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A TEMPORALLY CONSTRAINED SPATIAL ICA FOR SEPARATION OF SEIZURE BOLD FROM FMRI

Min Jing and Saeid Sanei

Centre of Digital Signal Processing, Cardiff University, UK
email: {jingm,saneis}@cardiff.ac.uk

ABSTRACT

Application of spatial Independent Component Analysis (ICA) to functional magnetic resonance imaging (fMRI) subject to the simultaneously recorded electroencephalography (EEG) signals as constraint, has been investigated in this work. In this novel approach, the closeness between the time course of spatial independent components of fMRI and EEG signals during epileptic seizure period is introduced as the constraint to the separation process. The performance of the algorithm has been tested on a set of simultaneous EEG and fMRI data and the results show a more accurate localization of the blood-oxygenated level-dependence (BOLD) regions, better algorithm convergence, and a higher correlation between the time course of spatial components and the seizure EEG signals than the conventional ICA method.

1. INTRODUCTION

As one of the advanced brain function monitoring modalities, fMRI provides high resolution spatial information which helps visualization of the brain activation. Blood-oxygenated level-dependence (BOLD) regions in fMRI result from event-related, movement-related, and abnormal brain activities such as seizures. The most widely used approach for fMRI data analysis was developed by Friston et al. (1995) [1], which is based on the general linear model (GLM). Based on this model, the prior knowledge or specific assumptions about the time courses contributing to the signal changes are required for model specification. Therefore, the appearance of false BOLD regions or lack of BOLD in places where the right stimulus cannot be modelled is inevitable by using this technique. This can happen in seizure detection and localization using fMRI, when the ictal duration is short and the seizure onset is difficult to be specified.

In comparison with the common fMRI analysis, for which the functional data are acquired from the designed experiments, the fMRI data from epileptic seizures are very different. As the spontaneous brain activation caused by certain functional disorders, the response of epileptic seizure is very difficult to be modelled or to be predicted. Although in some literature [2]-[3], some researchers have investigated the statistical parameter mapping of epileptic EEG and fMRI data, the seizure spike mapping in their methods was strictly limited by carefully choosing the functional data that have distinguishable periodic seizure spikes, so that the spikes can be used as the stimuli to construct the design matrix. Although these approaches can work for the mapping of epileptic spikes, but a very carefully chosen functional data and marking the spikes accurately by clinical expert are required. In such cases, a model-free method as ICA is more desirable to detect the seizure active area without any preassumptions about the seizure time course.

In contrast to the model-based GLM, the data-based model relies on the data instead of prior information on stimuli or predefined brain functions. Spatial ICA (SICA), which was proposed by McKeown et al. in [4] as the first application of ICA to fMRI data analysis, has raised more attention recently. In this model, the fMRI data are considered as the linear combination of a number of temporally or spatially independent components, and no preassumptions regarding the stimuli responses are required. This is favorable since the brain function and its hemodynamic response are too complicated to simply choose a fixed predefined HRF and to assume that the shape of HRF remains constant during the events for all brain voxels. Although some research have exploited temporal [8] and spatiotemporal [6] [12] ICA for the analysis of fMRI data, more work reside in the SICA due to the temporal dynamics of brain activities still remains unknown and the computational cost is extremely high in the temporal ICA approach.

The constrained ICA has also been applied to fMRI signal analysis in order to incorporate more prior information into separation process. The prior information could either take the fMRI time course into account, or as shown in this work, use the temporal information from the EEG data. Recent works have shown that the performance of ICA for fMRI analysis will improve if some prior information is incorporated into the estimation process [7]-[9]. Lu and Rajapakse [8] employed a predefined stimulus as the reference signal in the temporal ICA model such that the output source components are closest to the reference. Calhoun et al. presented a semi-blind spatial ICA [9], in which the constraint is introduced by incorporating the GLM design matrix which contains information on the fMRI time course. Although these methods provided some promising results, their constraint still relies on GLM, therefore they are only suitable for the case that the stimuli of the fMRI data can be prespecified. For an epileptic fMRI, these approaches cannot work due to the difficulties of specification of the epileptic seizures.

