Independent Component Analysis of BOLD fMRI Data

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1. Introduction

What an antithetical mind! - tenderness, roughness - delicacy, coarseness - sentiment, sensuality - soaring and groveling, dirt and deity - all mixed up in that one compound of inspired clay!

-Lord Byron

Independent component analysis (ICA) is a statistical method used to discover hidden factors (sources or features) from a set of measurements or observed data such that the sources are maximally independent. Typically, it assumes a generative model where observations are assumed to be linear mixtures of independent sources, and unlike principal component analysis (PCA) which uncorrelates the data, ICA works with higher-order statistics to achieve independence.

An example of ICA can be given by a scatter-plot of two independent signals s_1 and s_2. Figure 1.1a shows a plot of the two independent signals (s_1, s_2) in a scatter-plot. Figure 1.1b and c show the projections for PCA and ICA, respectively, for a linear mixture of s_1 and s_2. PCA finds the orthogonal vectors u_1, u_2, but does not find independent vectors. In contrast, ICA is able to find the independent vectors a_1, a_2 of the linear mixed signals (s_1, s_2), and is thus able to restore the original sources.

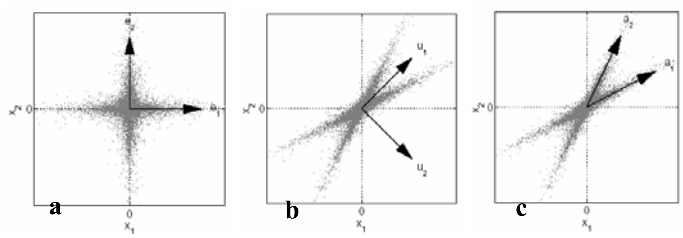


Figure 1.1: (a) The joint density of two independent signals, (b) PCA projection (u_1, u_2), (c) ICA projection (a_1, a_2) (adopted from [1])

A typical ICA model assumes that the source signals are not observable, statistically independent and non-Gaussian, with an unknown, but linear, mixing process. Consider an observed $M-$dimensional random vector is denoted by $\mathbf{x}=(x_1,\cdots x_M)^T$ which is generated by the ICA model $\mathbf{x}=\mathbf{A}\mathbf{s}$, where $\mathbf{s}=[s_1, s_2, \ldots s_N]^T$ is an N-dimensional vector whose elements are assumed independent sources and $\mathbf{A}_{M\times N}$ is an unknown mixing matrix. Typically $M >= N$, so that A is usually of full rank. The goal of ICA is to estimate an unmixing matrix $\mathbf{W}_{N\times M}$ such that $\mathbf{y}=\mathbf{W}\mathbf{x}$ is a good approximation to the 'true' sources, $\mathbf{s}$.

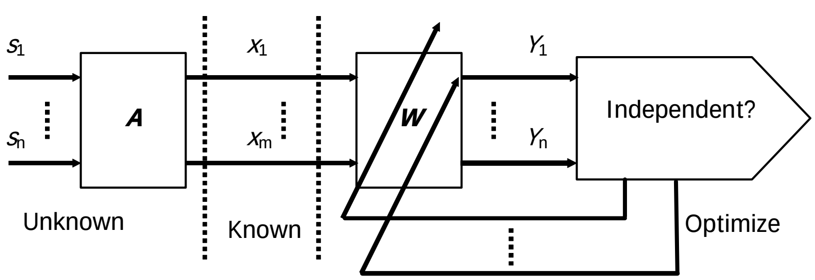


Figure 1.2: Basic ICA model for blind source separation

ICA is hence an approach to solve the blind source separation problem, which traditionally addresses the solution of the cocktail party problem in which several people are speaking simultaneously in the same room. The problem is to separate the voices of the different speakers, using recordings of several microphones in the room [2]. The basic ICA model for blind source separation is shown in Figure 1.2.

Popular approaches for performing ICA include maximization of information transfer—which is equivalent to maximum likelihood estimation, maximization of nongaussianity, mutual information minimization, and tensorial methods. The most commonly used ICA algorithms are Infomax [3], FastICA [4] and joint approximate diagonalization of eigenmatrices (JADE) [5]. The original Infomax algorithm for blind separation by [3] is better suited to estimation of super-Gaussian sources. To overcome this limitation, techniques have been developed for simultaneously separating sub- and super-Gaussian sources [6]. A flexible independent component analysis approach using generalized Gaussian density model method was introduced in [7]. These algorithms typically work well for symmetric distributions and are less accurate for skewed distributions. Recent extensions of ICA to overcome this limitation include non-parametric ICA [8] and kernel independent component analysis [9]. Other ICA models that adaptively vary the nonlinear functions (or activation functions) to better fit the underlying sources have also been proposed [10,11]. The variety of recent approaches for performing ICA and its applications in areas as diverse as biomedicine, astrophysics, and communications demonstrates the vitality of research in this area.

