Biological Parametric Mapping

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Introduction

Functional MR imaging (fMRI) has revolutionized the field of neuroscience and has emerged as a widely used research tool for the probing of neural function. Over the last several years additional functional imaging modalities have emerged including diffusion tensor imaging (DTI), perfusion imaging, T2 mapping, Voxel-based morphometry (VBM) and 3D spectroscopic imaging. Analysis methodologies, however, have remained modality specific. That is, analysis for each form of functional imaging data has proceeded to develop specific to that imaging modality. We describe a novel form of multimodal integrative image analysis called biologic parametric mapping (BPM). The basic idea behind BPM is to probe functional imaging data using biological measures from other imaging methodologies. We introduce the first version of our BPM toolbox that allows correlation, ANOVA and ANCOVA analyses of multimodal data sets, and present examples based on simulated and in-vivo data. The BPM toolbox probes functional imaging by using images from other modalities as regressors in a massively-univariate analysis.

Materials and Methods

The BPM toolbox was developed entirely in Matlab. It was designed to only use routines available in the standard Matlab distribution, and does not require any additional Matlab toolboxes. The BPM toolbox has a high degree of integration with SPM (1), and makes use of basic SPM I/O calls for file reading and writing, reslicing and smoothness estimation. Statistical estimation was implemented in the software application using the general linear model (2).

The main program is called from the Matlab command line by entering wfu_bpm. This brings up a user-friendly GUI that prompts the user for all analysis specific parameters. These include type of analysis (correlation, ANOVA, ANCOVA), number of imaging modalities (i.e., fMRI and VBM), and number of non-imaging regressors. The user then selects the images for each portion of the analysis. For simplicity, these can be provided as text files that contain the respective image filenames. The program then constructs the design matrix, and performs the computations on a voxel-wise basis, generating Beta maps to be used later during contrast specification. The BPM toolbox reads and writes Analyze format images. However, since the SPM I/O calls are used, it can theoretically read and write any format that the SPM read/write functions allow.

The major conceptual difference between the BPM analysis and a conventional SPM-style analysis is in the nature of the design matrix. In a conventional SPM analysis, the same design matrix is applied to each voxel. In the BPM analysis, the design matrix varies for each voxel. For example, in a correlation analysis using SPM, the same scalar correlation regressor is applied to each voxel in the primary modality. In BPM, the correlation regressor is dependent on the second imaging modality, and varies at each voxel. This is similar for a BPM ANCOVA analysis, in which the design matrix varies at each voxel based on the additional modalities. In order to permit flexibility in the specification of contrasts after statistical estimation, information on each voxel's design matrix is stored for later retrieval.

In order to facilitate viewing in the SPM software environment, a SPM insertion tool was created. This program takes any T-map and creates the appropriate files to allow the map to be viewed using the SPM result selector (i.e., SPM.mat). This allows for the use of the standard SPM viewing and statistical inference tools to examine the output of the BPM analysis.
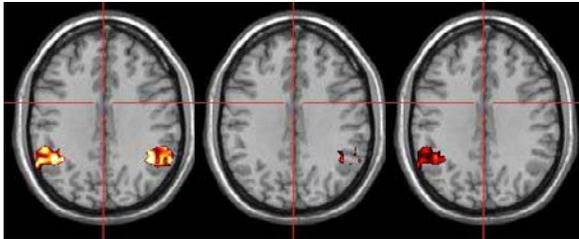

Figure 1 Results for simulated data. Left panel represents fMRI, middle panel is VBM, and right panel is BPM ANCOVA. (All data corrected at FDR of 0.05).
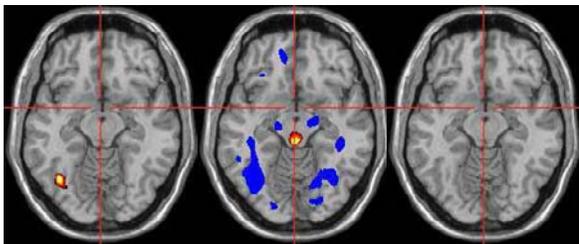

Figure 2 BPM results for a dyslexia study. Left panel represents fMRI, middle panel is VBM, and right panel is BPM ANCOVA (displayed at P< 0.001).

To illustrate the power of the BPM approach, we applied BPM to simulated and in-vivo data. In the simulated data example, two groups (12 subjects each × 2 modalities) of images (46×55×37 voxels) were generated from a Gaussian normal distribution with mean 0 and variance 1. A representative total brain mask was used from a previous in-vivo analysis to restrict the analysis. Activations were added to two regions (right and left parietal), and correlation of 0.8 between the first and second modalities was artificially created in the right parietal area. In the in-vivo data example, BPM was applied to compare two groups (15 dyslexics and 13 normals) of fMRI mages with corresponding grey matter VBM images as a covariate.

Results

The simulation results are shown in Figure 1. The left and middle panels demonstrate the results of the ANOVA analysis for each modality separately. The right panel shows the results of the BPM ANCOVA. The activation detected by ANOVA in the first modality (right parietal) was regressed out by the signal detected in the second modality. All images are corrected for multiple comparisons at FDR p<0.05.

The in-vivo results are shown in Figure 2. The left panel demonstrates a group difference in brain function in the left temporal lobe. The VBM demonstrates group differences in the temporal lobes bilaterally. The BPM ANCOVA analysis, however, demonstrates that the left temporal activation seen on the fMRI is explained by the variance in the grey matter differences in this region.

Conclusions

The BPM approach overcomes the modality specific nature of current analysis methodologies. It allows the use of information obtained from other modalities as regressors in a voxel-wise analysis, thereby allowing for more sophisticated scientific questions to be answered. In addition, the BPM toolbox has a high degree of integration with the SPM software package, and the SPM insertion tool feature permits the use of the SPM statistical inference and visualization tools.

References

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