INDEPENDENT COMPONENT ANALYSIS AND BEYOND IN BRAIN IMAGING: EEG, MEG, FMRI, AND PET

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Abstract

There is an increasing interest in analyzing brain images from various imaging modalities, that record the brain activity during functional task, for understanding how the brain functions as well as for the diagnosis and treatment of brain disease. Independent Component Analysis (ICA), an exploratory and unsupervised technique, separates various signal sources mixed in brain imaging signals such as brain activation and noise, assuming that the sources are mutually independent in the complete statistical sense [1]. This paper summarizes various applications of ICA in processing brain imaging signals: EEG, MEG, fMRI or PET. We highlight the current issues and limitations of applying ICA in these applications, current, and future directions of research.

Key Words: Blind signal and image processing, higher order statistics, independent component analysis, statistical independence.

1. INTRODUCTION

Functional brain imaging modalities, such as electroencephalography (EEG), magnetoencephalography (MEG), functional magnetic resonance imaging (fMRI), and positron emission tomography (PET) provides functional information about the activity of neurons or their population during sensory or cognitive tasks. One of the most important challenges of brain imaging is the localization of specific brain areas that carry out certain functions and monitoring the ongoing brain activity over time [2]. In order to achieve this, it is often necessary to separate the signals involved in brain processes from their artifacts.

In imaging neuroscience, mostly referred as *brain imaging*, as in other signal processing areas, a common task is to find an adequate representation of multivariate data for subsequent processing and interpretation. The transformed variables are then envisaged to optimally represent the essential structure of data, that can provide information about the process of generation of underlying events. The focus of this paper is the application of Independent Component Analysis (ICA) to the analysis of brain signals that presume that the brain processes and the other noise and artifactual components are mutually independent in complete statistical sense.

The basic model assumed in ICA for brain imaging is as follows:

$$\mathbf{x}(t) = \mathbf{A}\mathbf{s}(t) + \mathbf{r}(t) \tag{1}$$

where $\mathbf{x}(t) = (x_1(t), x_2(t), \ldots x_m(t))^{\mathrm{T}} \in \mathbf{R}^m$ indicates a zero mean vector of signals observed by the imaging modality at time t, $\mathbf{s}(t) \in \mathbf{R}^n$ denotes n number of sources, at most one Gaussian, that generate the observed brain signals, and $\mathbf{r}(t) \in \mathbf{R}^m$ indicate the noise embedded in the signal. The matrix $\mathbf{A}$ is a full column rank mxn matrix, ($m \geq n$), that represents a linear mixing of the sources embedded in the observed brain signals. The mixing is assumed instantaneous, i.e., that there is no time delay between the sources of events in the brain and the observed signals. The challenge of identifying brain signal sources can then be posed as the realization of source signals $\mathbf{s}(t)$, given the observations $\mathbf{x}(t)$ and an unknown mixing matrix $\mathbf{A}$. If no further assumptions are made, the noise can be included in the signals as a source signal component.

A set of sources is said to be independent in complete statistical sense if their joint density is equal to the product of the marginal densities. The concept of statistical independence may be defined by means of an independence criterion derived from the statistical properties of the data, such as entropy of output sources [3], non-Gaussianity [4], etc. Based on these properties, an objective function or *contrast function* is derived. To optimize this function, the source signals are separated to be as independent as possible. Entropy is a criterion based on the amount of information contained in some occurrences of a discrete random variable [5]. The invariance to invertible linear transforms and nonnegativity are introduced by using the concepts of negentropy and mutual information (MI) [3]. Minimizing the MI between the outputs of a system is equivalent to maximizing individual negentropies of its outputs, which can be proved by means of expressing the two items via the Kullback-Leibler divergence [6, 7].