More recently the relationship between hemadynamic and electrical activity has been investigated in animal [10] and humans [11], which has shown that the amplitude of hemodynamic response at the region of interest follows the change of the amplitude of the evoked electrical response. The connection between the components of ERP and fMRI spatial maps has been examined in [12]. The results from these studies suggested that hemadynamic response and electrical activity have certain connection. In this work, a novel constrained SICA (CSICA) method is proposed, in which the relationship between the simultaneous recorded EEG and fMRI has been introduced into separation process as the temporal constraint.

In the following sections, the SICA model is first briefly described and the development of the CSICA algorithm is explained. The experiment results are then presented. The proposed method is applied to a set of simultaneous EEG and fMRI data, the results are compared with an unconstrained SICA. The better performance of CSICA is illustrated in terms of algorithm improvement, correlation measurement and seizure BOLD mapping in the brain.

2. METHOD

2.1 Spatial ICA

The first application of the spatial ICA model for fMRI analysis was introduced by McKeown et al. in 1998 [4]. In this model, the brain areas executing different tasks are assumed to be spatially independent and the fMRI data are linearly combined by a number of independent components associated with their time course of activation. As in a conventional noise free instantaneous linear model, the mixing process of the spatial ICA can be expressed as:

$$\mathbf{X} = \mathbf{AS} \tag{1}$$

Where $\mathbf{X}$ is a $T \times V$ matrix of the mixtures, T is the length of the fMRI scan in terms of time samples, V is the number of brain voxels involved in the analysis. $\mathbf{A}$ is a $T \times N$ mixing matrix, N is the number of the unknown spatial independent sources. $\mathbf{S}$ is a $N \times V$ matrix of unknown sources. From this model, it can be seen that the fMRI signals can be decomposed into a number of spatial independent components $\mathbf{S}$ and their associated activation waveform (the time course of activation) $\mathbf{A}$. The unknown sources can be obtained by estimating an unmixing matrix $\mathbf{W}$ and computing

$$\mathbf{Y} = \mathbf{WX} \tag{2}$$

Where $\mathbf{Y}$ is an $N \times V$ matrix of the estimated sources, and $\mathbf{W}$ is an $N \times T$ unmixing matrix to be estimated. In an optimal case, $\mathbf{W}$ should be the pseudoinverse of $\mathbf{A}$, i.e. $\mathbf{W}^{\dagger} = \mathbf{A}$. († denotes pseudoinverse).

2.2 Constrained Spatial ICA

A recent work has shown that the performance of application of ICA to fMRI analysis will improved if a prior information is incorporated into the estimation process. As in [9], Calhoun et al. presented a semi blind spatial ICA. In the approach, the constraint is introduced by incorporating GLM design matrix which contains the information of fMRI time course. The columns of the mixing matrix are constrained according to the their closeness to the predefined design matrix time course. At each iteration of estimation, the weight parameters are updated not only based on the Infomax [13] learning rules, but also by comparing their cross-correlation with the time course from the design matrix. If the correlation is lower than certain threshold, the weights will be reupdated based on the constrained rule. However, this method cannot work for seizure fMRI data because their constraint still rely on the GLM.

In this work, we aim to incorporate the simultaneously recorded EEG data into the fMRI separation process as the constraint. As the columns of the mixing matrix represent the time courses of the spatial components, the temporal constraint can then be added to the columns of the mixing matrix such that EEG information can be taken into account.

The ICA algorithm is chosen as Infomax [13], in which the separating matrix is updated by using the natural gradient method as:

$$\mathbf{W}(k+1) = \mathbf{W}(k) - \eta(k)[I + \varphi(\mathbf{Y})\mathbf{Y}^H]\mathbf{W}(k) \tag{3}$$

Where $\mathbf{I}$ is the identity matrix, $\eta(k)$ is the learning rate at iteration k. $\varphi(\cdot)$ is a nonlinear function which is selected as $\varphi(\cdot) = 2tanh(\cdot)$. $(\cdot)^H$ denotes the conjugate transpose. A new constrained update rule is formulated as

$$\mathbf{W}(k+1) = \mathbf{W}(k) - \eta(k)[I + \varphi(\mathbf{Y})\mathbf{Y}^H + \alpha\Lambda]\mathbf{W}(k) \tag{4}$$

where α is an empirical adjustment factor which is adjusted based on the algorithm performance to ensure that the algorithm monotonically converge. $\Lambda = diag\{\Lambda_{ii}\}, i = 1, ..., N$, is a diagonal weight matrix containing the temporal information about EEG data, which works as the constraint. Λ can be formed as

