Dynamic Causal Modelling of fMRI data in SPM12

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Abstract

Dynamic Causal Modelling (DCM) is a widely used method for inferring effective connectivity from various kinds of neuroimaging data. This tutorial demonstrates a step-by-step walkthrough for using DCM to investigate group-level effective connectivity from a publicly available open-access fMRI dataset for face processing from 15 subjects. We illustrate a reproducible analysis pipeline that makes use of a hierarchical Bayesian framework called Parametric Empirical Bayes (PEB) to characterize inter-individual variability in neural circuitry. At the group level, we show various approaches for performing testing focused hypotheses on the estimated connectivity using Bayesian model comparison.

1. Introduction

This paper is a tutorial for Dynamic Causal Modelling (DCM) of fMRI data. DCM is a method for inferring effective connectivity between brain regions from neuroimaging data, and is part of the Statistical Parametric Mapping (SPM) free academic software (https://www.fil.ion.ucl.ac.uk/spm/), which is implemented in Matlab (The MathWorks Inc., 2018). We focus on basic DCM specification, estimation, Bayesian model reduction and Bayesian model comparison, using the recent Parametric Empirical Bayesian (PEB) framework for group-level inference across multiple subjects. Together with its companion document describing DCM of MEG data, this document extends the DCM PEB tutorial by Zeidman and colleagues (Zeidman, Jafarian, Corbin, et al., 2019; Zeidman, Jafarian, Seghier, et al., 2019; https://github.com/pzeidman/dcm-peb-example) to a multimodal dataset, and illustrates other features of DCM and PEB.

The dataset contains fMRI and MEG+EEG data on 15 subjects from a face-processing paradigm described in Wakeman & Henson, 2015. The raw data in BIDS format are available on OpenNeuro (https://openneuro.org/datasets/ds000117).[1] This tutorial continues a previous tutorial on the same dataset (Henson et al., 2019), which illustrated basic pre-processing and source localisation of MEG/EEG data in SPM. Here we assume this pre-processing has already been done, though you can download the pre-processed data as described below.

We describe practical steps using SPM's graphical user interface (GUI), its "batch" interface for linear pipeline creation and finally "scripting" in MATLAB for (parallelised) loops across subjects. We use version 12.5 of DCM in version 12 of SPM. The paper is organised into sections with a brief theoretical background followed by a detailed step-by-step walkthrough. The background is only brief because we refer to previous published papers, many of which are available from the SPM website: https://www.fil.ion.ucl.ac.uk/spm/doc/biblio/. We do not provide a full tour of all the available options in SPM for M/EEG, which is already present in Litvak et al. (2011). Rather, we focus on the typical steps for group-level DCM inference using PEB. Our experience with teaching SPM is that students appreciate having a concrete example, which they can then adjust to their own needs.

The steps below are also scripted in the "code" directory that you can download or clone from https://github.com/pranaysy/cognestic22_multimodal_dcm. This contains two sub-directories, one for fMRI and one for MEG, which themselves contain two groups of files: one of these are MATLAB files derived from SPM's "batch" interface (filenames beginning with batch*), in which various analysis steps (batch "modules") were created by the GUI, saved and then called from loops across subjects (all within the "spm_master_script_dcm_*_peb_batch.m"); the other consists of a script that implements exactly the same analyses, but with direct calls to underlying "spm*.m" functions, bypassing SPM's Batch interface (e.g., contained within the script in "spm_master_script_dcm_*_peb_direct.m").

2. The Multimodal Dataset

The dataset comes from a paradigm in which participants saw a series of faces and phase-scrambled faces, and made left-right symmetry judgments to each stimulus. There were 300 unique faces and 150 unique scrambled images. Half of the faces were famous and half non-famous, but we ignore this distinction in this tutorial. Each stimulus was presented for 900ms on average, followed by 2200ms on average. Each stimulus was repeated either immediately, or after 5-15 intervening stimuli, but again we ignore the effects of repetition here. Thus we only analyse two conditions: faces vs scrambled faces. See Lee et al. (2022) for DCM analysis of effects of repetition and recognition (familiar vs unfamiliar) in the fMRI data.

To give participants a break, the fMRI experiment was split into 9 runs, with approximately equal numbers of each condition per run, though to avoid delayed repetition across runs, a small number of

[1] There are 16 subjects on OpenNeuro, but we exclude one here because of missing fMRI data in one run.

these trials were dropped. In addition, in order to estimate the response versus inter-stimulus baseline, six periods of 20s of a fixation cross were added after a block of 9-20 trials. The MEG experiment was split into 6 runs, and there was no need for interspersing longer periods of fixation as in the fMRI experiment. For more details, see Wakeman & Henson (2015).

3. Background

3.1 DCM

DCM is a tool for inferring "effective connectivity" between brain regions of interest (ROIs), based on explicit network models and assumptions about neural dynamics. DCM is a state-space model, consisting of 1) first-order differential equations that relate changes in each latent neural variable to other variables in the network (depending on connections), and 2) an observation model that maps neural variables to the measured fMRI and M/EEG signals.

For fMRI, the neural model is based on simple exponential decay of activity within each area, offset by input from other areas, as captured by a simple bilinear approximation. For MEG, the neural model is much more complex (e.g, containing multiple differential equations relating many parameters within each ROI, based on knowledge of the neurophysiology of human cortical layers, with several variants; see Section 5).

For fMRI, the observation model is a temporal model that maps brief changes in neural activity to the more dispersed BOLD impulse response (a so-called HaemoDynamic Model, HDM). For MEG, the observation model is a spatial model that maps certain neural variables to electrical/magnetic fields recorded by sensors outside the head.

For more background on DCM, see David et al. (2006).

3.2 Current Network (model)

Here we focus on 4 ROIs: left and right occipital face area (OFA) and fusiform face area (FFA). These are the main four peaks that survive correction for multiple comparisons in the group analysis of the contrast of faces versus scrambled faces (see Supplementary Figure A2.1 of Henson et al. 2019; https://www.frontiersin.org/articles/10.3389/fnins.2019.00300/full#supplementary-material); the left FFA appears if the cluster threshold is reduced from 30 to 10 or fewer voxels. We could define the ROIs by saving each of them as thresholded clusters (as in Section 3.2 of Henson et al., 2019), but here, for fMRI, we just define them as spheres centred on significant peaks (see Section 4.3 below), while for MEG/EEG, we use the coordinates as the prior location of an equivalent current dipole (ECD) (see Section 5.2.1.3).

We connect the four ROIs as shown in Figure 1. This assumes bidirectional connections between OFA and FFA within each hemisphere, bidirectional connections between hemispheres for both OFA and FFA, but no direct connections between OFA and FFA in different hemispheres (based on neuroanatomical principles). Together with each ROI's (inhibitory) self-connection, these are the "A" connections in DCM. We further assume that all of these fixed connections can be modulated by the presence of faces (vs scrambled faces). Finally, we will assume that the input (for all stimuli) enters left and right OFA (but see Lee et al., 2022,) for more nuanced treatment of possible inputs to the network).

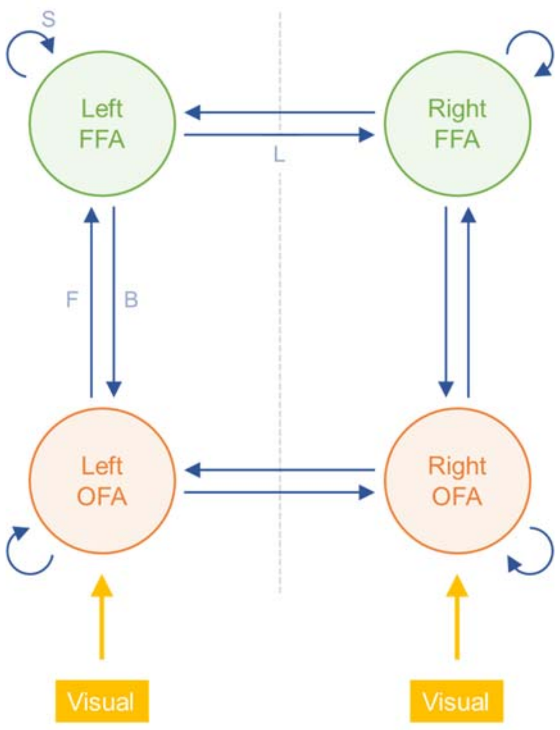


Figure 1. The 4-node DCM used for fMRI and MEG/EEG. F = forward, B = backward, S = self, L = lateral (note F, B and L only have different properties in DCM for MEG/EEG). OFA = Occipital Face Area; FFA = Fusiform Face Area.