2. Functional MRI

FMRI is a technique that provides the opportunity to study brain function non-invasively and is a powerful tool utilized in both research and clinical arenas since the early 90s [12]. The most popular technique utilizes blood oxygenation level dependent (BOLD) contrast, which is based on the differing magnetic properties of oxygenated (diamagnetic) and deoxygenated (paramagnetic) blood. When brain neurons are activated, there is a resultant localized change in blood flow and oxygenation which causes a change in the MR decay parameter T_2^*. These blood flow and oxygenation (vascular or hemodynamic) changes are temporally delayed relative to the neural firing, a confounding factor known as hemodynamic lag. Scientific interest rests primarily with the electrical activity in the neurons, which cannot be directly observed by any variant of the MRI procedure. Since the hemodynamic lag varies in a complex way from tissue to tissue, and because the exact transfer mechanism between the electrical and hemodynamic processes is not known, it is not possible to completely recover the electrical process from the vascular process. Nevertheless, the vascular process remains an informative surrogate for electrical activity. However, relatively low image contrast-to-noise ratio (CNR) of the BOLD effect, head movement, and undesired physiological sources of variability (cardiac, pulmonary) make detection of the activation-related signal changes difficult.

2.1 Types of Signal and Noise

There are several types of signals that can be encoded within the hemodynamic signals measured by fMRI. Some of these were identified by McKeown in the first application of ICA to fMRI [16]. In this paper, infomax [3] was utilized and separated signals were classified as task-related, transiently task-related, and motion related.

In general, fMRI data may be grouped into signals of interest and signals not of interest. The **signals of interest** include task-related, function-related, and transiently task-related signals. The *task-related* signal has already been mentioned and is the easiest to model. A reference waveform, based upon the paradigm, is correlated with the data. The responses of the brain to a given task may not be regular however, for example the signal may die out before the stimulation is turned off or change over time as repeated stimuli are applied, leading to a *transiently task-related* signal. It is also conceivable that there are several different types of transiently task-related signals coming from different regions of the brain. The *function-related* signal manifests as similarities between voxels within a particular functional domain (*e.g.*, the motor cortex on one side of the brain will correlate most highly with voxels in the motor cortex on the opposite side of the brain) [17]. An exciting application of this is for identifying synchronous auditory cortex activity [18,19] (see areas corresponding to the top time course in Figure 3.4). Most of these fMRI signals have been examined with ICA and other methods and have been found to be super-Gaussian in nature (except perhaps the artifacts mentioned in the next section).

The **signals not of interest** include physiology-related, motion-related, and scanner-related signals. *Physiology-related* signals such as breathing and heart rate tend to come from the brain ventricles (fluid filled regions of the brain) and areas with large blood vessels present, respectively. *Motion-related* signals can also be present and tend to be changes across large regions of the image (particularly at the edges of images). Finally, there are *scanner-related* signals that can be varying in time (such as scanner drift and system noise) or varying in space (such as susceptibility and radio-frequency artifacts) [21]. A number of such examples can be found online including slice dropout, motion artifact, and nyquist ghosting.

There are several types of noise one can characterize in an fMRI experiment. First, there is noise due to the magnetic resonance acquisition which can be discussed as 1) object variability due to quantum thermodynamics and 2) thermal noise. It can be shown that the thermal noise will result in white noise with a constant variance in the image dimension [22]. Additionally there is noise due to patient movement, brain movement, and physiologic noise (such as heart rate, breathing). It has been suggested that physiologic noise is the dominant factor in fMRI studies

[23]. In the ICA model these "noises" are often not explicitly modeled, but rather manifested as separate components, (see, e.g., [21,24]).

2.2 Statistical Properties of fMRI Data

Properties such as non-Gaussianity and spatial/temporal independence of sources need to be addressed for the application of ICA to fMRI data. If the "activations" do not have a systematic overlap in time and/or space then the distributions can be considered independent [25]. The temporal distribution of a task-related waveform is often nearly bimodal (off/on) and thus the algorithm needs to incorporate this fact. Some other basic assumptions of ICA have been considered in [16]. The assumption that components are spatially independent and add linearly was evaluated and it was concluded that the fMRI signals and noise are non-Gaussian and the accuracy of the ICA model may vary in specific regions of the brain. For example, cortex-based ICA assumes that cortical data are different from non-cortical data and processes a subset of the data determined by *a priori* information (see Section 3.4) [26]. The signals of interest in fMRI are typically focal and thus have a super-Gaussian spatial distribution. However, the artifactual signals will be more varied and potentially sub-Gaussian.