The current algorithms for ICA can loosely be classified in two categories. One category contains adaptive algorithms generally based on stochastic gradient methods and implemented in neural networks [3, 6]. The neural adaptive algorithms exhibit slow convergence and their convergence depends crucially on the correct choice of the learning rate parameters. The second category relies on batch computation optimizing some relevant criterion functions [8]. The statistical properties the ICA, such as consistency, asymptotic variance, robustness depend on the choice of the contrast function whereas the algorithmic properties, such as convergence speed, memory requirements, numerical stability, depend on the optimization algorithm.

Source separation consists of funding a demixing matrix $\mathbf{W}$, without resorting to any information about the mixing matrix $\mathbf{A}$, so that the elements of the estimated source vector become as independent as possible:

$$\hat{\mathbf{s}}(t) = \mathbf{W}\mathbf{x}(t) \qquad (2)$$

After performing ICA, it is expected that the separating matrix $\mathbf{W}$ converges to a fixed value which should ideally be equal to the pseudo-inverse of the mixing matrix: $\mathbf{W} = (\mathbf{A}^{\mathrm{T}}\mathbf{A})^{-1}\mathbf{A}^{\mathrm{T}}$. ICA involving higher-order statistics of sources is one of the approaches for Blind Source Separation (BSS). It sometimes only consider second-order statistics. An up-to-date review of the state of the art in BSS/ICA is provided in [9]; frontiers of research in this area are summarized in [10].

Applications of ICA show special promises in the areas of non-invasive human brain imaging techniques to delineate the neural processes that underlie human cognition and sensori-motor functions. To understand human neurophysiology, we rely on several types of non-invasive neuroimaging techniques: EEG, MEG, and functional MRI (fMRI). While each of these techniques is useful, there is no single technique that provides both the spatial and temporal resolution necessary to make inferences about the intracranial brain sources of activity. The application of ICA in brain imaging has two purposes: noise reduction and location detection of brain activation. Very recently, several research groups have demonstrated that the techniques and methods of BSS are related to those currently used in electromagnetic source localization (ESL) [1].

2. EEG AND MEG DATA PROCESSING

When a region of neural tissue (consisting of about 100,000 or more neurons) is synchronously active, detectable extracellular electric currents and magnetic fields are generated. These regions of activity can be modeled as "current dipoles" because they generate a dipolar electric current field in the surrounding volume of the head. These extracellular currents flow throughout the volume of the head and create potential differences on the surface of the head that can be detected with surface electrodes in a procedure called electroencephalography (EEG). One can also place super-conducting coils above the head and detect the magnetic fields generated by the activity in a procedure called magnetoencephalography (MEG). (see Figure 2).

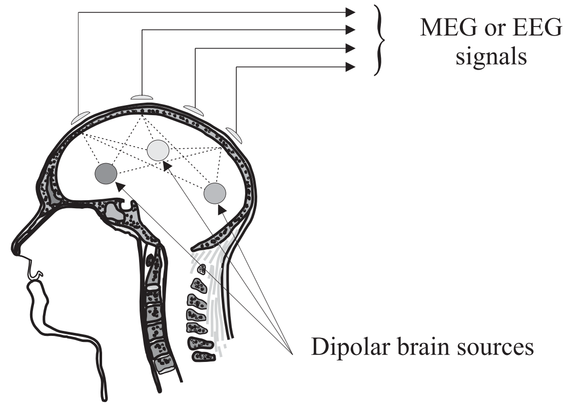

Fig. 1. Conceptual models for generation of EEG/MEG signals

Neural activity in the cerebral cortex generates small electric currents which create potential differences on the surface of the scalp (detected by EEG) as well as very small magnetic fields which can be detected using SQUIDs (SuperConducting QUantum Interference Devices). The greatest benefit of MEG is that it provides information that is complementary to EEG. In addition, the magnetic fields (unlike the electric currents) are not distorted by the intervening biological mass. Under certain circumstances, this allows precise localization of the neural currents responsible for the measured magnetic field.

