The Effect of De-noising FMRI Data Using Independent Component Analysis

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Abstract

Functional magnetic resonance imaging (FMRI) data is an important technique for non-invasive study of human brain activity, but its signal to noise ratio is quite low. Researchers have applied different statistical methods to de-noise FMRI data, identify the signal and correlate that signal with the stimuli and responses from behavioral experiments. We used Independent Component Analysis (ICA) to decompose the FMRI time series from a behavioral experiment into independent components. We then manually inspected each component and rated it on the likelihood that it was an actual signal or physiological, signal-related, or scanner related noise. We then show how the statistical maps of brain activation under several different stimuli change as we drop different proportions of the noise component from the data.

1. Introduction

Functional magnetic resonance imaging (FMRI) is an important tool used in many dfferent sciences including psychology, human physiology, biology and economics. Using FMRI gives us the opportunity to study brain function in a non-invasive way. In contrast to alternatives such as PET and EEG, it provides high resolution images of brain activation, with a reasonable amount of temporal resolution, but the FMRI scanner has a very low signal to noise ratio, on the order of 0.1 to 1%. The noisy signal gives low statistical power and can lead to inaccurate interpretations of signal-related activations. One way of increasing the ratio is to repeat the experiment and average the results, but repetition is expensive and tries the patience of the subjects. Another possibility is to use methods that attempt to de-noise the FMRI data before analysis. Independent Component Analysis (ICA) is one technique that can potentially separate the FMRI time series into independent components, some mainly attributable to signal, and others to noise. The noise components can then be excluded from the data prior to analysis.

The remainder of section 1 of this paper explains the collection of fMRI data and gives an introduction to its separation into components. Section 2 gives details on the experiment that generated the data we analyzed. Section 3 explains how we separated the data into independent components determined which to keep and which to drop, and provides examples of the various types of components. Section 4 starts with an explanation of how the results from the behavioral experiment were analyzed to produce statistical images of brain activations, and then shows how those statistical images change as we progressively exclude more noise related components from the analysis. Section 5 concludes.

1.1 Functional Magnetic Resonance Imaging

Functional magnetic resonance imaging (FMRI) gives us the chance to learn about the functions of the brain by producing images during stimulus and response. This technique was developed in the early 1990s (Kwong, 1992). The FMRI scanner consists of four main parts: a superconducting magnet to generate the static field, radiofrequency coils to collect the MR signal, gradient coils to provide spatial information in the MR signal, and shimming coils to ensure a uniform magnetic field. Basically, the scanner can measure the blood-oxygen level dependence (BOLD) because hemoglobin is diamagnetic when oxygenated but paramagnetic when deoxygenated (Owaga, 1990). A study by Pauls et al. (2001) has shown that neural firing

rate correlates with BOLD response in human brains. Therefore, the higher the detected BOLD response in a particular part of the brain, the higher the activation in that part of the brain.

The technology of the FMRI divides the brain into around 50,000 voxels, each around four cubic millimeters in size. The scanner can record the average BOLD response in each voxel every few seconds, and then form a temporal time series for each voxel. It produces a few hundred complete brain images per scanning session. The scanner stores the images in K-space by Fourier transformations, and then converts them to different formats by computer programs when being used as inputs for analysis in different analysis programs.

The FMRI is a very good way to study the brain because of its non-invasiveness and high resolution images of brain activation, with a reasonable amount of temporal resolution. The scanner, however, is very sensitive to movement, physiological noise, and scanner noises such as thermo noise. Even breathing by human subject and pulses will be detected by the machine. The sound generated by the FMRI scanner and background noises are also sources of noises that the scanner will capture. This results in a very low signal-to-noise ratio for FMRI data. In order to interpret the signals correctly, it is necessary to use statistical method to de-noise the FMRI data in order to extract the task-related data.

1.2 Independent Component Analysis and Components Classifications

Because FMRI is an example of digital signal processing, we can use a digital signal processing source separation technique to tackle the problem of low signal-to-noise ratio. If we can successfully separate the FMRI images, we can drop the components that arise from the noisy sources. Principle Component Analysis (PCA) and Independent Component Analysis (ICA) are useful techniques that can decompose digital signals into different components. We can apply these techniques to FMRI data, and separate the data into different sources components. After we identify the sources of the components, we can then drop the noise components to de-noise the data. Both PCA and ICA involve eigenvalue decomposition of the covariance matrix, with each eigenvector corresponding to one component, but the procedures for the two techniques are somewhat different. PCA uses orthogonal matrix decomposition, but ICA uses de-convolution to separate the components. Therefore, one main difference between PCA and ICA is that the components separated by PCA are non-correlated, while the components separated by ICA are independent. A study by Thomas et al (2001) compared the

images between PCA and ICA, and proved that ICA is better for isolation and removal of structured noise, while PCA is better for isolation and removal of random noise. In this paper, we will focus on using ICA to de-noise the FMRI data. The ICA of a random vector consists of searching the linear transformation that minimizes the statistical dependence between its components (Comon, 1992). ICA can decompose a single or multiple 4D data sets into different spatial-temporal components so that the observed data is a linear combination of the spatial-temporal components. In order words, each component is a 4D data set as well, showing the average brain activation at some region over time. As each final independent component is likely to be due to only one physical or physiological process, it should be possible to identify the source of the independent component (Beckmann).

We will use a computer program, FSL, to do the ICA. (See section 1.3.) Once we obtain the components, we can classify them into different categories. We can classify the components either by machine or by inspecting them manually. J. Tohka, et al. (2007) proposed a computer program to identify, classify and remove noise components in ICA. He constructed the program to remove noise components by different criterion considering the frequency of the component, without looking at the images. He also mentioned that the misclassification rate was between 20% and 30% for the components. To have more accurate results, we modified his classification criterion and classified the independent components manually. We modified Beckmann's classification (2001), and have a set of rules to classify and rate the independent components.[8] (Details in section 3)

1.3 FMRIB Software Library (FSL)

The four dimensional images generated by the FMRI scanner are used in the analysis by FMRIB Software Library(FSL), which is a set of software programs we used in our study. Ultimately, we will use the FMRI Expert Analysis Tool (FEAT) to get contrasts of activation in different behavioral conditions. A contrast is a set of brain images showing which region of the brain is activating significantly to a specific condition. To do that, a one-tailed t-test is applied to each voxel according to the time series. The voxels that show significant differences in activation under that condition will be indicated in red. In Figure 1.1, we have a sample FEAT report showing three contrasts that relate to different aspects of our experiment. The first contrast shows the significant activation for mandatory trials, the second contrast shows the significant

activation for voluntary trials, and the third contrast shows the significant differences between the first two.

A powerful program, FEAT includes features such as motion correct and data smoothing. The FEAT report shows brain images with statistically significant activations in the contrasts. Because of the noises in the FMRI data, however, the results might not be ideal for reflecting the task-related signals. That is so because too much noise in the data will reduce t-test power. Therefore, we first used the Multivariate Exploratory Linear Optimized Decomposition into Independent Components (MELODIC) to de-noise the FMRI data. MELODIC allows Independent Component Analysis which can separate the FMRI data into multiple components by their sources, and automatically estimates the number of interesting noise and signal sources in the data. By using a likelihood maximizing function, MELODIC will only show the number of independent components that are the most significant. The more components there are, the noisier the data. The components are arranged in descending order by the percentage variance of the component. After we go through all of the components, we can drop the unwanted components and run the FEAT again. We will compare the images generated by FEAT according to the proportions of noise we dropped. If we successfully identify and drop the noises while keeping the signals, the result will be a more powerful t-test and will show more significant activations.

