9.3.2 fMRI pre-processing and analysis

Introduction

Following acquisition of the data set, the images are processed offline using a MATLAB software package called Statistical Parametric Mapping (SPM) [36]. This software is freely available and is written by the members of the Wellcome Trust Centre for Neuroimaging (University College London) for the analysis and interpretation of functional neuroimaging data. To gain a better understanding of fMRI analysis, I analysed an old EPI-BOLD data set from a case I had observed at NHNN. This data set had been previously acquired from a volunteer who had performed a simple finger tapping motor task with his left hand on the Siemens Trio 3T scanner. The data was preprocessed in SPM by realigning and motion correcting, normalising to a MNI template (standard brain used from the Montreal Neurological Institute) and finally smoothing. These various steps and results are discussed in more detail in the methodology and results section. During my placement, I also gave a talk to my fellow trainees and training coordinator on fMRI preprocessing and analysis (presentation slides in appendix A3).

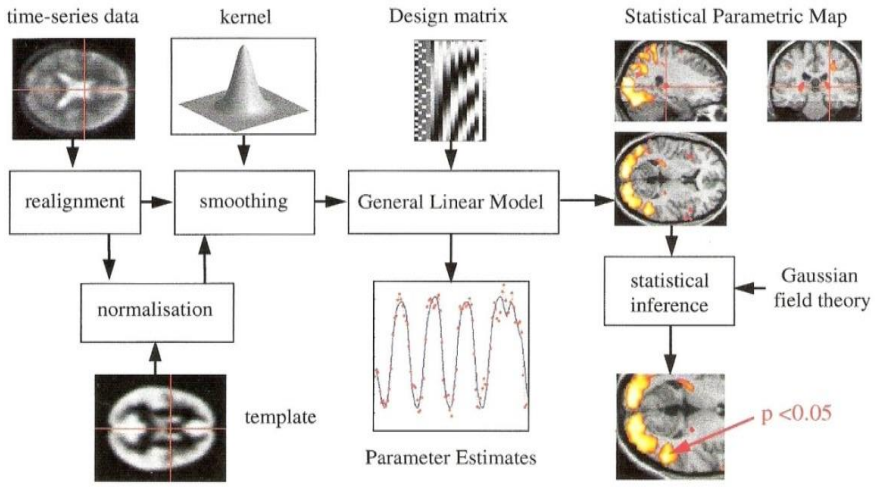


Figure 9.7 Flow Chart showing the different stages of SPM fMRI analysis

Methodology

A localiser and a Magnetization Prepared Rapid Acquisition Gradient Echo (MP-RAGE) T_1 weighted structural image were acquired, followed by a series of EPI images with the volunteer asked to remain as still as possible (TR/TE = 3200ms/40ms, 40 slices and 200 volumes). This is used for subsequent analysis of 'resting state' fMRI, to observe the default activation when the brain is at rest. The volunteer was then presented with visual instructions: 'go' (to start the finger tapping task) or 'rest' (stop the finger tapping task and remain still). A series of EPI-BOLD images are acquired (TR/TE = 4000ms/40ms, 49 slices, 96 volumes). I used the following pre processing pipeline to analyse the images on SPM:

Realignment for motion correction: The images need to be realigned to correct for subject movement during the scan. Before realignment, the first five BOLD volumes (including the M_0 image which is the first image acquired) were discarded. This was done to avoid T_1 equilibration effects. It is important that subjects are cooperative and remain as still as possible [36,37].

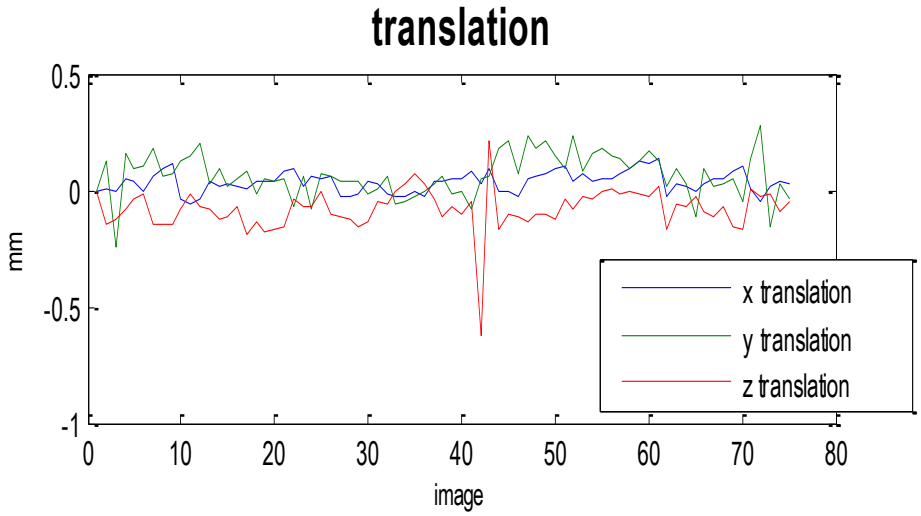


Figure 9.8 Realignment results from SPM showing less than 0.7 mm translational movement in the x,y,z direction during the scan