DCM proceeds by comparing different models of the data through (an approximate lower bound on) the Bayesian model evidence, where models typically differ in connections (parameters), e.g. which connections are modulated by an experimental manipulation (here, by faces). When there are multiple subjects, one can create a single hierarchical model, enabling an Empirical Bayesian approach in which the mean and covariance of parameters across subjects can act as a prior on individual subject parameter values. Since DCM also assumes multivariate normal error terms (so-called "parametric" assumptions), this approach is called Parametric Empirical Bayes (PEB); see papers by Zeidman and colleagues (Zeidman, Jafarian, Corbin, et al., 2019; Zeidman, Jafarian, Seghier, et al., 2019) for more details.

There are many models one could compare. For example, one could ask whether face processing modulates connections between ROIs, or whether it is sufficient to explain face-related responses in each ROI simply via modulations of each ROI's self-connections. If the latter "self-only modulation" model were more parsimonious (had higher model evidence), then there would be no need to assume that faces change the effective connectivity between regions (and the traditional voxel-wise analysis of univariate statistics would be sufficient, as in Henson et al., 2019).

The tutorial consists of two main sections: 1) specifying and estimating a single-subject DCM for fMRI, and 2) estimating group-level DCMs for fMRI with inference based on model comparisons.

4. DCM for fMRI

Preprocessing of the fMRI data is described in Supplementary Material of Henson et al. (2019) https://www.frontiersin.org/articles/10.3389/fnins.2019.00300/full#supplementary-material, but if you do not want to repeat that, you can download the preprocessed image files and first-level models from the Figshare link below. More practical help on DCM for fMRI can be found in Chapter 36 of the SPM12 manual, https://www.fil.ion.ucl.ac.uk/spm/doc/spm12_manual.pdf.

4.1 Preparation

In order to run this tutorial, there are two preparatory steps involved: setting up the software environment, and organizing data. For preparing the environment, install SPM12 from https://www.fil.ion.ucl.ac.uk/spm/software/download/ somewhere on your local system. The results in this tutorial were obtained with release "r7771". Once installed, clone or download the git repository at https://github.com/pranaysy/cognestic22_multimodal_dcm/ to a folder. These include a few minor updates to DCM functions. Launch MATLAB and change directory to the cloned or downloaded repository folder. We will refer to this folder as 'base_dir' in the tutorial as well as scripts.

Once the environment is ready, the data can be organized according to the level of pre-processing, with three possible starting points:

1. You could begin with raw data from OpenNeuro (https://openneuro.org/datasets/ds000117) and run the demo in the supplementary material of Henson et al. (2019) to preprocess the raw images into smoothed, normalised, slice-time corrected and realigned images. Note that the full data is about 85GB in size. Once you have downloaded and finished processing the data, you will have a BIDS directory tree with processed derivatives in the folder "ds000117 / derivatives / SPM12". We refer to this folder as 'derpth'.

   The data in this folder are not yet ready for fitting DCMs and need to be processed further. The SPM single-subject models will need to be reparametrized, their runs concatenated and re-fit to all the smoothed, normalised fMRI volumes created in Henson et al (2019), after which extraction of VOI time courses will be necessary. These steps are described in sections 4.2 and 4.3, with precise details given in the Appendix. DCMs can then be fit using the extracted VOI time courses and reparametrized SPM models.

If you are not starting with raw data from OpenNeuro and would like to proceed with pre-processed data, you have two choices:

2. You could download fMRI images that have already been preprocessed from Figshare in the file "fmri_data.tar.gz" (https://figshare.com/articles/dataset/fMRI_Data/20936143) and extract into the 'data' folder in 'base_dir'. Note this will take almost 17GB. The data folder should now have a directory tree that looks like 'data / derivatives / SPM12'. We refer to this folder as 'derpth'. Inside this folder there are 15 sub-directories called "sub-01", "sub-02" etc, each of which have a further sub-directory called "func", in which there should be three types of file for each of 9 runs: the 4D smoothed, normalised NIFTI images ("swsub-*.nii"), a MATLAB file with the trial definitions ("sub-*_run-*_spmdef.mat") and a text file with the 6 motion parameters from spatial realignment of the volumes ("rp_sub-*_run-*.txt"). Single-subject first-level models will need to be created using the same steps for reparametrizing, concatenating and VOI extraction as described in sections 4.2 and 4.3.

   Lastly, you could start directly with processed DCM-ready data which consists of extracted VOI time courses for the 4 ROIs: lOFA, rOFA, lFFA and rFFA, along with reparametrized SPM.mat files for each subject. If you use this dataset, you can skip sections 4.2 and 4.3 and proceed directly to section 4.4 for specifying DCMs. For this approach, download the file "derivatives_fmri_dcm_ready_VOIs_concatenated.zip" from Figshare (https://figshare.com/articles/dataset/Face_processing_M_EEG_data_for_Dynamic_Causal_Modelling/21333996), and extract into the 'data' folder in 'base_dir'. The data folder should now have a directory tree that looks like 'data / derivatives / SPM12'. We refer to this folder as 'derpth'. Note this will take up around 1.1GB of space after extraction. Each subject's data in consists of one SPM.mat file and one file each for the four VOIs along with masks. These are the same files that would be produced by running the steps described in sections 4.3 and 4.3.

4.1.1 Initialisation

Open "spm_master_dcm_fmri_peb_batched_script.m" from the "code/fmri" folder. There is some MATLAB code at the start that is necessary to start SPM & define some key variables. First start SPM12

```
SPM12PATH = <insert path to your local install of SPM12>
addpath(SPM12PATH);
spm fmri
```

Then define some paths where you have downloaded the code and data from above:

```
base_dir = '<path to where you have cloned the respository>'
derpth = fullfile(base_dir,'data','derivatives','SPM12')
% above will exist if you have run preprocessing scripts for Henson et
% al, 2019, or else create these directories and download and extract
% "fmri_data.tar.gz" from Figshare as above
```

Next, add the 'code' folder and all subfolders in it to MATLAB's path by running this line:

```
addpath(genpath(fullfile(base_dir, 'code')))
```

This ensures that all the code we provide is available in MATLAB's environment. This is necessary because our scripts for batch processing rely on functions in various files – some of which enable parallel processing, some are 'job files' used by SPM's batching interface while some are modified SPM functions, which have been updated for this tutorial. It is crucial to add this 'code' folder to the MATLAB path after your local installation of SPM has been added to MATLAB's path and launched. This sequence of operations will put our 'code' folder above SPM's on MATLAB's list of paths, which can be viewed by typing `pathtool` on the command line. Since the updated SPM functions we provide share the same filenames with the original SPM functions, adding the two in this exact order guarantees that when a function is to be executed, MATLAB will first look at our 'code' folder, since it is higher up, and then SPM's folders. Therefore, running any code that relies on our modified SPM functions, will always correctly use them and not the default SPM functions. A list of modified SPM functions with a brief overview of changes is provided in the README file on the GitHub repository for this tutorial, linked earlier.

Then you can run the lines below to define some variables:

```
% If you have all raw data
% BIDS = spm_BIDS(rawpth);
% subs = spm_BIDS(BIDS,'subjects', 'task','facerecognition');
% runs = spm_BIDS(BIDS,'runs', 'modality','func', 'type','bold',
'task','facerecognition');

% Else specify subjects and runs manually
subs = compose('%02g', [1:9, 11:16]); % subject 10 had fewer scans in
last run
nsub   = numel(subs);
subdir = cellfun(@(s) ['sub-' s], subs, 'UniformOutput',false);
```

Then, if you have access to multiple cores (parallel processing in Matlab), you can run below (if not, set "numworkers" to 0):

```
numworkers = nsub; % Number of workers for distributed computing
```

```
if numworkers > 0
    delete(gcp('nocreate')) % Shut down any existing pool
    parpool(numworkers);
end
```

4.2 Re-parametrising each subject's fMRI model

If you have downloaded the data and models from Henson et al. (2019), two further preprocessing steps are required before we can create DCM models: 1) re-parametrising the single-subject (1st-level) fMRI general linear model (GLM) for each subject, and 2) extracting the (adjusted) fMRI timeseries for each ROI and each subject.

The first step of re-parametrising the GLM involves defining two conditions: 1) all stimuli (faces and scrambled), to be used as the driving input for DCM ("C" matrix) and 2) faces (collapsing famous and unfamiliar), to be used as a modulatory input for DCM ("B" matrix). It also involves concatenating the 9 runs into a single run for convenience. These steps are described in Appendix 6.1, where they can either be implemented by running some MATLAB code on the SPM.mat files produced by the Supplementary Section 2 of Henson et al. (2019), or by re-creating the SPM.mat files from scratch using SPM's batch interface.

