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A Combined SPM-ICA Approach to fMRI

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***Abstract*-Independent component analysis (ICA) and statistical parametric mapping (SPM) are two commonly used methods of analyzing fMRI measurements. Typically, these methods are applied separately to the measurements to produce brain maps indicating active brain regions in response to a stimulus or a performed task. However, ICA can also be used to develop a hemodynamic response model that can be used as a regressor in SPM of fMRI measurements. This may lead to a more accurate method of localizing brain activity that corresponds to performing a task or to various pathologies. In this study, BOLD fMRI data were acquired from a subject performing a finger flexion task in a block design paradigm. Both spatial and temporal ICA was performed on the subject's BOLD fMRI measurements. Two hemodynamic response model signals were generated from ICA results to use as regressors in SPM of the subject data. IC maps and SPM-generated brain maps of the subject data using the canonical hemodynamic response model and the ICA-derived models were compared. In all cases, there was significant overlap in voxel activations.**

I. INTRODUCTION

Both independent component analysis (ICA) and statistical parametric mapping (SPM) are two existing methods of examining signals measured from the brain using blood-oxygen-level-dependent (BOLD) functional magnetic resonance imaging (fMRI) [1]. These types of analyses have typically been applied separately in fMRI studies, but the techniques can be combined.

A. Independent Component Analysis

ICA is a powerful technique that can be applied to systems that can be modeled as a mixture of source signals generated by statistically independent physical processes [2]. For instance, a signal measured in one voxel of an fMRI session may be comprised of activity from head motion, machine artifacts and cognition. In ICA, it is assumed that these component processes sum together in a linear fashion resulting in the mathematical model of ICA [3]

$$\mathbf{x} = \mathbf{A}\,\mathbf{s}\,. \tag{1}$$

Matrix **x** is the matrix of observations from each recording site, such as one voxel in an fMRI scan. Each row of **x** corresponds to measurements from one recording site and each column is a time sample. Matrix **s** contains the desired independent components where each row is one component. Components in **s** and observations in **x** are treated as random variables [3]. Matrix **A** is known as the mixing matrix that contains coefficients that mix source signals together in an unknown process. Both **A** and **s** are unknown, so the system must be solved by exploiting the statistical independence of each row of **s** [2, 3].

Methods that solve the ICA system of equations maximize or minimize objective functions that result in independent components. The objective functions implicitly exploit the Central Limit Theorem that states that the probability density function (pdf) of a sum of independent random variables becomes more Gaussian with increasing numbers of random variables in the sum [3]. To find each independent component in **s**, the inverse of the **A** matrix that produces independent components that are the least Gaussian is computed. The inverse of the **A** matrix is also known as the **W** matrix.

Several measures of nongaussianity are available. The measure of nongaussianity used in this study taken from information theory is known as entropy [3, 4]. Entropy is the average amount of information about a random variable that is not known [3]. The entropy of a continuous random variable y is [3]

$$H(y) = -\int p(y)\log(p(y))dy\,. \tag{2}$$

The function p(y) is the pdf of y. Computing independent components using entropy can be performed if the system is analyzed from a neural network perspective [3, 5, 6]. Neural weights in the **W** matrix are updated in an iterative fashion to achieve an optimal objective function result that is some measure of entropy in the ICA algorithms used in this study [3, 5, 6].

B. Statistical Parametric Mapping

Inferring results based on the SPM of fMRI measurements is another popular method of locating brain activations. This method contrasts with ICA in that it is based on hypotheses that are made about the data while ICA is a blind source separation technique that does not assume the data takes on any predetermined form [1]. This technique also involves a linear model given below [7].

$$\mathbf{Y} = \mathbf{G}\boldsymbol{\beta} + \boldsymbol{\varepsilon} \tag{3}$$

The matrix **Y** contains the fMRI measurements from each voxel (row of **Y**) sampled at every repetition time (column of **Y**). The **G** matrix is known as the design matrix that contains rows of functions called regressors that are intended to model the different signals the researcher expects to see in the fMRI recordings [7]. For example, these signals can model drift, high frequency noise and the signal of interest from the experiment [7]. The **β** matrix contains parameter

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estimates that are calculated when a statistical analysis has completed [7]. Parameter estimates indicate how closely a particular regressor matches the activity recorded in a voxel. The parameter estimates calculated are those that minimize some objective function such as ordinary least squares [7]. The remaining $\boldsymbol{\varepsilon}$ term contains error values that account for any differences between the measured BOLD signal intensities in $\mathbf{Y}$ and those accounted for by $\mathbf{G\beta}$ [7].