Normalisation: In order to carry out voxel based analysis, it is important that data from different subjects have come from homologous parts of the brain. The mean image of the series (obtained after realignment) is used to estimate warping parameters. The images are then moved and warped so that they match a brain template (MNI template) which already conforms to a standard space e.g. Talairach and Tournoux (version 2.4.2). Normalisation allows comparison between different subjects and intersubject averaging of data [36,37].

Smoothing: Smoothing involves convolution with a Gaussian kernel whose full width at half maximum (FWHM) is at least twice the voxel dimensions. e.g. for a 3 mm x 3mm x 3 mm voxel , the FWHM should be set to 6mm x 6mm x 6 mm. Increasing the kernel size will increase sensitivity for subsequent analysis but at the expense of spatial resolution. The images appear blurred due to averaging over neighbouring voxels which removes high spatial frequency noise from the BOLD signal [36,37].

The General Linear Model: The General Linear Model (GLM) describes the time varying signals in each voxel and is a linear combination of explanatory variables and residual error terms (assumed to be normally distributed). It can be represented in matrix form as**:** $\mathbf{Y} = \mathbf{X}\boldsymbol{\beta} + \boldsymbol{\varepsilon}$, where **Y** is the observed data matrix i.e. the BOLD signals at various time points in a voxel, **X** is design matrix (figure 9.9), **β** is the parameter matrix, **ε** is a matrix of error terms [34, 36]. **X** contains the BOLD time series data along with information about the predicted shape of the BOLD response, or in other terms the predicted variation in response to the task performed. This is obtained by convolving the haemodynamic response function (section 9.3.1) with the task timing described as the onset times in seconds: [0 40 80 120 160 200 240 280] and the 20 second duration for activation and rest. **β** contains different parameters which define the contributions of each component of **X** to the value of **Y**. The first column in **X** is the haemodynamic response function convolved with the task timing, the next six columns are the movement parameters for the head translation (in x, y, z) and rotation (about the x, y and z axis) during acquisition; the last column is a constant to take into account the constant component of the MR signal.

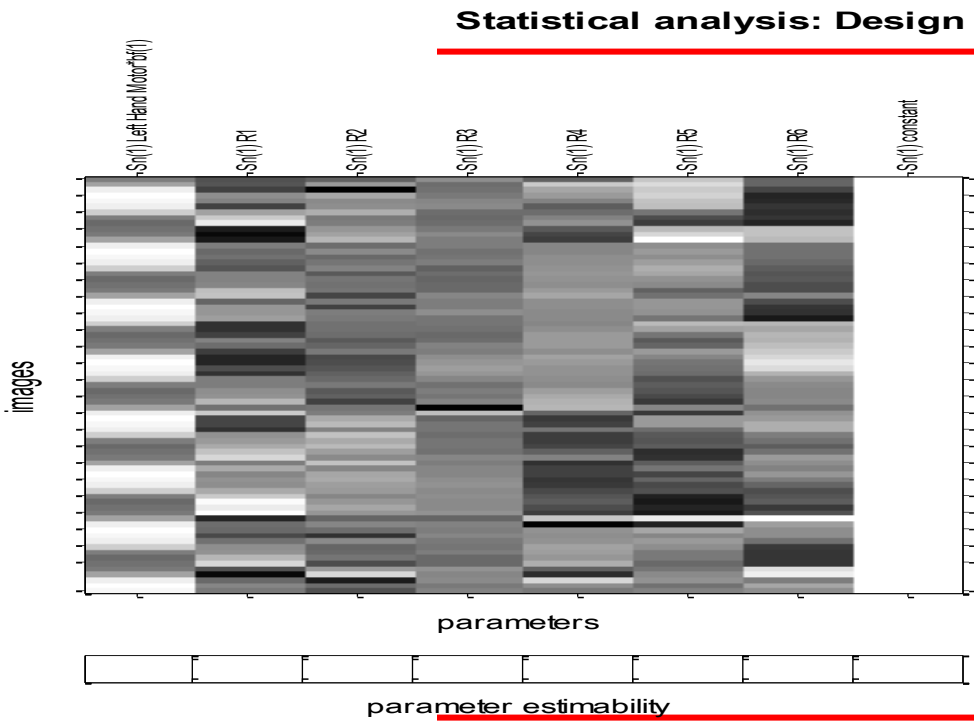
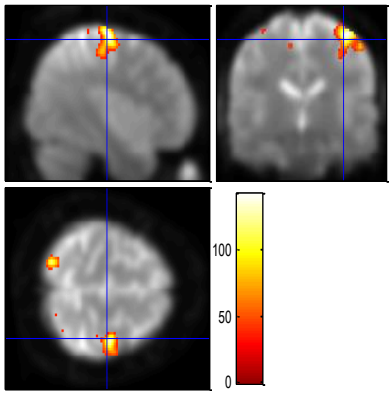