4.3 Defining ROI (VOI) timeseries

DCM fits fMRI timeseries for a number of ROIs. Those timeseries are extracted by taking the first temporal mode[2] across a number of voxels within a specified volume of interest (VOI) that defines the ROI. In SPM, a VOI can be defined by one or more constraints. The full options are described in chapter 36 (section 36.3.3) of the SPM manual (see also Zeidman, Jafarian, Corbin, et al. (2019)). Here we will define our VOI by two constraints: 1) voxels within a 10mm radius of the centre of a sphere centred on the peak T-statistic in the group analysis described in Supplementary Section 2 of Henson et al (2019), 2) voxels that also showed some effect of our experiment (defined by an "effects of interest" F-contrast that spans all conditions of interest) at $p<0.001$ uncorrected. The second constraint ensures that voxels within the sphere are likely to be gray-matter that is generally responsive to the stimuli (i.e, removing voxels within the sphere that are white-matter or CSF). Of course, further constraints could be added (e.g, a gray-matter mask), or other definitions used instead (e.g, a mask image created by thresholding each individual subject's contrast of faces versus scrambled), but they are not explored here.

SPM produces at VOI*.mat file for each ROI and each subject (e.g, "sub-01/fmri/VOI_lOFA_1.mat" for the lOFA), which are passed to DCM below. The precise steps needed to create these files are described in Appendix 6.2.

4.4 DCM definition: for single subject

Unfortunately DCM definition is not yet batched in SPM, so we need to go through SPM's GUI by pressing the 'DCM' button (the following mirrors the PDF available here: https://github.com/pzeidman/dcm-peb-example).

In MATLAB, use the file selector on the left hand side to change the working directory to sub-15. We now walk through each step involved in specifying the 'full' DCM model, which we will subsequently estimate.

• Click the big Dynamic Causal Modelling button in main SPM window. In the grey window that appears, click 'Action' and then specify.

[2] This is from a singular-value decomposition of the data to extract the first temporal and spatial singular vectors. If all the voxels were equivalent, the temporal mode would be equivalent to the average over all voxels.

• In the file selector, click the SPM.mat file from sub-15 on the right hand side and then click 'Done'. This provides DCM with the timing of the experimental conditions.

• You'll be asked for a name for the new DCM. Type: 'Full' and press enter.

• You'll be asked to select the VOIs (volumes of interest) for this subject. These are the timeseries for each brain region, which have already been prepared. The order is important - the same order will be used for the regions in the DCM. For consistency with this tutorial, select in order: lOFA, rOFA, lFFA, rFFA and click 'Done'.

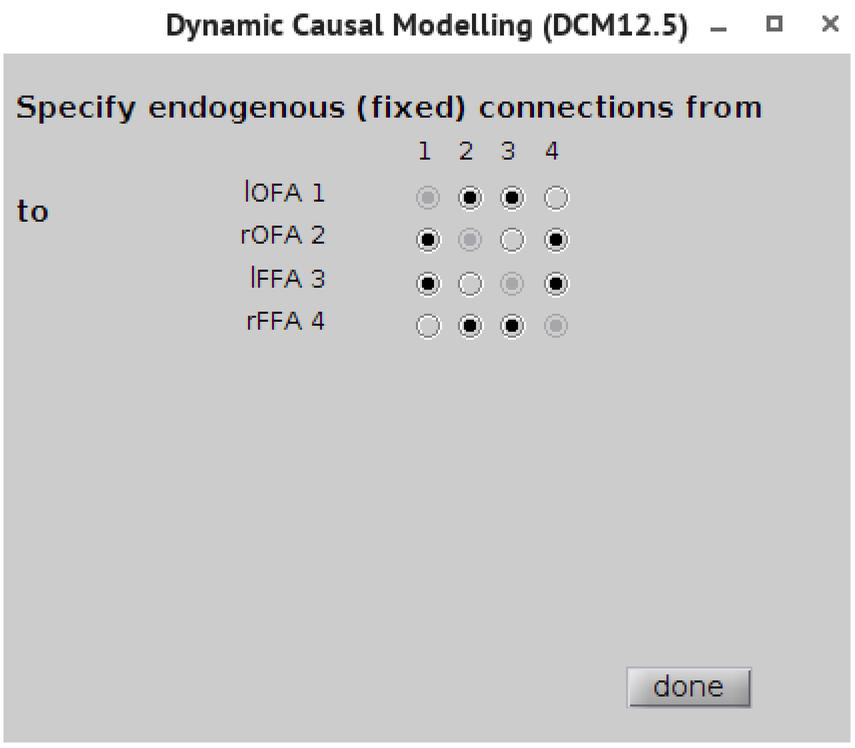
• Now you are asked which experimental conditions to include – include both "all" (faces+scrambled) and "faces".

• For VOI timings, keep 1 (second), ie half TR, since interpolated to middle slice

• For Echo Time (TE), change to 0.03 (30ms), which was used on this 3T scanner

• You are now asked to set certain options for the model. Keep defaults of bilinear, one state per region, no stochastic effects, no centred input, and fitting fMRI timeseries.

• You are now asked which connectivity parameters you want switched on (free to be informed by the data) and which you want switched off (fixed at their prior expectation of zero). These are connectivity parameters in matrix A from the DCM neural model, which is the average connectivity over experimental conditions. The self-connections (on the leading diagonal) are always switched on, and this screen asks you to select which between-region connections to include. Switch the connections on according to Figure 2 and then press done. (Tip: holding your mouse pointer over a button will identify the connection.)


Dynamic Causal Modelling (DCM12.5)

Specify endogenous (fixed) connections from

to		1	2	3	4
	lOFA 1	◉	●	●	○
	rOFA 2	●	◉	○	●
	lFFA 3	●	○	◉	●
	rFFA 4	○	●	●	◉

Figure 2: DCM specification for matrix A.

• Next you are asked about each of the experimental effects, starting with "all" stimuli. The buttons on the left are the driving inputs (matrix C), and the buttons on the right are the modulatory inputs (matrix

B), which increase or decrease the strength of particular connections. The connections you switched off in the previous step are hidden. Set all stimuli to drive lOFA and rOFA only, as in Figure 3 and press done.

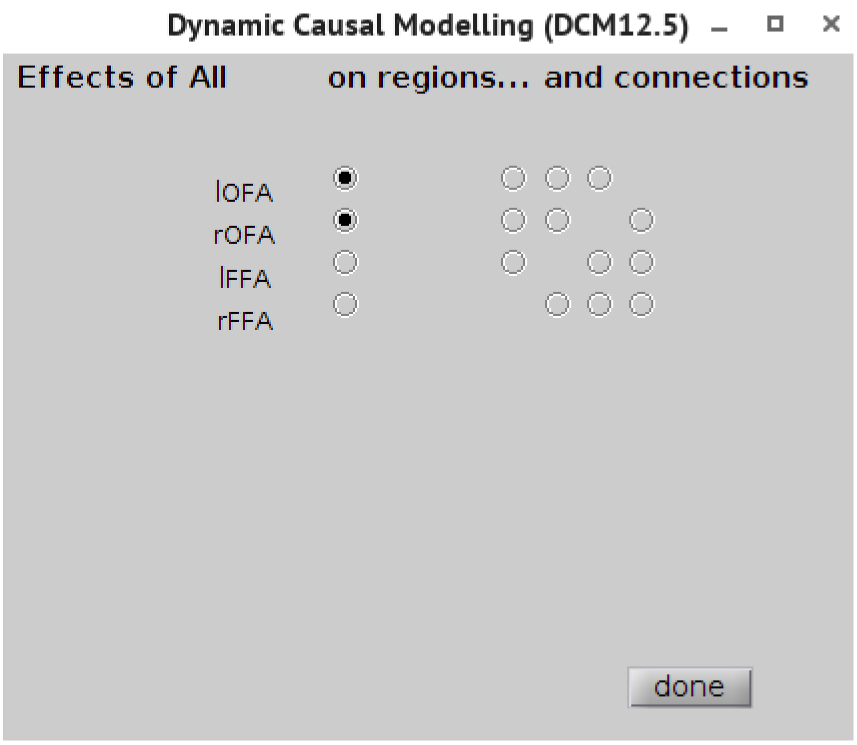

Dynamic Causal Modelling (DCM12.5)
Effects of All
on regions... and connections
lOFA
rOFA
lFFA
rFFA
done

Figure 3: DCM specification for driving inputs (C) for all stimuli.