Certain aspects of the fMRI signal are well known and could be incorporated into an ICA analysis. First, local spatial correlation exists in MR images due only to the acquisition process. It is often the case that partial k-space acquisitions involve sampling fewer frequency samples than the desired number of spatial samples. One can use the fact that the matrix of frequency data is Hermitian-symmetric to reconstruct the image using a partially acquired frequency matrix (with the trade-off being a decrease in signal-to-noise-ratio). Another well-known method involves sampling the lower frequencies and padding the high frequencies with zero (with the trade-off being a decrease in spatial resolution). This broadens the well described MRI spatial point spread function in one direction, although it has been suggested that there is a real gain in resolution when zero padding is up to as much as twice the original number of samples [27]. This results in spatial correlation of the MR signal.

In addition, spatial correlation is induced by the process being measured. The hemodynamic sources to be estimated have a spatial hemodynamic (vascular) point spread function. This is partially due to the hemodynamics, but is also a function of the pulse sequence and the parameters used. Differing degrees of sensitivity to blood flow and blood oxygenation as well as differences between low and high field magnets will measure different hemodynamics. The pulse sequence, parameters, and magnetic field strength are considered as constant to enable discussion of the hemodynamic point spread function without introducing the complexities of these parameters. There may also be some degree of temporal correlation. Temporal correlation is introduced by: 1) rapid sampling (a scanner parameter) on the time scale of the magnetic equilibrium constant, T_1 and 2) the temporal hemodynamic (vascular) point spread function (a physiologic variable). There are also other sources of temporal autocorrelations in the data which are yet to be understood fully [28]. These data properties, which often vary from subject to subject, can impose difficulties for modeling the temporal aspects of the fMRI signal.

FMRI provides a non-invasive surrogate measure of the brain's electrical activity. It is a diverse technique and research using fMRI is growing at a rapid pace. The richness of fMRI data is only beginning to be understood. We have provided a brief introduction to the fMRI technique and summarized some of the functionally-related brain signals. It is important to understand the properties of these signals when developing methods for analyzing this data.

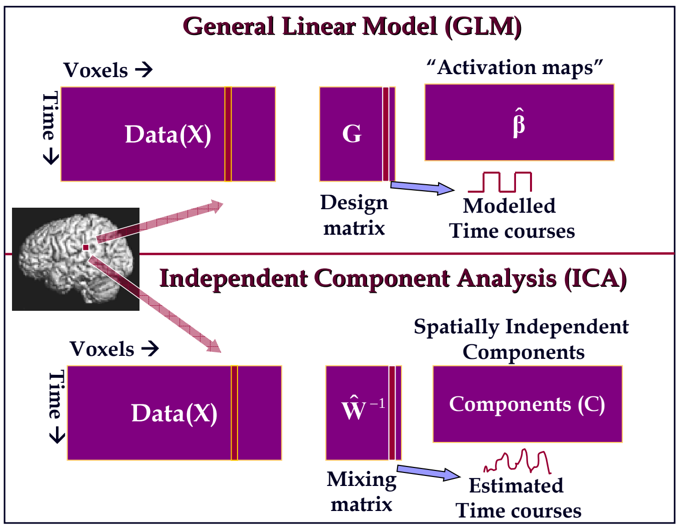
3. ICA of fMRI

Independent component analysis has shown to be useful for fMRI analysis for several reasons. Spatial ICA finds systematically non-overlapping, temporally coherent brain regions without constraining the temporal domain. The temporal dynamics of many fMRI experiments are difficult to study with functional magnetic resonance imaging (fMRI) due to the lack of a well-understood brain-activation model. ICA can reveal inter-subject and inter-event differences in the temporal dynamics. A strength of ICA is its ability to reveal dynamics for which a temporal model is not available [29]. Spatial ICA also works well for fMRI as it is often the case that one is interested in spatially distributed brain networks.

ICA has found a fruitful application in the analysis of fMRI data [30,31]. A principal advantage of this approach is its applicability to cognitive paradigms for which detailed a priori models of brain activity are not available. ICA has been successfully utilized in a number of exciting fMRI applications and in those that have proven challenging with the standard regression-type approaches. These include identification of various signal-types (e.g. task and transiently task-related, and physiology-related signals) in the spatial or temporal domain [32], the analysis of multi-subject fMRI data, the incorporation of a priori information [33,34], more recently for clinical applications [35,36] and for the analysis of complex-valued fMRI data.

