A Multivariate Approach to fMRI-Based Subject Discrimination

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Introduction

A novel multivariate approach to between-subject analysis based on the application of PCA to n-way fMRI data is presented. Our technique is compared to traditional univariate fMRI analysis and is shown to discriminate between subject groups in a two dimensional space without the use of a priori knowledge of the stimulus. Univariate analysis of fMRI data relies on an input stimulus time course from which voxels with statistically significant correlations to the input can be found. This approach has been successfully applied to test many physiological hypotheses. However, its efficacy is completely reliant on physiological a priori knowledge. Recently, there has been a large body of research devoted to data-driven analysis of fMRI. Typically, blind source separation techniques such as ICA have been applied to "tease out" physiological processes which are assumed to be independent and linearly mixed. These independent sources can then be used to test physiological hypothesis. However, it is also possible to use data-driven approaches to perform discrimination between subject groups in a physiologically relevant sense without the decomposition (or knowledge) of the underlying biological process. Herein we apply PCA for the sole purpose of providing a subspace in which we can discriminate between two subject groups. Our goal was to show the utility of the method for a general class of problems where subject discrimination in fMRI is desired (for example, normal vs. abnormal spatiotemporal BOLD activation).

Method

To test our approach, we hypothesized that men and women would exhibit different spatiotemporal BOLD activation when shown the same sequence of faces of both men and women (some attractive, some not). Using a traditional univariate approach, detecting a difference would be quite challenging. Our approach used a simple paradigm – we showed each subject a sequence of 50 faces (randomly male, female, attractive and unattractive) with durations of 4 seconds each. In order to compare this with a traditional analysis, we inserted two rest phases of 30 seconds each – one at the beginning and one after half of the faces had been presented (thus providing a simple block design). Using multi-way linear algebra, we formed each row of a multi-subject data matrix from the concatenation of each subject's intensity volume (expressed as a vector) at all time points. Thus each row was (t x v) in length for t time points and v voxels. PCA was then performed on this n by (t x v) matrix where n denotes the number of subjects. Each row was normalized to unit variance and the subject-wise mean was removed from each row. Each subject's row vector was correlated with the two eigenvectors of the covariance matrix of the data with the largest eigenvalues. This provided a two-dimensional representation of each subject's fMRI data. Our study used 6 subjects, 3 male and 3 female and gathered a 64 x 64 x 28 (3.75 x 3.75 x 4 mm resolution) volume of the brain at 130 time points with TE = 35 ms and TR = 2 seconds. Data was acquired using a GE 3T Signa HD scanner with 8 parallel receivers (GE Healthcare, Milwaukee, WI). For comparison, we also applied the same PCA approach to a previously conducted fMRI experiment where 3 subjects (all male and right handed) performed a block design of finger-tapping (30 second on, 30 second off, 64 x 64 x 28 volume at 90 time points with TE = 35 ms and TR = 3 seconds) in both the morning and evening. Here we hypothesized that despite a self – professed propensity for morning or night alertness from the subjects, there would be no difference in spatiotemporal BOLD activation. Again, with PCA, we found 6 two-dimensional data points (AM and PM measurements for each subject).

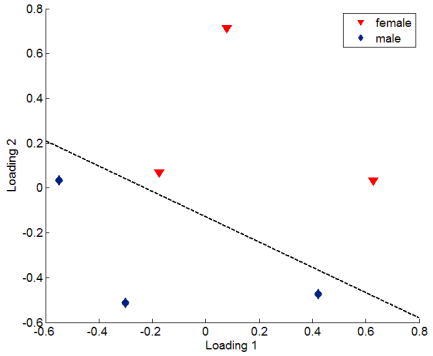

Figure 1. Loadings for females and males viewing faces (note that they are linearly separable)

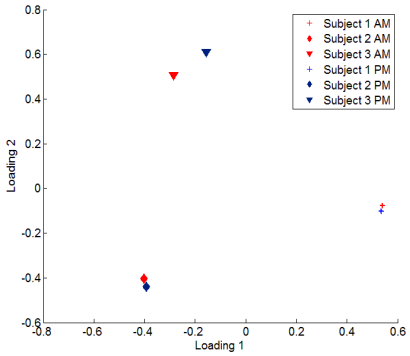

Figure 2. Loadings for 3 subjects performing finger tapping in the AM and PM

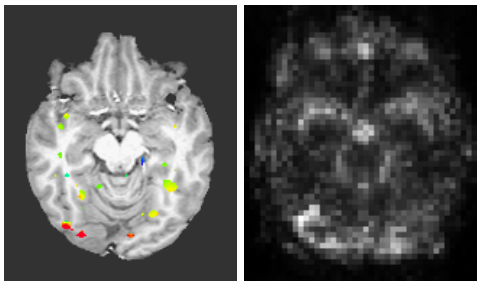

Figure 3. Activation in the right Fusiform Gyrus (a) T-test at each voxel (red indicates ~ 2% difference between males and females) (b) Variance of the time series at the slice in (a) from the first Eigenvolume.

Results & Discussion

As expected, a standard univariate analysis yielded a statistically significant activation in the right Fusiform Gyrus for both males and females. Additionally, a t-test at each voxel showed a 2 percent larger response (at p = .05 confidence) for males in a small area of the right Fusiform Gyrus (**Figure 3 (a)**). It is difficult to draw a significant conclusion from this analysis. However, our multivariate analysis resulted in a clear grouping of male and female subjects in the 2 dimensional loadings plot shown in **Figure 1**. The data is linearly separable, illustrating that our technique provides a data distribution of low "complexity". Assuming a uniform distribution of points throughout the two-dimensional space, the probability that the 6 points would group as they did by chance alone is only 5 %. As a further confirmation of the efficacy of the technique, **Figure 2** shows that when we expect there to be no significant differences in spatiotemporal activation (such as finger tapping performed in morning and evening) we see a close grouping of points in the loading space. **Figure 3 (b)** illustrates the variance of each voxel from the first eigenvolume at the same slice as **Figure 3 (a)** for the face experiment. Clearly, the major region of variation found from PCA is similar to the traditional analysis. However, in general, it is fallacious to attribute a specific physiological process to this variance, since it is the space spanned by the eigenvolumes which is relevant for the purposes of discrimination. In fact, an identical result would be obtained with any rotation of the eigenvolumes in the two-dimensional space, including the use of ICA in the reduced space. It is this lack of ability to attribute the results to a specific hypothesis about complex neurophysiology that gives the technique its power. This work illustrates that we can potentially perform clinically significant discrimination with a "black box" view of the underlying physiological process.