

Chapter 1

Face fMRI data

As a third and more sophisticated example, consider the data from a repetition priming experiment performed using event-related fMRI. Briefly, this is a 2x2 factorial study with factors ‘fame’ and ‘repetition’ where famous and non-famous faces were presented twice against a checkerboard baseline. The subject was asked to make fame judgements by making key presses. There are thus four event-types of interest; first and second presentations of famous and non-famous faces, which we denote N1, N2, F1 and F2. The experimental design is shown schematically in Figure 1.1.

Images were acquired using continuous Echo-Planar Imaging (EPI) with TE=40ms, TR=2s and 24 descending slices ($64 \times 64 \times 3 \text{mm}^2$), 3mm thick with a 1.5mm gap. The data archive is available from [This](#) contains 351 Analyse format functional images `sM03953_0005_*.img` of dimension $64 \times 64 \times 24$ with $3 \text{mm} \times 3 \text{mm} \times 4.5 \text{mm}$ voxels. A structural image is also provided `sM03953_0007.img` also in Analyse format.

To analyse the data, first create a new directory DIR eg. `c:\home\wpenny\fmri_analysis\face-rep\all`, in which to place the results of your analysis. Then create 3 subdirectories (i) `jobs`, (ii) `designs`, (iii) `classical` and (iv) `bayesian`. As the analysis proceeds these directories will be filled with job-specification files, design matrices and models estimated using classical or Bayesian methods. Additionally, in each of the `designs`, `classical` and `bayesian` directories create two subdirectories called `categorical` and `parametric` as we will show how this data can be analysed in two different ways. In the categorical analysis we will look at the main effects of fame and repetition and in the parameteric analysis we will look at responses as a function of ‘lag’, that is, the number of faces intervening between repetition of a specific face.

Start up matlab, enter your jobs directory and type `spm_fmri` at the matlab prompt. SPM will then open in fMRI mode with three windows (1) the top-left or ‘command’ window, (2) the bottom-left or ‘interactive’ window and (3) the right-hand or ‘graphics’ window. Analysis then takes place in three major stages (i) spatial pre-processing, (ii) model specification, review and estimation and (iii) inference. These stages organise the buttons in SPM’s base window.

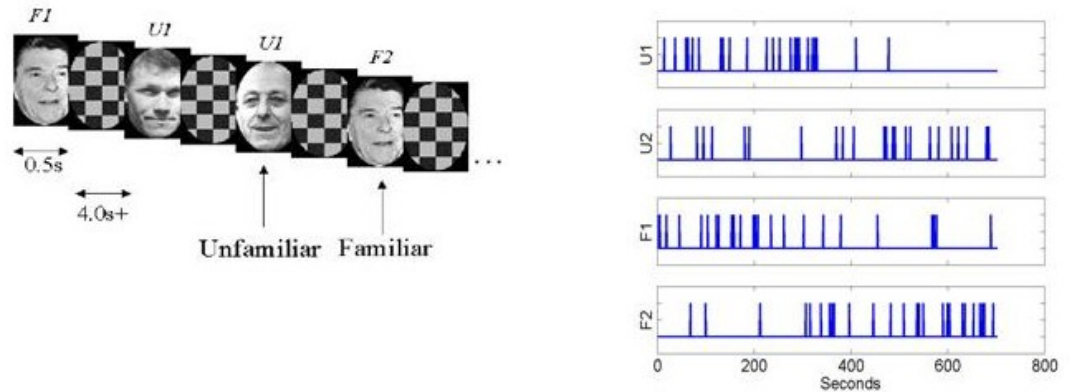


Figure 1.1: *Face repetition paradigm.* **Left** There were 2 presentations of 26 Famous and 26 Nonfamous Greyscale photographs, for 0.5s each, randomly inter-mixed. The minimal Stimulus Onset Asynchrony (SOA)=4.5s, with probability 2/3 (ie 1/3 null events). The subject made one of two right finger key presses denoting whether or not the subject thought the face was famous. **Right** The time series of events.

1.1 Spatial pre-processing

1.1.1 Display

Display eg. the first functional image using the ‘Display’ button. Note orbitofrontal and inferior temporal drop-out and ghosting. This can be seen more clearly by selecting ‘brighten if necessary’ from the ‘Effects’ tab at the top of the graphics window.

1.1.2 Realignment

Under the spatial pre-processing section of the SPM base window select ‘Realign’ from the ‘Realign’ pulldown menu. This will call up a realignment job specification in the graphics window. Then

- Select ‘New Realign:Estimate and Reslice’
- Open the newly created ‘Realign:Estimate and Reslice’ option.
- Highlight data, select ‘New Session’, then highlight the newly created ‘Session’ option.
- Select ‘Specify Files’ and use the SPM file selector to choose all of your functional images eg. sM03953_0005_*.img.
- Save the job file as eg. DIR/jobs/realign.mat.
- Press the RUN button in the graphics window.

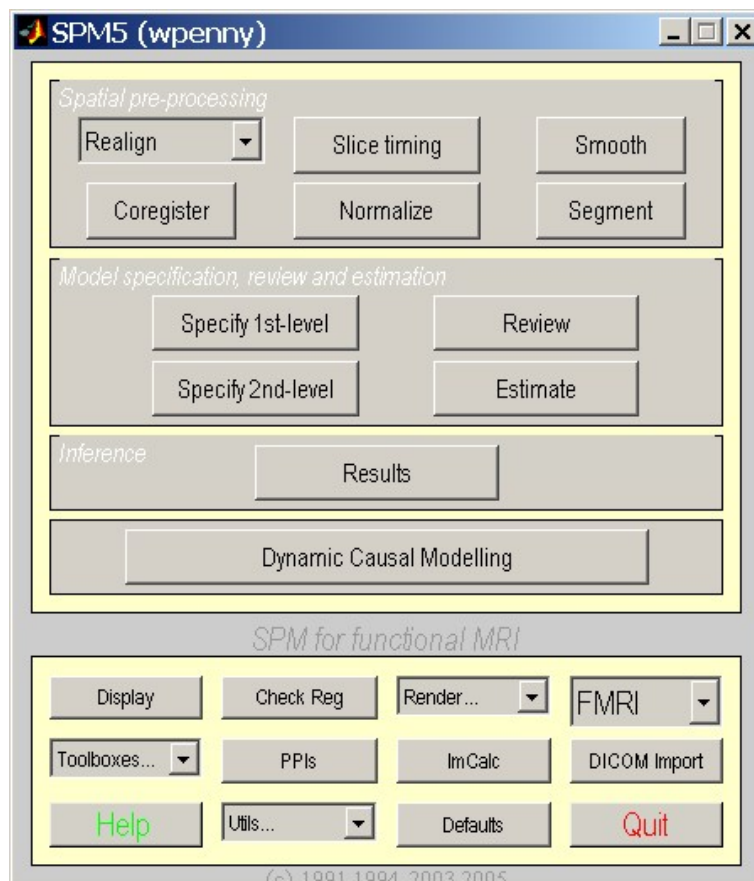
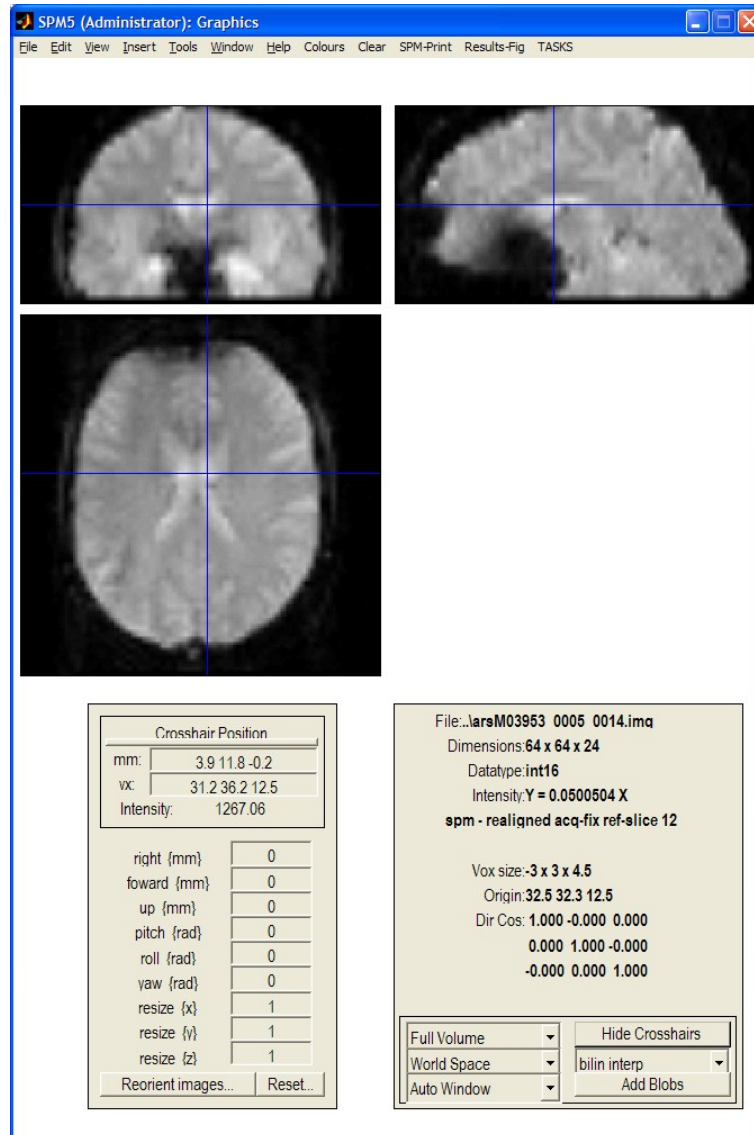


