Longitudinal Measurement of CBF and CBV Using Arterial Spin Labeling and Steady State Contrast Enhancement fMRI

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INTRODUCTION: Translation of fMRI into clinical research faces several challenges that require development of new modalities that provide quantifiable images of correlates of brain function that are stable over time. Longitudinal stability is crucial in monitoring slow-varying processes in the brain such as normal aging, disease progression, and therapeutic efficacy. We have developed a method that provides concomitant measurement of CBF and CBV by combining tissue specific arterial spin labeling (ts-ASL) perfusion fMRI with steady state contrast enhanced (SSCE) fMRI. Here we report on the **test-retest reliability of CBF and CBV images acquired on subjects from an older population, 90 days apart.**

METHODS: This study is part of a larger study whose overall goal is to investigate the effects of exercise and epicatechin on basal brain function in older populations. The recruitment target is 25 subjects/condition. Each subject is being imaged at 2 time-points, D_1 and D_{90}, 90 days apart. So far we have completed imaging for 7 subjects (age = 65 ± 6y, 2 men.) All subjects gave written consent according to our institutional guidelines. Prior to the start of the study, a SmartExam protocol was run on 10 age-matched volunteers to establish a 'trained' geometry to minimize the error due to different subject head-placement over time[1]. Image Acquisition: The following images were acquired on a 3T Philips scanner: Pre-contrast MPRAGE with voxel resolution 0.7x 0.7 x 3 mm^3; pCASL as per Osch et al.[2] with labeling duration=1.9s and post-labeling delay=1s; Post-contrast MPRAGE with the same parameters as the pre-contrast as previously described[3,4]. CBF Computation was done using a partial volume correction method that yields flow density images for gray (GM) and white matter (WM), independently[5]. CBV Computation: Pre-contrast MPRAGE was subtracted from the post-contrast and normalized to the sagittal signal[3,4]. Mean transit time (MTT) images were computed as CBV/CBF. Prior to the computation, the CBF and CBV images were normalized to the MNI space. All other analyses were done in subjects' native space. ROI analysis: In addition to global GM and WM measures, CBF and CBV values were obtained on ROIs selected based on power analysis considerations and their role in aging and dementia. For each subject, the ROIs were constructed based on the pre-contrast MPRAGE image using FreeSurfer[6].

RESULTS: Unlike ASL, for which several studies have reported test-retest reliability measures[7], this is the first study to report on the longitudinal stability of high-resolution CBV imaging. Therefore, to give a sense of the subject-level SNR over time, we show histograms (Fig.1) of the noise (computed as the difference between the pre-contrast MPRAGE images acquired at D_1 and D_{90}, respectively) and the CBV signal averaged over GM and WM, at both time-points from a randomly selected subject. In Fig.2 we show coregistered CBF and CBV images used to compute MTT. There was no significant difference in MTT across D_1 and D_{90} (p=.13). Whole brain GM and WM CBV values were 5.2% ± 2.1% and 2.2% ± 1.8%, respectively, on D_1 and 5.3% ± 2.1% and 2.1% ± 1.9% on D_{90}. Results of the ROI-analysis are summarized in Fig.3. There was no effect of time on both the CBF and CBV ROI values (p>0.13, for all). The correlation coefficient between CBV and CBF was r^2>0.7, for all ROIs.

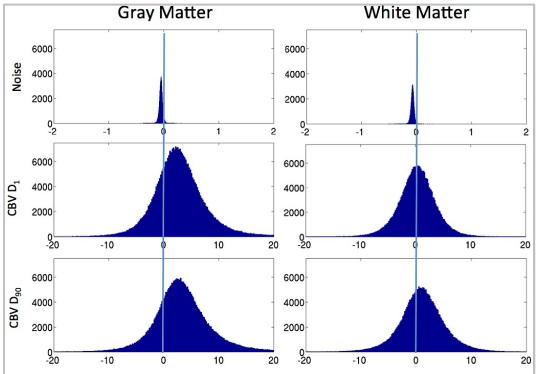

Fig.1: Histograms of noise (1st row), CBV at D_1 (2nd row), and CBV at D_{90} (3rd row), averaged over the whole-brain GM (left) and WM (right). Note the tissue difference in CBV, with GM CBV centered at ~5%.

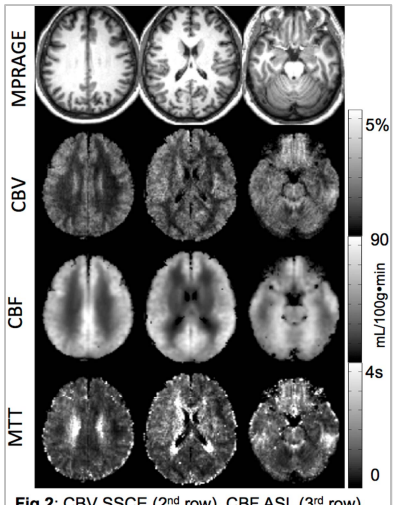

Fig.2: CBV SSCE (2nd row), CBF ASL (3rd row), and MTT=CBV/CBF (3rd row) images from a randomly selected subject. Pre-contrast MPRAGE (1st row) is shown for anatomical reference. Note the relatively long MTTs in WM compared to GM.

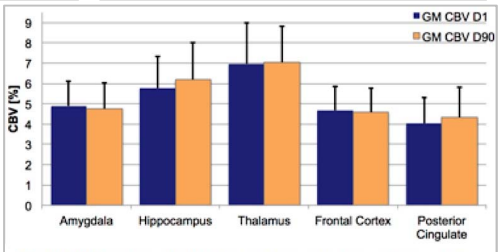

Fig.3: ROI were selected based on power analysis and their relevance in studies of aging and dementia. Note good ROI-wise stability of CBV over time.

DISCUSSION: Multimodal fMRI is important in studies of aging and disease where assumptions about basal coupling of physiological correlates might not hold. Here we provide e method that concomitantly provides whole brain quantifiable measures of CBV and CBF with high test-retest reliability.

REFERENCES: [1]Petersen ET, et al. Neuroimage (2010); [2] van Osch MJ, et al., MRM (2008); [3]Lin W, et al., JMRI (1999); [4]Asllani I, et al, SFN Meeting (2004); [5]Asllani I, et al., MRM (2008), [6]Fischl B, et al., Neuron (2002). [7]Borogovac A, et al., JCBFM (2010).