent application of these two modalities can form a more comprehensive picture of the behaviour of CBF, which will enhance the comprehension of brain mechanisms. This work accesses the fundamental aspects of both modalities, which establishes the foundation for systematic combination of them.

Materials and Methods

Animal preparation: Hooded Lister rats 250-300 g (N=4) were anaesthetised with urethane (1.25g/kg i.p.), tracheotomised, artificially ventilated and cannulated for mean arterial blood pressure (MABP) monitoring and intravenous infusion. Phenylephrine (0.13-0.26mg/hr) was infused to maintain MABP between 100-110mmHg. Rectal temperature was maintained at 37°C using a homeothermic blanket (Harvard). A thinned skull cranial window above the barrel cortex region (5~8mm contralateral to the stimulation, 1~4mm posterior to bregma) was formed. The barrel cortex was localised outside the magnet using optical imaging spectroscopy and LDF with 6-s whisker stimulation (1.2mA, 3Hz). The 1.5cm diameter transmit/receive MRI surface coil was affixed to the head, with the LDF probe at its centre. The cranial window was then filled with 1% agar solution to minimise magnetic susceptibility artefacts. *LDF:* The MRI-compatible LDF probe (Perimed, wavelength 780nm) had 4 receiver channels with separations of 140, 300, 600 and 800μm from the transmitter. The four channels were sampled synchronously at a rate of 30 Hz.

ASL-fMRI: A 3T, 16cm horizontal bore Magnex magnet equipped with a Magnex 10cm-id self-shielded gradient (10kHz/mm max per axis), and an MRRS console was used. Continuous ASL (CASL) [1,4] was implemented using separate actively decoupled imaging and labelling (fixed underneath the trachea) surface coils (diameters 1.5 and 1cm, respectively) with 2.5cm separation (submitted to ISMRM 2005). The LDF probe was located in high resolution images, and a 2mm-thick transverse slice through the centre of the LDF probe was selected for imaging. Single-shot, gradient-echo echo-planar imaging (EPI) was used for CASL with 64x64 matrix, FOV=3x3cm, TE=15ms, TR=3s, labelling period of 2.850s. Paired images (ASL and control) were acquired alternately by varying the sign of the offset frequency for the labelling RF pulse. A block design stimulation protocol was used with 32s stimulus duration, 180s ISI and 6 epochs with two current values (1.2mA and 1.6mA). 3-minute 10% hypercapnia was also performed. *Data analysis:* The EPIs were coregistered to a high resolution image of the same slice and CBF time-series maps were calculated from the ASL data as in [1], using λ=0.9, T_1=1.4s and α=0.8. An ROI coincident with the area of sensitivity of the LDF probe (2mm along the probe surface x 2mm penetration depth) was defined in the high resolution image for use in CASL data analysis. The recordings of the 4 LDF channels were averaged and subsampled to match the temporal resolution of CASL.

Results & Discussion

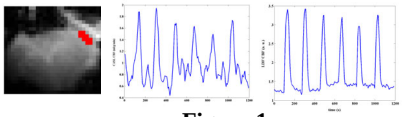

Figure 1

Figure 1 shows an EPI (left) with the area of the sensitive LDF region, used in the analysis. Concurrent CASL (middle) and LDF (right) time courses of a single trial for 1.6mA stimulation are also shown.

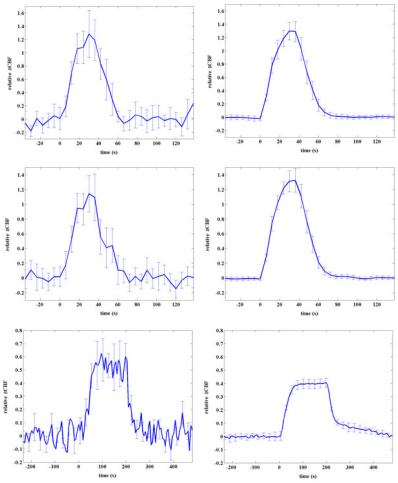

Figure 2

Figure 3 compares the average CASL (left column) and LDF (right column) responses for 1.6mA (top row), and 1.2mA stimulation and 10% hypercpania (bottom row). Although CASL measurements appear noisier than their LDF counterparts, these preliminary results clearly demonstrate that δCBF measurements using concurrent LDF and CASL show significant agreement in the magnitude and the shape of δCBF, for both activation and hypercapnia.

This project is ongoing and the next step is to refine the two techniques so that they are more comparable in terms of temporal and spatial resolution. First, the temporal resolution of CASL may be improved by labelling closer to the activation site and using small TR (<1s) pseudo CASL [5]. This will also improve the SNR of CASL, given that relaxation of the labelled arterial water may be significant noise factor at 3T (note that CASL studies of anaesthitised animals are performed at higher magnetic field strengths). Secondly, the spatial specificity of LDF may be improved, by using a spatially resolved variant of LDF, Laser speckle flowmetry (LSF)[6], which is a spatially resolved variant of LDF.

Conclusions

Measurement of activation-induced CBF changes using concurrent ASL-MRI and LDF has been performed for the first time in the rat. Careful selection of ROIs over the sensitivity area of LDF revealed significant agreement in the shape and magnitude of CBF responses between ASL-MRI and LDF. However CASL-MRI measurements were markedly noisier than their LDF counterparts. These promising preliminary investigations can benefit from refinements in both techniques, improving our understanding of cerebral haemodynamics.

References [1] Silva AC et al, *J Cereb Blood Flow Metab* 19: 871-879 1999 [2]]Haberl R et al, *Am J Physiol* 256: H1247-H1254 1989 [3] Mathiesen C et al, *J Physiol* 512: 555-566 1998 [4] Detre JA et al, *Magn Reson Med* 23: 23-45 1992 [5] Silva AC et al, *Magn Reson Med* 42: 425-429 1999 [6] Ayata C et al, *J Cereb Blood Flow Metab* 24: 744-755 2004 **Acknowledgments** This work is supported by the MRC (G0200484, G9825307).