

## ROBUST ICA ANALYSIS FOR EVENT-RELATED FUNCTIONAL MAGNETIC RESONANCE IMAGING DATA

N. EL-SHABRAWY<sup>1</sup>, A. S. MOHAMED<sup>2</sup>, A. M. YOUSSEF<sup>3</sup> AND Y. M. KADAH<sup>4</sup>

### ABSTRACT

Independent Component Analysis (ICA) revealed significant treatment of both structured and random noise. Nevertheless, this technique suffers from a fundamental limitation of not providing a consistent ordering of the signal components. This mandates human intervention to pick out the relevant activation components from the outcome of ICA, which poses a significant obstacle to the practicality of this technique. In this work, a simple yet robust technique is proposed for ranking the resultant independent components. This technique adds a second step to ICA based on white noise (WN) criterion as well as power spectral analysis. The proposed technique is verified using computer simulations as well as actual real event-related functional magnetic resonance imaging data from a healthy human volunteer and the results confirm the practicality and robustness of the proposed method.

**KEYWORDS:** Functional magnetic resonance imaging, independent components analysis, white noise criterion, spectral analysis, signals de-noising.

### 1. INTRODUCTION

Functional MRI “fMRI” based on blood oxygenation level dependent “BOLD” contrast has evolved into a leading technique for functional brain imaging due to its noninvasiveness, high spatial resolution, and relatively high temporal resolution. One of the most challenging aspects of fMRI is the extraction of the BOLD signal from the complicated susceptibility-weighted “T\*” MR signal. Various noise sources contribute to the complexity of this susceptibility-weighted signal. Those physiologic in origin include MR signal modulation due to respiration, the beating of the human heart, and gross subject movement. These physiological sources can modulate the susceptibility,

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apparent proton densities, and apparent relaxation times. Other potential noise sources are scanner instability leading to signal drift, signal oscillations, and other complex image artifacts.

The advent of functional magnetic resonance imaging “fMRI” has resulted in many exciting studies that have exploited its unique capability. It provides a valuable noninvasive tool for investigating brain function. The different magnetic properties of oxy-hemoglobin and de-oxy-hemoglobin are used to visualize localized changes in blood flow, blood volume and blood oxygenation in the brain [1-3]. These in turn, become indicators for local changes in neural activity. To observe these hemodynamic changes, the subject is exposed to controlled stimuli, which are carefully designed to affect only certain brain functions then rapid acquisition of a series of brain images is performed. The sequence of images is analyzed to detect such changes. The result is expressed in the form of a map of the activated regions, which represents sensory, motor, and cognitive functions in the brain [4]. fMRI analysis approaches range from model-based to exploratory, although model-based approaches are by far the most utilized[5]. Model-based approaches are extremely useful when the time course of the hemodynamic response can be inferred apriori, however the hemodynamics of the brain are still being studied and good a priori assumptions are sometimes not available [6]. Besides, the data are in general very noisy, much statistical research has been devoted to studying how the weak activation signals may be extracted with optimal sensitivity. Thus, the use of data-driven analysis in fMRI is inherently attractive because it does not rely on imposed assumptions about experimental conditions. The concept of data driven decompositions became familiar since principal component analysis “PCA” and independent component analysis “ICA” have been introduced to fMRI data analysis [7-8]. Both ICA and PCA are closely related to projection pursuit methods [9]. The underlying idea is to find interesting directions or components within the multi-dimensional data set. Both ICA and PCA use linear transformation to get the components of the observed signals [10]. The key difference is in the type of the components obtained. The goal of PCA is to obtain principal components, which are defined as the uncorrelated direction of highest variance. In ICA however, the stronger

constraint of statistical independence is imposed. It seeks to obtain statistically independent components. Hence, PCA algorithms use only second order statistical information, while ICA algorithms utilize higher order statistical information for separating the signals. Moreover, PCA gives projections of the data in the direction of the maximum variance. The principal components (PCs) are ordered in terms of their variances. The first PC defines the direction that captures the maximum variance possible. The second PC defines “in the remaining orthogonal subspace” the direction of maximum variance, and so forth. This provides a natural ranking for the resulting components “even though this might not provide information about the usefulness of the components since the variance of a signal is not necessarily related to the importance of the variable”. On the other hand, ICA involves an intermediate whitening step that does not make the ranking based on projection magnitude possible. Therefore, there is no consensus of how this ordering can be performed [11]. Several attempts were reported including the use of the value of higher order statistics. These methods were not proven useful in many applications including fMRI and electro physiology data [12]. The lack of consistent ordering of components results in different arrangement of independent components each time the analysis is performed even on the same data set, which mandates the intervention by the user to select the “interesting” components out of the analysis result. This is usually a cumbersome task that takes fairly long time and makes the technique subject dependent. Therefore, an analysis technique that would allow the robust ordering of independent components without the intervention of the user would be rather useful. In the present work, we present a simple yet effective method for functionally ranking the resulting components of the ICA algorithm. Using a new natural ranking that does not depend on any model-based fMRI tools is created. It depends on the nature of the data itself, applied to the outcome of ICA. This new technique enables the elimination of the limitations of other techniques and provides a robust model-free mechanism for analyzing fMRI data. The proposed technique is verified using computer simulations as well as actual real event-related functional magnetic resonance imaging data from a healthy human volunteer and the results confirm the practicality and robustness of the

proposed method. This power spectral technique as a post processing leads to provide a consistent and reproducible ordering of independent components and isolate the random noise components of the MR signal by ranking the result. Noise components then can be removed before subsequent reconstruction of the time series data.