If one knows the positions and orientations of the sources in the brain, one can calculate the patterns of electric potentials or magnetic fields on the surface of the head. This is called the forward problem. If otherwise, one has only the patterns of electric potential or magnetic fields, then one needs to calculate the locations and orientations of the sources. This is called the inverse problem. Inverse problems are notoriously more difficult to solve than forward problems. In this case, given only the electric potentials and magnetic fields on the surface, there is no unique solution to the problem. The only hope is that there is some additional information available that can be used to constrain the infinite set of possible solutions to a single unique solution.

Determining which regions of the brain are active, given EEG/MEG measurements on the scalp level is an important problem. An accurate and reliable solution to such a problem can give information about the higher brain functions and patient-specific cortical activity. However, estimating the location and distribution of electric current sources within the brain from EEG/MEG recordings is an ill-posed problem, because there is no unique solution and the solution does not depend continuously on the data. The ill-posedness of the problem and the distortion of sensor signals by large noise sources make finding a correct solution a challenging analytic and computational problem.

In the ICA approach, the sources of activation are considered temporally independent to artifacts and interferences: eye and muscle activity, line noise, and cardiac signals, which are assumed not to be time-locked to the sources of EEG activity conceived to reflect the synaptic activity of cortical neurons. Signal propagation is supposed instantaneously and summation of currents at the scalp sensors is considered essentially linear.

ERP time courses recorded from the human scalp are generally averaged prior to their analysis to increase their signal/noise ratio relative to other non-time and phase locked EEG activity and non-neural artifacts [11]. The source distributions are mostly super-Gaussian since an averaged ERP is composed of one or more overlapping series of relatively brief activations within spatially fixed brain areas performing separable stages of stimulus information processing. The super-Gaussian statistics of independent components of ERP data may indicate that brain information processing is dominated by spatially sparse, intermittently synchronous brain structures. The number of sensors is supposed to be at least equal to the number of signal sources, though this is highly questionable.

The statistical estimation of the source components from observed EEG signals should be performed irrespective of the physical locations or configuration of the sources. ICA is therefore useful in solving the elimination of artifactual signals and the source identification problem in EEG/MEG signal processing. The EEG/MEG data can be first decomposed into useful signal and noise subspaces using standard techniques like local and robust PCA, SVD and nonlinear adaptive filtering. Next, we apply ICA algorithms to decompose the observed signals (signal subspace) into independent components. The ICA approach enables us to project each independent component (independent "brain source") onto an activation map at the skull level.

2.1. Noise and Interference Cancellation

One important problem in brain imaging is how to automatically detect, extract and eliminate noise and artifacts. Another related problem is how to classify independent "brain sources" and artifacts. The automatic on-line elimination of artifacts and other interference sources is especially important for extended recordings, e.g., EEG/MEG recording during sleep. For each activation map, we can perform next an EEG/MEG source localization procedure, looking only for a single dipole (or 2 dipole) per map. By localizing multiple dipoles independently, we can dramatically reduce the complexity of the computation and increase the likelihood of efficiently converging to the correct and reliable solution.

ICA separates the source components based on the higher-order statistics of their distributions over time, which facilitates the differentiation between strictly periodical signals and regularly and irregularly occurring signals. Many artifactual signals in both EEG/ERP and MEG recordings are irregular in nature [12]. The assumption that EEG/MEG signals are different from artifacts and that their corresponding time courses are statistically independent enable their separation using the ICA. The independence of ERP signals and artifacts is valid in many cases by the known differences in physiological origins of those signals. Artifact-free EEG/MEG signals can be restored by back projection onto the data space of the remained estimated components after all presumable artifactual activities were discarded (Figure 2.1) [13]. The ICA method uses spatial filters after decomposition to filter artifactual signals and back-project only the significant source signals for their reconstruction. PCA is unable to completely separate eye artifacts from brain activity, particularly at comparable amplitudes, indicating that, in this application, the correlation is a weaker assumption.