• Next you are asked about the effect of Faces stimuli. We'll allow this experimental condition to modulate all connections in B except for inter-hemispheric lateral connections, as shown in Figure 4.

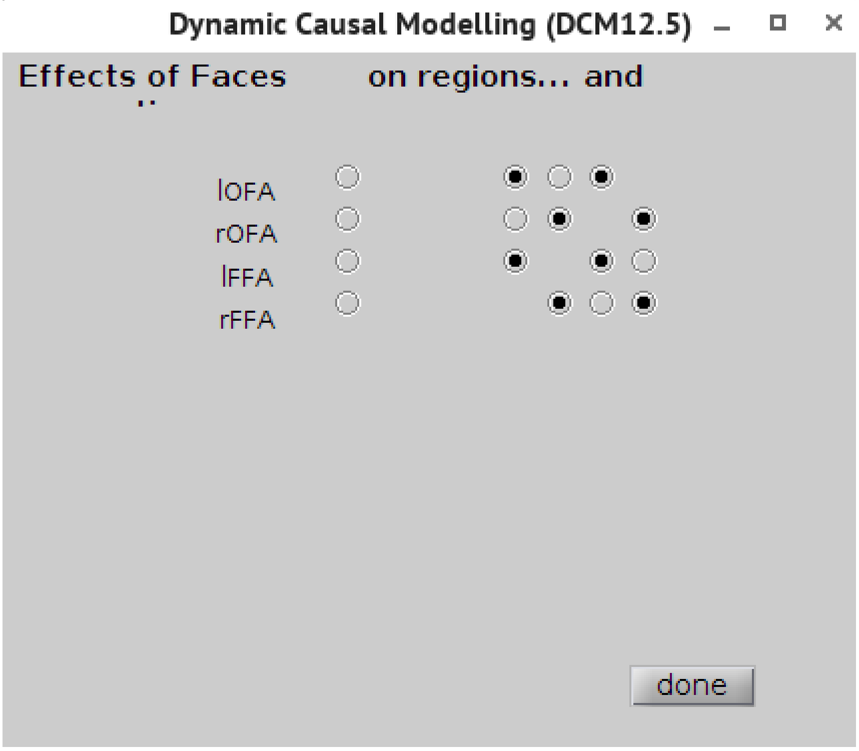


Figure 4: DCM specification for modulatory inputs (B) for faces only (in full model).

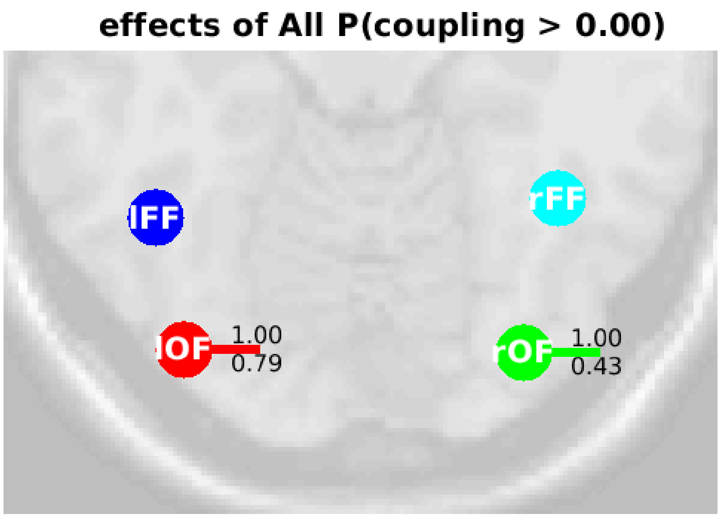
You will receive a polite ‘thank you’ and a file called “DCM_Full.mat” will have been created in this subject’s directory.

4.5 Estimating full model for single subject

Before running this step, copy “DCM_Full.mat” to a new file “DCM_Full_sub-15.mat” in the same sub-15 directory. This is because this way of estimating of a DCM will update that file with the posterior estimates, yet we do not want to use these posteriors when we re-fit all subjects later in this demo. To fit DCM to the data, you can press main DCM button, select “Action:… estimate (time-series)” and select the “DCM_Full_sub-15.mat” file. Or equivalently (to avoid copying), you could run this code:

```
load(fullfile(outdir,'DCM_Full.mat'));
DCM = spm_dcm_estimate(DCM);
save(fullfile(outdir,'DCM_Full_sub-15.mat'),'DCM');
```

Once estimated, press the main DCM button again, select ‘review’ and choose the ‘DCM_Full_sub-15.mat’ file. Select the option ‘effects of All’ under ‘review’, and you should see Figure 5. All stimuli (faces and scrambled) functioned as the driving input (C), which we specified to lOFA and rOFA, and the results show that both inputs were needed (posterior probability close to 1), as shown in top right panel of bottom section (top left panel of that section shows actual values, in Hz). There are no data on B connections, because we only allowed the second input (Faces) to modulate connections.



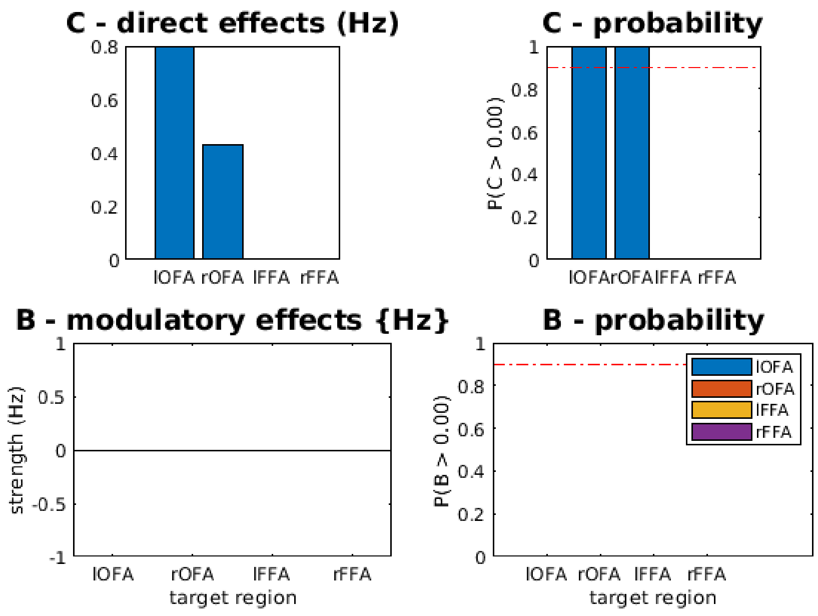


Figure 5. Single-subject fit of full model – Effects of All (Faces + Scrambled)

If you go back to “review” window, and select “effect of Faces” now, you will see Figure 6. In the bar graphs for the modulatory (B) connections (bottom right), you can see that some are needed (above the red dotted line for 0.9 probability), eg lOFA self-connection (first blue bar). Again, their values are shown in bottom left panel.