## 2. THEORY

### 2.1. Independent Component Analysis

Independent Component Analysis is a signal processing technique, created to separate a number of statistically “independent” sources that have been mixed linearly without further knowledge of their distributions or dynamics [13].

ICA assumes that there is  $N$  statistically independent inputs that have been mixed linearly in  $N$  output channels. Knowledge of joint distributions and statistical independence of latent variables is assumed [14]. If the matrix  $M$  represents the fMRI time series data in each voxel, then the decomposition can be thought of in terms of the matrix Equation:

$$M = WC \quad , \quad (1)$$

where  $W$  is the mixing matrix and  $C$  is the matrix containing the component map voxel values, where  $M$  is our data matrix where rows correspond to time and columns to spatial locations,  $C$  is the matrix of the independent components,  $W$  is the mixing matrix. In general, one wishes to solve for  $Z$  in the equation  $C = ZM$ , where  $Z$  is the inverse matrix of  $W$  and is a square matrix of full rank. Each column of  $Z^{-1}$  ( $=W$ ) returns the time course of modulation of its corresponding component map. These time courses may be correlated and non-orthogonal, but the distributions of voxel values in  $C$  are as statistically independent as possible. The ICA algorithm determines  $Z$  by an iterative method based on information theory principals, and the matrices  $C$  and  $Z$  provide a linear decomposition of the fMRI data. There are two types of ICA that can be calculated: Spatial ICA, in which the spatial components are constrained to be independent “ $C = ZM$ ”, and temporal ICA, in which the time courses of modulation are constrained to be independent “ $C = ZM$ ” [14,15].

## 2.2. White Noise (WN) Criterion

In order to determine which components of the decomposition can be considered white noise, we utilize an observed property of power spectra estimated by the multitaper method [15]. Empirically, it has been observed that if the power spectrum of a time series of random white noise is estimated by a straightforward Fourier transform with only one taper, the mean power across all frequency bins of the power spectrum is approximately equal to or greater than the standard deviation of the power across all frequency bins of the power spectrum. In the case of multitaper spectral estimation, in which there is a reduction in variance, one finds that the standard deviation of the power across all frequency bins of the power spectrum is frequently less than the mean power across all frequency bins of the power spectrum [15]. The WN criterion was met if the mean power across all frequency bins of the power spectrum was greater than the standard deviation of the power across all those frequency bins. If for any given component, if the WN criterion was met, then its power spectrum was considered essentially the spectrum of white noise and that component was scored as a relevant contributor to the overall noise content of the MR signal (i.e., the corresponding time mode component was considered a “noise” component). All data sets were processed with and without this criterion. If the WN criterion was not used, then only time-series components that contributed respiration and cardiac noise were considered noise sources.

The WN criterion was also used as a method for determination of a cutoff between relevant and non-relevant components in PCA-based denoising methods. This was defined as the point at which all components higher in rank passed the WN criterion for being non-structured (random) noise. These components were therefore labeled as non-relevant and were automatically zeroed for the data sets in which nonstructural noise was to be removed. Also, if nonstructural noise was to be considered for removal, then lower order components below the relevancy cutoff were also subjected to screening by the WN criterion.

### 3. METHODOLOGY

The algorithm implemented, all supporting routines were written in Matlab “math Works, Natick, MA”. This approach was applied to simulated fMRI datasets, one for event-related fMRI and the other for Block-design. In the simulation studies, the performance of the present approach was measured when used as a post process step after PCA/ICA to make its results easier to evaluate. In the experimental studies, the present approach was applied to activated time courses from experimental data obtained to illustrate its practical utility.

1) The computer simulations were performed whereby a computer generated ER-fMRI activation signal was added to an actual baseline data set. The number of epochs was 5 and the length of each epoch was 100. The generated activation was generated using a signal of the form (see fig.1 up to fig.3 for an example):

$$X(t) = (1 - \exp(\frac{-t}{T1}))^3 \cdot \exp(\frac{-t}{T2}) \quad , \quad (2)$$

where T1 and T2 are constants that can be adjusted to obtain the desired shape, and t represents the sampling times (i.e., the image number within an epoch). This signal was replicated for each epoch and added to either simulated Gaussian white noise or experimentally acquired baseline data as shown in Fig.1 and Fig.3. Also a computer generated Block design activation signal was added to an actual baseline data set as shown in Fig.4.