The regressors designed to represent the signals of interest are challenging to produce. Typically these signals are created by convolving a stimulus function with a hemodynamic response function [7]. The stimulus function is a boxcar function when the subject undergoes a block design fMRI experiment that has alternating periods of rest and task performance [1, 7]. The signal resulting from convolution ideally resembles the BOLD response the researcher is expecting in regions of the brain that are active during periods of task performance [7].

In order to determine the statistical significance of the parameter estimates, a t-test is performed. The t-test conducted in this study assesses whether the signal measured in a particular voxel during the task period is significantly different from resting brain activity [7].

II. METHODS

BOLD fMRI measurements were collected from a single healthy subject. An interleaved gradient echo-planar imaging sequence was performed using a 3.0T scanner (GE Sigma, Waukesha, WI) with the following specifications: 20 axial slices, 5mm slice thickness, 24cmx24cm FOV, single slice matrix 128x128 voxels, 1.875mmx1.875mm in-plane voxel area, 3.0sec two-shot repetition time (TR). The subject was instructed to perform a right hand finger flexion task for 12 seconds followed by 24 seconds of rest. The session began with the task block following a suitable amount of time for the scanner to reach steady state. The subject performed this block task for 5mins 24secs resulting in 108 time samples.

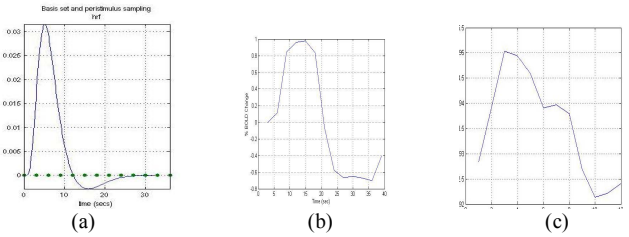
The measurements were preprocessed in order to properly acquire independent components. The image files had their slice timings adjusted first using SPM5 (Wellcome Dept of Imaging Neuroscience, London, UK). The slice timing adjustment aligns the BOLD signal time courses from each slice during one TR so that they appear to have been acquired simultaneously rather than consecutively [7]. This is necessary for a proper statistical analysis of the data as any delay in the measured signal in any voxel when comparing them with a hemodynamic response model will yield false positive and/or false negative results [7]. The output image files from SPM5 were then further preprocessed using FSL3.2β (fMRIB Analysis Group, Oxford, UK). FSL was used to high pass filter the data with a cutoff period of 120secs, spatially smooth the data with a Gaussian kernel of FWHM 8mm, do a brain voxel extraction and perform motion correction.

The subject went through the task-rest cycle nine times during which 12 time samples were taken each cycle. Slices acquired at the same time point in each cycle were averaged together using MATLAB 7.0 (Mathworks, Natick, MA) and the resulting images were run through fMRLAB (SCCN, San Diego, CA) to extract spatial ICs. The averaged images from 5 slices containing the expected brain region of interest were used as input to the FastICA software program (HUT, Helsinki, Finland) to extract temporal ICs. Averaging each cycle together will improve the BOLD signal SNR and allow a single cycle time course from task-related independent components to be extracted for use as described later. Twelve spatial ICs were derived using fMRLAB and 6 temporal ICs were obtained from FastICA.

Both temporal and spatial ICs corresponding to motor activity were identified based on the region of the brain the components displayed dominant activity and their corresponding time courses. Spatial component brain maps were displayed using fMRLAB and the spatial weight brain maps corresponding to each temporal component were displayed using MATLAB to illustrate voxels that are active for each component in all slices. Spatial weights computed for each temporal or spatial component are indicators of how brain activity is influenced by that component at that voxel [2, 4]. The spatial component weights were converted to z-values by subtracting the mean of each component's spatial weights from each weight and then dividing the result by the standard deviation of the weights [8]. The z-value indicates how strongly the component is activated (positive z-value) or deactivated (negative z-value) in that voxel [8]. Each spatial component was projected back onto voxels with positive z-values higher than a user-specified threshold so the average time course of the component could be viewed. Both time courses of the back-projected spatial components and time courses of the temporal components identified as task-related appeared correlated to the block paradigm task as expected.