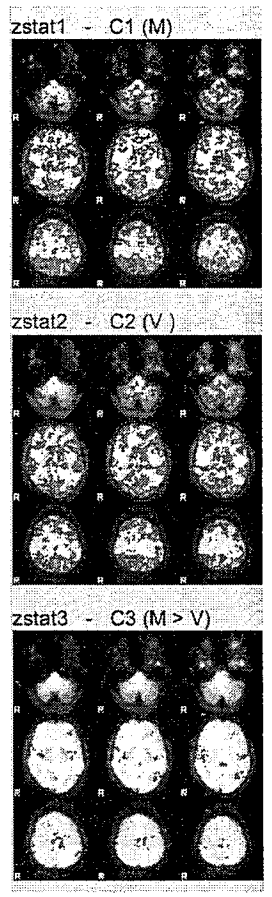


Figure 1.1

2. Sample Experiment Data

Although the focus of this paper is on ICA, an explanation of the experiment provides useful background. We used a sample of eighteen (18) students and gave them financial aid scholarships ranging from 50 USD, 100 USD, or 150 USD. All of the subjects demonstrated moderately high need and had high GPAs, but none of them had high financial need or had very high GPAs. We defined high GPA as between 3.0 and 3.8, and a very high GPA as a 3.8 or above. Therefore, none of the subjects was eligible for very high need or very high GPA scholarship funds.

In the experiment, we placed the student in the FMRI scanner, and they would make decision about the scholarships. Each person had 96 trials, 60 were mandatory, and 36 were voluntary. The 96 trials were divided into two runs of 48 trials each. Because FMRI data is noisy, there were many repetitions. One mandatory and one voluntary transfer would count for payoff, meaning that the student could get as much as 300 USD. During the trials, students were also reminded that their scholarship would reduce the amount available to other eligible students, by 50 USD, 100 USD, or 150 USD. As a result, they could reduce the amount for other eligible students by as much as 300 USD as well. The main screen reminded the students of their eligibility for the various scholarships. We want to find neural evidence according to the cost, qualification, and perceived stigma about the aid. We expect to see brain activation at the prefrontal cortex and anterior cingulate cortex.

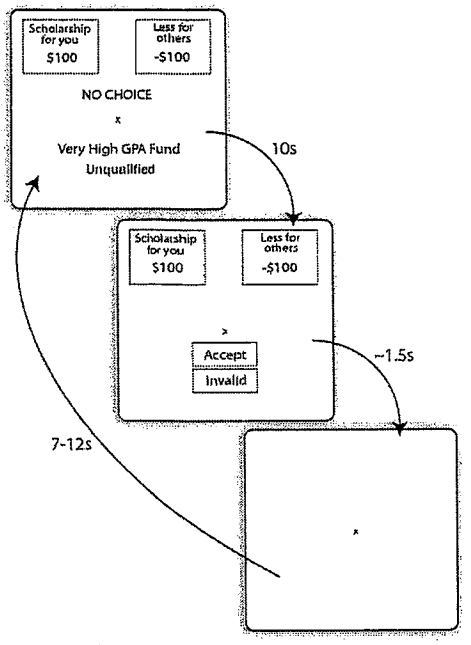
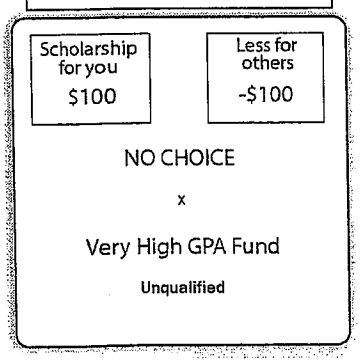


Figure 2.2
Experiment Process

During the experiment, the stimulus screen appeared every 20~25 seconds and remained visible for 10 seconds. Therefore, every component showing a peak at 4~5 or 10 on the power-spectrum is task-related.

For example, once the main choice screen appeared, it would be visible for 10 seconds. Then the subject had to decide whether to accept or reject the scholarship offer. The average response time was 1.5 seconds. Then the screen would remain blank for 7-12 seconds until the next stimulus choice screen appeared.

Figure 2.1
Stimulus choice window



3. Independent Component Analysis Methodology

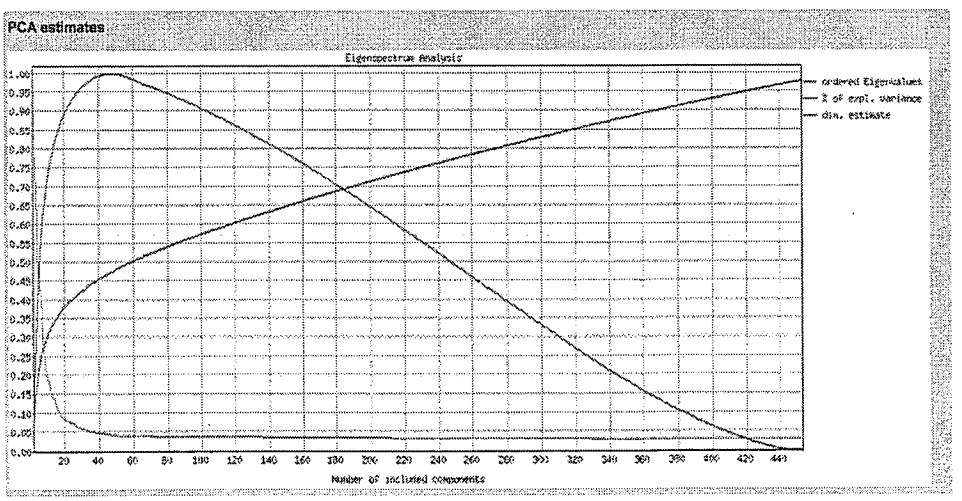
After the trials and after we run MELODIC, we will look at the components one by one in the MELODIC report (figure 3.1) and classify each component. Then we drop the noise related components to obtain cleaner FMRI data. Because

we classify all the components manually, we must have clear guidelines to classify the components to maintain consistent classification. We rate all of the components by seven criteria: head motion, eye movement, physiological noise, ghost (alternating pattern), dropout, outside brain (activation showing up outside the brain), and task-related stimulus. We then apply various rules to these ratings to decide what components to drop.

3.1 MELODIC Report

To classify the components, we will look at the MELODIC report of each component. There are 2 types of MELODIC reports: the subject report and the component report. The subject report shows the maximum likelihood function and the number of components. Each component report corresponds to an independent component. The component report consists of three main parts: the IC map, the temporal time course, and the power-spectrum of the time course. The IC map shows the brain images and the activation region for the component. Red/yellow means active and blue means inactive. The temporal time course shows the normalized activation according to different times. A spike on the time course indicates a head motion. The power-spectrum of the time course shows the frequencies of the component in one hundred seconds. For example, a power-spectrum showing a peak at five would mean that on average the activation increases five times in one hundred seconds, thus it activates every twenty seconds on average.

