Analysis of event-related fMRI data by incorporating physiological information in HDR models

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Introduction

Analysis of functional magnetic resonance imaging (fMRI) data has been performed using both model-driven (parametric) methods and data-driven methods. An advantage of model-driven methods is incorporation of prior knowledge of spatial and temporal properties of the hemodynamic response (HDR). Most statistical methods which analyze at an individual voxel level estimate, by performing tests, the probability that the time series of a single voxel being "different" from the null hypothesis of no response. The aim of this work is to develop a novel framework for fMRI data analysis that uses *a priori* knowledge of both the experimental paradigm and HDR to detect activation on a regional, rather than single voxel, basis. A clustering algorithm is proposed in which distances are based on parameters estimated when a chosen HDR model is fit to the time series. The benefit of this approach is the likely reduction of false detections, thereby producing "cleaner" activation maps.

Methods

Experimental details: The proposed method was tested using data from visual fMRI experiments conducted at the Indiana University School of Medicine using a 1.5T General Electric Signa LX Horizon imager. A visual surface coil was used to obtain 270 images of each of 10 slices (3.8mm thickness), perpendicular to the Calcarine fissure. Imaging was effected using a spiral echo-planar imaging (EPI) sequence (TR/TE=1000/40ms; FOV=24cm^2; acquisition matrix=64x64; flip angle=90°. A standard flashing checkerboard was presented to either the left of right visual hemifield of the subject in an alternating fashion.

Analysis procedure: The fifth slice of the experimental data was chosen based on a t-test map (Figs. 1, 2) generated for a blocked paradigm (30s ON, 30s OFF) conducted for the same subject in the same imaging session. The baseline and drift components (up to second order) of the magnitude signal were removed as a preprocessing step. Subsequently, the contrast-to-noise ratio was improved by averaging across trials (of 15s duration) for each stimulus. Brain voxels were identified from non-brain voxels by the strength of the baseline component, which was restored before fitting the model. As an initial implementation, the Gamma Variate model [1] was chosen to fit the time series for each brain voxel.

$$h(t;\delta,\tau) = x_0 + A\left(\frac{t-\delta}{\tau}\right)^2 e^{-\left(\frac{t-\delta}{\tau}\right)} u(t-\delta) \qquad (1)$$

u(.) is the unit step function. The physical significance of the parameters is: x_0−baseline signal, A−amplitude, δ−delay from stimulus presentation to onset of response and τ−spread i.e., half the delay from onset to peak of response. Non-linear regression using STATA software [2] was performed on an individual voxel basis to estimate the model parameters. The estimated parameters were used to generate an ideal response signal (using Eq. 1) at each brain location. During this process, voxels for which the correlation between ideal response signal and averaged measured signal dropped below a specified threshold were discarded. In addition, voxels were discarded whose parameters did not satisfy the feasibility constraints − $0 \le \delta \le 5$ (up to 5s delay to onset); $0 \le \tau \le 4$ (up to 8s lag from onset to peak); and $0.2\% \le A/x_0 \le 5\%$ (i.e., signal change as % of baseline). Finally the voxels were clustered on the basis of correlation of their computed ideal response signal (normalized by baseline).

Results

For stimulus 1 (right visual hemifield), a correlation coefficient (cc) threshold of 0.4 yielded six voxels at the clustering step. These were subsequently clustered and the cc between the ideal response signals for every pair of voxels in the red cluster was at least 0.95. The resulting three clusters are shown in Fig. 3. For stimulus 2(left visual hemifield), a cc threshold of 0.83 yielded eight voxels at the clustering step. (The data were strongly correlated for stimulus 2 for the chosen imaging session.) These eight voxels yielded two clusters as shown in Fig. 4 such that every pair of voxels in the orange cluster had cc≥0.96.

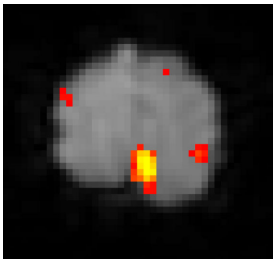

Fig.1: t-test map ($p<10^{-6}$) for stimulus 1.

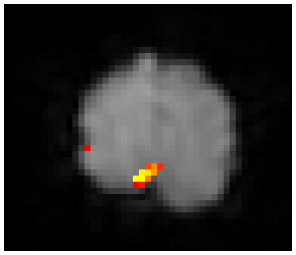

Fig.2: t-test map ($p<10^{-6}$) for stimulus 2.

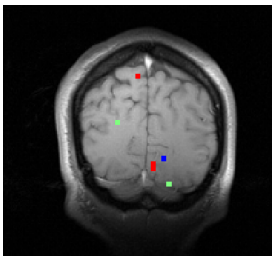

Fig. 3: Clusters obtained for stimulus 1.

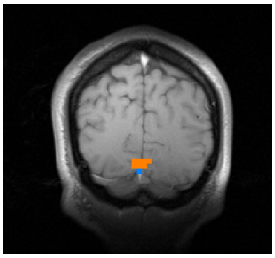

Fig. 4: Clusters obtained for stimulus 2.

Discussion

The results of the proposed procedure are consistent with the t-test activation maps which are used as a "gold standard" for comparison. Visual inspection of the obtained clusters indicates spatial contiguity although it was not enforced. The identification of activation maps is based on a parameters of a model fit to the data, rather than statistical parameters. Meaningful interpretations of the parameters of the model permit the estimation of an average response for the clusters showing activation, thereby characterizing the HDR completely. The procedure also permits the observation of co-activation (absent in the chosen data set) between different regions of the brain for the same task. Correlation could be replaced by a more appropriate distance metric that enforces spatial constraints on clusters. Identification of the cluster for activation could be defined in a more rigorous fashion, enabling a higher confidence in the results.

Conclusions

This work has presented a technique for activation detection in fMRI data using parametric modeling of the HDR. It exploits prior knowledge of the stimulation paradigm and properties of the HDR. Physiological constraints have been enforced (for the first time) on the HDR through the parameters. The results are consistent with the t-test maps. The framework allows further incorporation of more complex HDR models to impact the fitting process and subsequent identification of areas of common activation throughout the cortex, increasing confidence in the measured location and extent of activation.

References

1. Dale AM, Buckner RL, *Hum. Brain Mapp.*, **5**, 329-340, 1997.
2. StataCorp LP, College Station, TX, *http://www.stata.com*.