The next step was to prepare two models of the hemodynamic response function in MATLAB based on ICA results to use as regressors in SPM of the fMRI recordings. The conventional hemodynamic response function (HRF) is a canonical HRF shown in Fig. 1 [9]. This function is convolved with the stimulus function, in this case a square wave with an on time of 12secs and off time of 24secs, to yield a signal model that resembles BOLD activity in voxels contributing to task performance. The second model was the average BOLD signal from the region(s) of activity (known as the ROA+) of task-related independent spatial components with z-values ≥ 3.0 extracted from the averaged data. The third model was the time course of one task-related independent temporal component. Since the second and third models only had 12 time samples, the signal was repeated nine times to yield a model of 108 time samples. These two models are shown in Fig. 1.

The final step was to conduct SPM using each model in SPM5 separately. A t-test was chosen as the statistical test. The resulting parameter estimates were compared with the rest condition using the t-statistic to find significant voxel activations. The p-value threshold was set to 0.05, which is the corrected value that accounts for the multiple comparison problem when the 82643 voxels were tested in this study.



(a) (b) (c)

Fig. 1 (a) Canonical Hemodynamic Response (repeated 9 times) (b) Average ROA+ time course of Task-Related Spatial IC (repeated 9 times) (c) Task-Related Temporal IC (repeated 9 times)

III. RESULTS & DISCUSSION

Only one spatial IC and one temporal IC were necessary to account for the task-related BOLD activity in each case. The variance of the average ROA+ signal time course accounted for by the dominant spatial component was 98.25%. The component brain maps of each IC for the three slices depicting the largest amount of activity are shown in Fig. 2

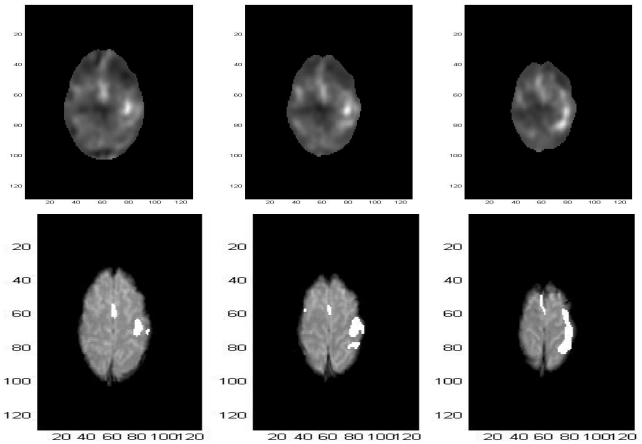


Fig. 2 (top) Temporal IC map (spatial dual) of Task-Related Component from Averaged Data Set (bottom) Back-projected Spatial IC map of Task-Related IC from Averaged Data Set (all images in radiological orientation)

The figures show excellent agreement with the strongest projection weights in the primary motor cortex in the left hemisphere of the brain. This is the region of the brain expected to be most active with right hand movements.

The SPMs resulting from using the temporal ICA-derived model, spatial ICA-derived model and conventional model were compared and showed activations in similar areas. The SPM results also show activation locations that are similar to those shown in the IC maps of Fig. 2. The same slices of Fig. 2 showing the voxels that were considered active simultaneously by each t-test are shown in Fig. 3.

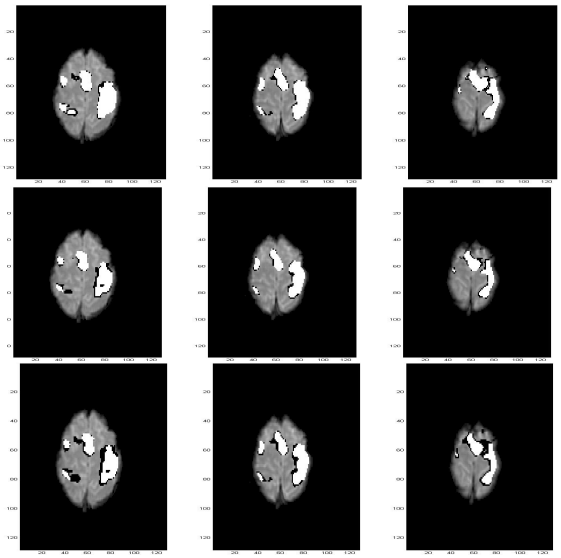


Fig. 3 (top) Contrast/Similarity map between SPM of spatial ICA-derived model and SPM using conventional model (middle) between SPM of temporal ICA-derived model and SPM using conventional model (bottom) between SPM of spatial ICA-derived model and SPM of temporal ICA-derived model.