Figure 9.9 The design matrix where the first column with equally spaced alternating bright and dark blocks depicts the paradigm for the experiment and the other columns are multiple regressors which use outputs from the realignment step for additional motion correction.

The error term is the difference between the observed data and the model. The parameters in **β** are estimated so as to minimize the error term using a least sum of squares method. These parameters provide information regarding the contrasts between the 'on' (finger tapping) and 'off' (rest) periods in the paradigm. The low frequency drift in the BOLD signal is removed by using a high pass filter. The statistical parametric maps produced at the end of the analysis indicate the probability of activation of voxels. A family-wise error (FWE) rate with $p<0.05$ was chosen. This means that if the same analysis is repeated 100 times, in 5% of the results there is 1 false positive, therefore all voxels in the parametric map have less than a 5% chance of being a false positive i.e. do not show activation even though the corresponding brain area is active. Figure 9.10(a) shows the statistical map overlaid on a smoothed volume showing activation in the motor cortex. The bright yellow region correspond to activations which are statistically significant.

a)



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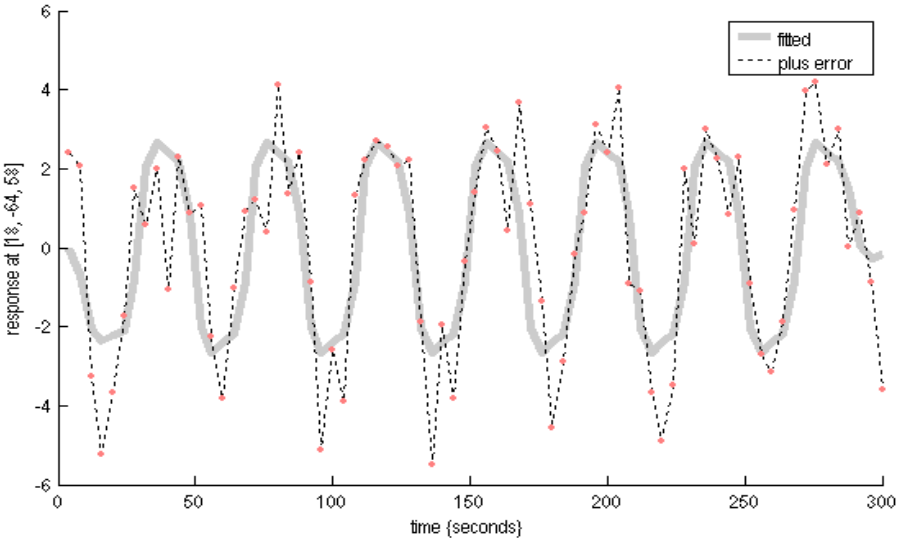

Figure 9.10 a) The statistical map overlaid on a smoothed volume showing activation in the motor cortex. The colour bar indicates the degree of significance of activation where bright yellow corresponds to activation which is statistically significant. b) Fitted responses (grey line) to the data (dotted lines) as a function of time for a selected voxel in the activated region.

Results and Conclusion

Table 9.1 The three clusters with the highest t statistic values and corresponding brain region where they are located

	Number of voxels	Coordinate			Brain Region
		X	Y	Z	
Cluster 1	845	40	-18	64	Broadmann area 4, Precentral gyrus
Cluster 2	243	16	-64	54	Broadmann area 7, superior parietal lobule
Cluster 3	199	-22	-70	60	Broadmann area 7, Superior parietal lobule

The coordinates quoted in table 9.1 are the voxels with the highest t statistic values for each cluster. Only the three most significant clusters are reported. In addition, the number of voxels are quoted for the cluster with the highest statistical significance. The freely available Talairach Client software (version 2.4.2) [38] can then be used to report the corresponding brain regions for the coordinates listed. The largest cluster was associated with Broadmann area 4 or precentral gyrus, a large part of which comprises the primary motor cortex. The function of this area is to execute movement. The smaller clusters 2 and 3 were associated with Broadmann area 7 in the superior parietal lobule which is part of the somatosensory association cortex and has a function in visuo-motor coordination.