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DETECTION OF NEURAL ACTIVITY IN FUNCTIONAL MRI USING CORRELATION ANALYSIS

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***Abstract**- Functional Magnetic Resonance Imaging (fMRI) is a recently developed neuro -imaging technique in Biomedical Engineering with capacity to map neural activity with high spatial precision. To detect brain activity in functional MRI data, a Canonical Correlation Analysis (CCA) is to be implied. A Canonical HRF framework for detecting brain activity in functional MRI data is presented. To locate active brain areas, the method utilizes local bl ood oxygenation changes which are reflected as small intensity changes in a special type of MR images. In this framework, a method based on canonical hemodynamic response function follows as a natural extension of established analysis methods is being used. To detect homogeneous regions of activity, the method combines a canonical approach of the hemodynamic response. It demonstrates by localizing brain areas which are involved in numerical mental calculation. It has been seen that Canonical Correlation technique is better compared to some other analysis techniques.*

Key words: fMRI, Neuro-Imaging, Neural Activity, Hemodynamic Response CCA, Homogeneous Regions

1. INTRODUCTION

Even though the significance of our brain has been reassessed during the past 2,000 years, most of its functionality still remains unknown. Techniques for non-invasive monitoring of the working brain have in recent years experienced a strong development. Such neuro-imaging tools open new possibilities to study brain functionality and to further advance our understanding of the brain. Among these methods, functional Magnetic Resonance Imaging (fMRI) holds a unique position due to its capacity to locate brain activity with high activity in fMRI data spatial precision. This dissertation presents novel methods for detecting brain. Now a day's fMRI data analysis is interesting as well as challenging task. Functional Magnetic Resonance Imaging (fMRI) is a relatively new tool with the purpose of mapping the sensor, motor and cognitive tasks to spacific regions in the brain [6]. The whole processes from analyzing the data to map the images are done in some steps. The processes are developed step by step. The data is analyzed and image obtained from the data. The image is affected by various types of noises. The images are smoothed and noises are eliminated. Then time series obtained from each and every pixel. After denoising the images canonical HRF is applied to determine the region responsible for any task. The Canonical hemodynamic response function detects the bold signal of the activated region of the brain with a high accuracy and less effected by noise or drift signal.

Over recent years there has been a growing interest within the computer science community in data processing for fMRI. One popular style of processing involves using Generalized Linear Models (GLM) as in Friston et al. (1995a, 1995b) and Bly (2001). Here a regression is performed for each voxel, to predict the signal value at that voxel, based on properties of the stimulus. The degree to which voxel activity can be predicted from stimulus features is taken as an indication of the degree to which the voxel's activity is related to the stimulus. Notice this regression problem (predict voxel activity given the stimulus) is roughly the inverse of the problem we consider here (predict cognitive state given all voxel activities) [2]. Others have used t-statistics to determine relevant active voxels, and yet others have used more complex statistical methods to estimate parameters of the BOLD response in the presence of noise (Genovese, 1999).

Various methods for modeling time series have been used for analyzing fMRI data. For example, Hojen-Sorensen, Hansen, and Rasmussen (1999) used Hidden Markov Models (HMM) to learn a model of activity in the visual cortex resulting from a flashing light stimulus. For example, Goutte et al. (1998) discussed the use of clustering methods for fMRI data. One particular approach (Penny, 2001) involved the application of Expectation Maximization to estimate mixture models to cluster the data. Others have used Principle Components Analysis and Independent Components Analysis

(McKeown et al., 1998) to determine spatial-temporal factors that can be linearly combined to reconstruct the fMRI signal.

2. LITERATURE REVIEW

2.1 Magnetic Resonance Imaging

The rate at which the resultant magnetic vector regrows is measured by a time constant T_1. The time constant T_2^* measures the combined effect of random nuclei interactions and magnetic field in homogeneities [1]. The time constants T_1 and T_2 are tissue type dependent. By making time constant maps covering a part of the body, images where different organs and tissues can be delineated are obtained, figure 2.1. This is the basis for clinical MRI.
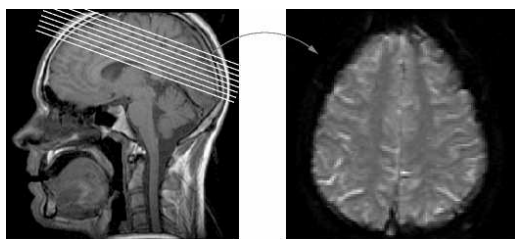

Fig. 2.1: Two examples of MR images acquired in two different slice orientations.