2) We added functions to the fastICA package as a post-processing step as shown in Fig.5. These functions will be included later with our practical implementation steps for our proposed technique [16].

3) The WN criterion observation [15] was extended to a rank criterion with help of correlation between the activation paradigm of the data and the output of the ICA as individual component to be a new rank method for the ICA output

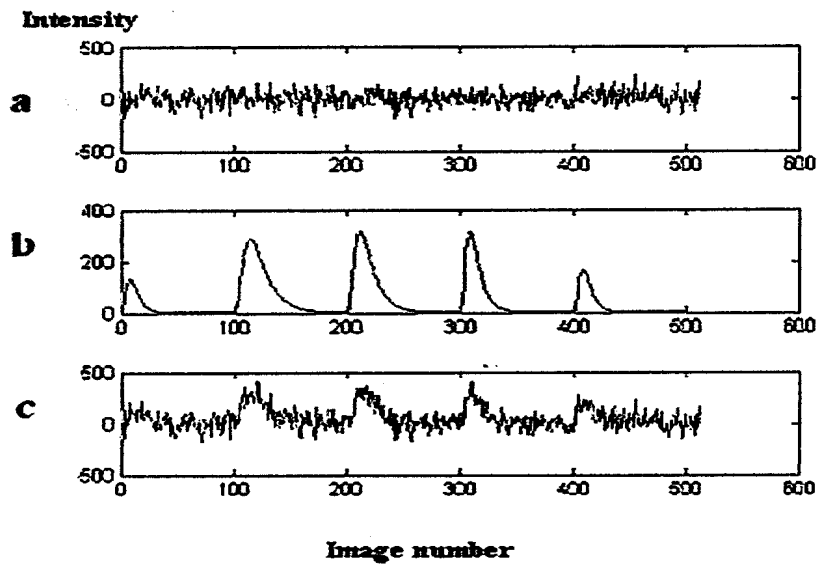


Fig.1. (a) experimentally acquired baseline noise.(b) The generated activation, (c) Simulated activation time course, where signal was replicated for each epoch and added to experimentally acquired baseline noise.

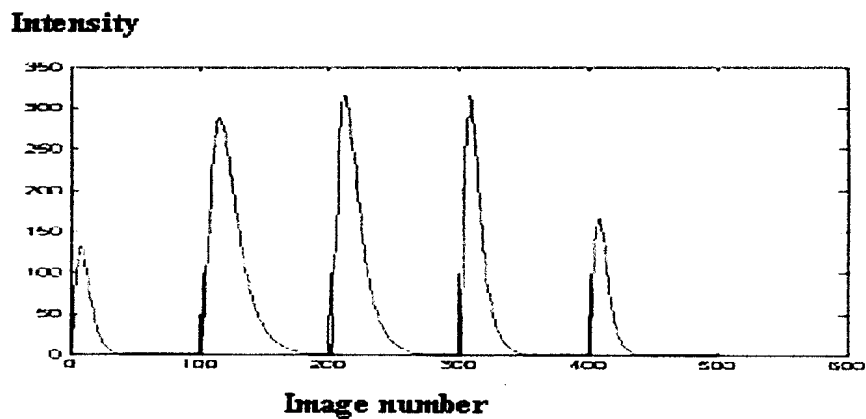


Fig.2. Stimulus marked on simulated activation.

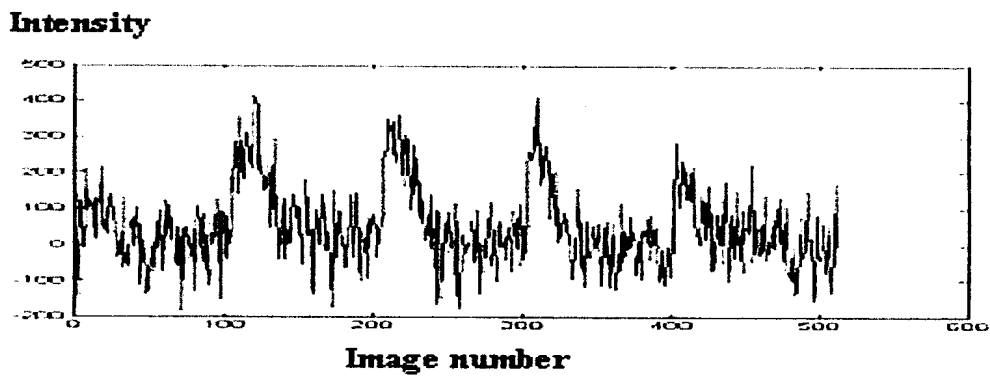


Fig.3. Computer generated ER-fMRI activation signal time course

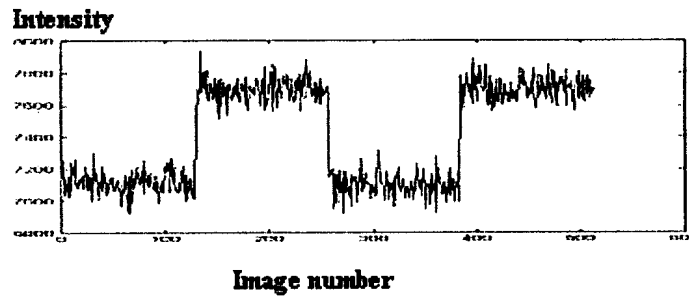


Fig.4. Computer generated Block design activation signal time course.