Figure 1.2: The SPM base window comprises three sections i) spatial pre-processing, (ii) model specification, review and estimation and (iii) inference.

Figure 1.3: *Signal dropout in EPI images.*

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 1.4. These data, the realignment parameters, are also saved to a file eg. `rp_sM03953_0005_0006.txt`, so that these variables can be used as regressors when fitting GLMs. To prepare for this copy the file into the `DIR\jobs\` directory and rename it `movepars.txt`. This allows movements effects to be discounted when looking for brain activations.

SPM will also create a mean image eg. `meansM03953_0005_0006.img` which will be used in the next step of spatial processing - coregistration.

1.1.3 Slice timing correction

Press the 'Slice timing' button. This will call up the specification of a slice timing job in the graphics window.

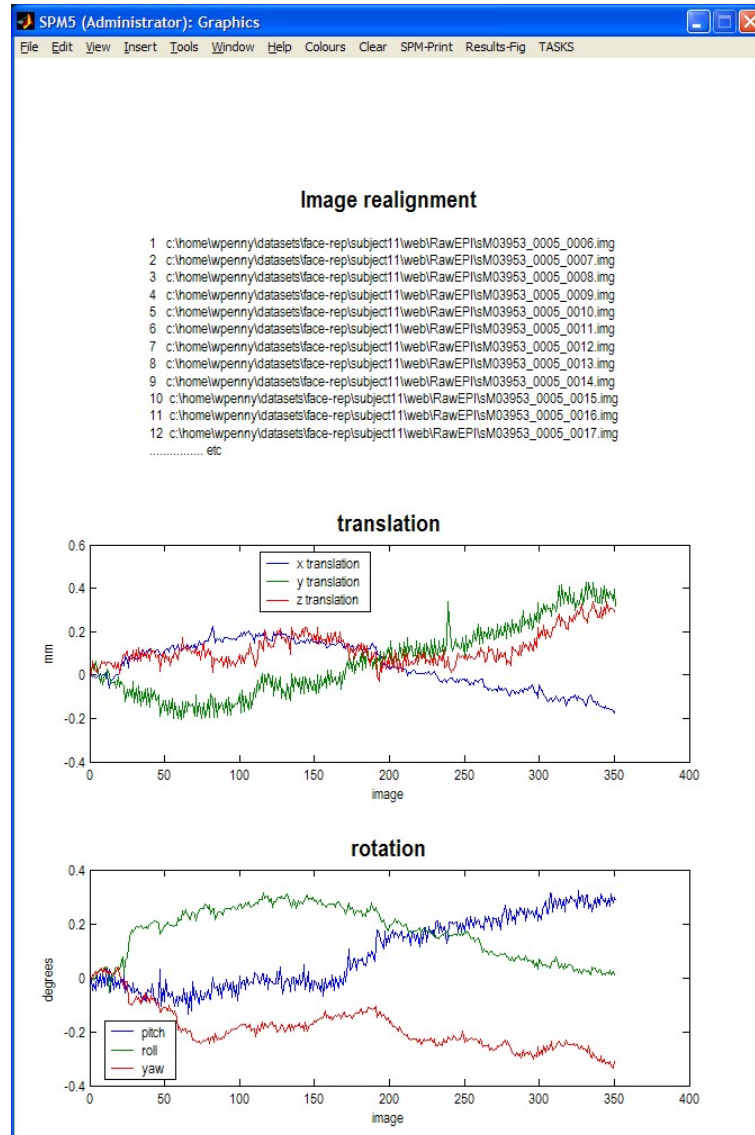
- Open the 'Slice Timing' option
- Highlight 'Data' and select 'New Sessions'
- Highlight the newly create 'Sessions' option, 'Specify Files' and select the 351 realigned functional images using the filter `^r.*`.
- Select 'Number of Slices' and enter 24
- Select TR and enter 2
- Select TA and enter 2
- Select 'Slice order' and enter 24:-1:1
- Select 'Reference Slice', and enter 12
- Save the job as `slice_timing.mat` and press 'Run'

SPM will write slice-time corrected files with the prefix 'a' in the functional data directory.

1.1.4 Coregistration

Press the 'Coreg' button. This will call up the specification of a coregistration job in the graphics window.

- Select New "Coreg:Estimate"
- Double-click on the newly created Coreg:Estimate
- Highlight 'Reference Image' and then select the mean functional image `meansM03953_0005_0006.img`
- Highlight 'Source Image' and then select the structural image eg. `sM03953_0007.img`.
- Press the Save button and save the job as `coreg.job`
- Then press RUN

Figure 1.4: *Realignment of face data.*

SPM will then implement a coregistration between the structural and functional data that maximises the mutual information. The image in figure 1.5 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 `sM03953_0007.img`.

1.1.5 Segmentation

Press the ‘Segment’ button. This will call up the specification of a segmentation job in the graphics window. Highlight the Data field and then select the subjects coregistered anatomical image eg. `sM03953_0007.img`. Save the job file as `segment.mat` and then press RUN. SPM will segment the structural image using the default tissue probability maps as priors. SPM will create, by default, gray and white matter images and bias-field corrected structural image. These can be viewed using the CheckReg facility as described in the previous section (press segment and select . Figure ?? shows the gray matter image, `c1sM03953_0007.img` along with the original structural.

SPM will also write a spatial normalisation eg. `sM03952_0007_seg_sn.mat` file in the original structural directory. This will be used in the next section to normalise the functional data.