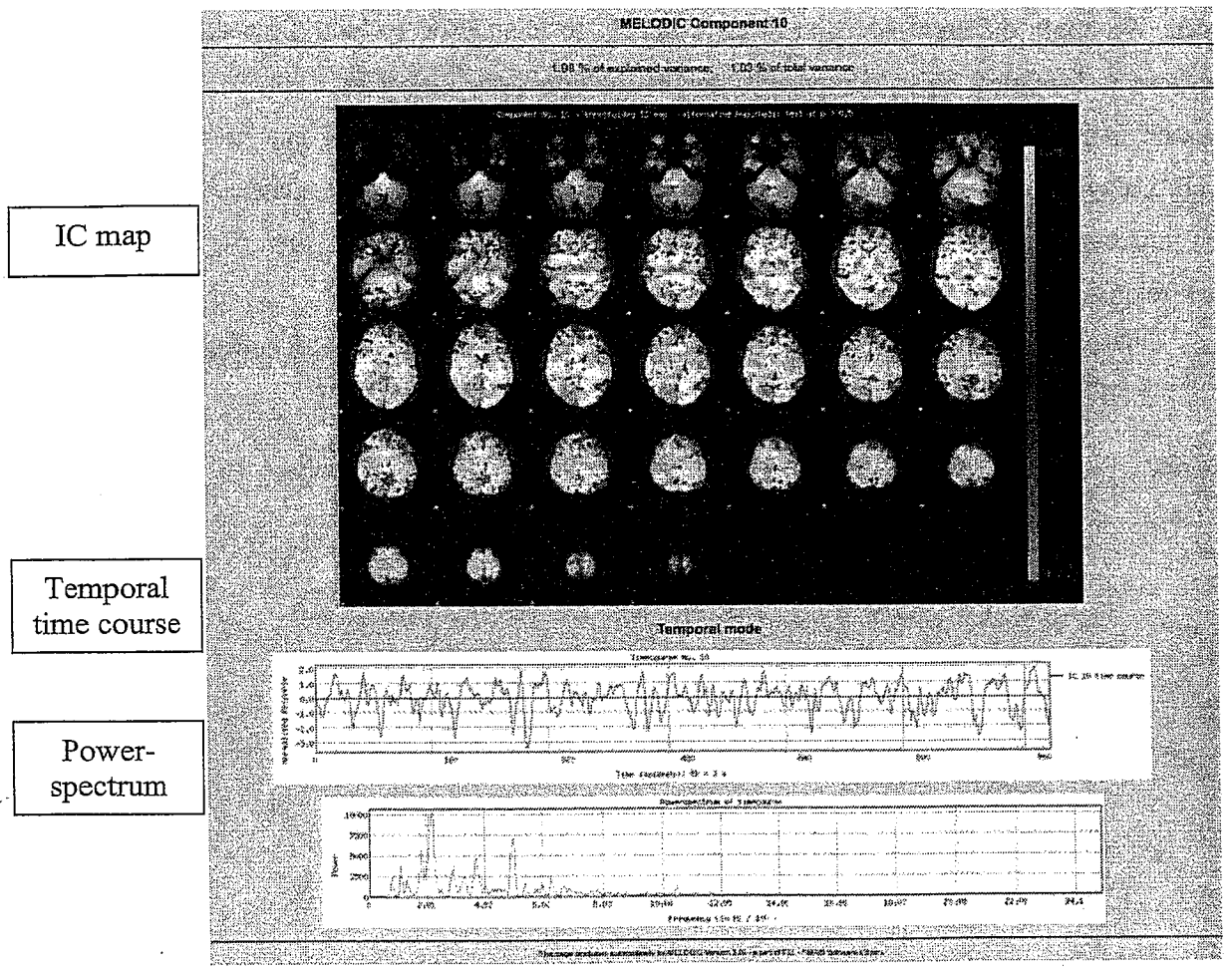
Figure 3.1 MELODIC Subject Report:



According to our experiment setup, we have 2 runs for each subject, 36 runs in total. Each run has 57.4 components on average (standard derivation=7.53, max=69, min=42). Two subjects showed over two hundred components on the MELODIC report. When we double-checked the FMRI data, we found many dropout components in the data, evidence that the

scanner was not functioning correctly during the scan. We dropped these two subjects from the analysis.

Figure 3.2 MELODIC Component Report



3.2 Independent Components Classifications

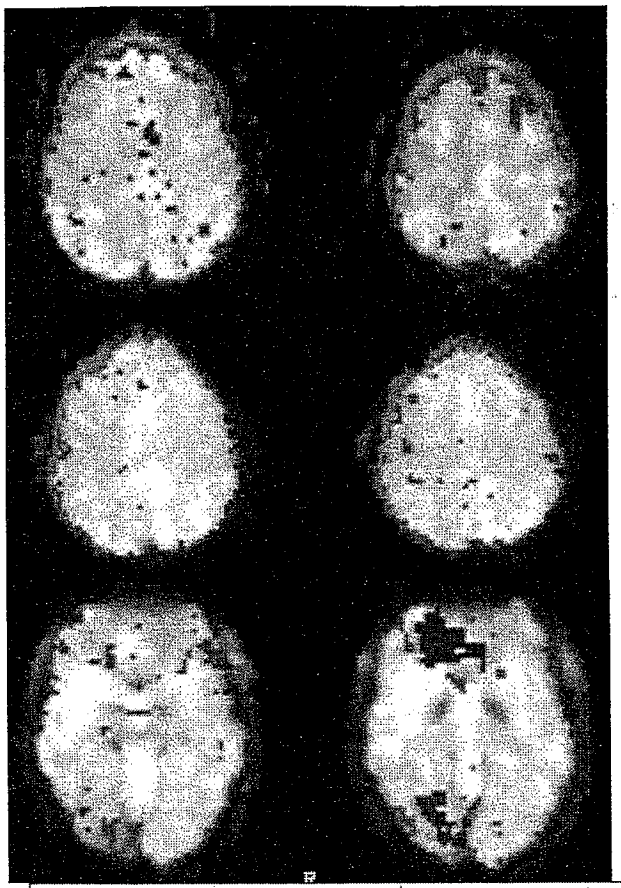
Beckmann (2001) gave examples of classified components to determine what kinds of components should be dropped. We modified his rules and came up with some manual guidelines to classify the components by looking at the IC map, temporal time course, and the power-spectrum of the time course for each independent component.

We then classified all the components according to seven categories: head motion, eye movement, physiological noise, ghost (alternating pattern), dropout, outside brain (activation showing up outside the brain), and task-related stimulus.