Voxels shown in white are those voxels determined to be active by both SPMs and those clustered in the same shade of grey or black are active according to either one or the other SPM. Grey and black were used to color code the voxels so that the SPM that activated a particular voxel can be deduced. There is significant overlap of active voxels in all cases, so the t-test results agree to a significant extent. Moreover, the most significant overlap is found in the primary motor cortex of the left hemisphere of the brain. A metric used to indicate the degree of overlap between the SPMs in each case is called the concurrence ratio (CR). The CR is found by taking the number of overlapping active voxels and dividing by the average number of active voxels from both SPMs [10]. The values are expressed as percentages in Table 1.

TABLE 1. CONCURRENCE RATIOS

CRs (%)	Conventi-onal Model	Spatial ICA-derived Model	Temporal ICA-derived Model
Conventi-onal model	n/a	87.23	83.56
Spatial ICA-derived Model	87.23	n/a	74.62
Temporal ICA-derived Model	83.56	74.62	n/a

Upon observing the CRs, the largest discrepancy between overlapping active voxels is seen between the SPMs resulting from statistical tests using the ICA-derived model waveforms. In addition, just over 60% of active voxels from t-tests using the ICA-derived models were in the same location while those that matched between SPMs using each

ICA-derived model and the conventional model was close to 75% in both cases. The two approaches to ICA seek very different forms of independence in the data. Temporal ICA endeavors to find time courses of activity in the data that are statistically independent and claim that each time course represents a different physical process. Conversely, spatial ICA finds clusters of voxels whose activity is statistically independent from other clusters. The overlap of these spatial independent component clusters in the brain is ideally minimized. This difference in what each ICA approach considers independent activity in the brain is likely the reason for the increased difference in matching active voxels when compared with a conventional model. What is encouraging, however, is that nearly all the voxels that did not match surrounded the region of overlapping voxels as shown in Fig. 3. For the spatial ICA case, the overlap region is quite dependent on the z-value threshold set in finding the ROA+ of the independent components. If the z-value is lowered from 3.0, the CR increases. The z-value must be carefully chosen to ensure that spatial ICs do indeed reflect as closely as possible the brain region(s) responsible for enabling the subject to perform the desired task.

The CR between the brain map computed using each ICA-derived model and the conventional model is quite significant. The use of each model in the t-test resulted in a similar number of voxel activations that overlapped to a great extent. This leads to the impression that a hemodynamic response model derived from ICA of data averaged over each task cycle may produce a reasonable representation of the task BOLD response. The canonical model has been used in many studies to compare to the BOLD signal measured in every voxel of every slice to extract regions of brain activity [9, 11]. However, the canonical model is not patient nor brain-region specific [11]. If a patient's BOLD response does not resemble the canonical model, several false negative or even false positive results may turn up when performing a statistical test on fMRI data. HR models derived from ICA are patient and brain-region specific, so they likely reflect BOLD signal time courses more accurately. In addition, ICs are not statistically tested during the ICA procedure. Using a statistical test, such as a t-test, to evaluate how closely the ICA-derived models resemble BOLD activity in various voxels results in a more confident assessment of the active brain regions.

IV. CONCLUSIONS

ICA and SPM are popular methods of analyzing fMRI measurements. In past studies, they have primarily been used separately to locate regions of the brain that are active in response to a stimulus, performing a motor task and even event-related studies. However these methods can be combined to find an improved method of localizing brain activity because the advantages of each technique are complementary and the mathematical system of equations of each is similar. ICA is a data-driven method, while SPM is by contrast a hypothesis-driven method [1]. In this study, hemodynamic response models derived from task-related independent components can be used as regressors to model the expected BOLD response. When voxel activations from t-tests done using temporal and spatial ICA-derived models were compared with voxel activations found from SPM with a canonical hemodynamic response model and with the IC brain maps, there was significant agreement between the active regions. The excess activated voxels surrounded the overlapping regions significantly and may reflect brain regions involved in the motor task more precisely than the conventional model.

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