To Smooth or Not to Smooth – ROC Analysis of Perfusion fMRI Data

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Introduction BOLD contrast has been widely used for visualizing regional neural activation. Temporal filtering and parameter estimation algorithms (1) are generally used to account for the intrinsic temporal autocorrelation present in BOLD data. Arterial spin labeling (ASL) perfusion imaging is an emerging methodology for visualizing regional brain function both at rest and during activation. Perfusion contrast manifests different noise properties compared with BOLD contrast, represented by the even distribution of noise power and spatial coherence across the frequency spectrum (2, 3). Consequently, different strategies are expected to be employed in the statistical analysis of perfusion fMRI data. In this study, the effect of different analysis methods upon signal detection efficiency, as assessed by receiver operator characteristic (ROC) measures, were examined for perfusion fMRI data. Simulated foci of neural activity of varying amplitude, spatial extent and temporal frequency were added to resting perfusion data, and the accuracy of each analysis was evaluated by comparing the results with the known distribution of pseudo-activations.

Methods Nine healthy subjects were studied while quietly resting with 8min perfusion and BOLD scans on a GE 1.5T Signa MR system. Perfusion data were acquired using a PASL technique as described previously (4) (FOV=24cm, 64x40 matrix, TR/TE=3000/18ms, 8slices of 8mm thickness and 2mm gap, 160acq), and perfusion image series were generated using "sinc subtraction" (2, 3). BOLD fMRI data were acquired using a gradient-echo EPI sequence (FOV=24cm, 64x40 matrix, TR/TE=2000/50ms, 21slices of 5mm thickness, 240acq). Activation time series with 4 design frequencies (30s, 1min, 2min and 4min OFF/ON) were added to approximately 5% of the total brain pixels, after the data were corrected for motion effects. A segmented gray matter ROI was used to constrain these activated foci within gray matter regions. Three cluster sizes of activation foci were tested with a 3D diameter of 1, 2 and 4 pixels respectively (0.11, 0.56 and 4.5cm^3). For BOLD data, the signal change between the resting and activation states was assumed to be 1.5%. For perfusion data, three levels of percentage signal change (25, 50 and 75%) were tested. The added time series was a boxcar function convolved with the hemodynamic response function (HRF) in both BOLD and perfusion data. Various kernel sizes (FWHM of 1, 2 and 4 pixels) were employed in spatial smoothing. Statistical analyses were carried out using the VoxBo software package (www.VoxBo.org). BOLD data analysis included notch filtering, HRF smoothing and 1/*f* modeling of the noise spectrum, followed by modified general linear model (GLM) analysis (2). The benchmark analysis of perfusion data consisted only of a conventional GLM analysis. Various pre-processing interventions were then assessed, including low pass, high pass filtering, temporal smoothing (moving average of 2-3 samples) and to set the mean global signal as a covariate in GLM. ROC curves were plotted based on the T-maps generated in each condition (number of detected activations vs. number of false-positive findings through ranked T scores), and a single parameter (area under curve, AUC) was used as the surrogate score for the efficacy of each method. Individual AUC measurements were averaged across 9 subjects to generate the mean ROC score.

Results and Discussion As expected, the power of perfusion fMRI increases with higher fractional signal change (Fig. 1). When spatial smoothing was applied, the accuracies of both BOLD and perfusion fMRI improve with larger activation cluster size (Fig. 2). In perfusion data, the peak ROC score was reached when the activation cluster size and smoothing kernel were similar. In BOLD data, however, the power generally decreases with heavier spatial smoothing. This result could be explained by previous observation that slow drifts in BOLD data are more spatially coherent which are magnified by spatial smoothing (3), thereby deleteriously affecting the accuracy of BOLD fMRI. As displayed in Fig. 3, the performance of perfusion fMRI is virtually the same at various task frequencies, whereas the power of BOLD fMRI decreases with increased interval between activation and rest in a block design. The cross point of approximately 4min interval in the curves of ROC scores of BOLD and perfusion data fits well with previous results (2, 5). Filtering or smoothing of the perfusion image series degrades the accuracy of perfusion fMRI, and high pass filtering is the most costly (mean ROC score reduction of 0.03). This result is consistent with the theoretical prediction that "whitening" the time series provides the most efficient parameter estimation (1). Finally, inclusion of the mean global time course as a covariate does not alter the efficacy of either BOLD or perfusion fMRI in this data.

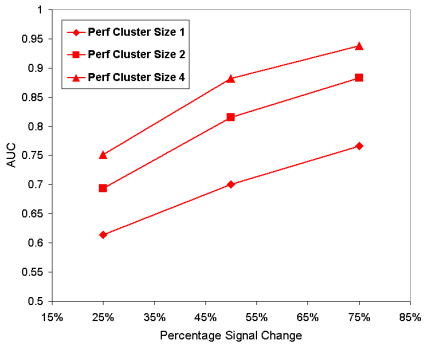

Fig. 1 Perfusion ROC score vs. signal change (30s OFF/ON, smoothing kernel of 2 pixels)

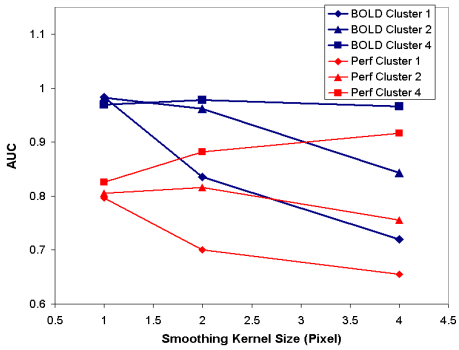

Fig. 2 ROC score of BOLD and perfusion data vs. smoothing kernel size (30s OFF/ON)

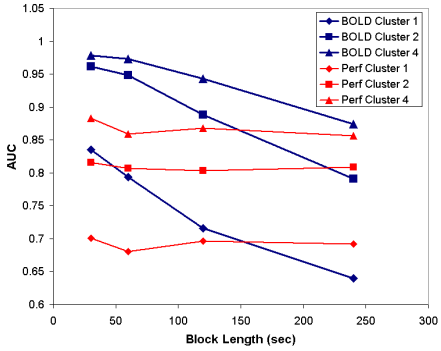

Fig. 3 ROC score of BOLD and perfusion data vs. task block length (smoothing kernel of 2 pixels)

References (1) Friston KJ et al. *Neuroimage* **12**: 196-208; 2000. (2) Aguirre GK et al. *Neuroimage* **15**: 488-500; 2002. (3) Wang J et al. *Neuroimage* **19**:1449-1462; 2003. (4) Wang J et al. *MRM* **48**: 242-254; 2002. (5) Wang J et al. *MRM* **49**: 796-802; 2003.