Are two tasks better than one?: Multi-task coupling of fMRI independent sources in schizophrenia

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Introduction

We propose a method to jointly analyze data from two different fMRI tasks, collected on the same individuals, which are "coupled" together by a shared loading parameter. We demonstrate our approach on a data set derived from healthy controls and schizophrenia patients, each of whom performed an auditory oddball task and a Sternberg working memory task. Results reveal one component that demonstrated significantly decreased connectivity in patients including temporal, frontal, thalamic, basal ganglia and cerebellar regions which have been implicated in several previous models of schizophrenia. Two dimensional task-by-task histograms of the identified voxels were consistent with increased task-specialization in controls (the between-task correlation was greater in patients). Such an approach can provide a more complete picture of the fMRI activation maps than subtractive analyses and enables new questions to be posed about fMRI data from multiple paradigms.

A functional MRI session often involves scanning participants during the performance of multiple tasks. Typical analysis approaches do not directly examine the joint (shared) information between different tasks, even though it makes intuitive sense that fMRI activation in different tasks for the same individual will contain some shared information (although not necessarily in the same voxels). A natural set of tools that avoid this problem include those that transform data matrices into a smaller set of modes or components. Such approaches include those based upon singular value decomposition [1] as well as more recently, independent component analysis (ICA) [2]. We introduce the idea of a second level, *feature-based* analysis of the fMRI activation maps (the features) generated from a first-level analysis. We propose a method that enables the decomposition of activation maps generated from two cognitive tasks into joint, maximally spatially independent components.). Examination of joint information between tasks may well reveal previously hidden relationships, explain some of the variability seen in existing research, and provide a more comprehensive understanding of brain function.

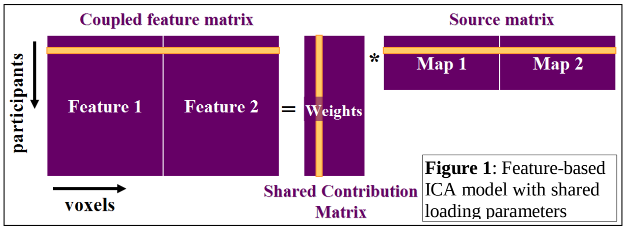

Figure 1: Feature-based ICA model with shared loading parameters

Theory

Our approach involves computing a set of joint parameters from different tasks. The standard ICA model attempts to estimate a source matrix, S=WX, which is unmixed from the data. One could estimate two W matrices (one for each task), but to interpret both results together, these matrices would then have to be combined somehow as they are computed independently of one another. Using a data-fusion approach, however, we compute a single optimal unmixing matrix that maximizes the joint likelihood function, $w^* = \arg\max_w \log p\left(x^{(1)}, x^{(2)}; w\right)$ and hence maximally uses the available information. It makes intuitive sense *not* to compute the parameters independently, since the activation maps from the two tasks are derived from the same participant. Thus we have a single W which fuses together the joint source (or, alternatively, basis vector common to the two tasks). One may use existing ICA analysis algorithms to perform a joint analysis by simply forming the overall data matrix by stacking features next to one another (see Figure 1). The identification of components with shared loading parameters, and the comparison of the associated maps, is a key means to identify couplings between brain image components of different tasks.

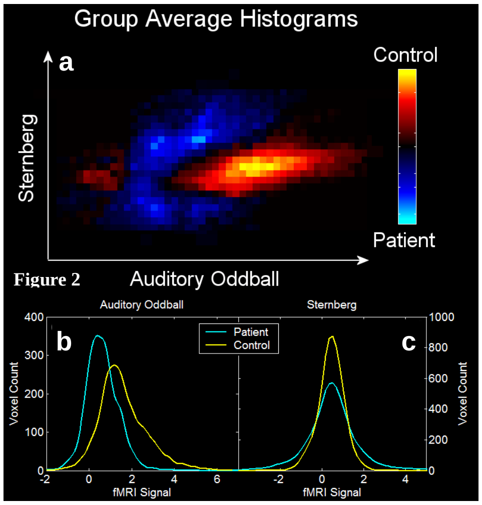

Figure 2

Methods

Fifteen healthy participants and fifteen outpatients with chronic schizophrenia provided written, informed, IRB-approved consent at Hartford Hospital. Participants were matched for age and gender and all were scanned on two fMRI paradigms [an auditory oddball task [3] (AOD), and a Sternberg working memory task [4] (SB)]. Both tasks have been found to show activation differences in schizophrenia patients. Scans were acquired on a Siemens Allegra 3T dedicated head scanner equipped with 40mT/m gradients and a standard quadrature head coil. Gradient-echo echo-planar-imaging functional scans were acquired (TR=1.86s, TE=30ms, FOV=24cm, matrix=64×64, flip=60°, slice thickness=3mm, gap=0.5mm, 36 slices, ascending acquisition). Scans were motion corrected, spatially normalized, and smoothed using SPM2.

Results

Only one component demonstrated significantly ($p<0.00044$) different loadings in patients and controls (loading for controls was higher than that for patients). Different spatial locations were identified for activation associated with the two tasks. For display, auditory oddball and Sternberg sources were converted to Z-values and thresholded at $|Z|>3.5$. The AOD tasks showed only regions with increases (including temporal lobe structures and cerebellum) and the SB task showed some regions with increases (basal ganglia, cerebellum) and others with decreases (visual cortex and occipito-temporal regions. Group-averaged joint histograms from the regions identified in the two tasks are presented in Figure 2a and the marginal histograms for the AOD and SB tasks are presented in figure 2b/c. In general, more AOD task voxels were active in the controls and the SB task showed an increased kurtosis for the patients (the number of voxels which were increased or decreased was greater). We also found significantly more correlation of activation between the two tasks in the patients ($p<0.000085$).

Discussion

Our novel data analytic approach revealed two important findings in the data that were undetected with traditional analyses. First, consistent with our hypotheses, schizophrenia patients demonstrate "decreased" connectivity in the joint network identified using the jICA approach. This network includes regions in temporal lobe, cerebellum, thalamus, basal ganglia, and lateral frontal regions, and these findings are consistent with both the cognitive dysmetria [5] and fronto-temporal disconnection [6] models. The current analysis reveals a single network, including portions of all of the regions mentioned above, which is diminished or attenuated in activation amplitude. This supports the idea that the pathophysiology of schizophrenia includes impaired brain connectivity [7]. A second finding is that for the voxels identified by the jICA analysis, the correlation between the two tasks was significantly higher in patients than controls. The degree to which a brain activation map is different from that of another task may reflect the degree to which performance on a task is "specialized" to a certain set of regions. A possible synthesis of both findings is that patients are activating less, but also activating with a less unique set of regions for these very different tasks. This is consistent with both a global attenuation of activity as well as a breakdown of specialized connections between anatomical regions subserving different cognitive domains.

We have demonstrated a novel method for examining joint activation across multiple tasks. This approach has enabled us to ask novel questions about fMRI data and provides a way to potentially help us gain a more complete understanding of brain function using different cognitive probes to elucidate how brain networks are shared between tasks.

References

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