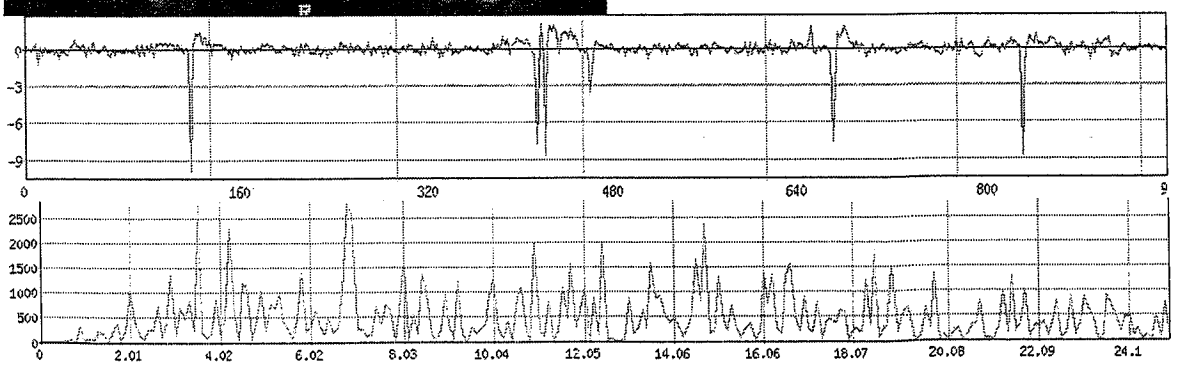
To decide what components to drop, one important consideration relates to task-related stimuli. A task-related component is correlated with the stimulus, and it can be either noise or signal-related. Moreover, a task-related signal is the type of component we would definitely keep. We apply different decision rules to decide to include or exclude the task-related noise, because task-related noise components might include some signal as well. For example, eye motion is usually correlated with a stimulus, and head motion/ghosting can be task-related as well. Using the power-spectrum, we try to determine whether the component is task-related. If the power-spectrum shows the same frequency as the signal frequency, then the component is task-related.

The following illustrations show examples of the criteria to classify a component by looking at the IC map, temporal time course (TC) and power-spectrum (P).

Head motion



Head motion is caused by random or structured head motion in the scanner. It can be task-related or non-task-related. The ring type head motion indicates up and down motion; the two-sided type head motion indicates left and right motion; the half-ring type head motion indicates one-sided head motion.

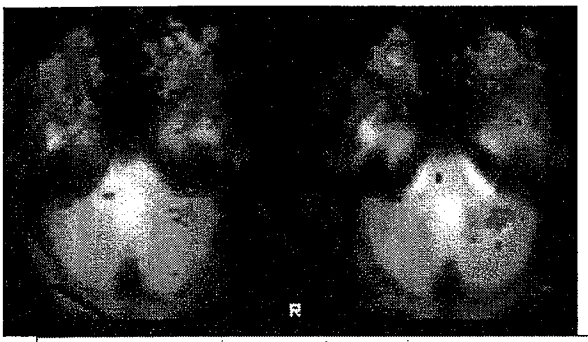


IC map: Activation as a ring on the skull/two-sided activation/half-ring activation

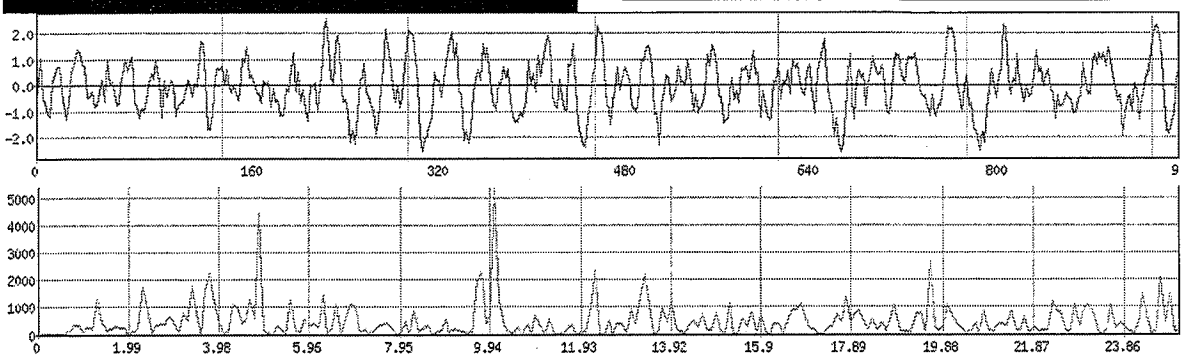
TC: A sharp spike indicates a sudden movement at the corresponding time in all the cases

P: Usually random or low frequency, might be task-related

Eye movement



Eye movement is usually task-related as subjects move their eyeballs mostly only when there is a stimulus. They were asked to focus at the middle of the screen.

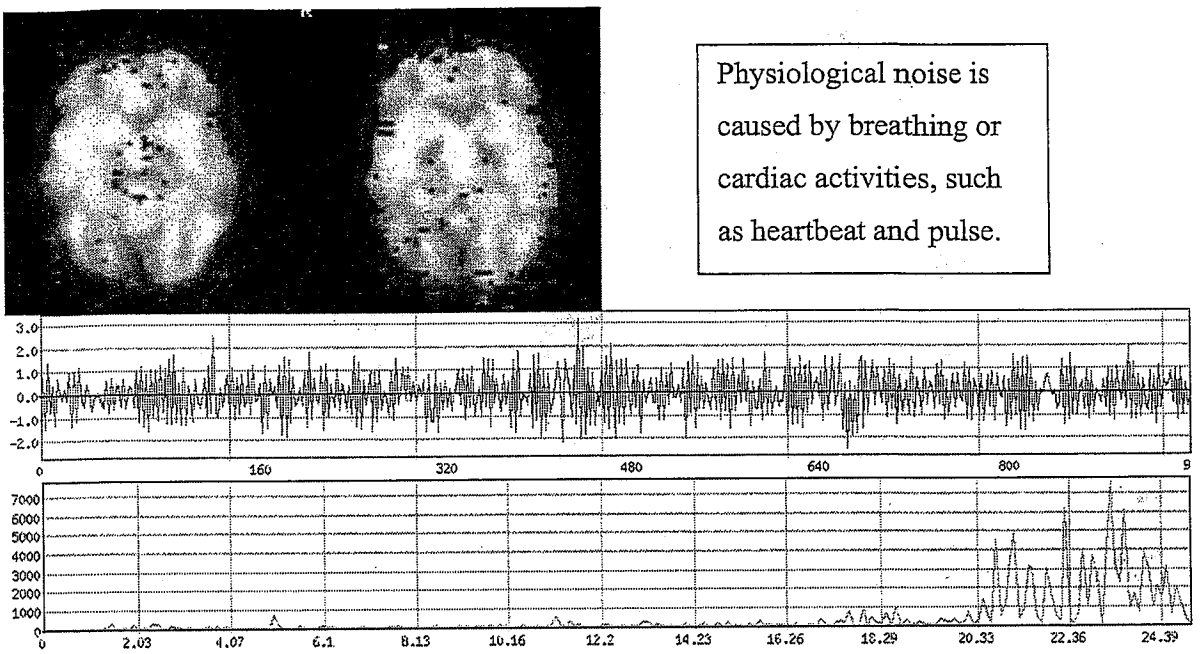


IC map: Activation right at the eye balls

TC: Regular, no extreme value and kind of periodic

P: Eye movements are mostly task-related, usually shows same peak frequency as the signal