Important in fMRI is the existence of a sequence sensitive to the T_2^* time constant, the gradient Echo Planar Imaging (EPI) sequence. The T_2^* time constant is generally not utilized for generating conventional anatomical MRI images since it is susceptible to local magnetic field in homogeneities, which depend on the geometry of the object placed in the MR scanner. EPI is also the fastest MRI sequence available, capable of capturing an image slice in less than 100 milliseconds and an entire brain volume in just a few seconds. The EPI sequence was devised by Mansfield (1977) but a decade of hardware development was required before the method became feasible in practice.

2.2 Functional MRI

The goal in fMRI is to locate brain activity. The first fMRI reports were given by Ogawa et al. (1990, 1993). Since, an ever growing interest in this method has been shown. The reasons are many but two of them are particularly important. First, fMRI is, to the best of our knowledge, a harmless technique. Second, an unsurpassed spatial resolution is obtained compared to other neuroimaging modalities such as Electroencephalography (EEG) and Positron Emission Tomography (PET). Furthermore, fMRI examinations can be carried out using what today can be considered as standard clinical MR scanners which are available at all modern hospitals and the procedure is completely painless. With the advent of fMRI as a tool for mapping brain activity, the neuroscience field has experienced a boost due to the possibility to study human brain function in a harmless way. Numerous experiments have been made addressing both basic sensory, visual and motor brain functions as well as higher cognitive functions such as language and memory. Another important application is pre-surgical examinations. Prior to the removal of for example a tumor, the brain functions located in the vicinity of the tumor can be mapped and the surgical approach can be optimized based on this information [1].

The fMRI technique relies on blood flow and blood oxygen concentration as indicators of brain activity. Local blood flow changes in active brain areas were predicted already in the end of the 19th century. The physiological basis of fMRI and how brain activity can be detected in MR images are further described below.

2.3 The BOLD signal

The neurons in the brain consume oxygen. The oxygen is attached to hemoglobin molecules in the blood and the flow of blood continuously provides new oxygen to the neurons. When the neuronal activity increases, so does also the demand of oxygen. To meet this demand, an increased flow of blood is regionally supplied to the population of active neurons [1]. The mechanisms underlying this very local regulation of blood flow is not yet fully understood. Important is however that an excess of oxygen is supplied to the active neurons, leading to an increased concentration of oxygenated blood in the capillaries surrounding the active brain area. This process is illustrated in Figure 2.2.

It is the difference in oxygenation concentration between a baseline state and an active state that can be measured with an MR scanner due to the different magnetic properties of oxygenated blood and deoxygenated blood. When oxygen is attached to the hemoglobin molecule an iron atom is shielded. In this state, the hemoglobin molecule is slightly diamagnetic and therefore almost magnetically inactive. Without oxygen attached, the hemoglobin's iron is exposed and the molecule becomes paramagnetic, which means that it interacts with and distorts an applied magnetic field. The oxygen concentration in the blood therefore affect the magnetic environment the hydrogen nuclei in the water molecules in the blood experience. At low oxygen concentrations there are many paramagnetic hemoglobin molecules that locally modulate the main magnetic field and as a consequence make the hydrogen nuclei excited by an RF-pulse diphase faster. Hence, the T_2' time constant becomes shorter in areas with low oxygen concentration and longer in areas with high oxygen concentration.
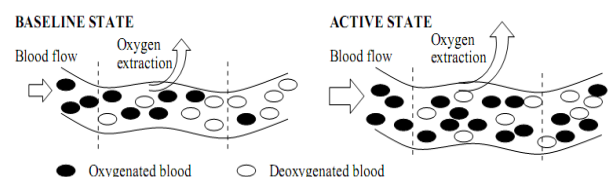

Fig. 2.2: Blood oxygen concentration in an active state compared to a baseline state.