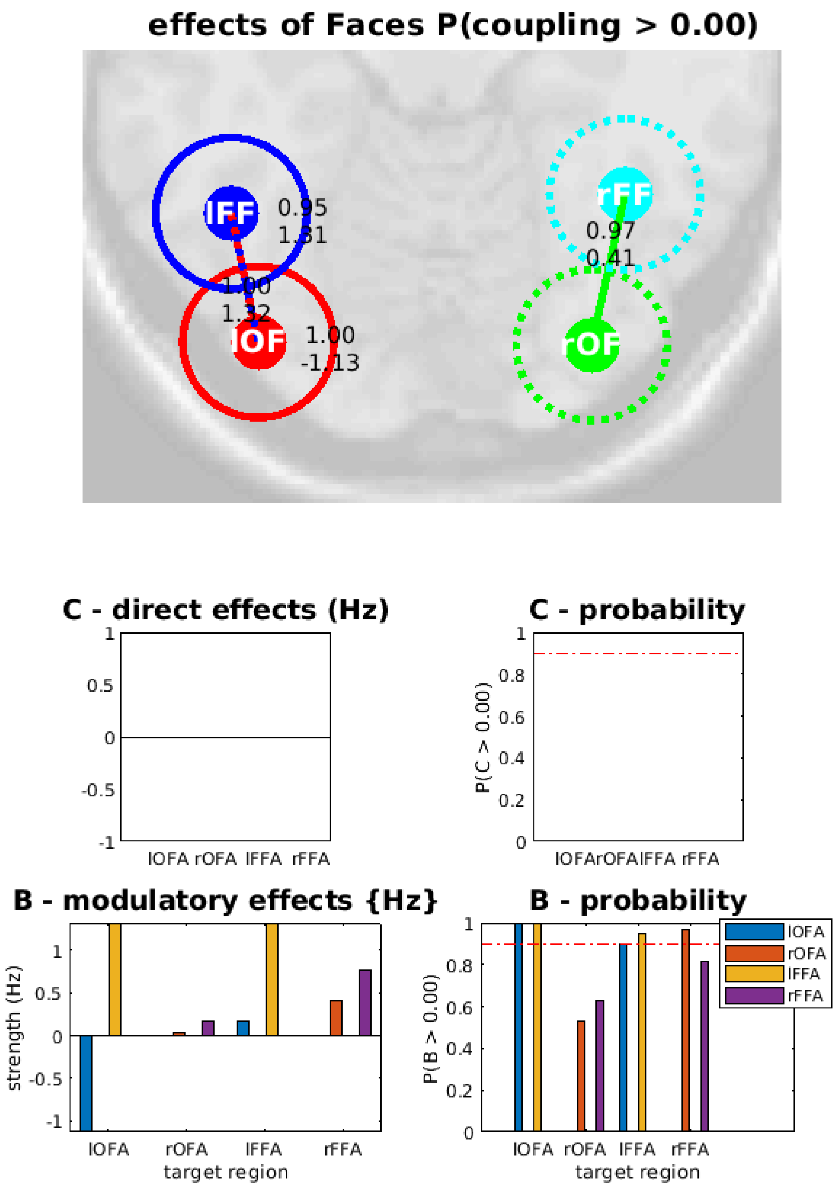


Figure 6. Single-subject fit of full model – Effects of Faces

You can review the "fixed (A) connections", but these are not very interesting in this context. You can also specify "contrasts of connections" (parameters), which we will not explore here (we will keep our inference at group level, across models; see later). You can also review "location of regions", and the "inputs" (from the SPM.mat) file, but more interesting are the "outputs", shown in Figure 7. The solid blue line shows how well DCM fits the data (dotted line) in each ROI. Finally, you can also examine the "kernels" if you're interested in the neuronal and haemodynamic parameters for each region (which we normally are not).

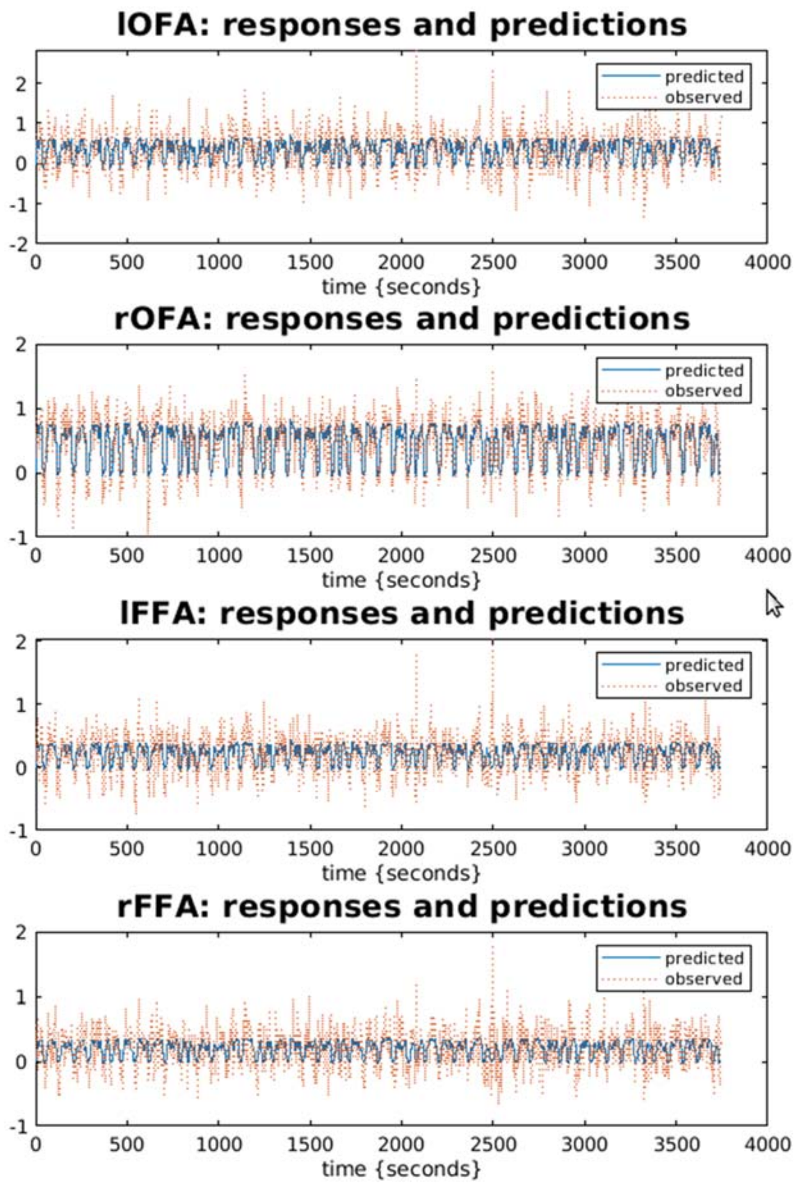


Figure 7. Single-subject fit of full model – Outputs

Make sure to quit the review window when finished.

You can also load the DCM file into MATLAB and run "spm_dcm_fmri_check(DCM)", which will show another window with the % variance explained across all ROIs (which is 62% in this case), as well as all the parameters posteriors and their posterior covariance.

4.6 Group DCM

4.6.1 GCM definition: Replicating across subjects

Having specified a 'full' DCM for a single subject, we can now use this as a template to specify the same DCM for every subject, and enter into a "Group Causal Model" (GCM). All subjects' models will be the same, except the timeseries and timing of the experimental input, which will be customized for each subject.

Open the batch GUI. From the menu at the top of the Batch Editor, click SPM → DCM → DCM specification → DCM for fMRI → Specify group:

• Output directory - double click Output directory to bring up the file selector. We will choose to store the GCM file in the templates folder located at 'fits/batch_gui/fmri/templates/GCMs/Full'. Navigate to this directory and pressing the single dot '.' (which indicates current directory). Then press Done.

• Output name - double click, then type "Full" and press OK.

• Full DCM - double click, then in the file selector, select the full DCM we made earlier for sub-15. It is named "DCM_Full.mat". Select this on the right hand side, then press Done.

• Alternative DCMs – leave empty.

• SPM.mat files - We will now select all subjects' SPM.mat files, which contain the timing information for each subject. Once in the base DCM directory, you should now see a list of all subject directories. Press the small 'Rec' button (for "recursive search"). This will search through all subject directories and pick out their SPM.mat files (since the "filter" is set for SPM.mat files only). Check that all 15 are selected at the bottom of the file selector window and press Done.

• Regions of interest - Now we'll select the timeseries (VOIs) for each subject. Click Regions of interest then click New: Region (VOI files). Do this four times, so you get four entries in the batch that say 'Region (VOI files)'. From the base DCM directory, edit the filter on the selection box from "^VOI_.*\mat$" to add "lOFA", ie to make "^VOI_lOFA.*\mat$" (this is a "regular expression" in linux that matches certain strings, here in the filenames). Then click Rec, which will search through all the subjects' folders selecting the 15 lOFA VOI files. Press Done.

• Repeat for the other three ROIs, just changing the filter name, but importantly the order you enter them must be rOFA, lFFA and then rFFA (to match order in DCM specification files).

• Click File → Save batch and save it in 'saved_from_batch_interface' sub-directory in 'code / fmri' as batch_dcm_create_gcm (just for record, eg to check in case any manual mistakes made).

Then press the green play button to run this module.[3] You'll see one DCM file in each subject's folder named "DCM_Full_m0001.mat" (the full model). Their filenames will also be collated into a single cell array and saved in a mat file named "GCM_Full.mat" in the templates directory.

4.6.2 Estimating GCMs

Having specified two DCMs for every subject, let's now fit them to the data. In the Batch editor, click File → New Batch. Then click SPM → DCM → DCM estimation. Fill out the batch as follows:

• Select GCM *.mat - double click, then select the file named "GCM_Full" we created earlier from the templates directory. Then press Done. The file we selected contains a cell array of DCM filenames.

• Output - single click Output, then click 'Create group GCM *.mat file' and for output, select the 'fits/batch_gui/fmri/' directory and name it "Full". For Estimation type, choose "Full + BMR (default)"; other items can be left on their defaults too.