Physiological Noise



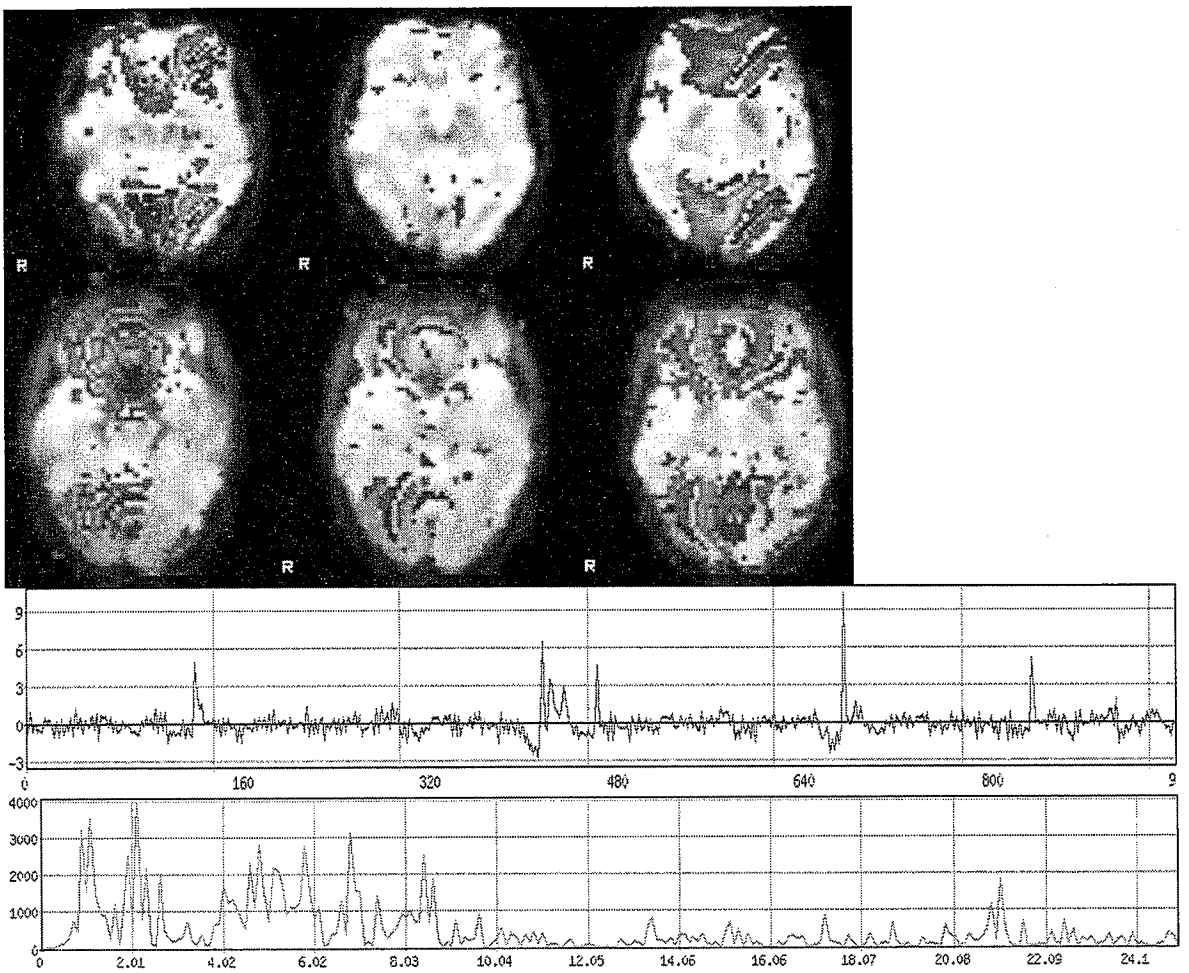
Physiological noise is caused by breathing or cardiac activities, such as heartbeat and pulse.

IC map: A lot of dotted activation or activation at the medulla oblongata (lower portion of the brainstem)

TC: Very high frequency

P: Peaks at around 20-25 (humans breathe once every 4-5 seconds)

Ghost



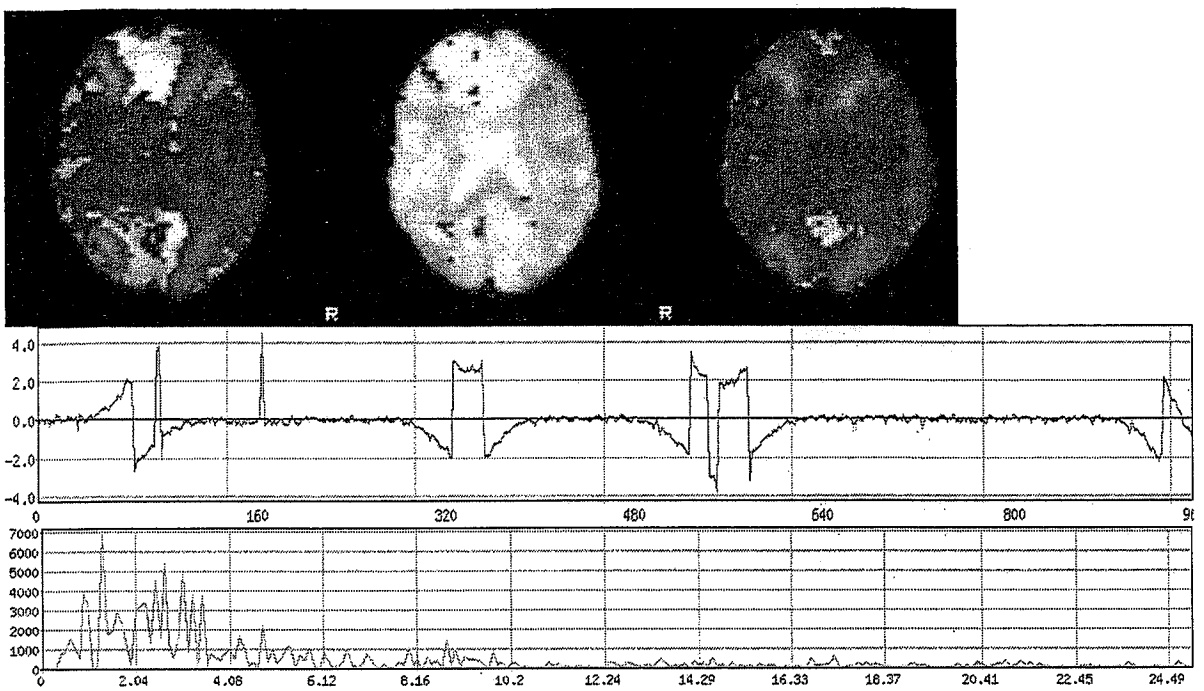
IC map: Wavy shape of activation, may have alternating pattern of activation on every other slice

TC: Kinked and spike

P: Random, usually low frequency, might be task-related

Ghosting is a special case of head motion and is caused by head motion parallel to the plane of the magnetic field.

Dropout



IC map: Activation on the entire brain images, with alternating pattern on every other slice

TC: Structured curve

P: Random, usually low frequency

Dropouts are caused by scanner malfunctions, especially mis-timings between gradient switching and signal acquisition. The slices lose intensity.