3.1 Spatial vs. Temporal

Independent component analysis is used in fMRI modeling to understand the spatio-temporal structure of the signal, and it can be used to discover either spatially or temporally independent components. Most applications of ICA to fMRI assume use the former approach and seek components that are maximally independent in space. In such a setting (shown in Figure 3.1), we let the observation data matrix be $\mathbf{X}$, an $N \times M$ matrix (where N is the number of time points and M is the number of voxels). The aim of fMRI component analysis is then to factor the data matrix into a product of a set of time courses and a set of spatial patterns. In principal component analysis this is achieved by singular value decomposition of the data matrix by which the data matrix is written as the outer product of a set of orthogonal, i.e., uncorrelated time courses and set of orthogonal spatial patterns. Independent component analysis takes a more general position and aims at decomposing the data matrix a product of spatial patterns and corresponding time courses where either patterns or time courses are a priori independent. ICA can also be compared with the widely used univariate general linear modeling approach which proceeds by deriving a temporal model/basis set and fitting this model to the data at each voxel by minimizing the least squared error [37]. The ICA approach does not attempt to explicitly parameterize the fMRI time course, which is estimated implicitly in the source separation algorithm (see Figure 3.1).



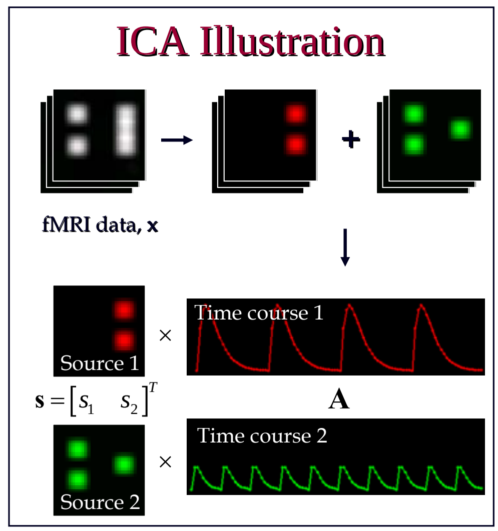


Figure 3.1: Comparison of GLM and ICA (left) and ICA illustration (right). The GLM (top left) is by far the most common approach to analyzing fMRI data, and to use this approach, one needs a model for the fMRI time course whereas in spatial ICA (bottom left), there is no explicit temporal model for the fMRI time course, this is estimated along with the hemodynamic source locations. (right) The ICA model assumes the fMRI data, x, is a linear mixture of statistically independent sources, s and the goal of ICA is to separate the sources given the mixed data and thus determine the s and A matrices

Since the introduction of ICA for fMRI analysis by McKeown *et al.* [24], the choice of spatial or temporal independency has been controversial. However, the two options are merely two different modeling assumptions. McKeown *et al.* argued that the sparse distributed nature of the spatial pattern for typical cognitive activation paradigms would work well with spatial ICA (SICA). Furthermore, since the proto-typical confounds are also sparse and localized, *e.g.*, vascular pulsation (signal localized to larger veins that are moving as a result of cardiac pulsation) or breathing induced motion (signal localized to strong tissue contrast near discontinuities: "tissue edges"), the Bell-Sejnowski approach with a sparse prior is very well suited for spatial analysis [38] and has also been used for temporal ICA [25] as have decorrelation-based algorithms [38]. Stone *et al.*, proposed a method which attempts to maximize both spatial and temporal independence [39]. An interesting combination of spatial and temporal ICA was pursued by Seifritz *et al.* [18]; they used an initial SICA to reduce the spatial dimensionality of the data by locating a region of interest in which they then subsequently performed temporal ICA to study in more detail the structure of the non-trivial temporal response in the human auditory cortex.

3.2 Choice of Algorithms and Preprocessing

As mentioned in the previous subsection, ICA of fMRI involves many preprocessing stages, and there are a number of choices both for those and the ICA algorithms that can be employed. Studies of how different algorithms and preprocessing stages impact the results have been performed by several groups [40,41]. The selection of which algorithm to use will also depend upon the assumed distribution of the sources. For example, fMRI data are commonly assumed to be super-Gaussian; that is the source distributions have a heavier tail that does a Gaussian distribution. This quality can be measured using the fourth statistical moment, called kurtosis (peakedness), which is zero for a Gaussian, negative for a sub-Gaussian, and positive for a super-Gaussian distribution.