The same image slice is repeatedly collected during a period of 5 to 10 minutes. Time series in active brain voxels contain a BOLD response while

time series in non-active voxels contain only noise [1].The rest and activity periods are indicated by the dotted signals.MR images reflecting the $T_2^{'}$ time constant are therefore brighter (longer $T_2^{'}$) when a brain area is in an active state compared to the baseline state. This effect is referred to as the Blood Oxygen Level Dependent (BOLD) signal. The effect is however very small, an intensity change of around 2-5 percent is expected, and it is therefore not detectable with a bare eye.
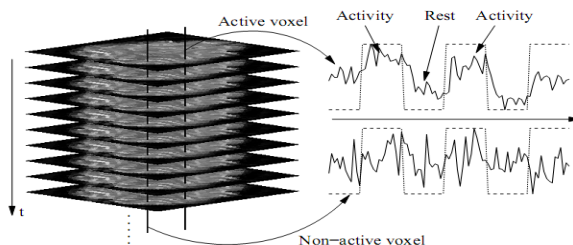

Fig. 2.3: A time series of intensity values is obtained in each voxel.

2.4 Detecting Brain Activity

To perform an fMRI experiment an MR scanner with the ability to acquire EPI images is required. A patient or volunteer is placed in the scanner and EPI images covering a volume of the brain are then continuously acquired during a period of 5 to 10 minutes. The in-plane size of the EPI images is 64×64 or 128×128 voxels and a stack of 10-40 slices are generally acquired [10]. Around 100-200 such image volumes are then repeatedly collected during the examination with a sampling period usually between 1 and 5 seconds. While the images are acquired the test subject is instructed to perform a task or some forms of stimuli are presented. For example, a visual stimulus can be presented on a screen during a period of 30 seconds and then a blank screen is shown for another 30 seconds. This activity/rest block is then repeated throughout the whole imaging session. Due to the BOLD signal effect, there will be a BOLD response in brain areas that are activated by the presented visual stimulus. Such areas will presumably be located in the visual cortex. Hence, in an EPI image collected when the visual stimulus is present, there should be higher image intensity values in voxels covering active brain areas compared to the intensities in the same voxels in an image collected during the resting period. As the same image slice repeatedly has been acquired during the experiment, there is a time series of intensity values in each voxel, see Figure 2.3. In a voxel covering a brain area participating in the processing of the presented visual stimulus, we expect a BOLD response, i.e. a variation in the time series, following the rhythm of the stimulus presentation.

2.5 Canonical Correlation Analysis

In 1936 H. Hotelling developed a general solution to this problem which is called canonical correlation analysis. Figure 2.4 shows how it can be applied in the context of functional MRI. Instead of analyzing single pixels

separately at the left hand side, a region of pixels is considered. Here we choose a 3×3 region. Analogous to the multiple correlations approach we now wish to construct two time-courses as linear combinations of pixel time-courses and basis functions respectively,

$$x(t) = w_x^T x(t) = w_{x1} x1(t) \ldots \ldots \ldots \ldots \ldots w_{xn} xn(t)$$
$$y(t) = w_y^T y(t) = w_{y1} y1(t) \ldots \ldots \ldots \ldots \ldots w_{yn} yn(t)$$

Just as in the previous section, y(t) is a time-course constructed using the basis functions. The time-course x(t) can be viewed as the output from a linear filter applied to the 3×3 region chosen in the image. The canonical correlation analysis find the linear combination coefficients $w_{x1} \ldots \ldots \ldots \ldots w_{xn}$ and $w_{y1} \ldots \ldots \ldots \ldots w_{yn}$ so that x(t) and y(t) correlates the most. Thus the canonical correlation analysis will for each region adaptively find a filter which reduces the noise and extracts a signal in the region to obtain good correlation.
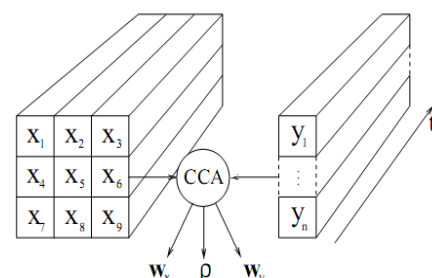

Fig. 2.4: A canonical correlation analysis between a set off MRI time-courses and a set of basis functions.

3. MATERIALS OF EXPERIMENT

In the fMRI studies considered here, data were collected from normal students from the university community. Typical studies involved between five and fifteen subjects, and it is generally selected a subset of these subjects with the strongest, least noisy fMRI signal to train the classifiers. Data were preprocessed to remove artifacts due to head motion, signal drift, and other sources. All voxel activity values were represented by the percent difference from their mean value during rest conditions (when the subject is asked to relax, and not perform any particular task). These preprocessed images were used as input to the toolbox.

