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Boost up the detection sensitivity of ASL perfusion fMRI through support vector machine

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Abstract- **Data analysis is challenging in arterial spin labeling (ASL) perfusion fMRI due to the intrinsic low SNR of ASL data. To boost up the detection sensitivity, this paper presented a multivariate method based group analysis approach to analyze ASL perfusion fMRI data. A spatial discriminance map (SDM) was first extracted for each subject by support vector machine learning (SVM) algorithm; a population inference about the discriminance was then given by a random effect analysis (RFX) on these individual SDMs. Evaluations were performed using 7 subjects' fingertapping ASL perfusion fMRI data, yielding similar activation patterns with enhanced sensitivity compared to the standard GLM based group analysis.**

I INTRODUCTION

ASL perfusion fMRI has been increasingly used in human brain function studies, especially those slowly changing brain functions studies [1,2,3,4] due to several superiorities compared to blood oxygen level dependent (BOLD) fMRI. Those superiorities include insensitivity to the low frequency drift of MR time series, less sensitivity to the across subject variance and better functional localization [1,4]. However, it is still challenging to process ASL perfusion fMRI data due to the intrinsic low SNR [4]. As a new modality of fMRI technique, current ASL perfusion fMRI just adopts the most widely used fMRI data analysis method, the voxel based univariate GLM method [5]. Each voxel of the whole image volume is handled separately without considering the spatial correlation between neighboring voxels. As multivariate data in nature, ASL perfusion fMRI may demand multivariate methods to boost up its sensitivity.

During the past several years, SVM has attracted more and more attentions in BOLD fMRI data analysis due to the successful brain state classifications using pre-feature selected data[7,9,10,11] or the whole brain data [8,12]. Unfortunately, no one has reported its applications in ASL perfusion fMRI. More importantly, current SVM based fMRI data analysis methods can not provide a population inference about the detected brain responses to functional stimuli. In this paper, we used SVM to explore the multivariate information structure of ASL perfusion fMRI data. Using the whole brain data, a spatial discriminance map (SDM) was extracted for each individual subject first, and a population inference about the brain state discriminance was then given by a random effect analysis (RFX). The proposed SVM based fMRI group analysis was then evaluated using seven subjects' fingertapping ASL functional data. Conventional GLM RFX was also performed as a comparison.

II THEORY

The SVM training steps for each individual subject's ASL functional data were similar to those used in [8,12]. A data reduction step was firstly applied to reduce the computation burden, followed by SVM classifier training.

A Data reduction

Standard principal component analysis (PCA) was used to extract the principal vectors and reduce the data dimensions through projecting the original data to these principal vectors. In the case of oversized dataset for computer memory space, a cascade recursive least squared network based PCA (CRLS-PCA) [13,14] can be used to sequentially extract the principal vectors.

Supposed we have an ASL perfusion fMRI data matrix $S_{N\times L}$ with one volume per column and one voxel per row. Here N and L are the number of within brain voxels and the number of timepoints, $N >> L$. Since S only has L nonzero eigenvalue associated principal vectors (eigenvectors) $E = (\mathbf{e}_1, \mathbf{e}_2, ..., \mathbf{e}_L)$, after PCA decomposition, S can be losslessly reduced to a $L \times L$ matrix $X = E^T S$, with one representation coefficient vector $\mathbf{x}_i = (x_{1i}, x_{2i}, ..., x_{Li})^T$ per column corresponding to one original image volume. These coefficient vectors are then subject to the SVM training or prediction process as stated below.

B Linear support vector machine

Consider the two class problem and label the

dimension reduced data as $\{\mathbf{x}_i, y_i\}, i = 1,...L$, $y_i \in \{-1,+1\}$ (-1 indicates task 1, +1 indicates task 2), a linear SVM [6] looks for a hyperplane $W \bullet \mathbf{x} + b = 0$ in the feature space $\Re^L$ with largest margin to separate the coefficient vectors with label +1 from those with label -1. Here, *W* is the weight vector normal to the hyperplane, which can be solved using the Lagrangian multiplier method, please refer to [6] for the solution details.