The problem formulation can be stated in the following form: Denote by $\mathbf{x}(t)$ the observed m-dimensional vector of noisy signals that must be "cleaned" from noise and interference. Here we have two types of noise. The first one is the so called "inner" noise generated by some primary sources that cannot be observed directly but is contained in the observations. They are mixtures of useful signals and random noise signals or other undesirable sources. The second type of noise is the sensor additive noise (observation errors) at the output of the measurement system. This noise is not directly measurable, either. We also assume that some useful sources are not necessarily statistically independent. Therefore, we cannot achieve perfect separation of primary sources by using any ICA procedure. However, our purpose here is not the separation of the sources but the removal of independent or uncorrelated noise components.

The scheme of noise and interference cancellation is shown in Figure (2). $y_j(t),\ j = 1, 2, \ldots n$ denote the separated independent components from data; $\tilde{y}_j(t)$ indicates the postprocessed components. The projection of interesting or useful independent components (e.g., independent activation maps) $\tilde{y}_j(t)$ back onto the sensors (electrodes) can be done by the transformation $\hat{\mathbf{x}}(t) = \mathbf{W}^{+}\tilde{\mathbf{y}}(t)$, where $\mathbf{W}^{+}$ is the pseudo-inverse of the unmixing matrix $\mathbf{W}$. In the typical case, where the number of independent components is equal to the number of sensors, we have $\mathbf{W}^{+} = \mathbf{W}^{-1}$. A common technique for noise reduction is to split the signal in two or more bands. The high-pass bands are subject to a threshold nonlinearity that suppresses low amplitude values while retaining high amplitude values [14].

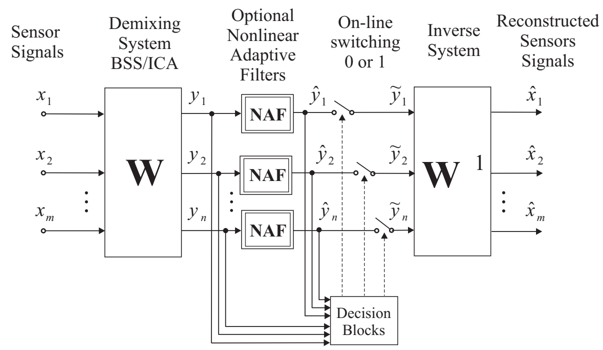

Fig. 2. Conceptual models for removing undesirable components like noise and artifacts and enhancing multi-sensory (e.g., EEG/MEG) data using nonlinear adaptive filters and hard switches .

Principal Component Analysis (PCA) is a standard technique for the computation of eigenvectors and eigenvalues of an estimated autocorrelation matrix of raw sensor data that enables not only reduction in the noise level, but also allows us to estimate the number of sources [15]. This approach has been applied to noise reduction in electroencephalographic signals. A problem arising from this approach, however, is how to correctly set or estimate the threshold which divides eigenvalues into the two subsets, especially when the noise is large, i.e., the SNR is low [15].

Recently, it has been realized that ICA or at least combining both techniques: PCA and ICA, is more appropriate for noise reduction and moreover such approach reveal the underlying structure of signals better than PCA alone [14], [16], [12]. Moreover, using ICA we can achieve better results in the sense that PCA use only second-order statistics, but ICA can estimate a better basis by taking into account higher-order statistics inherent in the data and allow to build nonlinear estimator instead of linear one. ICA algorithms can be also robust, what is very important for noise cancellation applications. ICA allows to separate sources $\mathbf{s}(t)$ based on observations $\mathbf{x}(t)$ using a maximum *a posteriori* method that is disposed of *a priory* information problem and allows to realize blind scenario. Using ICA we can find independent components, which are undesirable and can be thought of as noisy sources and eliminated.

It should be noted that the uncorrelated principal components are ordered by decreasing value, while independent components (ICs) are typically extracted without any order. We can apply first ICA and next ordering the independent components (ICs) according to the decreasing absolute value of their normalized kurtosis rather than their variances; since the normalized kurtosis $\kappa_4(y_i) = \frac{E\{y_i^4\}}{E^2\{y_i^2\}} - 3$ is a natural measure for Gaussianity of signals. Using $\kappa_4(y_i)$, we can easily detect and remove white (colored) Gaussian noise form raw sensory data. Optionally we can use more robust measures to detect and classify specific ICs [17].