This data set comprises whole brain BOLD/EPI images acquired on a modified 2T Siemens MAGNETOM Vision system. Each acquisition consisted of 64 contiguous slices ($64 \times 64 \times 64$ 3×3×3 mm3 voxels). Acquisition took 6.05s, with the scan to scan repeat time (TR) set arbitrarily to 7s. 96 acquisitions were made (TR=7s) from a single subject, in blocks of 6, giving 16 42s blocks. The condition for successive blocks alternated between rest and auditory stimulation, starting with rest. Auditory stimulation was bi-syllabic words presented binaurally at a rate of 60 per minute. The functional data starts at acquisition 4, image fM00223_004. Due to T1 effects it is advisable to discard the first few scans (there were no "dummy" lead-in scans). A structural image was also acquired: sM00223_002. This data set was the first ever collected and analyzed in the Functional Imaging Laboratory (FIL)

and is known locally as the mother of all experiments (MoAE).

4. EXPERIMENTAL METHODS

4.1 Spatial Preprocessing

The spatial pre-processing has the following steps:

Realignment: This routine realigns a time-series of images acquired from the same subject using a least squares approach and a 6 parameter (rigid body) spatial transformation. The first image in the list is used as a reference to which all subsequent scans are realigned. The reference scan does not have to the first chronologically and it may be wise to choose a "representative scan" in this role.

The aim is primarily to remove movement artifact in fMRI and time series (or more generally longitudinal studies). The headers are modified for each of the input images, such that they reflect the relative orientations of the data. The details of the transformation are displayed in the results window as plots of translation and rotation. This will run the realign job which will write realigned images into the directory where the functional images are. These new images will be prefixed with the letter "r". SPM will then plot the estimated time series of translations and rotations shown in Figure 4.1. These data are also saved to a file e.g. rp_fM00223_004 so that these variables can be used as regressors when fitting GLMs. This allows movements effects to be discounted when looking for brain activations.
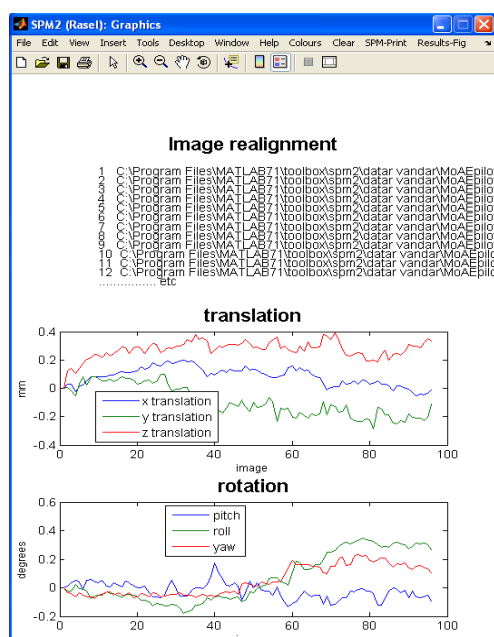

Fig. 4.1: Realignment of Auditory data

Coregistration: In the coregistration step, the sessions are first realigned to each other, by aligning the first scan from each session to the first scan of the first session. Then the images within each session are aligned to the first image of the session. The parameter estimation is performed this way because it is assumed (rightly or not) that there may be systematic differences in the images between sessions.

At the end of coregistration, the voxel-to-voxel affine transformation matrix is displayed, along with the histograms for the images in the original orientations, and the final orientations. The registered images are displayed at the bottom.
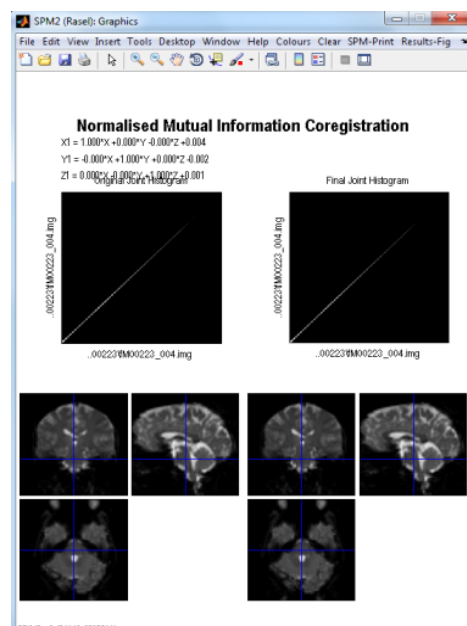

Fig. 4.2: Mutual Information Coregistration of Auditory data.