1.1.6 Normalize

Press the ‘Normalize’ button. This will call up the specification of a normalise job in the graphics window.

- Select a New “Normalise:Write” field. This allows previously estimated warps to be applied to a series of images.
- Highlight ‘Data’, select New “Subject”
- Open ‘Subject’, highlight ‘Parameter File’ and select the `sM03952_0007_seg_sn.mat` file that you created in the previous section
- Highlight images to write and select all of the slice-time corrected, realigned functional images ‘`arsM*.img`’. Note: This can be done efficiently by changing the filter in the SPM file selector to `^ar.*`. SPM will then only list those files beginning with the letter *r* ie. those that have been realigned. You can then right click over the listed files, choose ‘Select all’ and press ‘Done’.
- Open ‘Writing Options’, and change ‘Voxel sizes’ from [2,2,2] to [3,3,3].¹
- Press ‘Save’, save the job as `normalise.mat` and then press ‘Run’.

SPM will then write spatially normalised files to the functional data directory. These files have the prefix ‘w’.

If you wish to superimpose a subject’s functional activations on their own anatomy² you will also need to apply the spatial normalisation parameters to their (bias-corrected) anatomical image. To do this

¹This step is not strictly necessary. It will write images out at a resolution closer to that at which they were acquired. This will speed up subsequent analysis and is necessary, for example, to make Bayesian fMRI analysis computationally efficient.

²Beginners may wish to skip this step, and instead just superimpose functional activations on an ‘average structural image’.

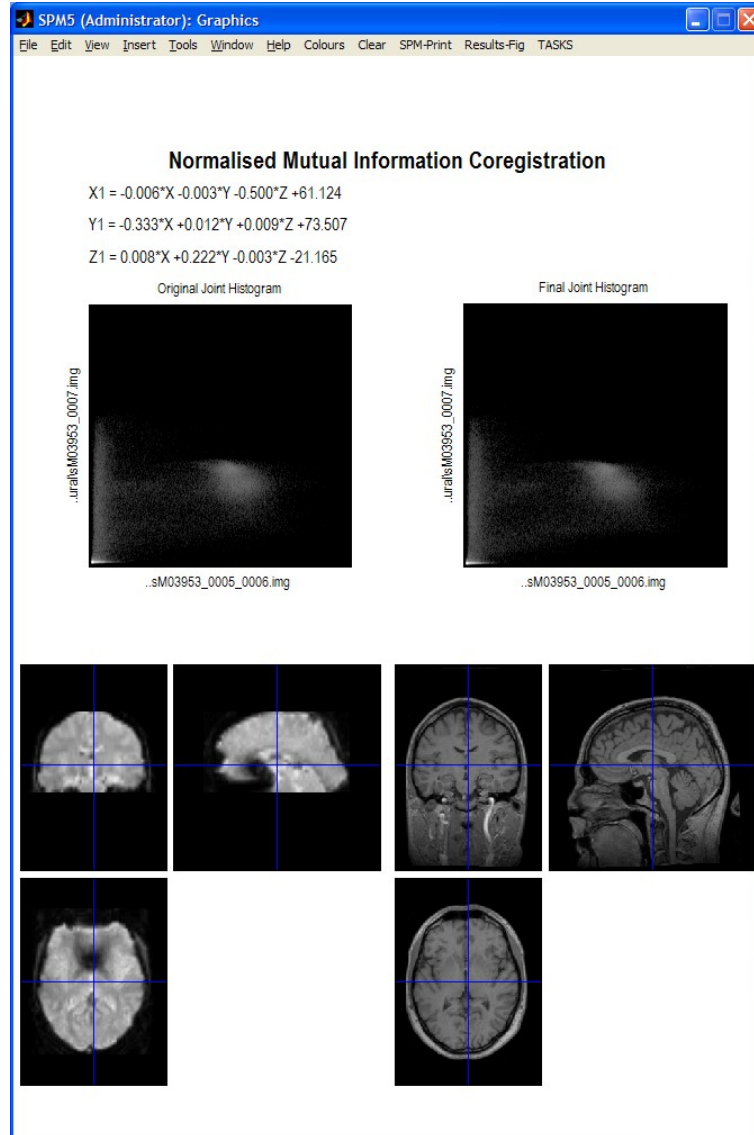


Figure 1.5: *Mutual Information Coeregistration of Auditory data.*

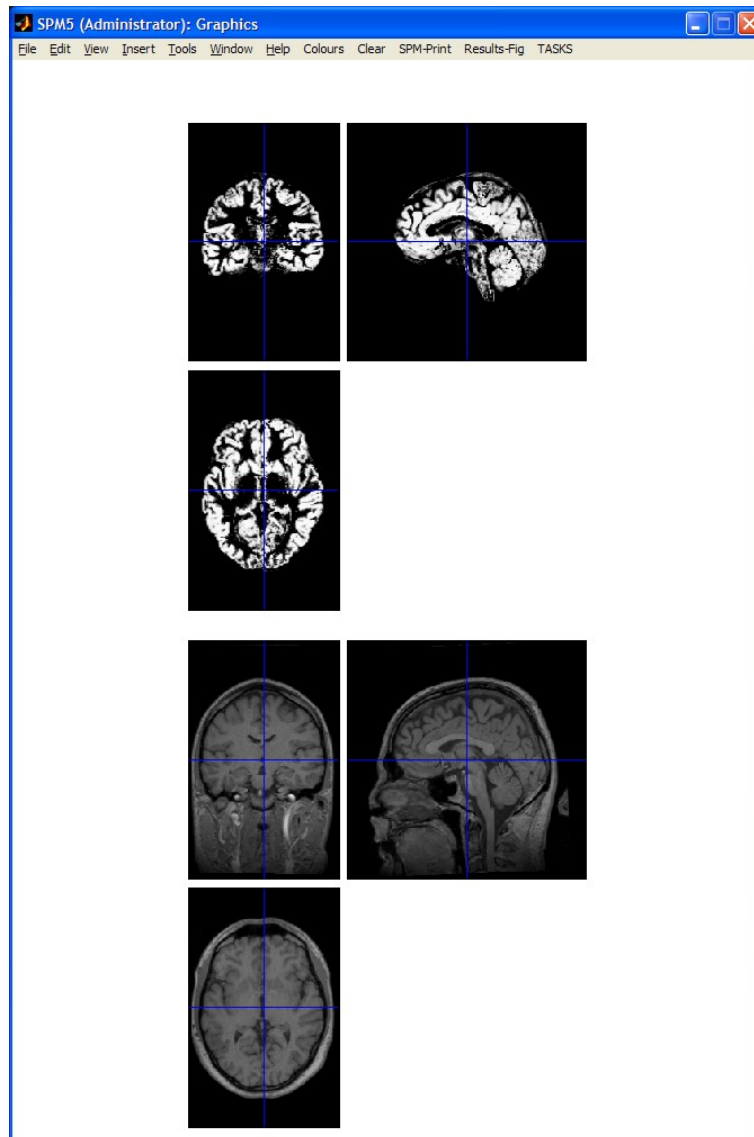


Figure 1.6: *Gray matter image and 'registered' structural image.*

- Press ‘Normalise’, select New ”Normalise:Write”
- Open ‘Normalise: Write’, highlight ‘Data’, select New ”Subject”
- Open ‘Subject’
- Highlight ‘Parameter File’, select the `sm03952_0007_seg_sn.mat` file that you created in the previous section, press ‘Done’.
- Highlight ‘Images to Write’, select the bias-corrected structural eg. `msM03952_0007.img`, press ‘Done’.
- Open ‘Writing Options’, select voxel sizes and change the default $[2\ 2\ 2]$ to $[1\ 1\ 1]$ which better matches the original resolution of the images $[1\ 1\ 1.5]$.
- Save the job as `norm_struct.mat` and press ‘Run’.