2.2. Source Localization

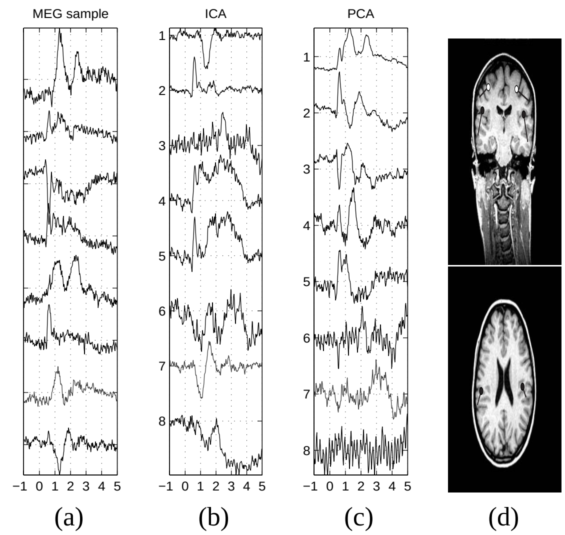

Fig. 3. (a) A subset of 122-MEG channels in an auditory experiment. (b) Independent and (c) Principal components of data. In (d) the superposition of the localizations of the dipole originating and IC2 onto MRI of the subject.

Figure 3 illustrates an example of a promising application of blind source separation (BSS) and independent component analysis (ICA) algorithms for localization of the brain source signals activated after the auditory and somatosensory stimulus applied simultaneously. In the MEG experiments performed in collaboration with the Helsinki University of Technology, Finland, the stimulus presented to the subject was produced with a sub-woofer, and the acoustic energy was transmitted to the shielded-room via a plastic tube with a balloon at the end [15]. The subject had his hands in contact with the balloon and sensed the vibration. In addition, the sound produced by the sub-woofer was listened to by the subject, constituting the auditory stimulation. Using ICA, we successfully extracted auditory and somatosensory evoked fields (AEF and SEF, respectively) and localized the corresponding brain sources [15] (see Figure 3).

In addition to denoising and artifacts removal, ICA/BSS techniques can be used to decompose EEG/MEG data into separate components, each representing a physiologically distinct process or brain source. The main idea here is to apply localization and imaging methods to each of these components in turn. The decomposition is usually based on the underlying assumption of statistical independence between the activation of different cell assemblies involved. An alternative criterion for decomposition is temporal predictability or smoothness of components. These approaches lead to interesting new ways of investigating and analyzing brain data and developing new hypotheses how the neural assemblies communicate and process information. This is actually a very extensive and potentially promising research area, however these approaches still remain to be validated at least experimentally.

Recent results have shown by means of ICA that some features of an evoked response may actually be produced by event-related changes in the autocorrelation and cross-correlation structure of the ongoing EEG processes [18]. This reflects that synchronous activity in the brain occurs continuously in some brain regions or by small perturbations in their dynamics. It comes out that applying ICA to EEG/ERP data may constitute a potential source of information on mechanisms of neural synchronization.

3. FUNCTIONAL MRI AND PET

Although EEG/MEG signals are good for monitoring the electrical and magnetic field activity over the skull, spatial resolution depicted by EEG/MEG signals over the brain is limited. Based on the change of local blood supply for active neurons, PET and fMRI provide brain imaging signals from the whole brain at a much higher resolution. By means of short-lived isotopes that emit positrons, PET allows measuring the rate of blood flow through particular regions of the brain. The basic framework for the analysis of imaging time series was developed in PET neuroimaging and thereafter extended up to fMRI. The basic assumption is that an increase in neuronal activity within a brain region entails an increase in local blood flow, leading to reduced concentrations of deoxyhemoglobin, which has a differential magnetic susceptibility in relation to the surrounding tissue. Therefore, relative decreases in deoxyhemoglobin concentration attract a reduction in local field inhomogeneity and a slower decay of the MR signal, resulting in higher intensities in T2 weighted images.

