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Detection of CBF Changes due to Activation over One Month Using ASL Functional MRI

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INTRODUCTION: Arterial spin labeling (ASL) offers several advantages over BOLD fMRI: 1) Theoretically, ASL lacks signal drift due to 1/f noise[1], 2) ASL offers better localization of the activated areas, 3) ASL yields absolute quantification of the observed signal change in physiological units, 4) ASL has a lower intersubject variability of the activation contrast. ASL stability combined with its absolute quantification of CBF is highly relevant for studies where changes in CBF over long period of time need to be detected, such as studies of disease progression or detection of pharamacological effects. Feasibility of ASL for detection of CBF changes due to activation separated from baseline by 24 hours has already been shown by Wang et al[1]. Our group has shown changes in CBF due to 48 hours of sleep deprivation. The aim of this ongoing study is to investigate the feasibility of using ASL to detect changes in CBF due to motor and visual stimulation where activation was separated from baseline by 4 weeks. Arterial transit times to motor and visual cortex were estimated using a multiple labeling duration experiment.

METHODS: ***Subjects:*** CASL functional data were acquired on 4 subjects (age 26 ± 4 years, 1 male). CASL multi-LD data were acquired on 5 subjects (26 ± 2 years , 3 male). Written consent was obtained as approved by the institutional IRB. ***MRI:*** Images were acquired on a 3T Philips Achieva using a standard transmit-receive coil. Single shot SE-EPI CASL images were acquired in ascending slice-order with: TR/TE=4.3/30ms, θ=90, FOV=240x210 mm2, acq. matrix=64x56, slice thickness/gap=8mm/1.2mm. Activation data were acquired using 13 slice acquisition, PLD=0.5s and LD=1.8s. Single slice positioned at motor cortex was acquired using PLD=20ms and 12 different labeling durations ranging from 150-1900ms. Additional single slice positioned at visual cortex was acquired using PLD=20ms and 8 different labeling durations ranging from 150-1500ms. Adiabatic inversion of water spins and correction for off-resonance effects in control images were done as described by Alsop et al[3]. For each subject, a high resolution, 3D MPRAGE: TR/TE=6.7/3.1ms, TI=0.8s, FA=8°, res: 0.9x0.9x0.9 mm^3, FOV=240x162x190, Recon=288x288 and 180 slices, was also acquired. All EPI images were motion corrected, co-registered to the corresponding MPRAGE and spatially normalized to MNI standard space using SPM5. Each control-label pair yielded a CBF image using the formula by Wang et al[4] and correcting for slice-dependency of PLD and transit time. ***Arterial transit time estimation:*** Slice-wise average ASL percent change signal was computed for each LD acquisition. The data were then fit to the one-compartment theoretical model[1] by minimizing the sum of square errors. ***Activation data acq. and processing:*** Data were acquired during two separate sessions, 4 weeks apart. Each session consisted of 5 OFF/ON blocks. During each OFF block, 13 images of baseline CBF were acquired. During each ON block, 13 activation CBF images were acquired while subject performed self-paced sequential right-hand button-pressing and observed 8Hz reversing checkerboard. CBF images were smoothed by 6mm Gaussian kernel. Subject specific voxelwise analysis of the functional data was carried out to identify voxels with a significant response to the motor and visual cortex simulation compared to the baseline acquired 1 month apart. Similar voxelwise analysis was performed comparing baseline CBF images across the 2 sessions, as well as within session activation. The analysis employed the general linear model and used an appropriate single covariate function of resting state and activation. The individual subject contrasts were then combined in random effects analysis using a one-sample t-test. Additionally, ROI analysis was performed to compare baseline and activation CBF in motor and visual cortex across the two sessions. The visual and motor ROIs were based on voxels having significant activation (T>4.8, P<0.001, uncorrected) for within session ON-OFF voxelwise analysis.

RESULTS: The best fit of multiple LD data to the theoretical model yielded best-fit arterial transit times of 1023±198ms and 649±125ms to motor and visual cortex, respectively. Plots of the fit for representative subject is shown in Fig.1. The estimated transit times are in good agreement with values reported using multi-PLD experiment[5]. Group voxelwise analysis comparing baseline CBFs acquired 1 month apart yielded no activated voxels at P<0.001, uncorrected. The group random effects analysis was able to detect activation when ON and OFF were acquired 1 month apart, while within-subject comparisons showed contamination with false-positives (data not shown). Fig. 2 shows the resulting SPM{T} map in the motor cortex. ROI analysis showed that motor activation on average induced highly significant, 58% increase in CBF (Fig. 3), while visual induced a smaller CBF increase of around 20% (data not shown).

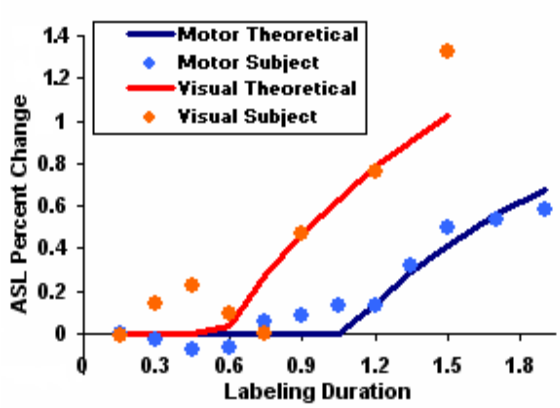

Fig.1: Estimation of arterial transit time by fitting ASL signal obtained in multi-LD experiment to theoretical model. Figure shows best fit for single subject.

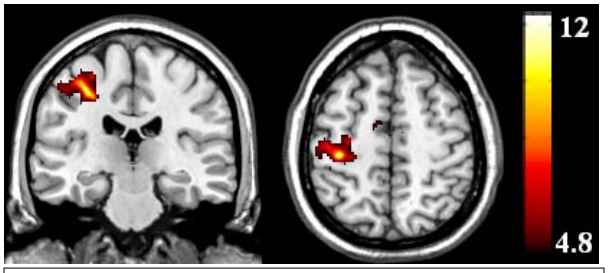

Fig.2: SPM{T} map (T>4.8, P<0.001, uncorr.) of group data comparing baseline and activation acquired 4 weeks apart.

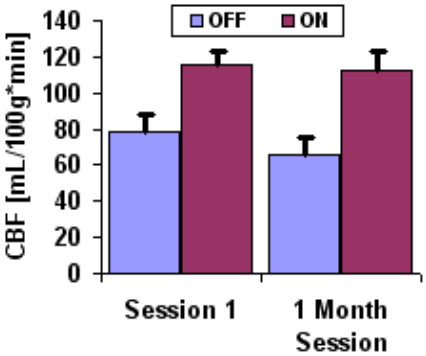

Fig.3: ROI analysis showing baseline (blue) and activation (red) CBF in motor cortex for 2 sessions 4 weeks apart. Error bars denote standard error.

DISCUSSION: We have demonstrated the relative insensitivity of the CASL CBF measurement to the 1/f noise over a period of 4 weeks, and affirmed the viability of the technique for use in group longitudinal studies tracking changes in CBF over this time scale. Further work is necessary to validate flat noise spectrum of ASL signal over even larger time scales.

REFERENCES: 1) Wang et al, MRM 49 (2003) 2)Asllani et al ISMRM06 3) Alsop et al, JCBFM 16(6) (1996) 4) Wang et al, MRM 48 (2002) 5) Gonzalez-At et al, MRM 43 (2003)