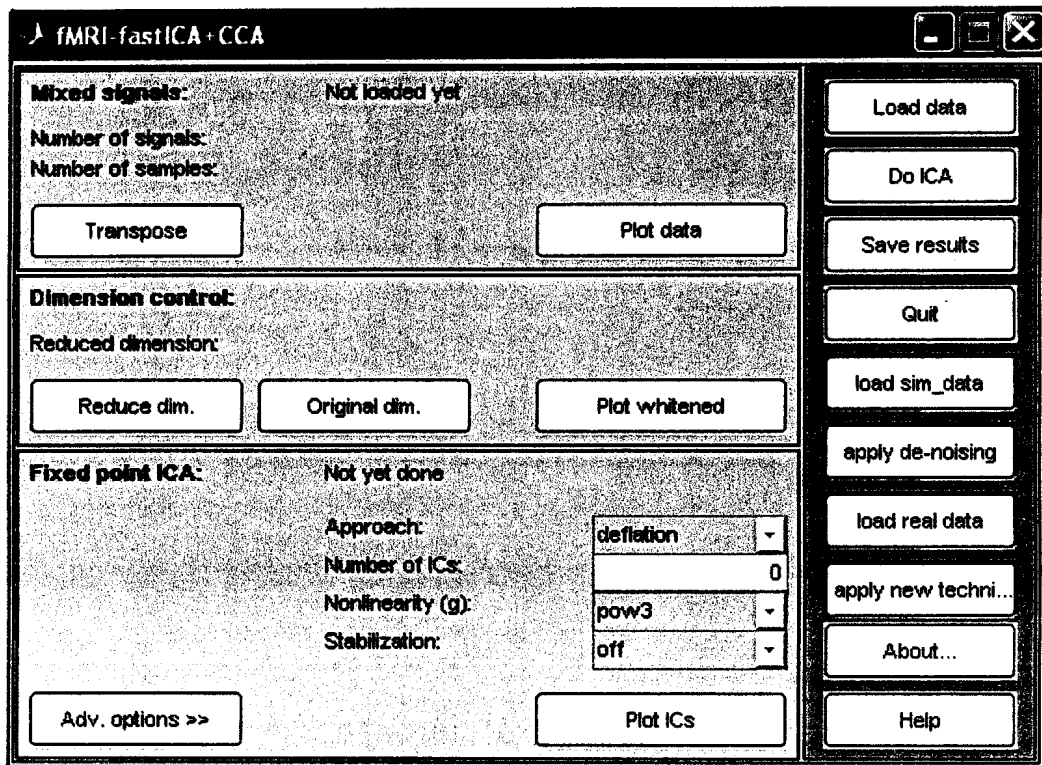
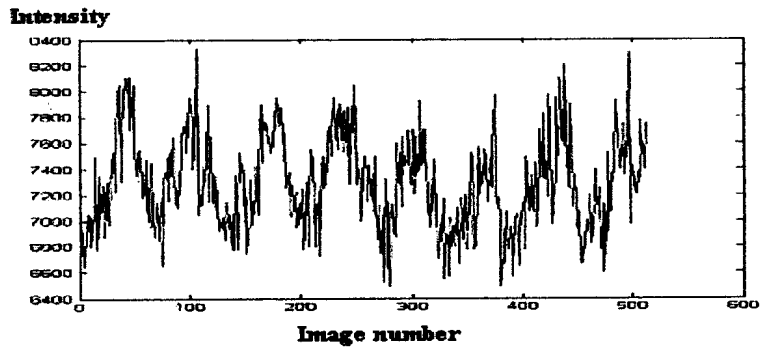


Fig.5. Functions has been added to fastICA as a post process step

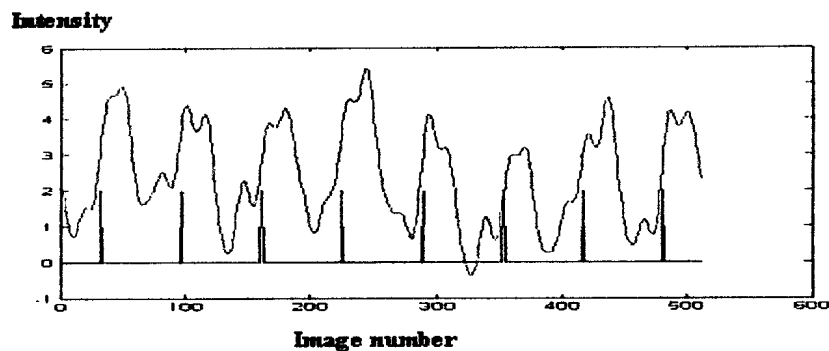
4) The activation signal seems to be our helper as from the experimental data we have the information needed to extract the stimulus paradigm activation, where the subject performed rapid finger movement cued by flashing LED goggles. The study consisted of 31 epochs, with 64 images per epoch. Temporal data from only 8 epochs of pixels in both the motor and visual cortices were processed using the new method therefore the stimulus created for the correlation are shown in Fig. 6-b for the real data which represented in Fig 6-a, also for simulated data the stimulus created is shown in Fig. 2 .