1.1.7 Smoothing

Press the ‘Smooth’ button³. This will call up the specification of a smooth job in the graphics window.

- Open ‘Smooth’, select ‘Images to Smooth’ and then select the spatially normalised files created in the last section eg. `war*.img`.
- Save the job as `smooth.mat` and press ‘Run’.

This will smooth the data by 8mm in each direction, the default smoothing kernel width.

1.2 Modelling categorical responses

Before setting up the design matrix we must first load the Stimulus Onsets Times (SOTs) and movement parameters into matlab. SOTs are stored in the `sots.mat` file in a cell array such that eg. `sot{1}` contains stimulus onset times in TRs for event type 1, which is N1. Event-types 2,3 and 4 are N2, F1 and F2⁴.

- At the matlab command prompt type ‘load sots’
- Then type ‘load movepars.txt’

Now press the ‘Specify 1st-level’ button. This will call up the specification of a fMRI specification job in the graphics window. Then

- Open the fMRI model specification option
- Open the ‘Timing paramaters’ option

³The smoothing step is unnecessary if you are only interested in Bayesian analysis of your functional data.

⁴Also included with this data set are variables describing two event-types of no interest - the (rare) errors made by this subject on the fame-judgement task. We will not, however, be using these in our analyses.

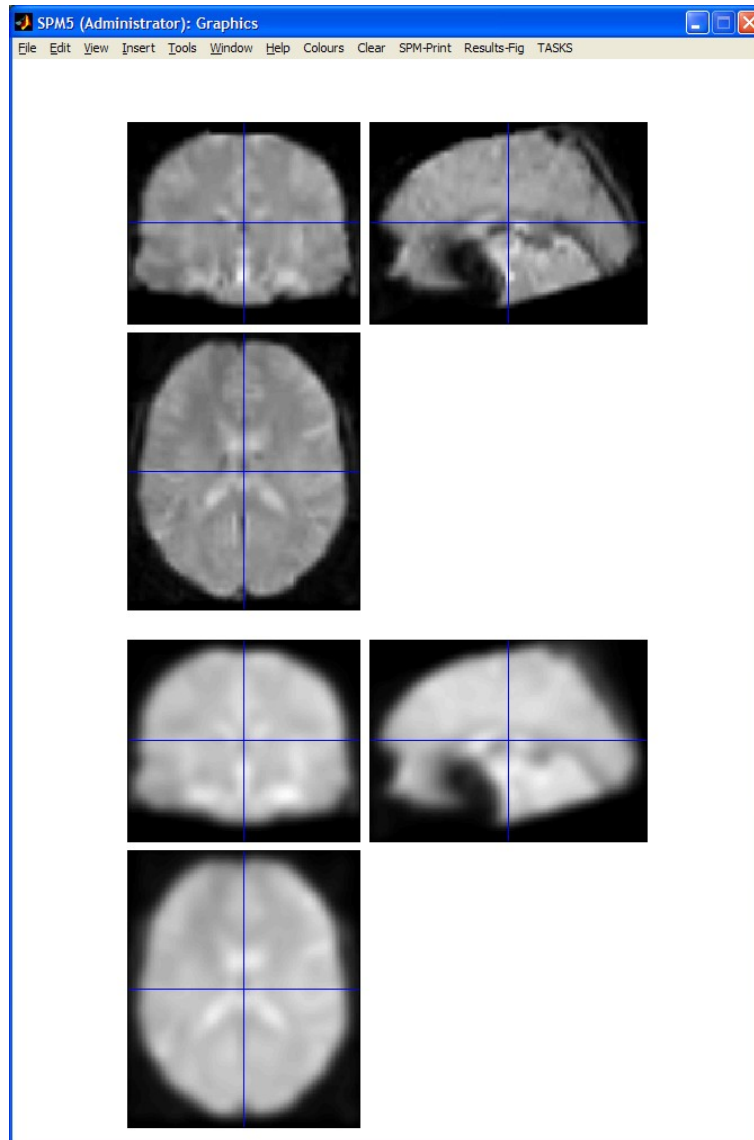


Figure 1.7: *Functional image (top) and 8mm-smoothed functional image (bottom). These images were obtained using SPM's 'CheckReg' facility.*

- Highlight 'Units for design' and select 'Scans'
- Highlight 'Interscan interval' and enter 2
- Highlight 'Microtime resolution' and enter 24
- Highlight 'Microtime onset' and enter 12. These last two options make the creating of regressors commensurate with the slice-time correction we have applied to the data.
- Highlight 'Data and Design' and select 'New Subject/Session'. Then open the newly created 'Subject/Session' option.
- Highlight 'Scans' and use SPM's file selector to choose the 351 smoothed, normalised, slice-time corrected, realigned functional images ie `swarsM.img`. These can be selected easily using the `^swar.*` filter, and select all. Then press 'Done'.
- Highlight 'Conditions' and select 'New condition'
- Open the newly created 'Condition' option. Highlight 'Name' and enter 'N1'. Highlight 'Onsets' and enter 'sot{1}'. Highlight 'Durations' and enter 0.
- Highlight 'Conditions' and select 'New condition'
- Open the newly created 'Condition' option. Highlight 'Name' and enter 'N2'. Highlight 'Onsets' and enter 'sot{2}'. Highlight 'Durations' and enter 0.
- Highlight 'Conditions' and select 'New condition'
- Open the newly created 'Condition' option. Highlight 'Name' and enter 'F1'. Highlight 'Onsets' and enter 'sot{3}'. Highlight 'Durations' and enter 0.
- Highlight 'Conditions' and select 'New condition'
- Open the newly created 'Condition' option. Highlight 'Name' and enter 'F2'. Highlight 'Onsets' and enter 'sot{4}'. Highlight 'Durations' and enter 0.
- Highlight 'Regressors', select 'New Regressor', open the newly created 'Regressor' option, highlight 'Name' enter 'tx', highlight 'Value', enter `movepars(:,1)`
- Highlight 'Regressors', select 'New Regressor', open the newly created 'Regressor' option, highlight 'Name' enter 'ty', highlight 'Value', enter `movepars(:,2)`
- Highlight 'Regressors', select 'New Regressor', open the newly created 'Regressor' option, highlight 'Name' enter 'tz', highlight 'Value', enter `movepars(:,3)`

- Highlight ‘Regressors’, select ‘New Regressor’, open the newly created ‘Regressor’ option, highlight ‘Name’ enter ‘pitch’, highlight ‘Value’, enter `movepars(:,4)`
- Highlight ‘Regressors’, select ‘New Regressor’, open the newly created ‘Regressor’ option, highlight ‘Name’ enter ‘roll’, highlight ‘Value’, enter `movepars(:,5)`
- Highlight ‘Regressors’, select ‘New Regressor’, open the newly created ‘Regressor’ option, highlight ‘Name’ enter ‘yaw’, highlight ‘Value’, enter `movepars(:,6)`
- Highlight ‘Factorial Design’, select ‘New Factor’, open the newly created ‘Factor’ option, highlight ‘Name’ and enter ‘Fam’, highlight ‘Levels’ and enter 2.
- Highlight ‘Factorial Design’, select ‘New Factor’, open the newly created ‘Factor’ option, highlight ‘Name’ and enter ‘Rep’, highlight ‘Levels’ and enter 2⁵.
- Open ‘Canonical HRF’ under ‘Basis Functions’. Select ‘Model derivatives’ and select ‘Time derivatives’.
- Highlight ‘Directory’ and select the `DIR/designs/categorical` directory you created earlier.
- Save the job as `categorical_spec.mat` and press ‘RUN’

SPM will then write an `SPM.mat` file to the `DIR/designs/categorical` directory. It will also plot the design matrix, as shown in Figure 1.8.