In [42], using hybrid data, an evaluation of different preprocessing stages and ICA algorithms was performed using the Kullback-Leibler (KL) divergence. In the case of real fMRI data, validation is difficult as the true source distributions are unknown. However, one can move in this direction by superimposing simulated source(s) upon real fMRI data to create a "hybrid" fMRI experiment (see Figure 3.2). Sources are estimated, extracted (by ranking components by their correlation with the known sources) and compared with the actual sources. While this approach is limited, it is useful in providing a quantitative ICA performance measure. Figure 3.2 shows a thresholded "true" source (a) and its mixing function (b). Also shown is a plot of the "hybrid" fMRI data for a voxel close the "true" source maximum (c). The contrast-to-noise level is calculated as the ratio of the source amplitude to the standard deviation (over time) of a voxel within the brain. In general, it is noted that certain choices and combinations make a difference in results. In this work, infomax outperformed (in approximation and variability) FastICA, and PCA outperformed clustering. The best overall combination for this case appears to be Infomax and PCA.

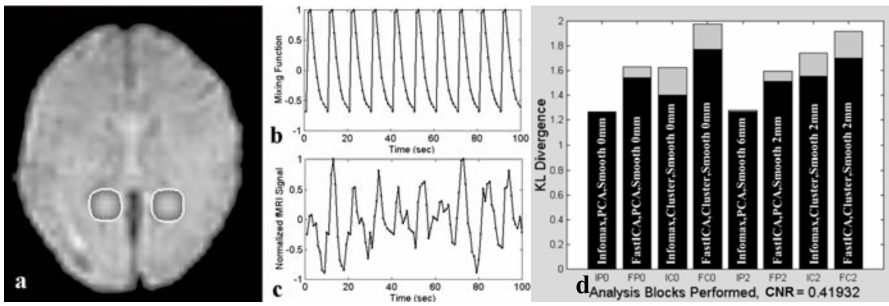


Figure 3.2: (a,b,c) Hybrid-fMRI experiment in which a known source is added to a real fMRI experiment (from [29]). (d) Comparison of algorithms and preprocessing using hybrid data.

In [43], the performance of various ICA and blind source separation algorithms is studied for application to fMRI analysis. The algorithms tested were the extended Infomax [6], FastICA [4], joint approximate diagonalization of eigenmatrices (JADE) [5], simultaneous blind extraction using cumulants (SIMBEC) [44], and AMUSE [45] in the user-friendly environment of a Matlab-based toolbox, group ICA of fMRI toolbox (GIFT) [46] incorporating the implementations from ICALAB toolbox [47]. The comparison study used both simulated fMRI-like data and actual fMRI data from seven individuals performing a four-cycle visual stimulation task.

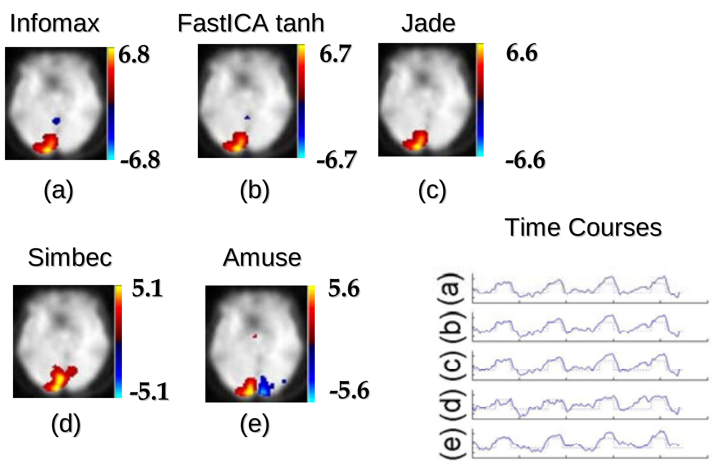


Figure 3.3: FMRI single slice results (left visual cortex)