5) Practical implementation steps





(a)



(b)

Fig.6. (a) actual data time course, (b) stimulus marked on the real uncorrupted signal

The following are the steps needed to implement the new technique:

- Step 1) select the area of interest to be examined for a real activation, 2x2 pixels at a time.
- Step 2) recall the data and perform PCA /ICA technique for the selected time series using modified fastICA module [16].
- Step 3) compute the mean power for the output from ICA across all frequency bins of the power spectrum.
- Step 4) compute the standard deviation of the power for the output from ICA across all those frequency bins of the power spectrum.
- Step 5) the power spectra of each component were evaluated with the modified WN “white noise” criterion.
- Step 6) divide the standard deviation by the mean as a ratio.
- Step 7) search the signal for WN “white noise” criterion.

Step 8) classify the ICA output by applying the t-test among all components of the ICA output.

Step 9) correlate the results with the actual stimulus paradigm activation and get the hypothesis, as well as the signal significances to the hypothesis,

Step 10) rank the signal according to step “6” and step “9”.

Step 11) arrange the signals in descending order according to the new nature ranking created from step “10”.

Step 12) the higher the value of the rank the higher the relation with the activation paradigm stimulus a certain grade is assigned for each IC based on its relation with the activation paradigm and display the output as shown in Fig.7 and Fig.8.

Step 13) These components which classified as a noise were therefore labeled as non-relevant and were automatically zeroed for the data sets in which noise was to be removed.

Step 14) The components which classified as a signal were therefore labeled as relevant and were returned a certain activation value to the activation map corresponding to the probability of correlation with the activation paradigm stimulus as shown in Fig.10.

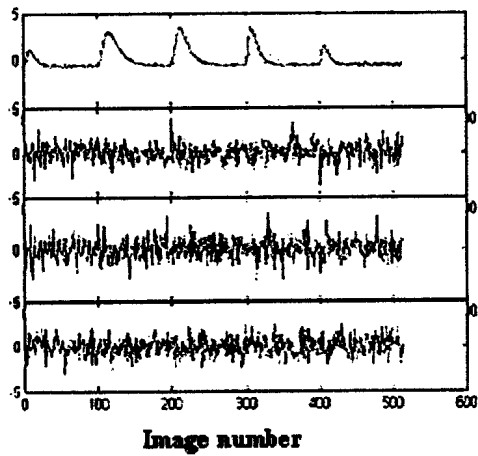
Step 15) repeat the steps from 1-14 for the rest of pixels.

#### **4. RESULTS AND DISCUSSION**

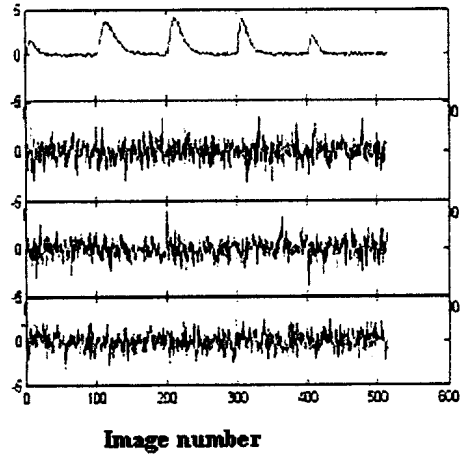
The proposed technique was verified using computer simulations as described before in methods as well as actual data from a human volunteer. The computer simulations were performed whereby a computer generated ER-fMRI activation signal was added to an actual baseline data set. The baseline data were collected on a healthy human volunteer using an echo planning imaging “EPI” sequence “TE”echo time” / TR”repeat time” =25/500 ms”, Matrix=64x64, field of view (FOV) =20 cmx20cm, slice thickness=5 mm, 640 images on a Siemens Magnetom Vision 1.5 T clinical scanner. The number of epochs analysed was 8 and the length of each epoch was 64. The generated activation was designed to include interepoch variations in both the

magnitude and width of the activation signal in order to test the performance of the new technique in preserving such variations. The actual data were obtained from an activation study performed on a volunteer using a Siemens 1.5T clinical scanner. In this study, an oblique slice through the motor and the visual cortices was imaged using a T2\*-weighted EPI sequence (TE/TR= 60/300ms, Flip angle=55°, FOV=22cmX 22cm, slice thickness=5 mm). The subject performed rapid finger movement cued by flashing LED goggles. The study consisted of 31 epochs, with 64 images per epoch. Temporal data from only 8 epochs of pixels in both the motor and visual cortices were processed using the new method. Temporal ICA was applied to process groups of pixels within a user-specified region of interest of size 2x2. The proposed ranking method based on the new method was used to order the outcome of ICA, which came in different order each run. The results of ICA before and after applying the ordering technique are shown in fig. 7 for simulated data, and fig.8 for an actual real data were obtained from an activation study performed on a volunteer using a Siemens 1.5 T clinical scanner. As shown, the components are consistently ordered in these examples. Furthermore, in each of these examples, even though the order of ICA components came different from the data before the application of the proposed technique, the results after its application were exactly the same each time. This suggests that the addition of the proposed method as a post-processing step after ICA makes the technique more practical for use in clinical settings.