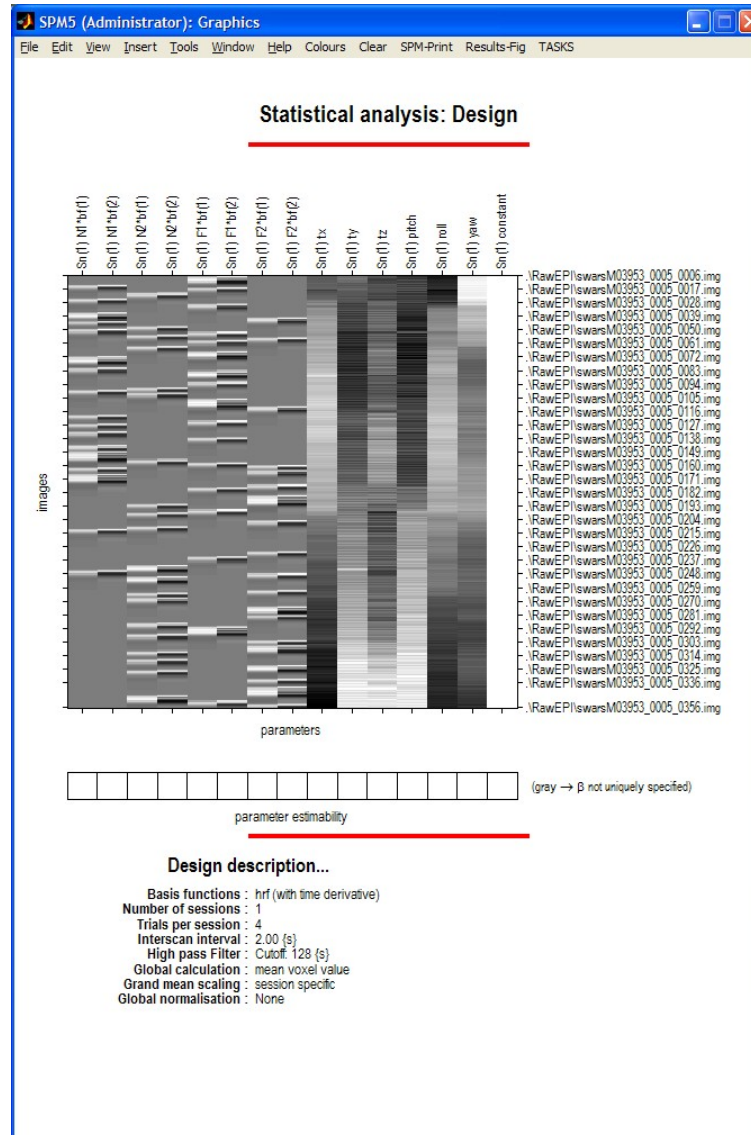
At this stage it is advisable to check your model specification using SPM’s review facility which is accessed via the ‘Review’ button. This brings up a ‘design’ tab on the interactive window clicking on which produces a pulldown menu. If you select the first item ‘Design Matrix’ SPM will produce the image shown in Figure 1.8. If you select ‘Explore’ then ‘Session 1’ then ‘N1’, SPM will produce the plots shown in Figure 1.9.

1.2.1 Estimate

Press the ‘Estimate’ button. This will call up the specification of an fMRI estimation job in the graphics window. Then

- Open the ‘fMRI model estimation’ option
- Highlight the ‘Select SPM.mat’ option and then choose the `SPM.mat` file saved in the `DIR/designs/categorical` directory
- Highlight the ‘Directory’ option and then choose the `DIR/classical/categorical` directory

⁵The order of naming these factors is important - the factor to be specified first is the one that ‘changes slowest’ ie. as we go through the list of conditions N1,N2,F1,F2 the factor ‘repetition’ changes every condition and the factor ‘fame’ changes every other condition. So ‘Fam’ changes slowest and is entered first.

Figure 1.8: *Design matrix.*

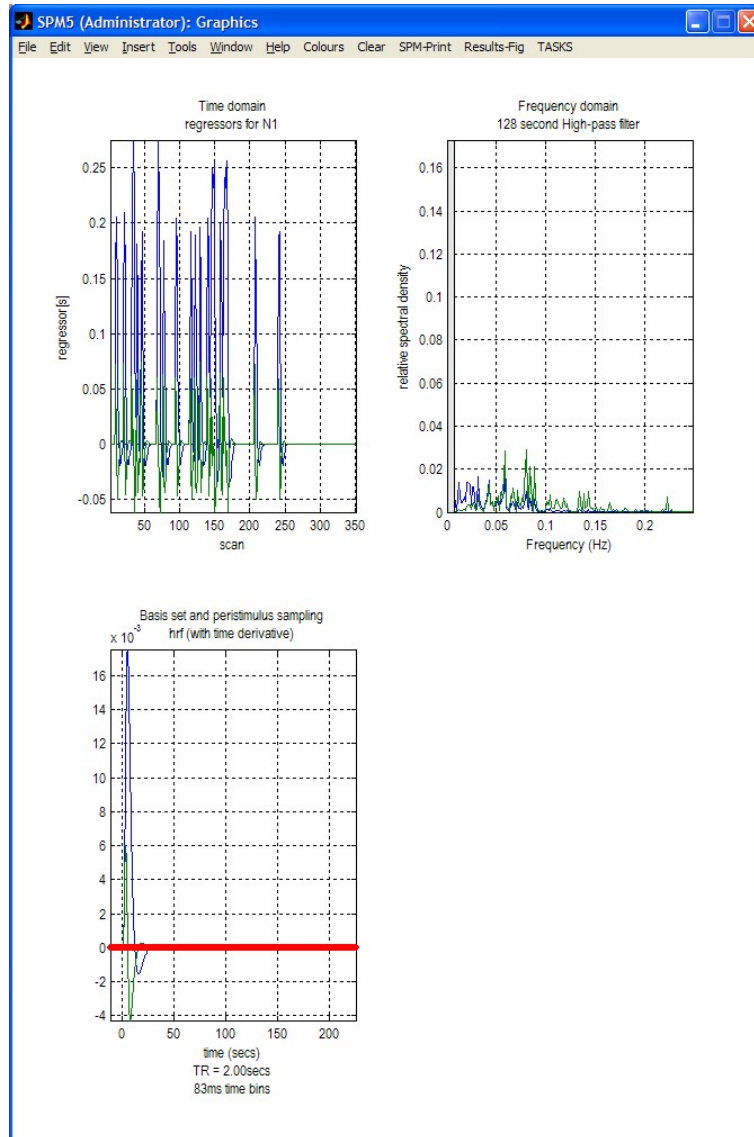


Figure 1.9: Exploring the design matrix in Figure 1.8. This shows the time series of the ‘active’ regressor (top left), a frequency domain plot of the active regressor (top right) and the basis function used to convert assumed neuronal activity into hemodynamic activity. In this model we used the default option - the canonical basis function. The frequency domain plot shows that the frequency content of the ‘N1’ regressor is above the set frequencies that are removed by the High Pass Filter (HPF) (these are shown in gray - in this model we accepted the default HPF cut-off of 128s or 0.008Hz).