SPM will then implement a coregistration between the structural and functional data that maximizes the mutual information. The image in figure 4.2 should then appear in the graphics window. SPM will have changed the header of the source file which in this case is the structural image sM00223_002.hdr.

Normalization: This function can be used for bias correcting, spatially normalizing or segmenting the data. This routine produces spatial normalization parameters (* seg_sn.mat files) by default. These can be used for writing spatially normalized versions of the data, via the "Normalize: Write" option. This mechanism produce superior results than the "Normalize: Estimate" option. In addition, it also produces files that can be used for doing inverse normalization. If an image of regions defined in the standard space, then the inverse deformations can be used to warp these regions so that it approximately overlay the image.

Generally, the algorithms work by minimizing the sum of squares difference between the image which is to be normalized, and a linear combination of one or more template images. For the least squares registration to produce an unbiased estimate of the spatial transformation, the image contrast in the templates (or linear combination of templates) should be similar to that of the image from which the spatial normalization is derived. The registration simply searches for an optimum solution. If the starting estimates are not good, then the optimum it finds may not find the global optimum.

The first step of the normalization is to determine the optimum 12-parameter affine transformation. Initially,

the registration is performed by matching the whole of the head (including the scalp) to the template. Following this, the registration proceeded by only matching the brains together, by appropriate weighting of the template voxels. This is a completely automated procedure (that does not require "scalp editing') that discounts the confounding effects of skull and scalp differences. A Bayesian framework is used, such that the registration searches for the solution that maximizes the a posteriori probability of it being correct i.e. it maximizes the product of the likelihood function (derived from the residual squared difference) and the prior function (which is based on the probability of obtaining a particular set of zooms and shears).

All normalized *.img scans are written to the same subdirectory as the original *.img, prefixed with a 'w' (i.e. w*.img).The normalized structural image is shown in figure 4.3.

Smoothing: Though the data is noisy, it might need to apply a smoothing algorithm to expose its features, and to provide a reasonable starting approach for parametric fitting. The smoothing process attempts to estimate the average of the distribution of each response value. The estimation is based on a specified number of neighboring response values.

The FWHM of the Gaussian smoothing kernel (mm) applied to the images before estimating the realignment parameters (MRI images typically use a 5 mm kernel).

4.2 fMRI Model Specification

Statistical analysis of fMRI data uses a mass-univariate approach based on General Linear Models (GLMs). It comprises the following steps (1) specification of the GLM design matrix, fMRI data files and filtering (2) estimation of GLM parameters using classical or Bayesian approaches and (3) interrogation of results using contrast vectors to produce Statistical Parametric Maps (SPMs).
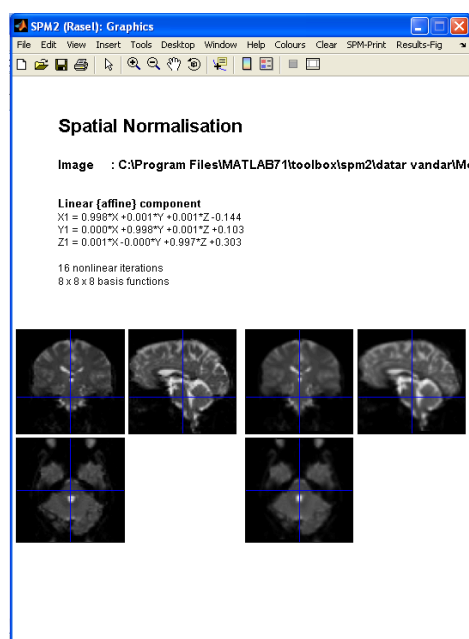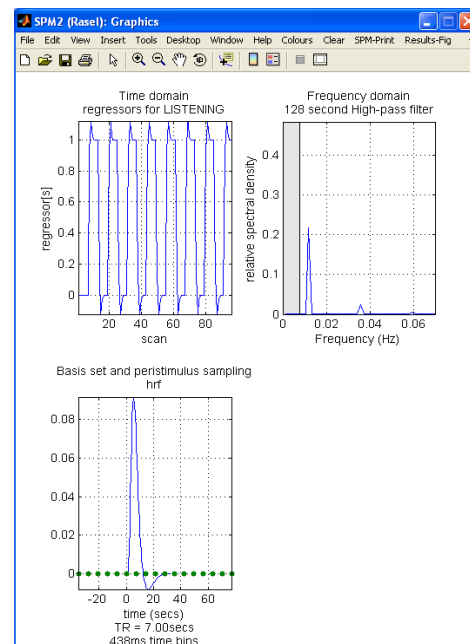

Fig. 4.3: Normalized Structural image

Fig. 4.4: Exploring Design Matrix.