The experiment on simulated data included two data sets: a set of five sources and another of eight sources consisting of highly super-Gaussian, Gaussian, and sub-Gaussian sources with time courses representing sources typical to fMRI data as discussed in Section 2.1. The separation performance is measured in terms of correlation of the estimated sources with the original sources both spatially and temporally. All five algorithms were able to achieve some separation of the sources, with significant performance differences especially for the set with larger number of sources. Infomax consistently yielded reliable results, followed closely by JADE and FastICA. In the comparison with fMRI data, group ICA was performed on subjects performing an alternating left-right visuomotor task [19]. In Figure 3.3, we display that component from the results of each algorithm which contains the left visual cortex activation from group results from three subjects. For this case, Infomax, FastICA, and JADE again successfully identify the task-related components in the left and right visual hemifields. It is also worthwhile noting that the *Z*-scores for Infomax are higher than the other algorithms for the task-related source, indicating that Infomax achieves a higher contrast to noise ratio. SIMBEC identifies the two task-related sources in the right and left hemifields; however it splits the left hemifield task-related source into two components, one of as shown in Figure 3.3 (d). AMUSE also finds the two task-related sources but places both in the same component (Figure 3.3 (e)), which might be due to the similarity of the left and right activations for the task-related source have similar spectra.

The comparisons indicate that Infomax performs most reliably, followed closely by JADE. FastICA whereas the performance of SIMBEC and AMUSE did not prove to be robust as different combination of sources and their numbers seemed to affect their performance significantly. SIMBEC, however, may prove to be useful to identify the sub-Gaussian sources, i.e., artifacts in fMRI data as its performance for these sources has been consistently very good. The performance of AMUSE is highly dependent on the differentiability of the spectra of the sources for a given delay and its performance suffers a great deal when the condition is not met.

Another approach for comparing algorithms is proposed by Esposito *et al.* in [40]. Linear correlation and receiver operating characteristics are used to compare temporal and spatial outcomes, respectively. The infomax approach appeared to be better suited to investigate activation phenomena that are not predictable or adequately modeled by inferential techniques.

3.3 Group ICA

ICA has been successfully utilized to analyze single-subject fMRI data sets, and recently extended for multi-subject analysis [19,48-50]. Unlike univariate methods (e.g., regression analysis, Kolmogorov-Smirnov statistics), ICA does not naturally generalize to a method suitable for drawing inferences about groups of subjects. For example, when using the general linear model, the investigator specifies the regressors of interest, and so drawing inferences about group data comes naturally, since all individuals in the group share the same regressors. In ICA, by contrast, different individuals in the group will have different time courses, and they will be sorted differently, so it is not immediately clear how to draw inferences about group data using ICA.

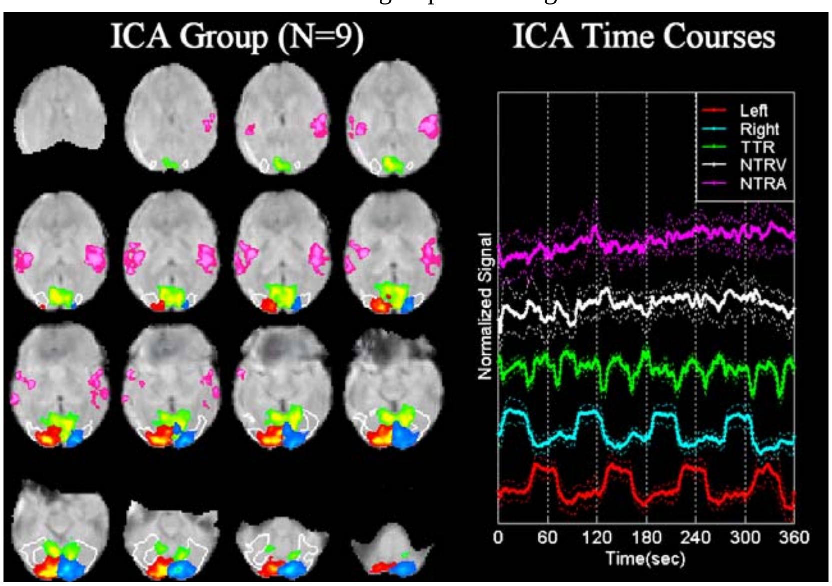


Figure 3.4: fMRI Group ICA results (from [19])

An approach was developed for performing an ICA analysis on a group of subjects [19]. In order to reduce computational load, data reduction was first performed for each subject's data then a second, aggregate model order reduction was performed. Back-reconstruction and statistical comparison of individual maps and time courses is performed following the ICA estimation. This approach is implemented in a Matlab toolbox [46].