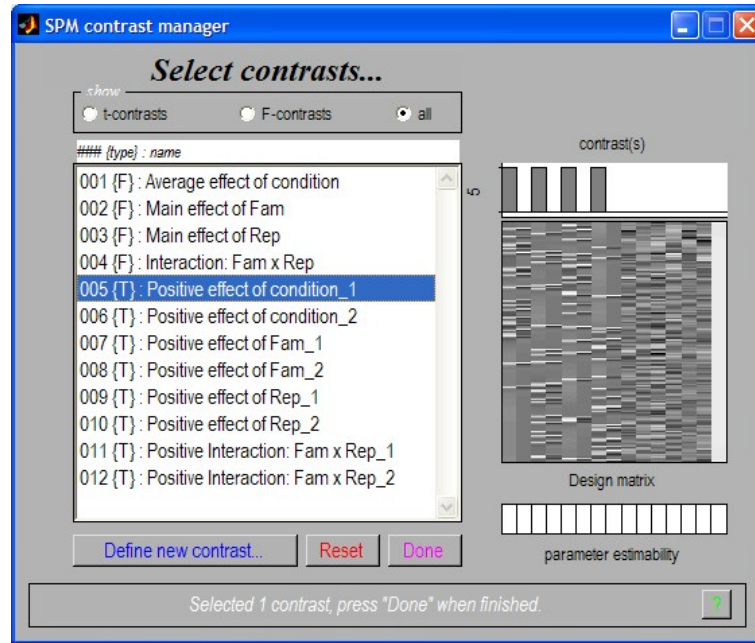


Figure 1.10: *Contrast Manager containing default contrasts for categorical design.*

- Save the job as `categorical_est.job` and press Run

SPM will write a number of files into the selected directory including an `SPM.mat` file.

1.3 Inference for categorical design

Press ‘Results’ and select the `SPM.mat` file from `DIR\classical\categorical`. This will again invoke the contrast manager. Because we specified that our model was using a ‘Factorial design’ a number of contrasts have been specified automatically, as shown in Figure 1.10.

- Select contrast number 5. This is a t-contrast **Positive effect of condition_1**. This will show regions where the average effect of presenting faces is significantly positive, as modelled by the first regressor (hence the `_1`), the canonical HRF. Press ‘Done’.
- *Mask with other contrast ? [Yes/No]*
- Specify No.
- *Title for comparison ?*
- Enter ‘Canonical HRF: Faces > Baseline’
- *p value adjustment to control: [FWE/FDR/none]*

- Select FWE
- *Corrected p value(family-wise error)*
- Accept the default value, 0.05
- *Extent threshold {voxels} [0]*
- Accept the default value, 0

SPM will then produce the MIP shown in Figure 1.11.

1.3.1 Statistical tables

To get a summary of local maxima, press the ‘Volume’ button in the p-values section of the interactive window. This will list all clusters above the chosen level of significance as well as separate (>8mm apart) maxima within a cluster, with details of significance thresholds and search volume underneath, as shown in Figure 1.11 The columns in volume table show, from right to left:

- x, y, z (mm): coordinates in Talairach space for each maximum
- voxel-level: the chance (p) of finding (under the null hypothesis) a voxel with this or a greater height (T- or Z-statistic), corrected (FWE or FDR)/ uncorrected for search volume.
- cluster-level: the chance (p) of finding a cluster with this many(ke) or a greater number of voxels, corrected / uncorrected for search volume
- set-level: the chance (p) of finding this (c) or a greater number of clusters in the search volume

1.3.2 F-contrasts

To assess the effect of presenting faces, as characterised by both the hrf *and* its temporal derivative, an F-contrast is required. Again, because we have told SPM that we have a factorial design, this required contrast will have been created automatically.

- Press ‘Results’ and select the SPM.mat file in the DIR/classical/categorical directory
- Select contrast number 1, as shown in Figure 1.12. Press ‘Done’.
- *Mask with other contrast ? [Yes/No]*
- Specify No.
- *Title for comparison ?*
- Enter ‘HRF + deriv: Faces > Baseline’
- *p value adjustment to control: [FWE/FDR/none]*
- Select FWE

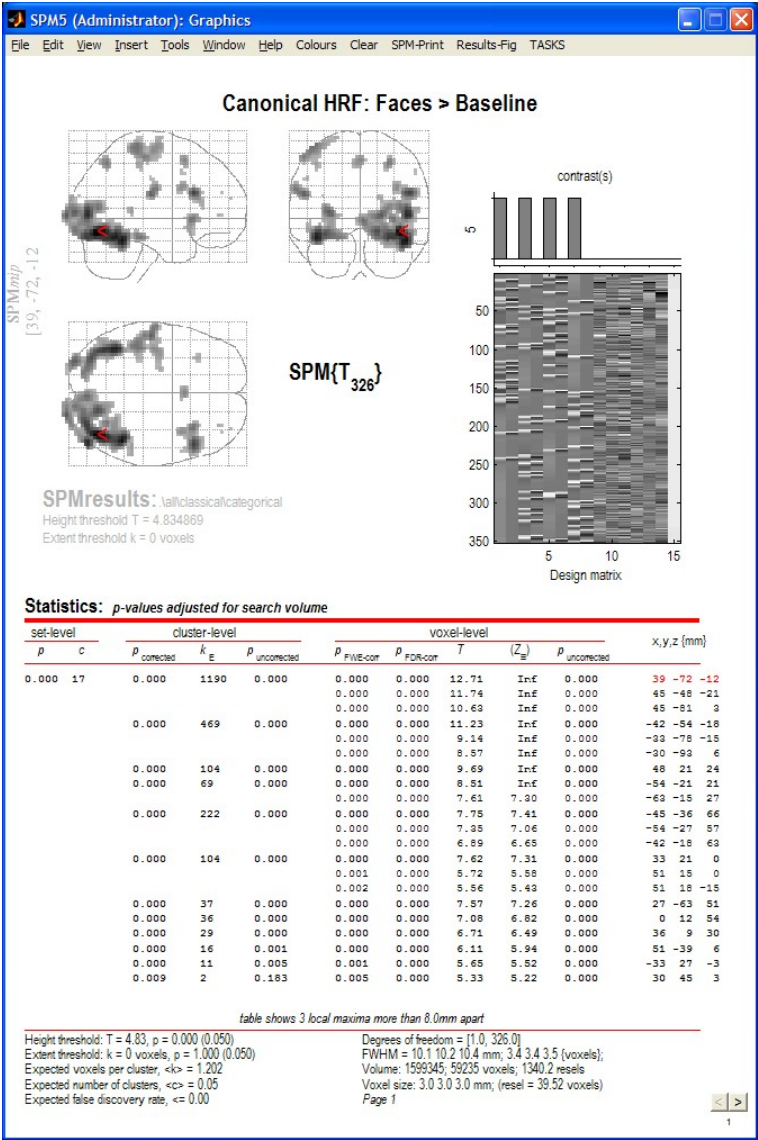


Figure 1.11: MIP and Volume table for Canonical HRF: Faces > Baseline.