FMRI data carry spatio-temporal information of responses of the brain responses activated by some functional tasks. FMRI data are always confounded by physiological signals such as cardiac, respiratory, and blood flow, the electronic noise of the scanners and other environmental artifacts [19, 20, 21, 22]. The detection of the brain activation is usually performed by statistically comparing time-series corresponding to each brain voxel with the input stimuli and generating statistical maps. The simplest of these approaches is the correlation analysis [23]. In order to correct for multiple comparisons and spatial correlations, the statistical maps are further analyzed using the Gaussian Random Field (GRF) theory, whose approach is referred to as the *statistical parametric mapping* (SPM) [24]. Prior to the simple correlation analysis or the SPM analysis, fMRI data is required to be preprocessed using appropriate denoising or smoothing filters and correct for artifacts. These preprocessing techniques are still mostly ad hoc and tend to alter the original data.

Recently, ICA has become an increasingly promising data-driven approach for the analysis of fMRI data because of its capability of separating the components of interest, that are due to task-related brain activation, from other components that are due to interferences and artifacts [20]. Therefore, it is unnecessary to preprocess fMRI data before using the ICA technique for the detection of brain activation. Figure (4) shows separation of independent components on data obtained on a simple visual task: an alternating checker board pattern with a central fixation point was projected on an LCD system; subjects were asked to fixate on the point of stimulation. Further experimental details are available in [21].

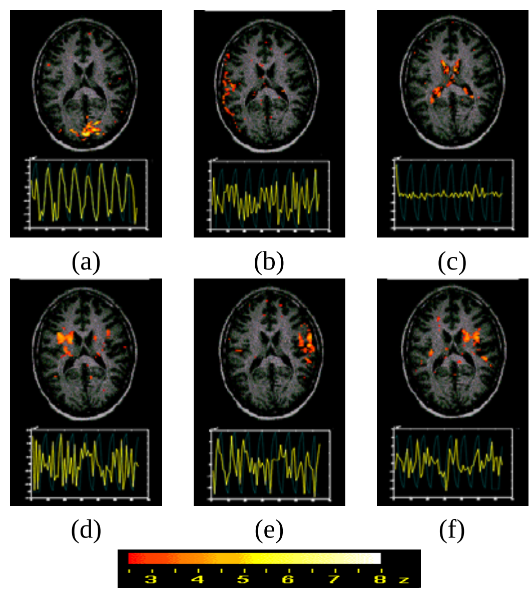

Fig. 4. Various activation maps and corresponding time-series separated by spatial ICA in a visual experiment. (a) 33th component indicating activation in the visual cortex, (b) 7th component indicating head motion artifacts, (c) 9th component indicating flow artifacts, and (d) 25th component indicating significant noise. (e) and (f) indicate components of motor activation.

3.1. Temporal, Spatial and Spatio-Temporal ICA

FMRI data is essentially spatio-temporal as a series of brain scans are acquired over time during a functional experiment. Recently, there has been a growing interest in applying ICA to analyze fMRI data in two different ways: spatial ICA (SICA) and temporal ICA (TICA) [20, 25, 26]. The premise of ICA application in fMRI analysis is that the task-unrelated components in fMRI data are either independent in spatial-domain (SICA) or independent in the time-domain (TICA) to the task-related components. The data is decomposed into a set of spatially independent components in SICA whereas the TICA decomposes fMRI data into a set of temporally independent components.