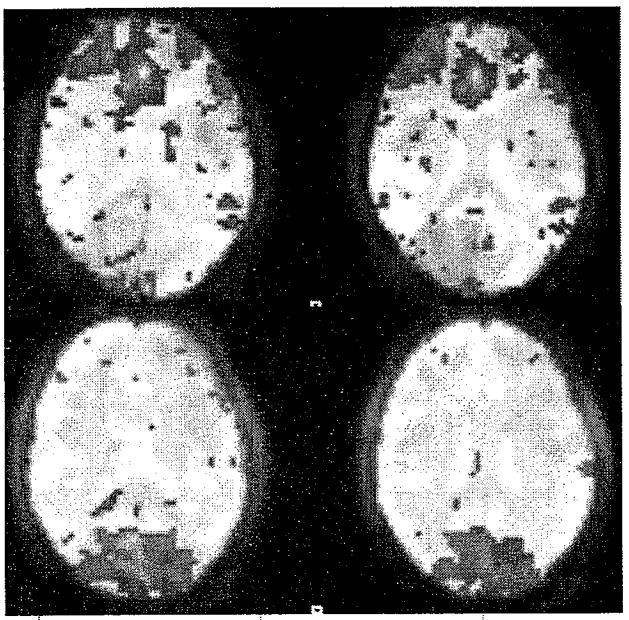
Outside Brain

IC map: Lots of activation outside the brain

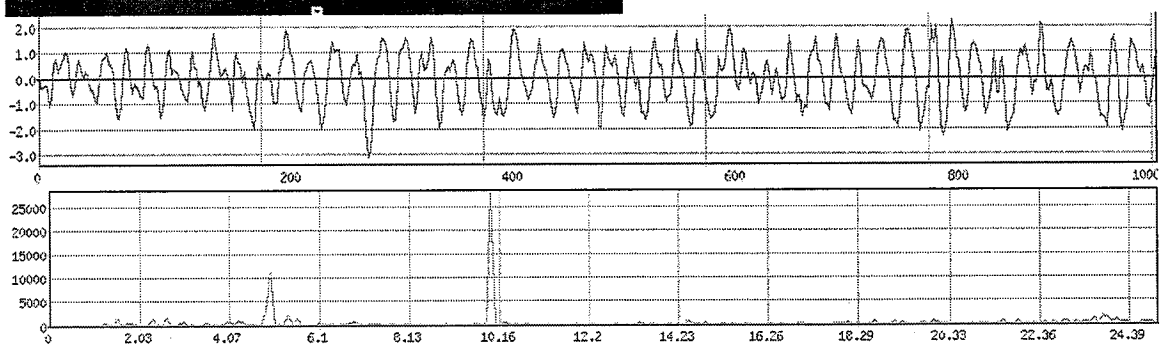
TC & P: No special feature

Outside brain is usually due to head motion or scanner malfunction.

Task-Related Stimulus



Activation of prefrontal cortex and anterior cingulate cortex are the regions involved in decision making.
The occipital lobe is the region responding to a visual stimulus.



IC map: Activation at prefrontal cortex (usually two sides on the front of the brain), anterior cingulate cortex (at the middle front) or occipital lobe (back of the brain)

TC: Regular, smooth, kind of periodic

P: Showing peaks at the signal frequency, which is 4~5 and 10 in our experiment

3.3 Independent Components Rating System

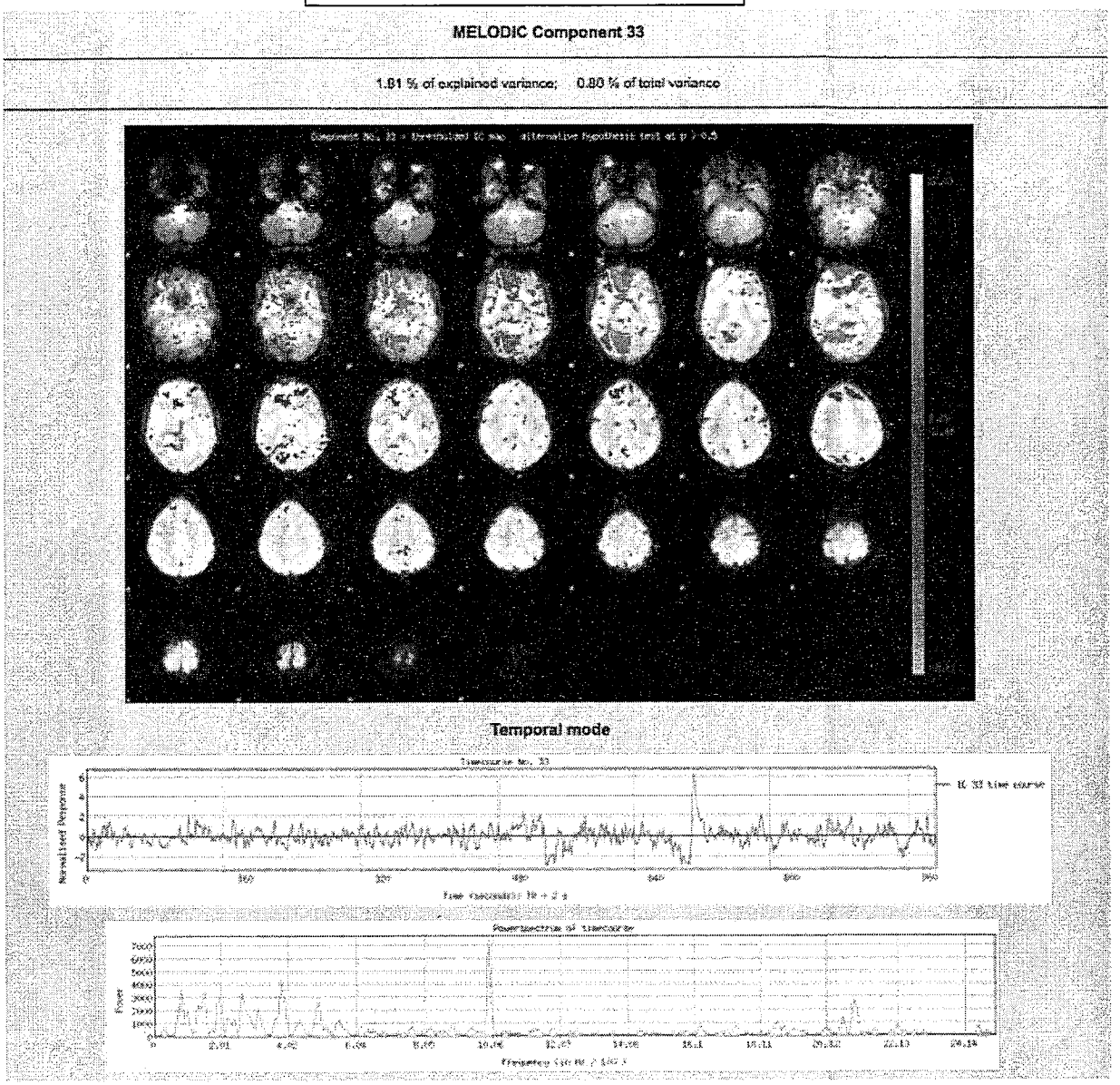
Our goal is to classify each independent component to determine which to exclude. Most components, however, cannot be identified as purely one type; they are often mixed with two or more features. Moreover, the degree of noise may vary among components. That is why we introduced a rating system for independent components. We give rating on a 0-3 points scale (3: most obvious, 2: moderate, 1: least obvious, 0: none) to each components according to the above seven criteria.