Group maps for an ICA analysis of a four cycle alternating left/right visual stimulation task collected from a 1.5T Phillips scanner are presented in Figure 3.4. The number of components is estimated to be twenty-one by the two information-theoretic criteria employed: the minimum description length and Akaike's information criterion. Thus, the aggregate data are reduced to this dimension and twenty-one components were estimated. Both maps are thresholded at $p<0.001$ ($t=4.5$, $df=8$). Several interesting components were identified within the data. Separate components for primary visual areas on the left and the right visual cortex (depicted in red and blue, respectively) were consistently task-related with respect to the appropriate stimulus. A large region (depicted in green) including occipital areas and extending into parietal areas appeared to be sensitive to changes in the visual stimuli. Additionally some visual association areas (depicted in white) had time courses which were not task related. A comparison of group ICA approaches is found in [51].

Higher order tensor decompositions (also known as multidimensional, multi-way, or n-way), probably the first class of algorithms that performed ICA successfully [52], have received renewed interest recently, although their adaptation to group and multi-group fMRI data is still being explored. Recently, a tensorial approach was developed to estimate a single spatial, temporal, and subject-specific 'mode' for each component to attempt to capture the multidimensional structure of the data in the estimation stage [53].

3.4 Applications to Clinical Research

ICA has more recently been applied to address some clinically relevant questions [54]. For example, ICA has been used to study differences in brain activation due to pain in healthy individuals vs. those with chronic pain [55] and even to distinguish between Alzhiemer's patients and healthy controls by examination of the brain's 'default mode' estimated using ICA [35,56]. We now give an example of using ICA to classify schizophrenia patients from healthy controls.

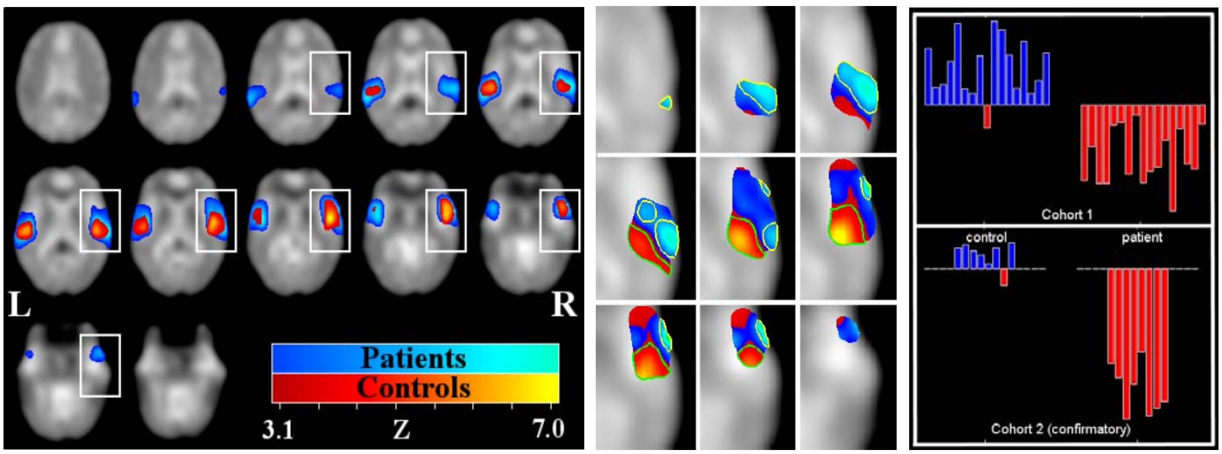


Figure 3.5: (left) Mean activation maps from patients with schizophrenia and healthy controls. Right auditory cortex demonstrated the greatest difference (white box); (middle) Right auditory cortex difference maps with optimized boundaries; (right) Individual classification results for cohort 1, and replication in cohort 2. Schizophrenia classification is indicated with the color red.

Among the most prominent features of schizophrenia brains are abnormalities in temporal lobe structure and function; in particular in the superior temporal gyrus (STG). In this study, we attempted to examine temporal lobe function utilizing an intrinsic, task-uncorrelated measure. Using functional magnetic resonance imaging data collected from a 1.5T GE Scanner, we calculated synchronous hemodynamic independent maps (SHIMs) of temporal lobe in 17 patients and 17 matched controls while they performed an auditory oddball task (for more details see [36]). These maps are computed using ICA, which resulted in one of the components showing large values in superior temporal lobe. Patient SHIMs revealed greater synchrony in anterior and lateral STG regions; control SHIMs had greater synchrony in posterior and medial regions. Right auditory cortex difference maps indicate regions where controls > patients (orange) and where patients > controls (blue) [see Figure 3.5, right]. Also shown are boundaries (in green and yellow) depicting intra-individual comparison regions determined by thresholding difference maps that maximized discrimination between the 2 groups.