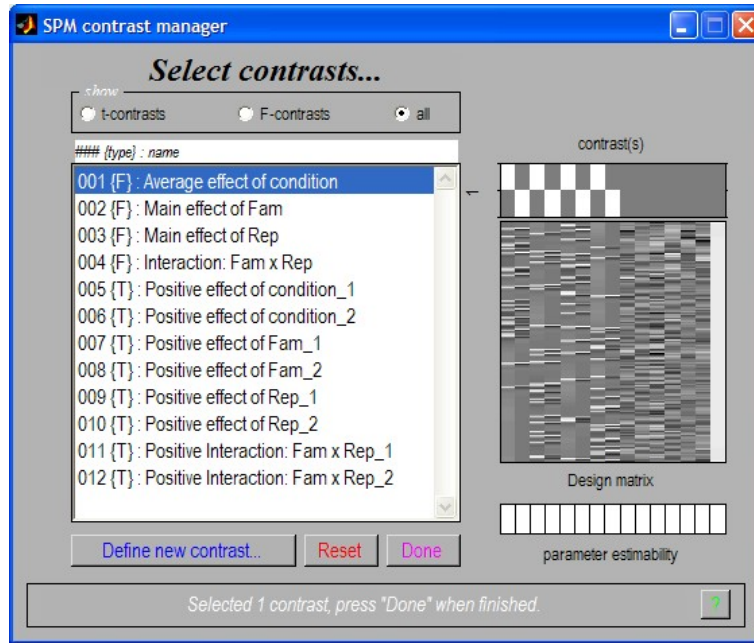


Figure 1.12: Contrast manager showing selection of the first contrast 'Average effect of condition', also known as 'HRF + deriv: Faces > Baseline'.

- Corrected p value(family-wise error)
- Accept the default value, 0.05
- Extent threshold {voxels} [0]
- Accept the default value, 0

Again, when the MIP appears, press 'Volume'. This should result in the display should in Figure 1.13.

Although the MIP of this F-contrast looks similar to the previous t-contrast, note that the present contrast shows the areas for which the mean of the parameter estimates for the canonical hrf *or* its temporal derivative for the four conditions are different from zero (baseline). In other words, the F-contrast is two-sided, and tests two t-contrasts simultaneously. Also note that an F- (or t-) contrast such as [1 1 1 1 1 1 1], which tests whether the mean of the canonical hrf AND its temporal derivative for all conditions are different from (larger than) zero is not sensible. This is because the canonical hrf and its temporal derivative may cancel each other out while being significant in their own right. Finally, note that single F-contrasts can be regarded as t^2 -contrasts, so that the F-contrasts [1 0 -1 0 1 0 -1 0] and [-1 0 1 0 -1 0 1 0] are equivalent.

The relative contributions of the canonical hrf and its temporal derivative may also be assessed using the following F-contrast approach. This will allow us to plot the estimated effect sizes at a given voxel.

- Press 'Results' and select the SPM.mat file in the DIR/classical/categorical directory

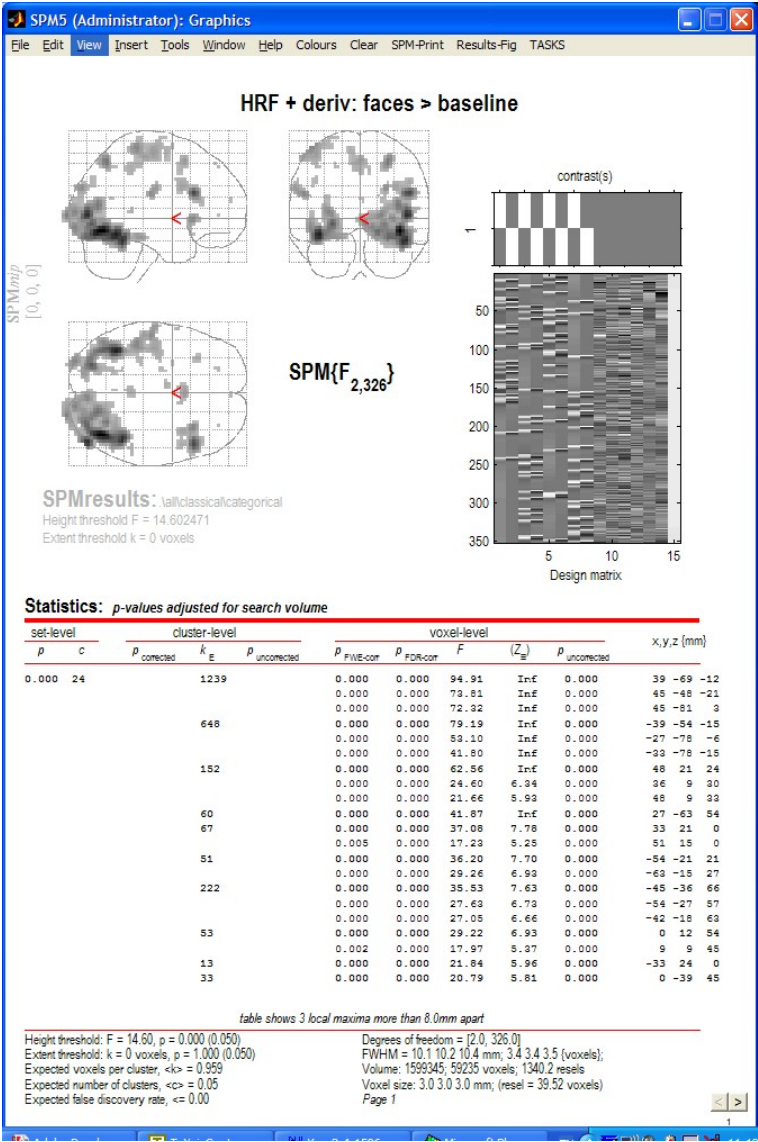


Figure 1.13: MIP and Volume table for Canonical HRF: Faces > Baseline.

Figure 1.14: *Contrast manager showing specification of ‘All effects of interest’.*

- Press ‘Define new contrast’, enter the name ‘All effects of interest’, press the ‘F-contrast’ radio button, enter [9:15] in the ‘columns in reduced design’ window, press ‘OK’, press ‘Done’.
- *Mask with other contrast ? [Yes/No]*
- Specify No.
- *Title for comparison ?*
- Accept what is offered
- *p value adjustment to control: [FWE/FDR/none]*
- Select FWE
- *Corrected p value(family-wise error)*
- Accept the default value, 0.05
- *Extent threshold {voxels} [0]*
- Accept the default value, 0

Again, when the MIP appears, press ‘Volume’. This should result in the display should in Figure 1.15.

1.3.3 Plotting parameter estimates at a voxel

Move the cursor to e.g. the anterior right fusiform blob (the R fusiform face area) by clicking the second set of coordinates in the cluster (45 -48 -21) and press the ‘plot’ button in SPM’s interactive window. Select ‘Contrast of estimates and 90% CI’ and select ‘All effects of interest’. This will produce the plot in Figure 1.16. A positive coefficient for the canonical indicates a positive response to faces, whereas a positive coefficient for the derivative indicates a later peak response to faces. Note, however, the large amplitudes and smaller error bars of the canonical hrfs compared to the temporal derivatives. This suggests that, for this region at least, the timing of the canonical model is adequate. Also note the repetition x stimulus type interaction; F1 seems larger than F2, whereas there is no difference between N1 and N2.

1.3.4 F-contrasts for testing effects of movement

To assess movement-related activation

- Press ‘Results’, select the SPM.mat file, select ‘F-contrast’ in the Contrast Manager. Specify e.g. ‘Rotation-related activation’ (name) and in the ‘contrasts weights matrix’ window, or ‘1:11 15’ in the ‘columns for reduced design’ window.