Save this batch by clicking File, Save Batch as "batch_dcm_fit_gcm" in 'saved_from_batch_interface' sub-directory in 'code / fmri' for record, and press green play button. This will take a long time, though if you have multiple cores, you can speed up DCM estimation by using MATLAB's parallel computing: this "use_parfor" switch has been on in the modified version of spm dcm fit.m in the "code" directory.

[3] In the accompanying tutorial on MEG, we will demonstrate the use of "dependencies" within SPM's batch interface, where the output(s) from one module can be specified as the input(s) to subsequent modules, even though those output files have not yet been created, in order to create a single "pipeline" of modules before running it.

This will fit each full model to the subject's data independently. The results will overwrite the DCM files in each subject's folder.

4.6.3 Diagnostics

Having completed the estimation of the first-level DCMs, it is a good time to perform some diagnostics on the models. First, in the main Matlab window, change to the analyses directory ('/fits/batch_gui/fmri') and load the 'GCM_Full.mat' file and then execute following SPM command within Matlab console: 'spm_dcm_fmri_check (GCM)'.

The output of this command will be similar to that shown in Figure 8.[4] This is a graphical representation of the GCM file, where the long coloured bar indicates the explained variance of the DCM for each subject, and the columns correspond to models per subject, in our case just the one 'Full' model. This column will have the explained variance calculated (averaged across all ROIs). Here we clicked on the model for subject 1, who had explained variance 77.52%. (Depending on your SPM version, you may get slightly different explained variance.) The lowest of 18.08% is for subject 11, while the highest is 77.52% for subject 1. As explained in DCM literature, % variance explained is not the ideal criterion (model evidence captures this accuracy, but also "adjusts" for model complexity), but as a rule-of-thumb, one might be concerned if DCM explained <10% of the variance (e.g, there could be excessive noise in data from one participant, or incorrect GLM specification, or just poor DCM choice)

After clicking on a participant's full model (left hand column of the figure), you can click the Diagnostics button, to further explore, eg, the predicted timeseries, as we did for the single subject DCM fit for subject 15 in Section 3.4.

[4] Press "CTRL-" or "CTRL+" on "SPM Figure" menu if font too big/small.

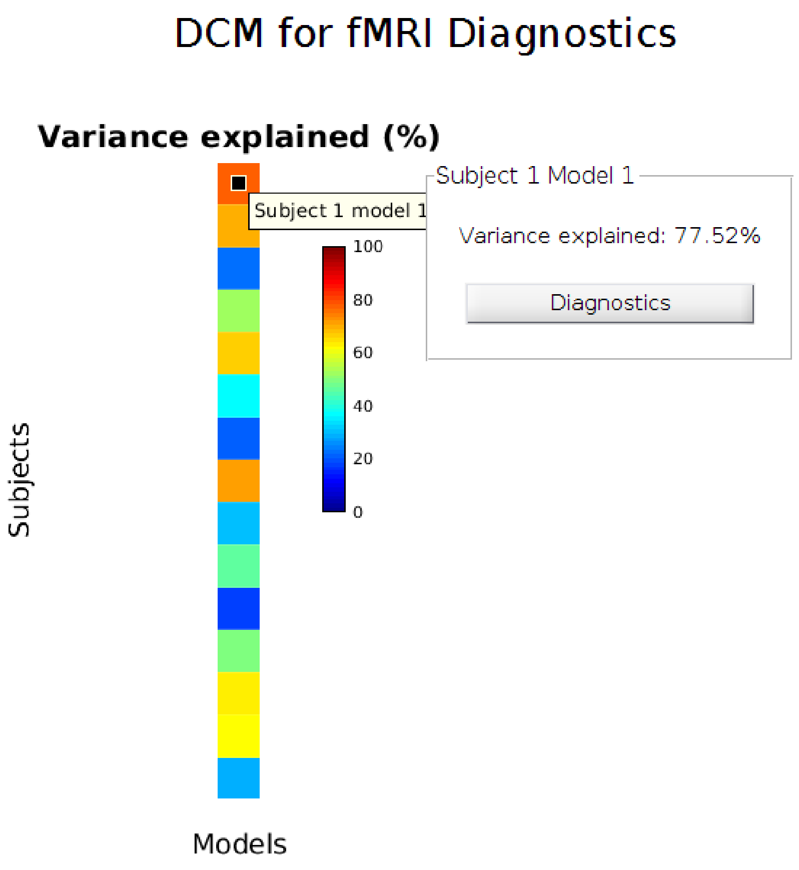


Figure 8. Diagnostics of fits of full model for each participant

4.7 Second level analysis: PEB

Having estimated each subject independently in the previous section, we now want to get a single measure of model evidence at the group-level (hierarchical) model. We might also want to examine differences between subjects by specifying group covariates like age or sex (see later for an example), though for now we just estimate the simple group average, for simplicity.

4.7.1 PEB model specification

Go to the main SPM window and click Batch. Then click SPM → DCM → Second level → Specify / Estimate PEB.

• Name - This is a name for the analysis, which you can enter “Full”, since SPM with prepend “PEB” to create file “PEB_Full.mat”.

• DCMs - Double click, then navigate to the ‘fits/batch_gui/fmri’ folder and select the file named “GCM_Full.mat”.

• Selected DCM index - Leave this on the default value of 1.

• Covariates – keep as “none”, but later below, we will add age here.

• Fields - We're only going to take parameters from DCM matrix B to the group level. Click Fields, then click 'Enter manually'. Double click 'Enter manually' and type: {'B'} including the curly brackets, then press OK.

• Rest as default

Now save the batch by clicking File, Save Batch and give it a name like 'batch_dcm_fit_peb'. Then run the batch by pressing the green play button. This will create and estimate the group-level PEB model and store the results in a file called "PEB_Full.mat".

4.7.2 Model comparison: automatic search

To make use of the PEB model, we need to perform a model comparison. The simplest form of model comparison to run is an automatic search, which will prune parameters from the PEB model that do not contribute to the model evidence. The software will specify and compare hundreds of candidate reduced PEB models, in which different combinations of parameters have been switched off. This search can be performed quickly owing to a method called Bayesian Model Reduction (BMR), in which the parameters and model evidence for any nested model can be estimated from the full model fit by simple equations, without needing to re-fit each nested model to the data. Moreover, we can also average the parameters (connection strengths) across the whole model space, weighted by the model evidence for each model; a process called Bayesian Model Averaging (BMA).

In the batch editor, click File → New Batch then click SPM → DCM → Second level → Search nested PEB models. Fill it out as follows:

• Select PEB file – Select "PEB_Full.mat" created above

• DCMs - Select the file "GCM_Full.mat" – this file is only needed because it contains information about the full model needed for graphical output.

• Null prior variance - This determines the null hypothesis for each connectivity parameter - i.e. what prior variance constitutes a connection being 'switched off'. Set this to 0 (zero).

Save the batch as "batch_dcm_peb_bmr_search" and press the green play button. This will produce a file called "BMA_search_PEB_Full.mat", as well as three windows:

1. The window titled 'BMR - all' (Figure 9) details the 256 candidate PEB models from the final iteration of the automatic search (the full number of models searched is 2^8, since 8 B parameters were estimated during PEB stage). The top left plot shows the log model evidence for each PEB model and the top right shows these values converted to posterior probabilities. Note that no single model wins (in sense of conventional probability >.95), though a few models are much more likely than remaining ones.

The second row shows the parameters of the PEB model before the search (left) and after the search (right). Only two parameters have been pruned away because they did not contribute to the model evidence (free energy) – the second and sixth. We will return to the identity of these parameters shortly.

The bottom left plot shows the parameters that were switched on (white) and switched off (black) in each model from the final iteration of the search. For example, B(1,1,2) - the modulatory effect of faces on self-connection of lOFA - was switched off in the first 128 models and switched on in the second 128 models. Finally, the bottom right plot shows the posterior probability for each PEB parameter. This is computed by comparing the evidence for all models (out of the final 256) which had the corresponding parameter switched on, versus all models which had that parameter switched off.