A within-participant subtractive comparison of these two sets of right hemisphere temporal lobe regions (optimized for cohort 1 using a minimum probability of error criterion) differentiated schizophrenia from healthy controls with 97% accuracy initially (further validated by a re-test of the healthy controls) and performed with 94% accuracy in a confirmatory study of new subjects scanned at a different site. These results shed new light on STG functional differences in schizophrenia, suggest that aberrant patterns of coherence in temporal lobe cortical regions are a cardinal abnormality in schizophrenia, and have the potential to provide a powerful, quantitative clinical tool for the assessment of schizophrenia.

3.5 Incorporation of Prior Information

The incorporation of prior information into ICA methods is important as it can provide improved separability and allow *selective* exploratory analysis. In addition, ICA methods make assumptions about, e.g. the distributional shape of the sources, and thus it is important to both assess the impact of such assumptions and modify them based upon given fMRI data.

There have been a number of applications of ICA that have attempted to utilize prior information for fMRI analysis. For example, using a reference function to extract only a single component is proposed in [57]. A more general Lagrange-based approach for constraining the spatial sources is found in [58]. Stone *et al.* propose a skewed symmetric nonlinearity (i.e., assume that the source distributions are skewed). This makes sense if one is interested in components that consist largely of either activations or deactivations [59]. Formisano *et al.* propose performing ICA upon data extracted from the cortex (where the activation is expected to be occurring) using a tessellation model of the brain cortex derived from a high resolution structural image [26]. Duann *et al.* examine time-locked temporal structure and propose a visualization approach to evaluate trial-by-trial variability [60]. An advanced mean field approach was invoked for handling situations with adaptive binary source signals [61]. In temporal mode this method can separate on/off signals while in spatial mode the approach leads to an algorithm that shares many features with Fuzzy clustering. Bayesian methods provide a useful way to incorporate prior information into ICA and may prove useful for fMRI analysis [62].

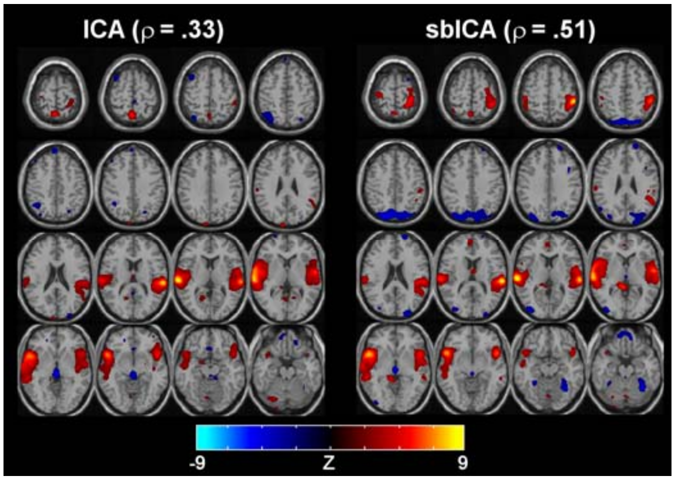


Figure 3.6: Comparison of ICA and sbICA in one participant

It is also useful to impose constrains directly upon the mixing matrix in a spatial ICA fMRI analysis. For example, a component selective constraint of the ICA model mixing matrix such that one or more specific components are constrained to be “close” to a paradigm-derived time course is shown in Figure 3.6 [33]. The degree of closeness is specified by the user based upon amount of confidence placed in the information provided. Such an approach can also be formulated using a Lagrange framework. Results from our approach are shown below for an fMRI experiment for an auditory detection task. The participant was responding to the target with a button press.

The left side of the figure demonstrates the task-related component for an unconstrained ICA analysis. On the right is the constrained (or semi-blind) analysis showing additional regions including motor cortex towards the top of the figure [33]. The temporal correlation with the paradigm is much higher for the constrained analysis as expected. These results demonstrate the utility of incorporating mixing matrix constraints in an fMRI analysis.

4. Conclusion

The application of ICA to fMRI data has proved to be quite fruitful. However there is still much work to be done in order to take full advantage of the information contained in the data. Additional prior information about multiple expected sources (both interesting and non-interesting) and their properties (fMRI properties, physiologic recording, etc) can be utilized. In addition to incorporating appropriate assumptions (and moving towards a semi-blind source separation) it is important to relax inappropriate assumptions (such as having a fixed temporal delay for each source). One of the strengths of ICA of fMRI is its ability to characterize the high-dimensional data in a concise manner. Continuing to do this and developing ways to mine the unexpected information in fMRI data will provide an exciting future for ICA of fMRI.

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