If the time series corresponding to the i th brain voxel is $\mathbf{x}_i = (x_{1i}, x_{2i}, \ldots x_{mi})^{\mathrm{T}}$, the fMRI data set is given by the matrix, $\mathbf{X} = [\ \mathbf{x}_1\ \mathbf{x}_2\ \ \ldots\ \mathbf{x}_P\ ]$ where P is the total number of brain voxels and m is the total number of scans collected over time. SICA is based on the fact that input data is decomposed into n spatially independent components, $\mathbf{s}_j,\ j = 1, 2, \ldots n$ such that

$$\mathbf{X} = \mathbf{A}\mathbf{S}^{\mathrm{T}} \tag{3}$$

where $\mathbf{A}$ is the mixing matrix and $\mathbf{S} = [\ \mathbf{s}_1\ \mathbf{s}_2\ \ \ldots\ \mathbf{s}_n\ ]$ is the matrix of the independent component maps. $\mathbf{x}_j = (s_{1j}, s_{2j}, \ldots s_{Pj})^{\mathrm{T}}$ denotes the j th spatial component map. The decomposition made by TICA can be given by

$$\mathbf{X}^{\mathrm{T}} = \mathbf{S}\mathbf{A}^{\mathrm{T}} = \mathbf{A}_t\mathbf{S}_t. \tag{4}$$

Thus, by taking the transpose, we change the roles of the mixing matrix and the independent components. In fact, we consider both matrices as being independent variable entities as much as possible. This is the basic idea in spatio-temporal ICA [15].

In SICA, the multifocal brain areas activated due to a sensory or cognitive task are presumed to be unrelated to the brain regions that are affected by the artifacts and confounds. The signals due to heartbeat, respiration, and blood flow can be considered as mutually independent in time-domain because they have frequencies that are different from the task. On the other hand, the spatial independence of the effect of these signals in the brain is questionable because the influence of noise and interference is common to most regions of the brain. Furthermore, the motion artifacts which may be transiently task-related, appear in the most part of the brain indiscriminately. Therefore, some of the sources in fMRI data are deterministic in nature and the associated component maps may not be unrelated spatially but may be independent in time because their characteristics differ in time-domain. Therefore, it is more appropriate to assume that these noise and interference sources involved in fMRI data are independent in time-domain rather than in the spatial-domain. However, to date, SICA has dominated most applications, mainly, because the computational requirements of TICA has been much higher than those of the SICA. The SICA approach is biased towards finding relatively sparse and discrete components, and the task-related component might split into several ICA components associated to smaller active areas with closely related time-courses [20]; if a number of independent brain processes are active during the task, the task-related activation may appear in different component maps. Furthermore, if two component processes contributed by the input stimulation appear in a well-overlapped brain area, the ICA may split the resulting activation areas into many component maps.

In general, TICA is preferable to SICA because most non-task related signals are more likely to be independent in time-domain. However, because the number of voxels of fMRI data in the spatial domain is large, applications of TICA is prohibitive in practice. In simple experiments like the finger tapping paradigm, it has been demonstrated that SICA and TICA produce similar results [27]. However, a recent study [26] using especially designed visual activation paradigms each consisting of two spatio-temporal components that were either spatially or temporally uncorrelated has shown that the independent components produced by different ICA approaches may be task-dependent. Therefore, the independent components of fMRI data, produced by SICA and TICA, may be valid depending on the task. A combination of SICA and TICA has also been considered by Stone et. al. [28], but its limitations are obvious as it is more difficult to design both spatially and temporally independent task approaches that are independent to other interference and noise as well.

3.2. Detection and Significance of Activation Maps

ICA-based decomposition of fMRI signals is consistent with fundamental neurophysiological principles concerning the spatial extent of neural activity during the performance of psychomotor tasks. Artifacts that make up the bulk of the variability in the measured fMRI data should have spatial patterns of activity separate from the localization of brain areas involved in task-related activation. After separation of independent components, it remains to select the map corresponding to actual brain activation. This is currently done post hoc, correlating the time-series corresponding to component maps with those of the input stimuli and finding the component giving rise to the maximum correlation [20]. An attempt to incorporate the input stimuli as reference signal is also reported in [29]. This approach has the computational advantages by producing only the task-related component in ICA.