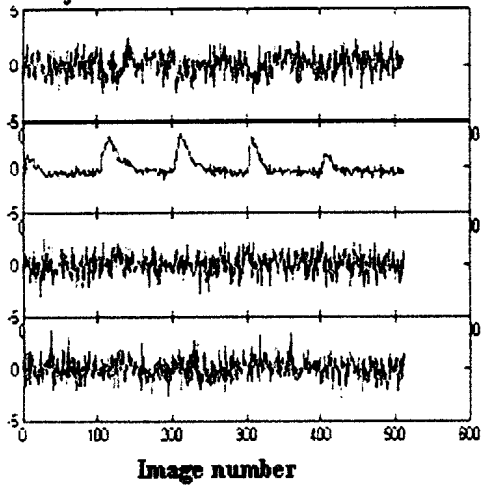
Generated ICs before applying new technique



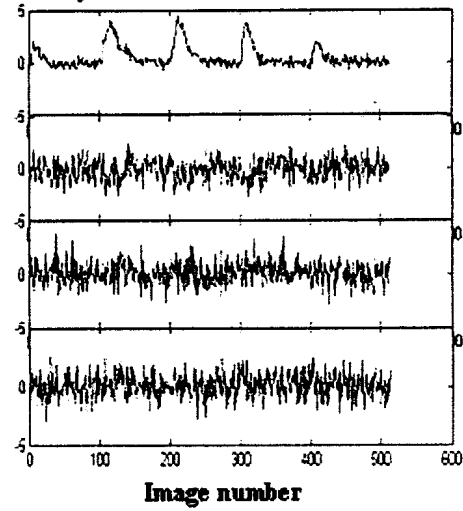
Generated ICs after applying new technique



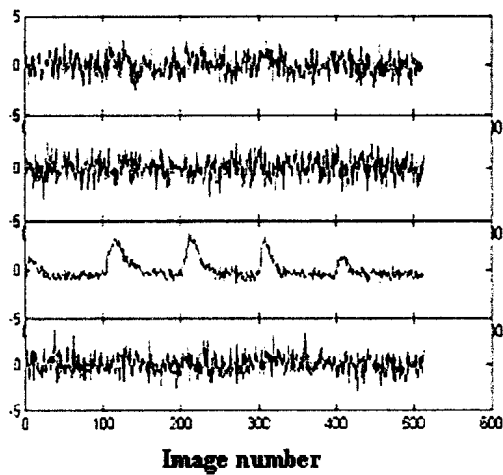
Intensity



Intensity



Intensity



Intensity

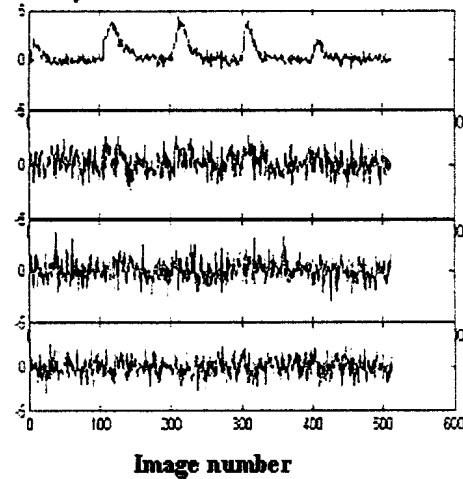


Fig.7. The generated ICS without ordering “left side”, the generated ICS after applying the new technique “right side” for simulated data, X-axis represent image number, Y-axis represent amplitude.