C Spatial discriminance map

The separating weight *W* described above represents the direction along which the training samples of both classes differ most. Since it has the same dimension as the training samples, this discriminance between different classes (corresponding to different brain states) can be extracted as an SDM, also called "discriminating volume" in [12]. If the training vectors $X = (\mathbf{x}_1, \mathbf{x}_2, ..., \mathbf{x}_L)^T$ are directly from the original voxel space, *i.e.*, each coordinate of the feature space is a voxel, *W* can be directly treated as an SDM, representing the direction along which the image volumes from different brain states (task 1 and 2 for the two class problem) differ most. Each voxel's value of the SDM can be then treated as a projection of the entire brain discriminance between different states to the corresponding coordinator of the feature space, with positive value meaning higher activation during the task 2 than task 1, negative value meaning lower activation during task 2 than task 1. Since the separating weight is trained as a unit, this spatial discriminance mapping intrinsically provides a spatial connected activation pattern of brain functions, carrying more information about the functional connectivity or neural coupling than standard GLM. Since the training vectors are actually from the eigenvector space spanned by *E*, the separating weight vector *W* should be mapped back to the original voxel space to get the SDM through: SDM = EW^T.

D SDM based group analysis

Population inference on the spatial discriminance can be performed using an RFX model [5], i.e., the individual SDM is treated as a random effect. By training SVM classifiers for each subject separately, this SVM based group analysis, called SDM RFX in the following texts, treats the inter-subject difference (either structural or functional) as between subject variance just like the conventional GLM RFX, instead of treating it as a potential discrimininance during the classification for all subjects' data as in the multiple subject SVM classification method [12].

III EXPERIMENT AND METHODS

A fMRI experiment

Imaging experiments were performed on a 3T Siemens Trio whole body MR scanner with an amplitude modulated CASL perfusion imaging sequence [15] (label time=1.2msec, post label delay=0.8msec, field-of-view (FOV)=22cm, 64x64x12 matrix, bandwidth=3kHz/pixel, flip angle=90° , TR=3sec TE=17msec, slice thickness 7 mm, inter-slice space 1.25 mm).

High resolution 3D T1-weighted anatomical images using the MPRAGE (TR/TE/TI = 1630/3/1100msec) sequence were additionally obtained for each subject for spatial image normalization.

Seven healthy volunteers (3 male, 4 female) gave written informed consent before scanning following an IRB approved protocol for the associated experiment. Visual stimuli with an 8 Hz reversing black and white checkerboard were presented periodically with duration of 72 sec. The subject was also asked to perform a self-paced right hand only fingertapping task during visual stimuli. Total functional scan time was 7.2 min, resulting in 72 control/label image pairs.

B Preprocessing and General linear model analysis

The functional images (72 pairs for each subject) were motion corrected, coregistered with the T1 images, and smoothed with an isotropic Gaussian filter (FWHM=8 mm) using the SPM2 software (Wellcome Department of Cognitive Neurology, London, UK, http://www.fil.ion.ucl.ac.uk). The perfusion weighted images and the CBF images were calculated from the label/control image pairs. Group analysis was performed on those individual GLM beta maps using SPM2.

C SVM based group analysis

A mask was first used to remove the outside brain voxels to reduce the computation burden. Each spatially normalized CBF image (without the outside brain voxels) was then reformatted into a column vector. These image vectors were also grand mean normalized by each subject's own global CBF value and centered before PCA decomposition. Each image vector was projected into the eigen space spanned by the extracted eigenvectors to get a representing coefficient vector.

The SVMlight software [16] was used to train a linear SVM classifier and extract the separating weight vector in this paper. The source code of this software was modified to allow reading binary image representation coefficients, and calculating SDMs.

Group analysis was performed through the random effect analysis routine provided by SPM2.

IV RESULTS

Fig. 1 shows several slices of the superthresholded spatial t maps of SDM RFX and GLM RFX, overlapped onto the same structural template. The threshold is P<0.005 (uncorrected) for both group maps. Voxels with t value greater than 10 were clipped in both maps for a better visualization, considering the large range of the t value in both maps. Note there, the red regions cover the whole green regions. Both maps yielded similar activation patterns, while SDM RFX has a little bit broader activation regions than GLM RFX and larger peak t values than GLM RFX as also listed in Table 1. An averaged t value calculated using a visual cortex ROI and motor cortex ROI was also shown in Table 1. The SDM RFX yielded higher on average t value in visual cortex and motor cortex functional foci. The difference within motor cortex is even much more significant than that within visual cortex. We also noted that the cluster corresponding to the vision task in the t map of GLM RFX is bimodal with the peak t value located in nearly the edge of the visual cortex, while SDM RFX yielded a unimodal cluster with peak t located in the center.

Table 1: Peak t value, cluster extension and within ROI average t value list of GLM based and SVM based random effect analysis results with a threshold of t>5.21 (P<0.001 uncorrected). "ext" stands for cluster extension.