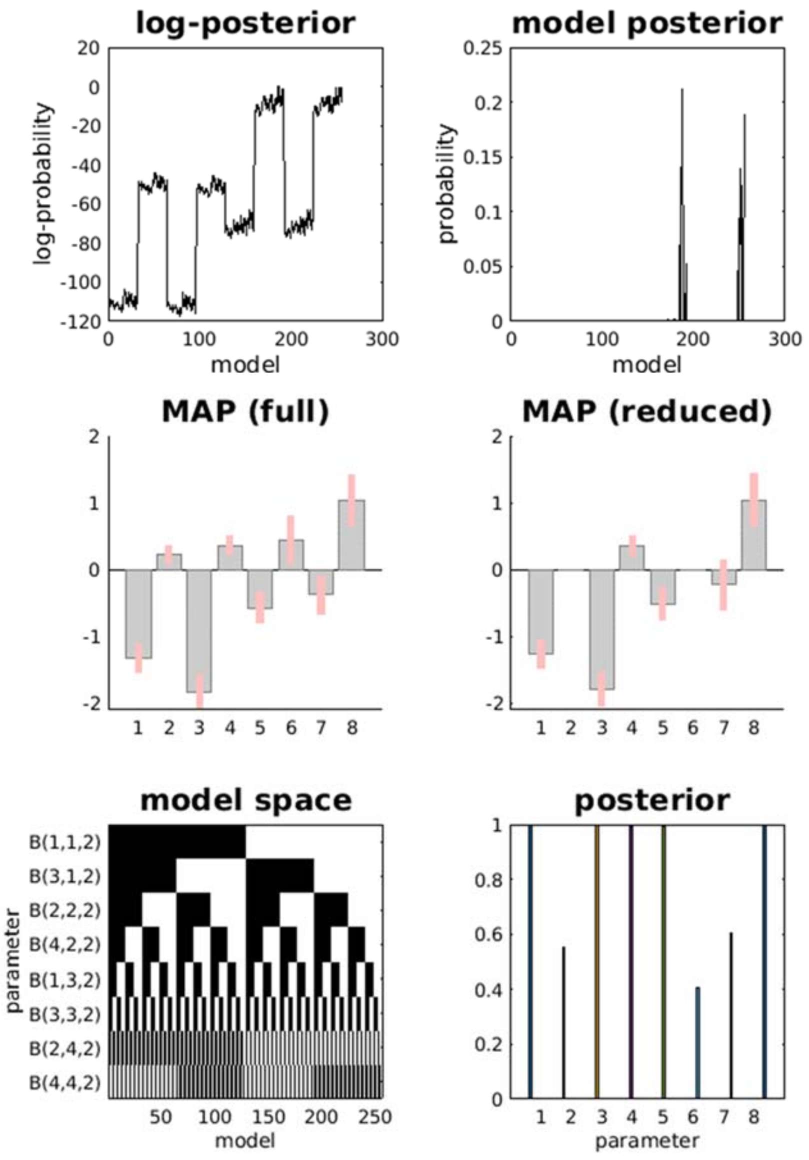


Figure 9. PEB BMR automatic search of whole model space: "BMR-all" window

With a large model comparison such as this, it is unusual to find one model that is the overall winner. Instead of considering the individual models, it is generally more informative to consider the BMA - the weighted average of the parameters over models. The window titled BMC (Bayesian Model Comparison, Figure 10) shows this average, with plots organised into three rows. The top row shows parameters from the estimated PEB, while the middle row shows parameters from the BMA, with their respective posterior probabilities in the bottom row. The bottom row shows posterior probabilities for each parameter as described above. While parameters 2 and 6 have been pruned, other parameters have become less strong, eg credible interval for parameter 7 now overlaps 0. The bottom row shows the posterior probability for each parameter (as described above), and all except first parameter (and two pruned) have probabilities close to 1, suggesting all needed.

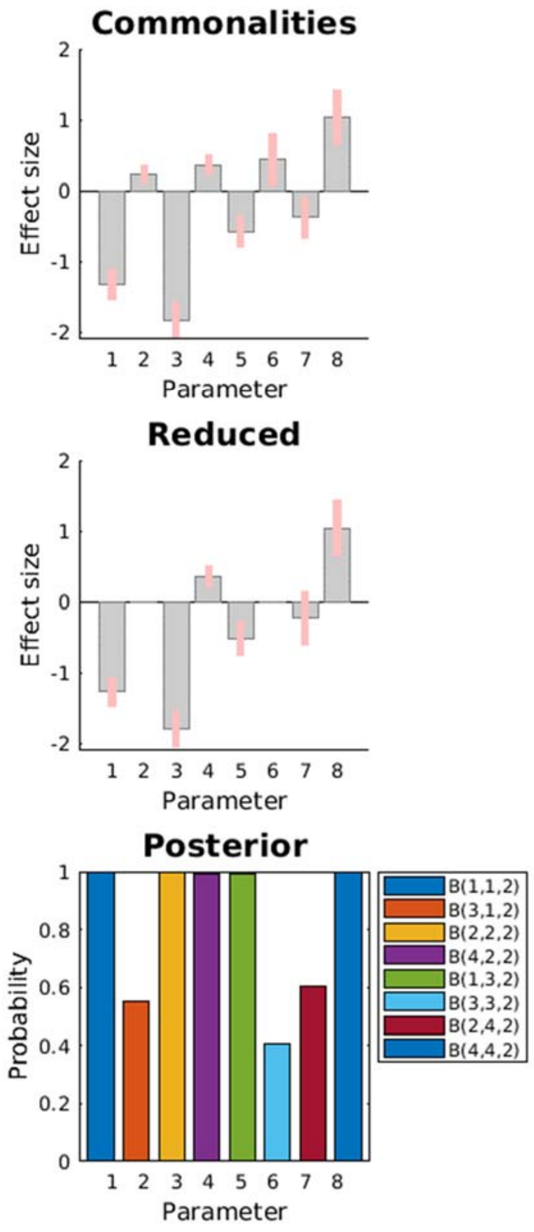


Figure 10 PEB BMR automatic search of whole model space: "BMC" window

The final window, titled 'PEB - Review Parameters' (Figure 11), is an interactive tool that provides an easier way to explore the results (should you need to open this tool yourself at a later stage, then the command is: 'spm_dcm_peb_review(BMA, GCM)', after loading the PEB and GCM files into Matlab).

• The boxes in top left give the number of regressors (covariates – just single group mean here) in the between-subjects design matrix, the number of DCM parameters (8 B parameters passed to PEB) and the number of subjects (15). The between-subjects design matrix is shown below, with one subject per row and one covariate of mean across subjects.

• The estimated between-subject covariance matrix. The diagonal is the estimated between-subjects variance for each parameter, where the more white they are, the greater the between-subjects variability. Clicking on each item identifies the corresponding parameter (e.g, the backward connection from rFFA to rOFA is most variable across subjects).

• The parameters are grouped by covariate, but here only one, so select "Commonalities".

• Optionally, the parameters can be thresholded to just focus on the most probable effects. The first drop-down menu switches between thresholding based on the free energy (model comparisons with/without each parameter) and thresholding based on the posterior variance (the pink error bars). Where possible, we recommend selecting free energy, to accommodate interactions between parameters. The menu on the right is used to select the threshold, eg >.95.

• The bars are the parameters relating to the selected covariate. Pink error bars are 90% credible intervals. Clicking on a bar shows the name of the parameter, its expected value, and its probability calculated using the option selected above. Parameters 2, 6 and 7 have no evidence.

