Assumption Free Analysis of fMRI Data Sets

B. B. Biswal[1], D. Ward[2]

[1]Radiology, UMDNJ, Newark, NJ, United States, [2]Biophysics Research Institute, Medical College of Wisconsin, Milwaukee, WI, United States

Introduction

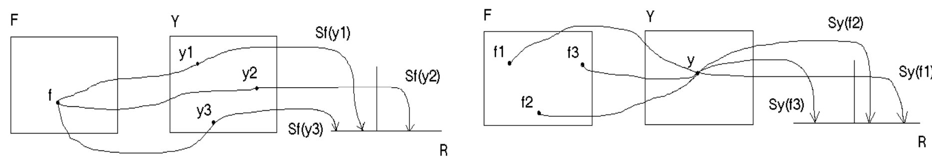
A large number of statistical tests (including t-test, cross-correlation, F-test, deconvolution, etc.) are currently used in functional Magnetic Resonance Imaging (fMRI) to localize and quantify task-induced signal changes. These statistical tests are subject to a number of assumptions including: i) errors are independent (no temporal autocorrelation of the noise); ii) the noise has a Gaussian distribution with constant variance; iii) the distribution of the noise is homogenous throughout the brain; iv) the statistical model utilized is adequate to account for task-induced signal changes. Violations of any of these assumptions will lead to unreliable (either over or under) estimation of significance levels. In this study, we have developed a novel method for detecting and estimating task-induced signal changes without making assumptions about the nature of the measured response under the null hypothesis.

Theory

In functional MRI it is currently believed that changes in the signal intensity during task activation reflect regional changes in blood flow and oxygenation. Thus, presentation of a stimulus/paradigm leads to a concurrent increase in signal intensity in the appropriate eloquent cortex. Statistical tests are then performed relating a fixed input function with the measured output function, and a probability of significance determined. If the relationship is found to be significant, it is assumed that output was caused by input. However, this approach does not establish causality, since the standard methods only establish that the model tested is better (in a statistical sense) in explaining the variation in the data. A number of other assumptions are often made, such as: no temporal autocorrelation of the noise; homogenous Gaussian distribution of the noise throughout the brain; and the adequacy of the model itself. Although attempts have been made to mitigate these assumptions, but they have generally introduced new assumptions in the process.

Using Classical statistical techniques, the input function is taken as fixed and multiple output functions are used (from different voxels) to generate a statistical significance. In the method proposed, the output data is taken as fixed, while input function is taken to be a realization of a random process. Given the measured output, a large number of “test” input functions are generated which are consistent with the actual input function. These test input functions are used to calculate statistics and significance level on a voxel-by-voxel basis.

This yields the distribution of the parameter of interest under the null hypothesis. Using this, a significance level can then be assessed for the actual input and measured output functions, which allows us to reliably determine if the causal relationship is significant. In contrast to traditional statistical methods, this method is unbiased.



Method

To test the validity of this method both computer simulation and actual human data were used. Comparison was done between classical methods (cross-correlation and F-test) and the proposed method, while the data set had non-homogenous distribution of errors, non-constant variance, temporal dependence. Four healthy volunteers (3 M, 1F) were scanned after written informed consent was obtained. This study was approved by the IRB at this institution. Images were obtained using a GE Signa 1.5T imaging system. Single shot gradient echo (GE) axial EPI images (64×64, TR=2s, TE=27.2 ms, FOV= 24 cm, slice=7 mm, 3 slices) were acquired over 288 seconds. The scan was obtained while subjects were instructed to perform bilateral finger tapping for 30 seconds, alternating with 30 seconds of rest. For the second scan, a binary random stimulus with equal number of zeros and ones were used.

Results

For all the simulations performed it was observed that the proposed method was able to more reliably detect task-induced signal changes. Figure 1(a) and (b) show the performance of a traditional statistical tests compared with the proposed method, when the measurement noise has temporal autocorrelation (in fact, it is a first order autoregressive process). It is seen that the proposed method yields a much more accurate evaluation of the statistical significance than traditional methods.

For all four subjects, it was observed that activation map generated using both cross-correlation and F-test method could reliably map the sensorimotor and its associated cortex. Very few voxels (<5) were present outside of the sensorimotor cortex. Further these voxels were randomly distributed without belonging to any fixed anatomical location. Using traditional analysis it was seen that although activation map in the sensorimotor cortex was apparent, a number of voxel near the sagittal sinus passed the threshold.

Discussion

This study demonstrates an unbiased methodology for detecting and estimating task-induced signal changes. Experimentation with bilateral finger tapping and calculations suggests the usefulness of this method for fMRI analysis. Using computer intensive methods, accurate statistical parameters can be obtained without making any assumptions used by traditional statistical methods that are not always true.