$$\Lambda = diag(cor(\mathbf{W}_i^{-1}, \mathbf{u})) \tag{5}$$

where $cor(\cdot)$ denotes the correlation measurement and $\mathbf{u}$ represents the seizure EEG reference after processing. $\mathbf{W}_i^{-1}$ represents each column of the mixing matrix $\mathbf{A}$ as $\mathbf{W}$ is the pseudoinverse of $\mathbf{A}$. Based on this constraint, the temporal information from EEG is taken into account in fMRI separation because the columns of the mixing matrix represent the weights of the time course of the components. The optimization process is subject to the correlation between the i^{th} column vector of the mixing matrix and the processed EEG time series $\mathbf{u}$. The seizure signal $\mathbf{u}$ has to be selected carefully either by using a seizure detection technique, or by choosing the seizure component from separation of multichannel EEG data, or based on the prior clinical information about the seizure. In this work, $\mathbf{u}$ is chosen based on the prior clinical information.

Therefore, according to Eq. (4), the constraint is added into the Infomax algorithm learning process. In each update iteration, $\mathbf{W}$ will be updated not only based on the Infomax principle, but also based on the closeness of the columns of $\mathbf{W}^{-1}$ to the processed EEG signal.

3. EXPERIMENTS AND RESULTS

3.1 Data detail

The simultaneously recorded EEG and fMRI data were obtained from National Society for Epilepsy, University College London (UCL). The fMRI data were acquired on a modified 3T GE Horizon system and EEG data were recorded by Brain Product system. The length of EEG-fMRI data is approximately 5 mins before the seizure onset. The functional data was acquired starting from the 16^{th} scan. In this experiment, the functional data was truncated from the acquisition 20^{th} till 107^{th}, which is the scan just before seizure onset. The first four scans were discarded in order to remove the initial gradient effect in the fMRI recording. Each acquisition consists of 47 contiguous slices, the dimension of the images is $64 \times 64 \times 47$, the voxel size is $3.75mm \times 3.75mm \times 2.5mm$. The interval between each scan, RT (Repeat Time) is 3 sec. The simultaneous 64 channel EEGs are sampled by 250Hz, and the scanner artifacts have been removed by data provider.

3.2 Preprocessing

(1)The raw fMRI sequences were processed in both spatial and temporal domains using SPM (Statistical Parameter Mapping). The preprocessing procedure included slice timing and realignment in order to mitigate the motion artifacts. (2) The off-brain voxels were excluded from the image data to reduce the data dimension. The data were then converted from 4D to 2D format to be ready for application of the spatial ICA. (3) In order to construct the reference vector $\mathbf{u}$ in Eq. (5), the signals from electrodes F8 and P8, which contain the most significant seizure information, were selected based on the clinical consultant suggestion. (4) The reference signal was filtered by a lowpass filter with the edge frequency of 15 Hz to keep the important seizure information (because the frequency of seizure is in the range of 2.5 to 15 Hz [14],[15]). (5) The difference in resolution between the EEG and fMRI signal was solved by down-sampling the reference EEG and up-sampling the column of mixing matrix.

3.3 Results

The SICA and the proposed CSICA were applied to the processed fMRI data. In each iteration of CSICA, the correlation between the column vectors of $\mathbf{W}^{-1}$ and EEG reference vector was measured as the factor of constraint. Then the unmixing matrix $\mathbf{W}$ was updated according to Eq. (4). The performance of the two algorithms is compared in terms of convergence (weights change), the correlation between the seizure EEG reference and the corresponding columns of the mixing matrix, and the mapping of the dominant component from separation.

Fig. 1 gives the algorithm convergence graph. It clearly shows that the proposed CSICA algorithm converges to a lower minimum than that from SICA. Fig. 2 illustrates the region of activation obtained from both algorithms. The level of the activity is represented by the normalized standard deviation (z-value). The activation area is the brain area in which the voxles have the z-value higher than the threshold (1.5 in this experiment). The mapping of component (active area) is then displayed by overlaying the area on the top of high solution structure images. Based on the advices of the clinical consultant, the highlighted part in the left frontal area is caused by the MRI scanner noise, and the right temporal area is verified to be within the epileptic zone. This has been verified by clinical consultant. Also based on the clinical investigation, the small patch at the right temporal region is more focussed in the result obtained from the CSICA.

