Group Analysis of ASL Perfusion fMRI Data based on Permutation Testing in individual subjects

Z. Wang[1], J. Wang[1], and J. A. Detre[1]

[1]Center for functional neuroimaging, University of Pennsylvania, Philadelphia, PA, United States

Introduction

Arterial spin labeling (ASL) perfusion fMRI suffers from relative low sensitivity through the conventional general linear model (GLM) based statistical analysis due to the intrinsic low SNR [1,2]. Permutation testing is flexible and requires a minimal assumption of noise distribution, therefore offer advantages over traditional parametric methods [3]. Due to the absence of temporal noise correlation under the null-hypothesis [4], each ASL perfusion MRI signal can be considered as an independent observation; consequently, permutation testing [3] is eligible for ASL data analysis at individual subject level [5]. This work reports the group analysis results based on permutation testing of ASL perfusion fMRI data at the individual level.

Materials and Methods

Imaging experiments were performed on a 3T Siemens Trio whole body MR scanner with a standard transmit/receive (Tx/Rx) head coil (Bruker BioSpin, USA). An amplitude modulated CASL perfusion imaging sequence optimized for 3.0T was used for perfusion fMRI scans [] with parameters of: labeling time = 1.6 sec, post-labeling delay = 800 ms, field-of-view (FOV)=22cm, matrix=64x64x12, bandwidth=3kHz/pixel, flip angle=90^o, TR=3sec TE=17, slice thickness 7 mm, inter-slice space 1.25 mm. Seven normal subjects with written informed consent underwent perfusion fMRI scanning for 7.2 mins with concurrent visual stimulation and self-paced right hand fingertapping. A block design was used, consisting of 3 task blocks (1.2 min each) interleaved with baseline blocks. The visual stimuli during the task state was an 8 Hz reversing black and white checkerboard. 72 control/label image pairs were obtained for each subject. High resolution 3D T1-weighted anatomical images were also obtained for each subject for spatial image normalization.

ASL data processing was performed using an SPM based ASL data processing toolbox, ASLtbx (described in another abstract submitted to ISMRM this year). Raw control/label images were realigned to the first control/label images separately. Spatially smoothing was then performed with an isotropic 3D Gaussian kernel with an FWHM of 8 mm^3. CBF images were calculated using sinc-subtraction method [4] and used for GLM based statistical analysis. Each subject's functional CBF images were randomly permuted 2000 times. GLM analyses were conducted to obtain 2000 corresponding parametric maps. A probability map was subsequently calculated by calculating the proportion of the permutation parametric map values that are no less than the original GLM parametric map value [3]. After spatial normalization, the permutation probability maps generated in individual subjects were grouped to provide a population inference through the random effect analysis (RFX) [6]. Conventional group analysis was also performed as a comparison using the spatially normalized original GLM parametric (contrast) maps. These two different analysis approaches were termed as PMU GLM RFX and GLM RFX, respectively in the following text.

Results and discussions

Table 1 lists the peak t-value and average t-value of GLM RFX and PMU GLM RFX in the same regions of interest (ROIs) determined from GLM RFX results with a threshold of P<0.0001. PMU GLM RFX yielded markedly improved sensitivity in both visual cortex and motor cortex than GLM RFX. Since the permutation probability map is independent of the activation strength, it therefore has less across-subject variability, which subsequently contributes to the higher sensitive group analysis results compared to GLM RFX. However, PMU GLM RFX can not be used to infer the activation strength alone due to the independence of activation magnitude. Combined with GLM RFX, PMU GLM RFX provides a thresholding tool for choosing the appropriate significance level to detect activated voxels corresponding to the functional tasks. Figure 1 shows several slices of the t map of PMU GLM RFX with a threshold of P<0.05 (family wise error (FEW) correction). Besides providing group inference on the activation probability, such thresholded map can be further used to mask the GLM RFX results, which never survived FWE correction for such a small sample size as 7.

Reference

[1] Wong EC, Functional MRI, 63-69, 1999. [2] Buxton R. Introduction to Functional Magnetic Resonance Imaging. Cambridge Univ. Press, 2002. [3] Nichols TE et al., Hum Brain Map, 15, 1-25, 2002. [4] Aguirre G.K et al., NeuroImage, 2002, 15, 488-500. [5] Aguirre GK et al., Int Rev Neur, 2005, 66, 213-236. [6] Holmes AP and Friston KJ, Neuroimage, 7, S754, 1998.

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Table 1. Peak t-value and average t-value within the same ROIs located in the visual cortex and motor cortex. GLM RFX means conventional GLM based group analysis; PMU GLM RFX means the permutation probability map based RFX.

Method	Visual cortex		Motor cortex	
	Peak t	Average t	Peak t	Average t
GLM RFX	20.85	6.01	12.96	5.85
PMU GLM RFX	1364.87	31.370	173.56	27.63

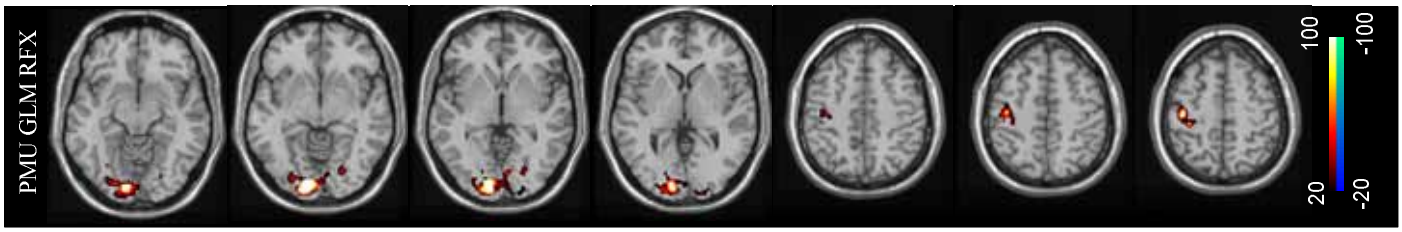

Figure 1. T map of PMU GLM RFX thresholded by P<0.05 (PWE corrected). The display window was set to 20~100 and -100~-20 for easy visualization due to the large range of t value in the suprathresholded clusters.