FEASIBILTY OF DUAL-ECHO PCASL AND PASL BOLD-RCBF FMRI IN OLFACTORY EXPERIMENTS

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Introduction: BOLD fMRI presents dropout of signal near air-tissue brain interfaces due to magnetic susceptibility artifacts. In olfactory experiments, the study of the primary olfactory areas such as enthorrinal cortex is difficult because of its location in medial temporal lobe, highly affected by magnetic field inhomogeneities causing both local image distortion and signal dropout [1]. Arterial Spin Labeling (ASL) is a promising quantitative fMRI technique, above all in these distorted brain areas due to its shorter TE (3.3ms) respect to optimal BOLD fMRI in 3T acquisition (TE=25-30ms). However, ASL-fMRI is challenging due to its low SNR [2]. In this work, simultaneous dual-echo BOLD-rCBF fMRI acquisition with spiral readout using pCASL and PASL were tested in an olfactory experiment in healthy volunteers.

Methods: *Subjects:* Three healthy subjects (mean age 32±1years) participated in this study.

Stimuli and experiment: Olfactory stimulus was administered using a custom-built olfactometer. The odor is delivered to the subject's nose, where the change from clean air to odorized air with rapid temporal features. Three different odorants (butanol, mint and vanilla) were randomly administered during the experiments synchronizing the odor supply with the subject inspiration monitored with respiratory gating. The stimulation paradigm was an block-design consisted of nine 9-s activation periods with no less than 25s interstimulus intervals (the stimulus is sent in next inspiration after 25s after next stimulus).

Image acquisition: Scanning was performed on a 3T GE scanner using the body coil for excitation and an 8-channel quadrature brain coil for reception. A dual-echo ASL 2D spiral-out gradient-echo sequence (spep, UCSD) [4] was used. Ten axial slices beginning from the inferior temporal lobe were acquired using two labeling techniques with and without background suppression: (a) pCASL parameters were: TR/TE1/TE2/voxel dimensions/label time/post labeling delay/volumes = 3.6s/3.3ms/30ms/3.3x3.4x3.4mm/1.5s/1.5s/100; (a) PASL, PICORE QUIPSS II, parameters were: TR/TE1/TE2/voxel dimensions/TI1/TI2/volumes = 2.2s/3ms/30ms/3.3x3.4x3.4mm/700ms/1.5s/150. A T1-weigthed image was also acquired to aid in anatomical localization. In addition, a whole brain image (at the same locations as the ASL-fMRI time series images) was acquired to improve the coregistration of the functional data and the T1-weigthed anatomical images.

Image preprocessing: rCBF and R2* for TE1 and BOLD for TE2 4D images were obtained using the interpolated subtraction (rCBF) and the average methods (R2* and BOLD) proposed by Lu et al. [3]. Functional imaging preprocessing was carried out using FMRIB's Software Library (FSL). Common preprocessing steps were: movement, spatial smoothing (FWHM=6mm) and temporal high pass filtering. Prewhitening was only applied for R2* and BOLD timeseries images.

Image analysis: Voxel-wise GLM analysis was performed to the preprocessed functional timeseries using regressors (and their time derivatives) for the different odors and four contrasts were calculated (one per odor and one for all of them). The number of activated voxels ($p<0.05$) and the peak Z stat value was extracted for each kind of acquisition.

Results: Figure 1 shows the results from BOLD-rCBF fMRI olfactory experiment. It can be observed that there are overlapped results for R2*, BOLD and rCBF in regions of medial temporal lobe such as the amygdala indicated by the arrows. In Figure 2, one representative voxel timecourse for the three contrasts is shown together with the olfactory stimulus model. The rCBF timeseries is the noisiest but, as Figure 1 shows, statistically significant results are also obtained in the regions of interest. In Table 1, we showed a comparison among the 4 different acquisition approaches used in this study. We obtained more activated voxels and higher z-values for PASL acquisition (no significant differences between background/non-background suppression). For pCASL series the number of activated voxels were higher for rCBF and the use of background suppression doubled the number of activated voxels.

Discussion: Simultaneous measurements of R2*, BOLD and fMRI allow to improve the location of activated brain areas in olfactory experiments which are difficult to observe with BOLD fMRI. The number of activated voxels when using PASL acquisition was higher than for pCASL acquisition for all the contrasts, probably due to the shorter TR in PASL. However, the ratio between BOLD and rCBF activated voxels is less than 1 for PASL and greater than 1 for pCASL. We hypothesize that this is related to the higher SNR in pCASL approaches (and higher with background suppression even when this is not totally effective in 2D acquisitions).

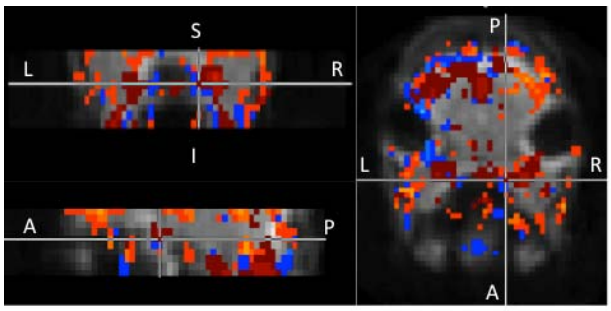

Figure 1: ASL-BOLD fMRI statistical maps for R2* (blue), BOLD (red) and rCBF (orange) in the olfactory experiment. (p<0.01,uncorrected)

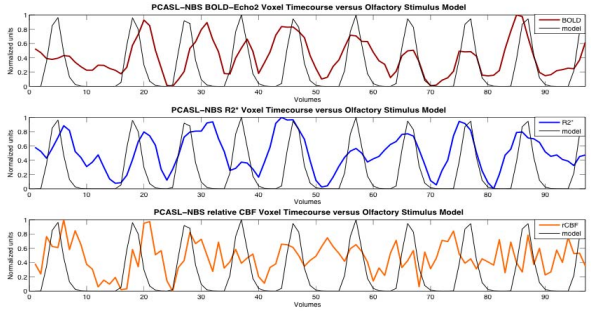

Figure 2: Representative voxel timecourses for R2*, BOLD and rCBF versus the olfactory stimulus model.

	PASL (bs)			PASL (nbs)			pCASL (bs)			PCASL (nbs)		
Number of activated voxels (p<0.05)	**R2***	**BOLD**	**rCBF**	**R2***	**BOLD**	**rCBF**	**R2***	**BOLD**	**rCBF**	**R2***	**BOLD**	**rCBF**
	6353	6933	5623	6329	6997	5800	612	502	2276	565	369	1007
Peak Z score	5.59	6.33	6.69	5.54	5.95	7.5	4.55	3.94	6.5	4.12	4.18	5.7

Table 1: Comparative between PASL (bs/nbs) and PCASL (bs/nbs) in number of activated voxels (p<0.05, uncorrected) and peak Z score for R2*, BOLD and rCBF contrasts.

Conclusion: In this study we have shown that the use of a dual-echo BOLD-rCBF fMRI is feasible for both PASL and pCASL acquisition approaches to study brain areas affected by magnetic field inhomogeneities. This suggests that this technique might be applied to evaluate the perfusion effect of drugs in temporal lobe. Furthermore, BOLD-rCBF fMRI can give quantitative measurements that could make an impact to the utility of fMRI into the Clinics, such as in neurodegenerative diseases.

References: [1] Glover GH et al. MRM 2001; [2]Detre JA et al,Clinical Neurophys 2002; [3] Lu et al. MRM 2006