Figure 3.3 Sample spreadsheet

	A	B	C	D	E	F	G	H
	component	head motion	eye motion	physiological	ghosts (alternating and waves)	dropout	outside brain	stimulus
2	1	3	0	0	0	0	0	3
3	2	2	0	2	0	0	0	0
4	3	1	0	0	0	0	0	2
5	4	3	0	0	0	0	2	2
6	5	1	0	0	0	0	0	1
7	6	3	0	0	0	0	0	2
8	7	0	0	3	0	0	0	0
9	8	3	0	0	0	0	0	3
10	9	3	0	1	0	0	0	0
11	10	1	0	0	0	0	0	2
12	11	3	0	0	0	0	0	2
13	12	0	0	0	3	0	0	3
14	13	0	0	0	0	0	0	3
15	14	0	0	0	3	0	0	1
16	15	0	0	2	0	0	0	0
17	16	1	0	0	0	0	0	2

For each subject, we will have a spreadsheet like the one shown above. With the rating system, we are able to group the components by their degree of noise.

Figure 3.4 Sample components 1

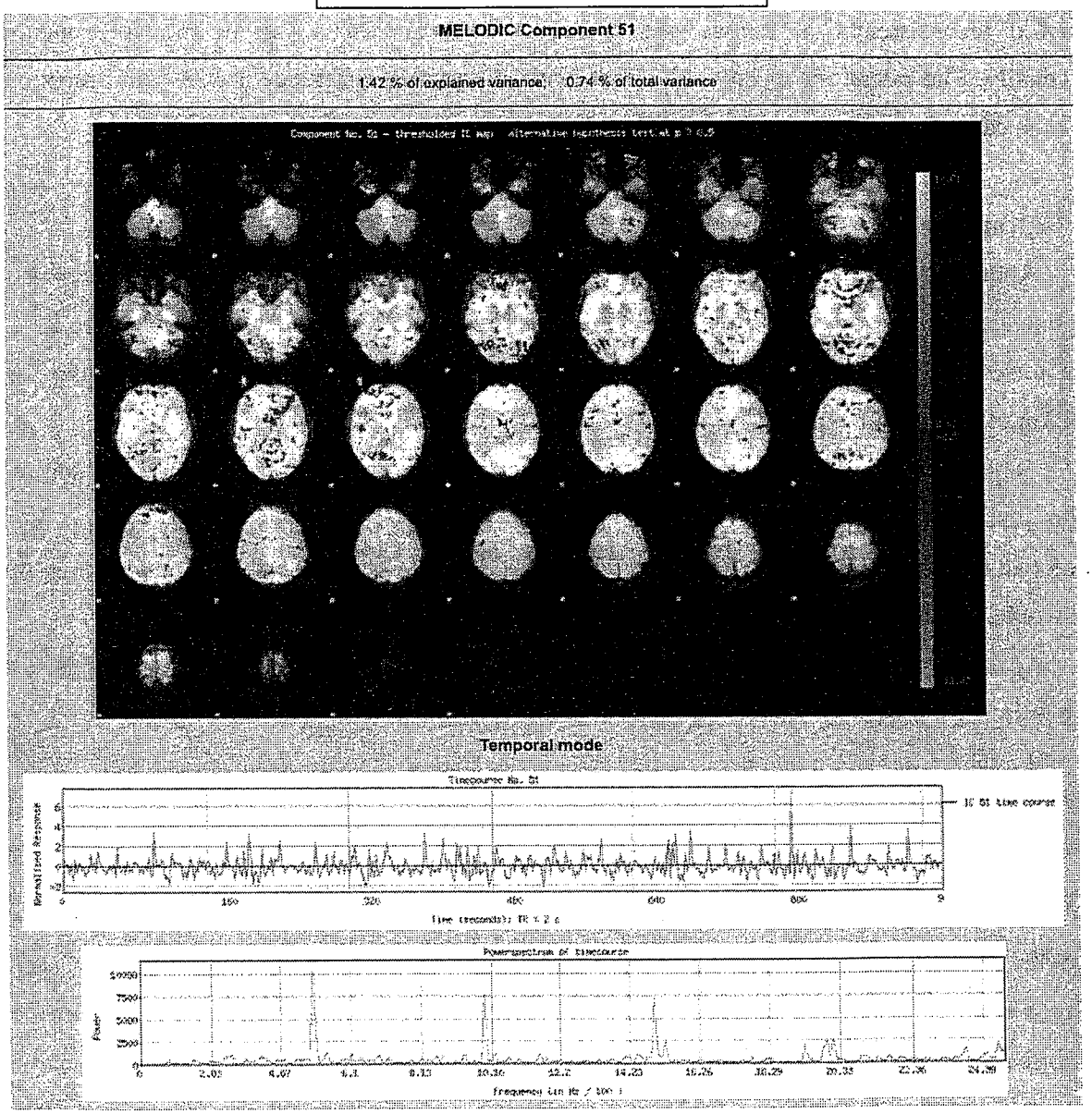


To rate the component illustrated above, we observe from the IC map that there is a strong ghost image pattern. Also, we see that there is activation around the border of the brain and a little bit outside of the brain. Looking at the time course, we see an obvious spike, indicating a head motion. The power-spectrum shows a peak at 10, indicating this component is mostly task-related. Therefore we will have a rating like this:

Component	Head motion	Eye movement	Physiological	Ghost	Dropout	Outside brain	Stimulus

33	2	0	0	3	0	1	3

Figure 3.5 Sample components 2



Not all the components look as clear as those in the previous illustration. In IC map for the above component (Figure 3.5), we see obvious eye movement, some ghosting, and a small head motion ring. But the power-spectrum has peaks at 5 and 10, meaning that this component is mostly task-related. Therefore, we use the following rating:

Component	Head motion	Eye movement	Physiological	Ghost	Dropout	Outside brain	Stimulus

51	1	3	0	2	0	3	3

To avoid inconsistency in ratings, we trained two raters who rated all the components individually. The raters are mostly consistent, with an average difference at 0.9 score, most of the errors came from the ratings between 1 and 2.

3.4 Dropping Noise Components

After we go through all of the components and rate them, we can drop the classified noise components. We then do two different FEAT analyses of the de-noised data when we drop 20% of the noises and 70% of the noises, and compare the results and contrasts of activation under the condition of interest.

At the 20% level, we dropped all the components with non-task-related noise, such as random head motion, physiological noises, non-task-related ghost, outside brain, and dropouts. We kept all the task-related noise, such as tasked-related eye motion and task-related ghosting. In other words, we dropped all the components with a rating of 0 in task-related stimulus.