When a correlation approach is used in fMRI, it is customary to express the activation with a certain level of significance. The ICA model does not provide a significance estimate for the activation of each separated component, what obscures the result interpretation. In fMRI applications, by placing ICA in a regression framework, it may be possible to combine some of the ICA benefits with the benefits of the hypothesis-testing approach.

4. CURRENT AND FUTURE DIRECTIONS

There is a current trend in linear ICA/BSS to investigate the average eigen-structure of a large set of data matrices which are functions of available data (typically, covariance or cumulant matrices for different time delays). In other words, the objective is to extract reliable information (like for example, estimation of sources and/or the mixing matrix) from the eigen-structure of a possibly large set of data matrices. However, since in practice only a finite number of samples of signals corrupted by noise is available, the data matrices do not exactly share the same eigen-structure. Furthermore, it should be noted that determining the eigen-structure on the basis of one or even two data matrices leads usually to poor or unsatisfactory results because such matrices, based usually on arbitrary choice, may have some degenerate eigenvalues and they usually discard information contained in other data matrices. Therefore, from a statistical point of view, in order to provide robustness and accuracy, it is necessary to consider the average eigen-structure by taking into account simultaneously a possibly large set of data matrices. Several very promising algorithms like Robust SOBI, JADE with time delayed cumulants, and SEONS exploit average eigen-structure and enable us to estimate reliable sources and the mixing matrix for noisy data [1].

Very recently, research and development has moved the field toward more general non-independent and/or nonlinear source separation approaches. The main objective is to develop and investigate novel criteria which enable to separate sources which are not precisely independent by using various criteria like linear predictability, smoothness, Kolmogorov complexity, and sparsity. Also semi blind concepts are further investigated where some *a priori* knowledge is exploited, e.g., knowledge about the source distribution.

There are still many open and challenging problems like the following:

1. What are meaningful cost functions which enable us to estimate brain sources which are not completely independent.

2. Are brain signals nonlinearly mixed?

3. If yes, which nonlinear model is valid.

4. How to estimate the number of sources and their waveforms if recorded biological data is corrupted by a large amount of noise, and external and internal interference (e.g., on- going brain activities).

5. How to facilitate the linear or nonlinear BSS problem by incorporating prior knowledge?

The independence assumption may not provide a unique decomposition of the data and may not be the desired representation of the brain imaging data. Nevertheless, ICA may be useful in noise cancellation or in discerning activation in an exploratory manner. For example, to determine differentially activated brain regions such as those transiently task related due to arousal and alertness, or independent brain processors involved during a particular task.

The ICA approach is meaningful only if the amount of data processed by the algorithm is large enough and the independence assumption holds. Even so, the results are influenced by the assumption that the sources of artifacts and cerebral activity remain spatially stationary through time, which is not always true all over the trials. There should be some means to validate ICA decompositions. One way is to simulate the conditions under which IC is likely to fail like simulated EEG recordings generated from a head model and dipole sources that include intrinsic noise and sensor noise, when the number of sources is larger then the number of sensors. Another approach is based on simultaneously recording and analyzing the correlation of concurrent types of signal, such as EEG and fMRI, which have good temporal (EEG) and good spatial (fMRI) resolution, respectively.

5. CONCLUSIONS

ICA identifies sources with independent and sparse dynamics that may or may not be neuro-anatomically/functionally segregated. ICA effectively removes artifacts and separate the sources of the brain signals on the basis of minimal suppositions on their underlying distributions and further decomposes the remained mixed signals into subcomponents that may reflect the activity of functionally distinct generators of physiological activity. The limits of the usefulness of ICA for EEG, MEG, fMRI and PET analysis will ultimately depend on the matching between the underlying assumptions of the analysis and the composition of the experimental data. ICA appears to be well-suited for noise reduction; whether it is a good approach to detect brain activation remains to be further investigated and validated.

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