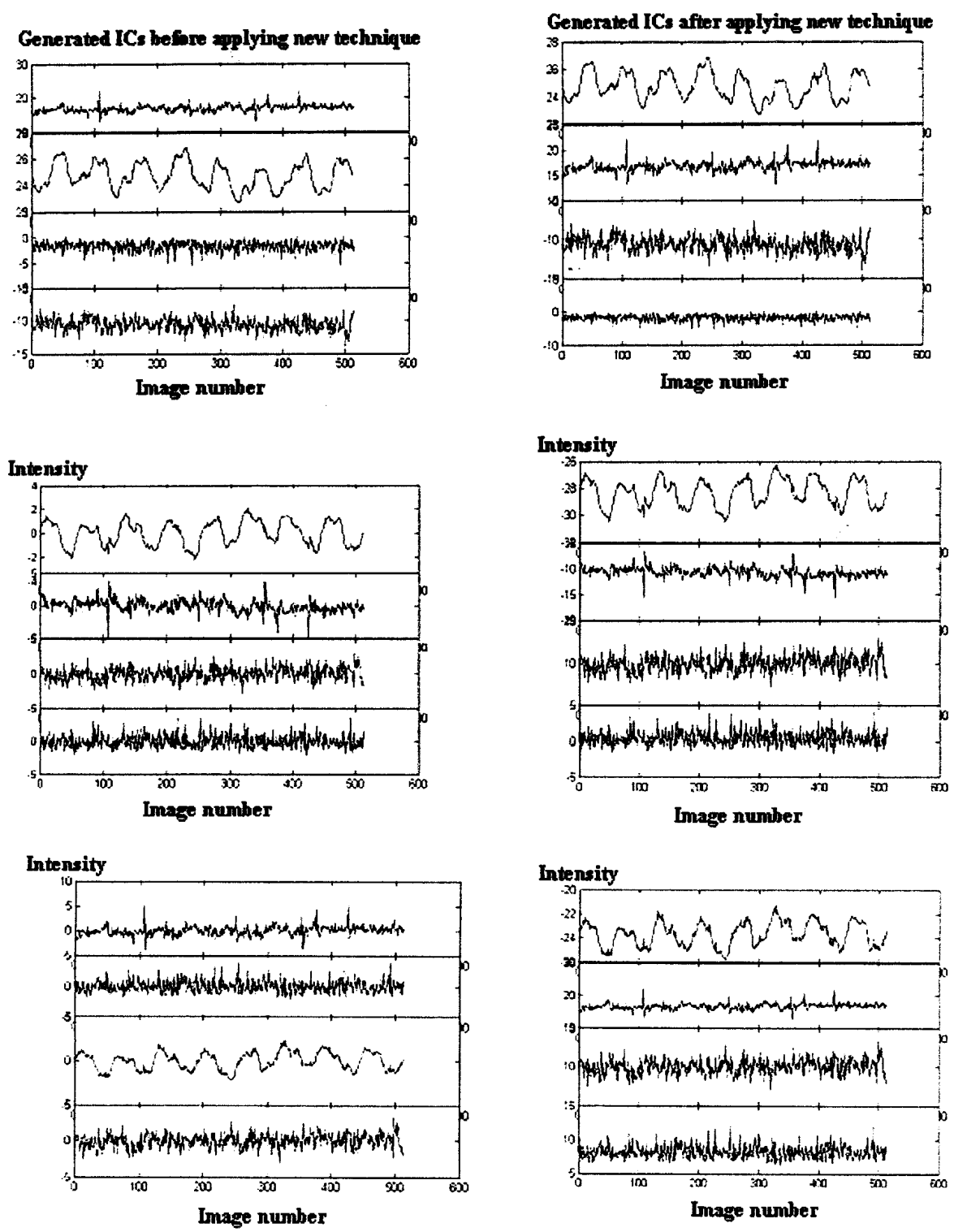


Fig.8. The generated ICS without ordering “left side”, the generated ICS after applying the new technique “right side” for real data, X-axis represent image number, Y-axis represent amplitude.

## 5. CONCLUSION

The major implications of these results can be summarized in a few key conclusions. The most fundamental finding is that component analysis of the fMRI BOLD signal, followed by deletion of undesirable components then the reconstruction of the data, can be used successfully as a way to help separate task-related voxel variations from non-task-related noise. We demonstrated algorithms that automatically select ICA components that are more likely to contain noise and mark them for subsequent deletion. A procedure for noise identification was tested for noise. This procedure was based on Fourier analysis of the time variation of each component's activity, followed by examination of the structure of the power spectrum. Extraction of various kinds of noise by using ICA is one of the most interesting features of the tested methods. These results seem to indicate that component-analysis-based on a natural ranking system depending on the nature of the data avoiding any assumption. This is different from the other technique that depends on basis function model that may lead to problems with noise especially in fMRI environment. That is mainly because of the noise that may have a strong correlation with some signal in that model. So, some signal that looks like that component can deceive the system and give a very high correlation with a noisy component while results will convert this high correlation factor to high grade for this component as an activation response. This gives wrong result which need applying any measurement technique to measure the similarity between the data and the model accordingly our proposed technique might be a valuable addition to the family of post-processing techniques which are used to improve the recovery of information from the BOLD-based fMRI signal. This may provide a more complete picture of the extent of each region's activation by task-related activity. As our proposed technique for ordering the outcome of temporal ICA is subjected to further correlation with the activation stimulus for the same data. The power of this technique is that it does not need to correlate with all components of the output of ICA as in the canonical correlation analysis (CCA) technique but the correlation here is between the output of ICA based on individuals basis. The results

obtained in our experiments suggest that this technique to be highly robust, which makes it suitable as a Post processing step after ICA to make its results easier to evaluate and the technique more practical to use.