	Visual			Motor		
	Peak	ext	average	Peak	ext	average
SDM	24.28	427	6.52	21.85	113	**5.57**
GLM	20.85	480	6.31	12.96	109	4.97

V DISCUSSIONS AND CONCLUSIONS

In this paper, we used a multivariate pattern recognition method, SVM, to analyze the ASL perfusion fMRI data for the first time. A spatial discriminance map (SDM) was calculated for each individual subject, and a population inference about these spatial discriminance was performed through a random effect analysis. Group analysis through conventional voxel based GLM (GLM RFX) was performed as a comparison for the SVM based group analysis.

The proposed method yielded similar activation patterns to standard GLM based group analysis, while demonstrated highly improved statistics sensitivities. This is mainly due to the match of multivariate processing and the multivariate nature of fMRI data. In another words, the activation patterns carried by SDM is detected as a whole unit instead of detecting the activation pattern on each voxel separately, which neglects the abundant coupling effect of the voxels within the activated brain regions, and these couplings can actually be used to improve the detection sensitivity in the case of low SNR signal as in ASL perfusion fMRI. Additionally, the spatial activation map detected as a whole unit could also provide a potential tool for detecting brain functional connectivities, which may be further evaluated in future work. The evaluation results also showed higher improvement in motor area compared to the visual area by using SDM RFX. One reason could be due to the ASL signal decay. Using a sequentially axial slice acquisition starting from inferior to superior, the top slices covering the motor cortex were scanned later than the bottom slices covering the visual cortex and due to the T1 decay of the tagged arterial spin, the signal magnitude within the motor cortex was also smaller than that within the visual cortex, which consequently causing a large detected activation difference between these two regions using the general linear model. Another reason could be due to the task couplings involved in the experiment. The subjects were asked to start fingertapping when they saw the flashing checking board, which introduced some functional couplings in both tasks. Due to the multivariate processing, SVM RFX could use these couplings to improve the activation detection in both regions.

Using the whole brain data, the proposed method requires no pre-feature selections, subsequently requires no a prior assumptions about activation location are required, so that the SVM based methods may provide the potentials of discovering unsuspected brain activation patterns which might provide more comprehensive understanding to the cognitive process of interest. As shown in the top right figure of Fig. 1, SDM RFX detected amygadala activations, though they are not targeted in the experiment design. Applying to ASL perfusion fMRI, the proposed SVM based group analysis method can also be used to analyze BOLD fMRI data with appropriate detrending approach for the low frequency drift of BOLD fMRI.

Although we only explored the discriminating weight of the SVM trained model, other useful information like what used in [8] can be also used in the proposed methods in future work, which may provide more insights into the mechanism of brain functions from different point of views.

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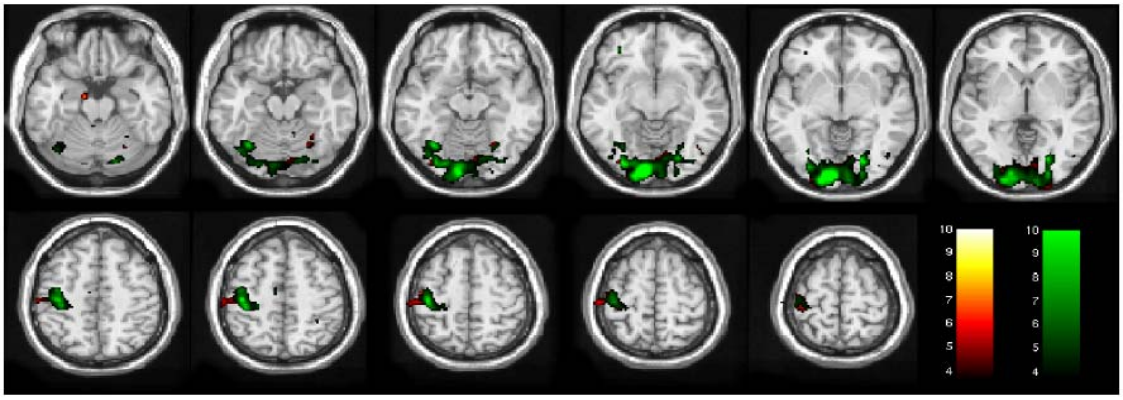

Fig. 1 Functional activation overlapped maps of SDM RFX (red) and GLM RFX (green). The display window for activation maps is 3.71-10. P<0.005 (uncorrected).