FINER DISCRIMINATION OF BRAIN ACTIVATION

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Introduction: Several recent fMRI studies have demonstrated that more information is contained in multi-voxel response patterns than single voxel [1, 2, 4]. However, conventional univariate analysis of fMRI data treats each voxel as a separate entity, totally ignoring the fine-scale patterns information contained in the local regions. Further, spatial smoothing standardly used in univariate analysis may obscure fine-scale patterns of weak effects that contain neuroscientifically relevant information. Consequently, univariate analysis always fails to detect the fine changes of the activity patterns resulting from stimulus. In the present study, a local multivariate distance mapping (LMDM) technique based on Fisher discriminant analysis (FDA) is proposed to distinguish the distinct brain activity patterns. Compared to the univariate analysis, LMDM employs Fisher's linear discriminant function (FLDF) as the statistic to discriminate the local activity patterns evoked by different conditions and map brain activation, rather than only relying on the individual voxel or combining the local information with spatial smoothing simply.

Method: For a voxel v_0 in the volume, the joint activity of all voxels within a small neighborhood $N(v_0)$ centering on v_0 constitutes a spatial pattern. Thus, the multi-voxel patterns of the small neighborhood measured in the condition X can be regarded as the data sampling from a multivariate variables $\mathbf{X}=(X_1,..., X_i,..., X_K)$, i=1, 2,…, K, where i stands for the index of the voxels in $N(v_0)$. All measurements across trials and time points under condition X construct a sample set $\mathbf{S}_X$. To find where in the brain the local activity pattern changes resulting from different experiment conditions are significantly separated, we use FLDF as the statistic to quantify the degree of separation between the response patterns **X** and **Y** which correspond to conditions X and Y, respectively. Given sample sets $\mathbf{S}_X$ and $\mathbf{S}_Y$, FDA projects them from K dimensions of space onto the discriminant axis which gives the best separation of the two sets (Fig. 1). FLDF statistic, which indicates distance or separability of the two sets on the discriminant axis, is computed as: $z = (\mathbf{u}_X - \mathbf{u}_Y)^T \Sigma^{-1} (\mathbf{u}_X - \mathbf{u}_Y)$, where $\mathbf{u}_X$ and $\mathbf{u}_Y$ are mean vectors of $\mathbf{S}_X$ and $\mathbf{S}_Y$, Σ is the pooled sample covariance matrix[1,5]. Computing FLDF for each voxel with its neighborhood, a continuous FLDF map will be obtained. Then, a permutation test is performed to obtain a map of P values of the FLDF statistic. fMRI data is resampled 1000 times in such way that the spatial patterns of the data are unaltered, but their temporal sequences are randomly permuted. To account for multiple comparisons, the P map from randomization is thresholded to ensure the average FDR will not exceed q = 0.05.

Experiment: Subjects (six normal adults) continually fixated on a central cross while viewing picture of faces or houses (3 face blocks & 3 house blocks). Each block lasted for 30s and has 20 pictures. Each picture was presented for 500ms. Baselines (crosshair fixation) lasted ~10 seconds. Whole brain fMRI data were acquired with a T2*-weighted gradient echo EPI sequence (slice thickness=4mm, TR =2000ms, FOV=240×240mm, matrix = 64×64).

Results: After being preprocessed, fMRI data were analyzed using GLM with no smoothing, GLM with Gaussian kernel (GK) of FWHM = 9mm smoothing and LMDM with K=27 voxels (v_0 and its 26-connexity neighborhood). As expected, all three approaches found the major blobs of brain activity evoking by the experiment conditions (face and place regions; [2, 3, 4]) (Fig. 2). It could be observed that univariate GLM analysis with no smoothing roughly localized the activated regions, whereas the activation maps showed salt-and-pepper phenomenon seriously (Fig. 2a). Smoothing the data with GK resulted in the clean maps and foci regions of activations (Fig. 2b). However, LMDM highlighted more voxels which were extended alongside the region of activations detected by GLM. The outcomes indicate that there are many voxels containing the effects related to the experiment conditions in fine-grained structure of the activity patterns (Fig. 2c). The univariate GLM with GK smoothing failed to detect these voxels because the fine-scale information was discarded when the data were smoothed. Across the subjects, activation regions detected by LMDM were all more extended than that detected by the GLM. But there were some varieties among subjects because at the fine spatial scale of millimeters with no spatial smoothing, activity patterns are unique to each individual. How to do multi-subject group averaging at fine scale is still an open issue, and will have to be investigated further.

Conclusion: Results from real fMRI data demonstrated that our LMDM method could dramatically increase the sensitivity of detection of fine-scale brain activity patterns which contained subtle information about the experiment conditions and showed distributed structures.

Reference: [1] Carlson, T. A. et al. J. Cogn.Neurosci. 2003; 15(5):704–17. [2] James V. Haxby et al. Science 2001; 293(5539) :2425-30.. [3] Kanwisher N. et al. Journal of Neuroscience 1997; 17(11):4302–11. [4] Nikolaus Kriegeskorte et al. PNAS 2006; 103(10):3863–68. [5] William F. Auffermann et al. NeuroImage 2002; 17(2): 583–91.

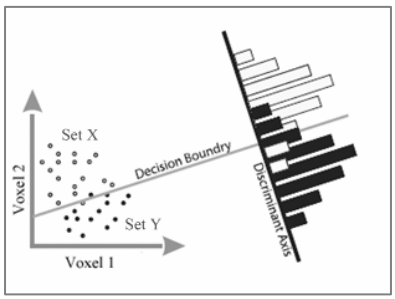

Fig. 1: FDA projects two-class samples onto the optimal discriminant axis (shown for the first two dimensions).

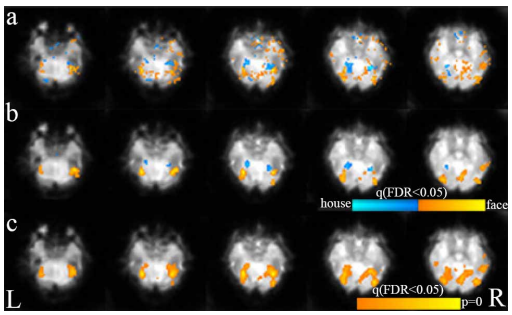

Fig. 2: Activation maps for an individual subject. (a) t maps from GLM with no smoothing, (b) t maps from GLM with GK of FWHM = 9mm smoothing, (c) FLDF maps from LMDM with K = 27 voxels.