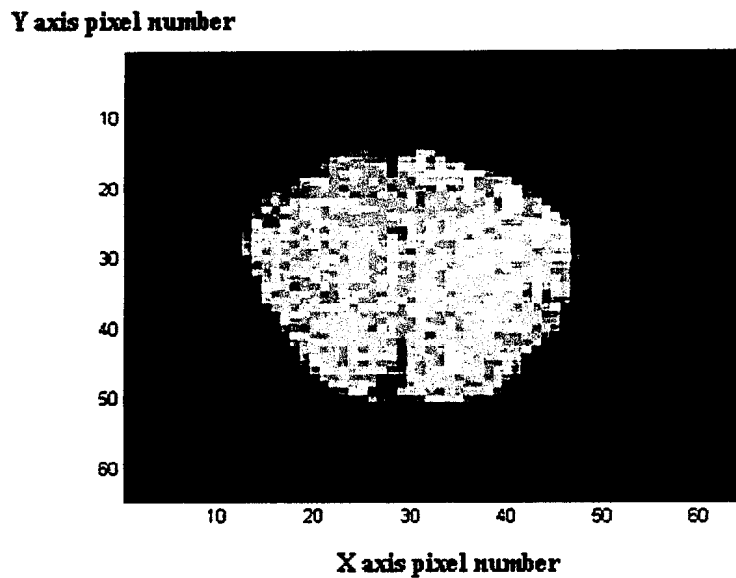


Fig.9. Brain cross section before mapping the activation, X-axis and Y-axis represent pixels number.

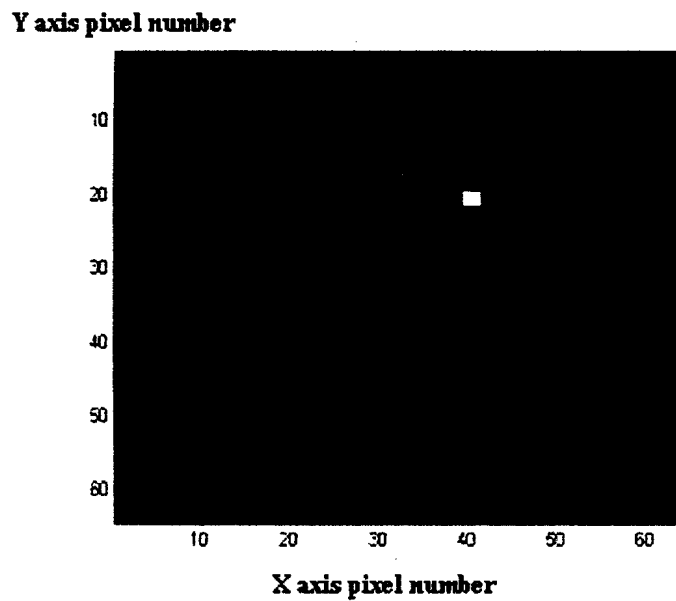


Fig.10 Activation map for returning a 2x2 pixels detected as activated pixels, X-axis and Y-axis represent pixels number.

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### التحليل الدقيق للمكونات الاساسية لبيانات التصوير الوظيفي بالرنين المغناطيسى

يقدم البحث استراتيجية جديدة فى مجال التصوير الوظيفي باستخدام الرنين المغناطيسى والمفهوم الذى يستند اليه الرنين المغناطيسى الوظيفي هو تحديد النشاط المخى عن طريق رصد التغيرات المصاحبة له فى مستوى الاكسجين بالدم وهذا التغير ينتج عن النشاط العصبى الذى يحدث بدوره اثناء الاستثارة .

ويهدف البحث الى تقديم استراتيجية جديدة لها القدرة على حل احدى مشكلات تقنية تحليل المكونات الاساسية الغير معتمدة على بعضها البعض وهى تقنية هامة جدا فى مجال الرنين المغناطيسى الوظيفي ولكن تعاني من مشكلة كبيرة وهى عدم اعطاء ترتيب للمخرجات يعتمد على علاقة الاشارة الصادرة من المخ مما يتطلب التدخل المستحم فى فحص المخرجات واقتناء ما هو يدل على اشارات حقيقية واستيعاد ما هو شوشرة الامر الذى يضيف تعقيدا كبيرا فى حالات الرنين المغناطيسى الوظيفي نظرا لوجود كم هائل من البيانات وقد مكنت الاستراتيجية الجديدة من حل هذه المشكلة والحصول على خريطة تربط بين مناطق محددة بالمخ ووظائف معينة .

وقد تم تحقيق الاستراتيجية المقترحة عن طريق المحكاة باستخدام بيانات استرخاء وايضا بيانات رنين مغناطيسى وظيفي وكذلك بيانات حقيقية مأخوذة من متطوعين . وقد اوضحت النتائج قيمة الاستراتيجية المقترحة فى مجال التصوير الوظيفي باستخدام الرنين المغناطيسى الوظيفي.