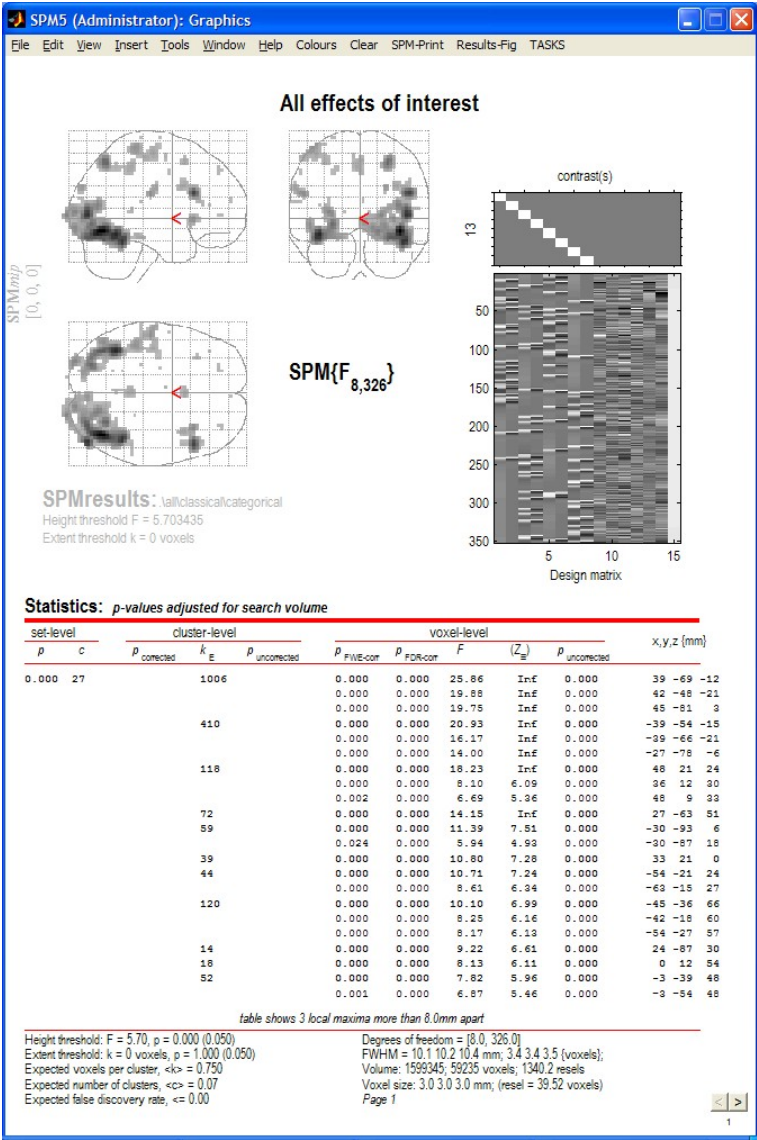


Figure 1.15: MIP and Volume table for ‘All effects of interest’.

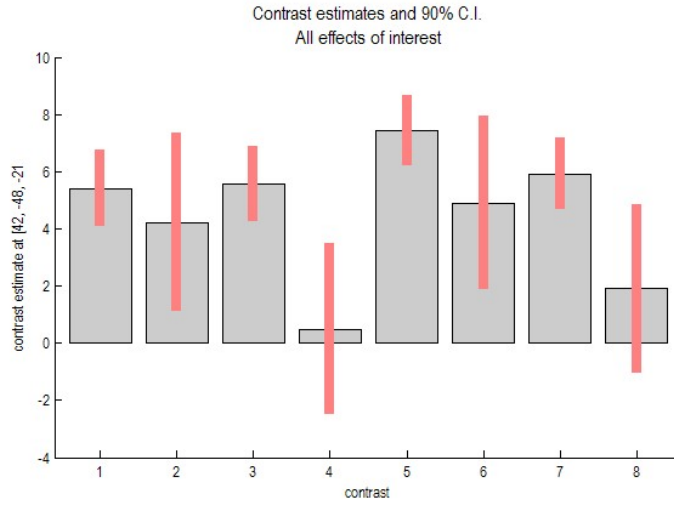


Figure 1.16: *Estimated effect sizes and 90% confidence intervals for all effects of interest. Columns 1,3,5,7 are the canonical hrfs for N1 (non-famous faces, first presentation), N2 (non-famous faces, second presentation), F1 (famous faces, 1st presentation) and F2 (famous faces, 2nd presentation), whereas columns 2,4,6,8 are the temporal derivatives.*

- Submit and select the contrast, specify ‘mask with other contrasts?’ (no), ‘title for comparison’ (accept default), ‘corrected height threshold’ (FWE), and ‘corrected p-value’ (accept default).
- When the MIP appears, select ‘sections’ from the ‘overlays’ pulldown menu, and select the normalised structural image `wmsM03953_0007.img`

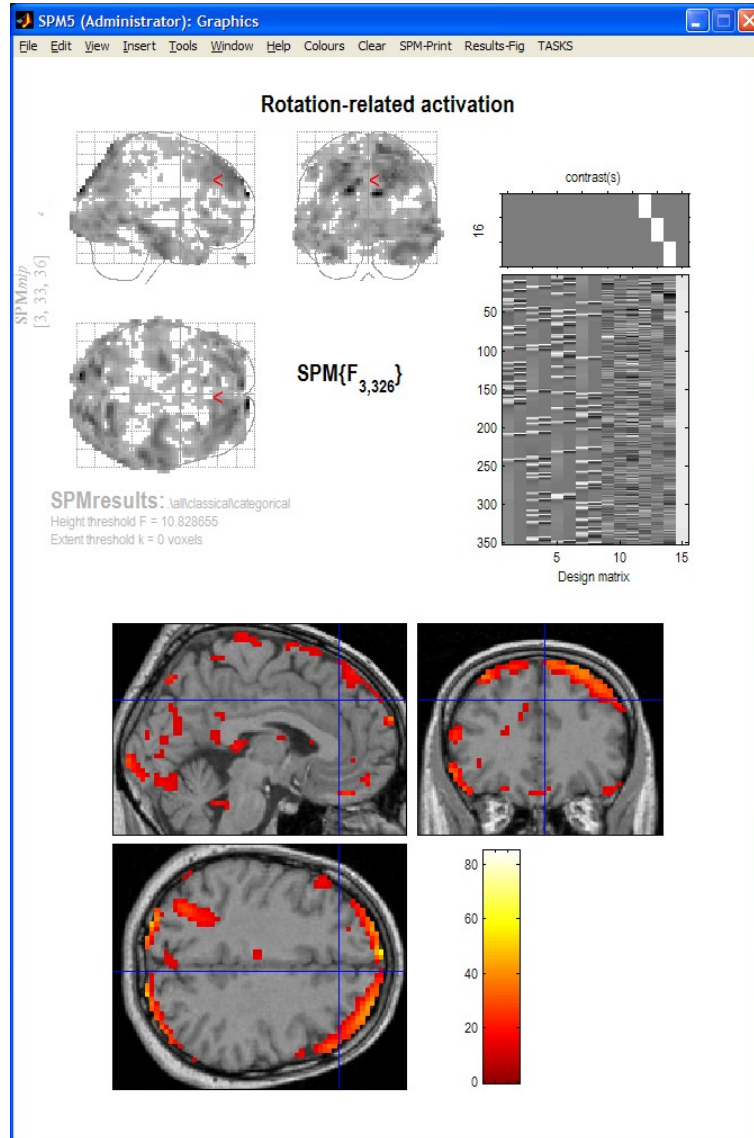


Figure 1.17: *Rotation-related activations. These spurious ‘activations’ are due to rotation of the head during the scanning session. Many of these effects occur at tissue boundaries and boundaries between brain and non-brain, as this is where contrast differences are greatest. Including these regressors in the design matrix means these effects cannot be falsely attributed to neuronal activity.*