Table 1 gives the maximum correlation coefficients between the column vectors of mixing matrix and the EEG reference, which were obtained by averaging five trials of each algorithm. It can be seen that CSICA provides the higher correlation between the columns of $\mathbf{W}^{-1}$ and the seizure EEG signal than that from the SICA.

Table 1: The maximum correlation between the EEG reference and column vectors of the mixing matrix.

SICA	CSICA
0.181	0.195

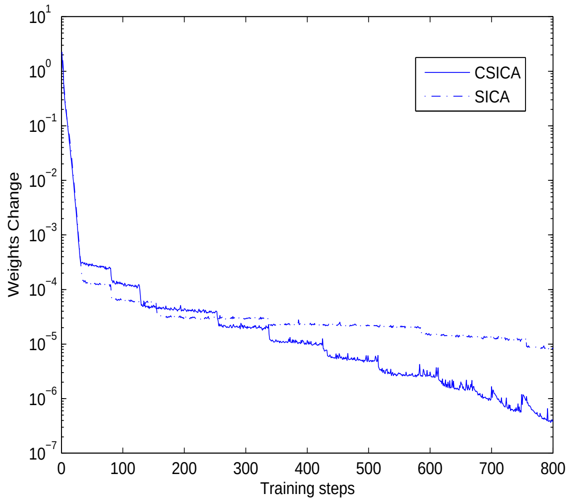

Figure 1: Comparison of algorithm convergence for the SICA and the CSICA.

4. CONCLUSIONS

In this paper for the first time the simultaneously recorded EEG seizure signal has been incorporated as the temporal constraint into the separation of fMRI sequences and localization of BOLD due to seizure using spatial ICA. The correlation between these two modalities and its application is indeed a challenging problem. The experimental results have shown that the BOLD region as the result of seizure onset, has been clearly highlighted using the proposed constrained spatial ICA approach. This algorithm outperforms the existing unconstrained SICA algorithm in terms of algorithm convergence and the closeness between the component time course and the seizure EEG signals. Further improvement in the performance may be achieved if a better mathematical modelling of the relationship between seizure EEG and fMRI can be developed. More comprehensive evaluation of the proposed method can be done if more dataset can be examined. This can be an agenda for future research in this area. Nevertheless, the results presented here still are very promising and can be further exploited in both separation and localization of seizure signals in joint EEG-fMRI signal processing.

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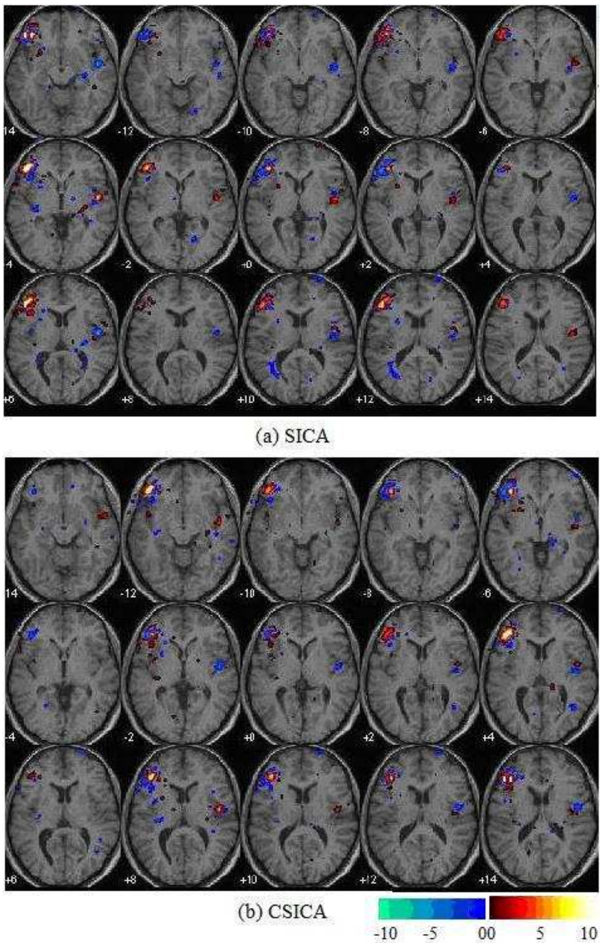

Figure 2: The BOLD obtained from the separation of fMRI data by using (a) SICA and (b) the proposed CSICA which incorporates the EEG signals as the constraint into the update equation

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