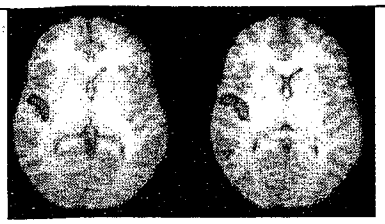
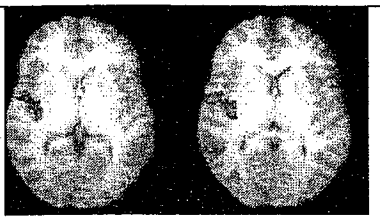
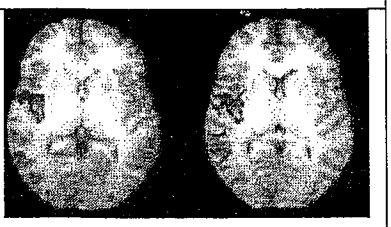
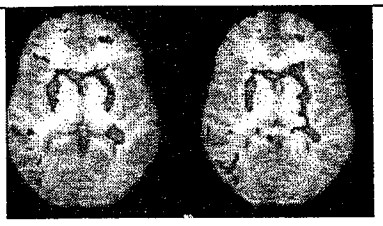
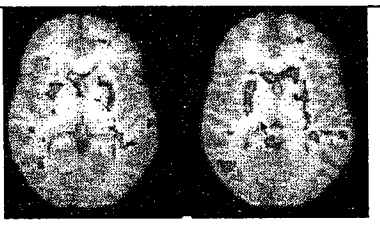
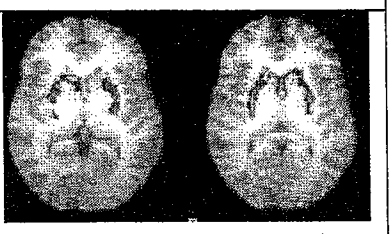
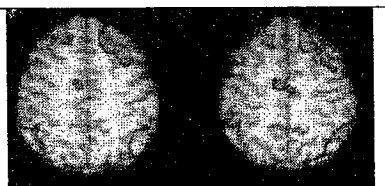
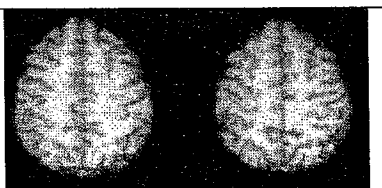
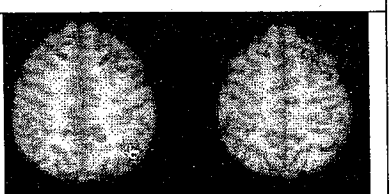
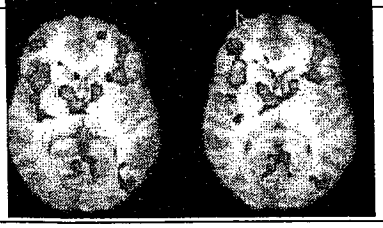
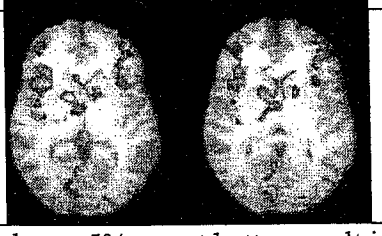
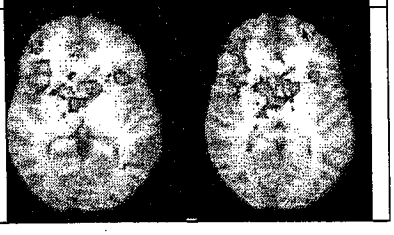
At the 70% level, we dropped all the components, except the task-related brain stimulus with a rating of 3 ***only***.

We then compared the contrasts of parameter estimates of each level respectively.

4. Results

In our study, we find that ICA improves the analysis results with a larger activation region and more significance, but the changes are not large. Six contrasts in our experiment are worthy of note: 1) Mandatory > Voluntary; 2) Voluntary > Mandatory; 3) Qualified > Unqualified; 4) Voluntary Qualified > Voluntary Unqualified; 5) Efficiency (where benefit greater than cost); 6) Mandatory Efficiency > Voluntary Efficiency. We will use a cluster analysis in FEAT, with Z-threshold at 1.6, p-value at 0.10, so that the resulting images only show significant normalized activations greater than 1.6 at the 90% confidence level.

Resulting images when we dropped different amount of noises

	0%	20%	70%
1			
2			
3			
4			
5 *			
6			

*: Used non-clustered analysis, p-value at 5% to get better result images

Explanations

1) This contrast shows the region where the brain activation with mandatory stimuli is greater than the one with voluntary stimuli. We can see the activation area increases as more noise related components are being dropped.

2) In contrast to 1), this contrast shows the region where the brain activation with voluntary stimuli is greater than the one with mandatory stimuli. While we dropped more noise components, we can see the brain images become less noisy.

3) This contrast shows the region of brain activation when the subject is qualified is greater than the region of activation when the subject is not qualified. The images become less noisy.

4) We expected that 4) is similar to 3) since 4) is a sub-stimulus of 3). We can see the noise reduction is similar to the case of 3).

5) This contrast is the most interesting case. The brain images show the region that is associated with efficiency. That is the behavioral condition when the gain of the scholarship is greater than the cost to others. Before we dropped any noise components, we saw activation at the prefrontal cortex and the occipital lobe. At the 20% level, we dropped all the non-task-related noises such as random head motion and physiological noises. Then we could see the visual stimulus overwhelms the signal stimulus in the prefrontal cortex. Then at the 70% level, we only kept the task-related signal and dropped all the task-related noises. In this case the task-related signal overwhelmed the visual stimulus and showed up on the images again.

6) This contrast shows the region having higher activations for mandatory efficiency than voluntary efficiency. This is just one more illustration of how dropping noise related components resulted in cleaner brain images.

5. Summary

The resulting images illustrate that Independent Component Analysis can be used to de-noise FMRI data and shows a less noisy image from the FMRI analysis. We can see that the regions expected to have task-related signal activation became larger as well. Moreover, the rating system we introduced can help us to perform ICA more efficiently. We can drop different components and see the effects of different type of noise on the analysis as well as the images. We still need to improve our approach, however, for there are potential problems with it.

The first potential problem involves unidentified components. This is a big concern of using ICA because we cannot always easily classify the components appropriately. One reason for that limitation is that there are a lot of non-task-related neural activities captured by the scanner, such as non task related emotion. We should be very careful when we decide whether to drop a component.

Another problem is that one component might not correspond only to one source. As I mentioned in section 3.2, the components may show mixed sources such as a component showing a task-related signal with eye motion and head motion at the same time. When we drop the components, there is also the potential risk that we may reduce the task-related signal.

As we need to look through all the components manually, this is a labor-intensive job. For example, our experiment has a total of 1837 components. It takes around 30 seconds to rate one component, and about 15 hours to rate all of the components for a small sample size of 16. As we increase the sample size, we will need more workers to go through all the components. This could lead to other potential issues, such as the fact that ratings are subjective and it is easy to make manual mistakes. Therefore, it is important that people working on the ICA are properly trained and use cross validation with multiple rates.

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