The design matrix (Explored in figure 4.4) defines the experimental design and the nature of hypothesis testing to be implemented. The design matrix has one row for each scan and one column for each effect or explanatory variable. (e.g. regressor or stimulus function).

5. RESULTS ANALYSIS

In Figure 4.4 it has been shown that the time series of the "active" regressor (top left), a frequency domain plot of the active regressor (top right) and the basis function used to convert assumed neuronal activity into hemodynamic activity. In this model it is used the default option - the canonical basis function. The frequency domain plot shows that the frequency content of the "active" regressor is above the set frequencies that are removed by the High Pass Filter (HPF)

After the model has been specified there must be define a contrast and then it is to be selected either 'active > rest' or 'rest > active'. It has been selected 'active > rest' and 't-contrast' from contrast manager display. Then it is to be given a threshold value.

Finally all the smoothed images are given to SPM input and visualize the output either in 'slices', 'sections' or 'render'. In Figure 5.1 there have been shown the sectional images i.e. either sagittal, coronal or transaxial images and show the activated region by bright color. In figure 5.2 there have been shown 3D volume rendered brain showing the activated region.
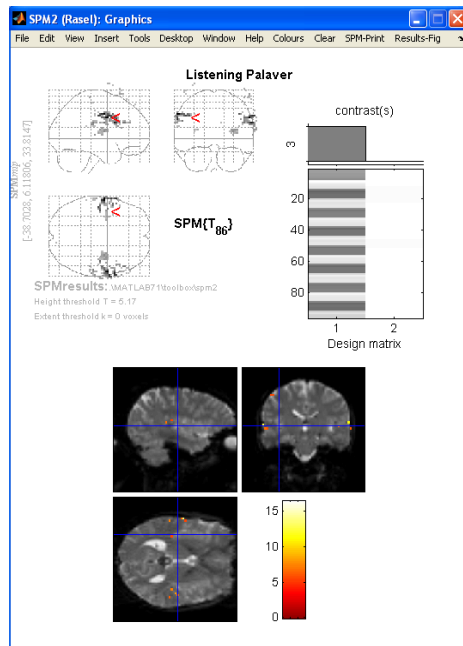
Fig. 5.1: Sagittal (upper right), Coronal (upper left), Tran-axial (down) sections.
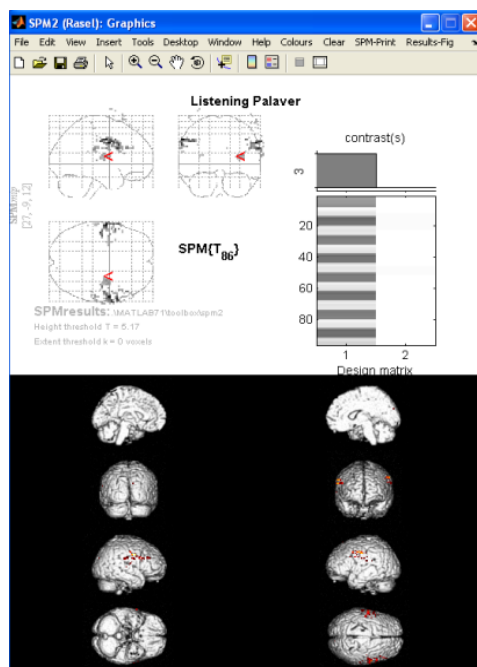

Fig. 5.2: 3D volume rendered brain

6. CONCLUSION

In this paper, it has been determined the portion of the brain which is responsible for any specific task using canonical correlation analysis. The functional MRI area attracts researchers from many diverse disciplines and a large number of methods have been devised for the analysis of fMRI data. Very few of these methods are however used in practice. There are a number of properties that a method must possess in order to be successful. Three such main properties are simplicity, good performance and computational efficiency. The method used here is based on the generalized linear

model. The result obtained by this approach is more accurate and clear than other methods.

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