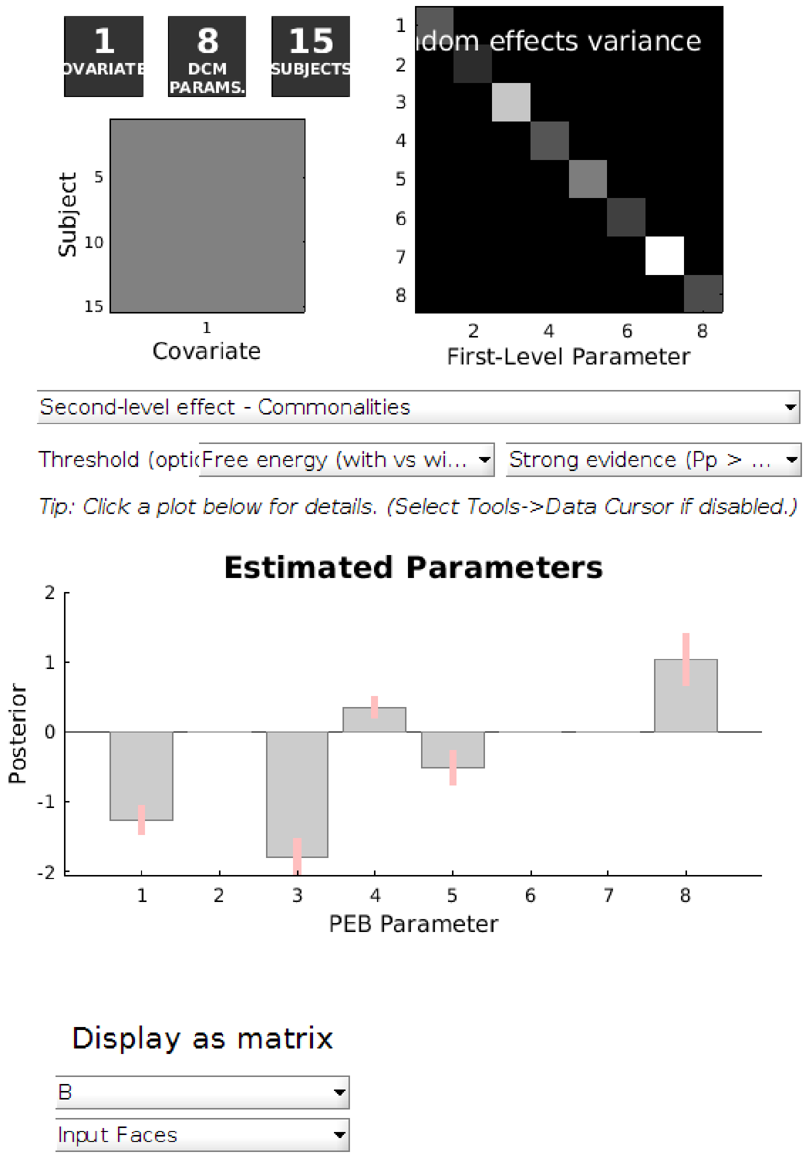


Figure 11 PEB BMR automatic search of whole model space: "PEB - Review Parameters" window

• Use the menus at the bottom of the window to display the parameters as a connectivity matrix. This is the same information as displayed in the bar chart, but shown in the same format as the connectivity matrices in DCM. Each column is an outgoing connection and each row is an incoming connection.

First use the selector higher up in the window to choose the "second-level effect" of Covariate 1 (which is simply the mean across participants). Then click 'Please select a field' and choose the parameters of interest - e.g. 'B' for the modulatory inputs (matrix B of the DCM neural model). A small window will pop up to select the input (modulator), which defaults to the first input (all faces and scrambled), which we did not allow to modulate, so need to change to "Input Faces", will update the popup window with the connectivity matrix to match Figure 12. This shows posterior probability for each connection, coloured by positive or negative sign.

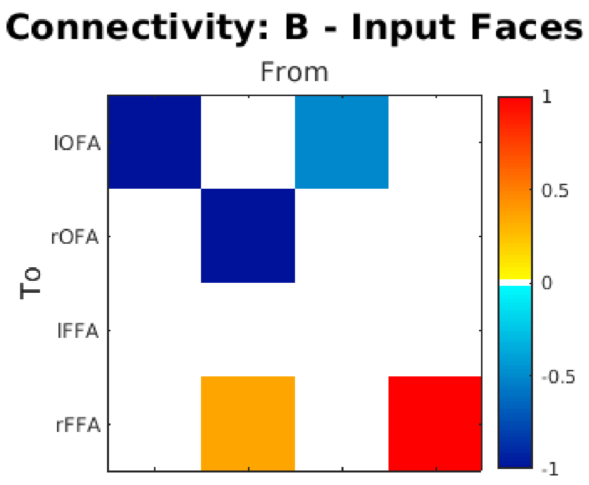


Figure 12 PEB BMR automatic search of whole model space: Thresholded B connectivity matrix

One can see that all self-connections (on leading diagonal), except that for lFFA, are needed, and are negative for both OFAs but positive for rFFA. A negative modulation means less self-inhibition when faces occurred, which will tend to result in greater activity for that region (though this also depends on modulations of afferent connections from other regions). This is because, in DCM, the total self-connection strength is -0.5 * exp(A_ii + B_ii) Hz, so if B_ii decreases with faces, the connection strength because less negative.

One between-region (off-diagonal) connection from rOFA to rFFA is positive, , while the one from lFFA to lOFA is negative.

4.7.3 Binary model comparison

The automatic search of all possible reducible models from the full model may not be sufficient to answer your questions. While it can return BMA estimates of connections that are needed, one might have a more general question that spans more than one connection, e.g, "Do we need (modulation of) any backward connections from OFA to FFA?", or "Do we need any lateral connections between hemispheres?". Here, we are going to ask the question "Do we need any modulations of connections between ROIs, in addition to modulations of self-connections?" – i.e., use DCM to ask whether there is any evidence of effective connectivity during face processing. Here, we will start by answering this question by a simple, binary comparison of two models: the full model and a reduced 'self-only' model that only contains modulation of self-connections by Faces (later we will ask the same question by comparing "families" of models).[5]

[5] Another advantage of specifying a smaller model space a priori, rather than relying on exhaustive search across all possible reduced models as in the previous section, is that it minimises the problem of "model dilution", i.e,

First we create the reduced 'self-only' model. You could repeat the steps for specifying the 'full' DCM from section 4.4, except when you come to the "Faces" input on modulatory connections, where you should not click on off-diagonal elements of the B matrix, as shown in Figure 13. Make sure you save this model as "DCM_Self" under 'fits/batch_gui/fmri/templates/DCMs', so as not to overwrite the "DCM_Full" created previously.

However, a quicker way is to type in Matlab (or see equivalent code in "spm_master_script_dcm_fmri_peb_direct.m"):

```
cd sub-15
load DCM_Full.mat
DCM.b                   % Just to remind you of current modulatory
connections, where first matrix in third dimension is for "All" and
second matrix in third dimension is for "Faces"

DCM.b(:,:,2) = eye(4)   % Leave only leading diagonal for modulation
by "Faces"

outf = fullfile(base_dir, 'fits/batch_gui/fmri/templates/DCMs/DCM_Self')
save(outf,'DCM') % base_dir is the root folder of the repository
cd ..
```

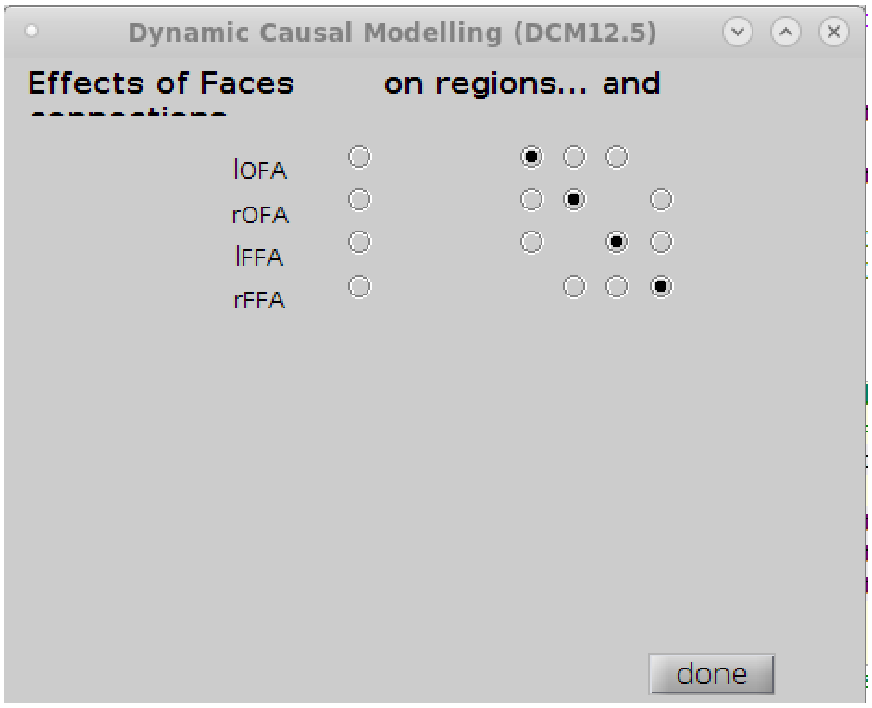


Figure 13: DCM specification for modulatory inputs (B) for faces only (in reduced, "self only" model).

Next, we define our model space consisting of the full and the 'self-only' model for each subject by specifying them as a GCM cell array. This can be done via the steps outlined in section 4.6.1 by keeping all options same except for 'Alternative DCMs'. For this option, specify the reduced 'DCM_Self.mat' file located under 'fits/batch_gui/fmri/templates/DCMs/'. Set the output directory of this GCM to 'fits'batch_gui/fmri/templates/GCMs/Full_vs_Self/' with the name 'Full_vs_Self'. Press the green

reduced probability of finding a single best model when a large number of similar models are compared (many of which might be implausible a priori).

button to run this module. Once completed, a GCM file called ‘GCM_Full_vs_Self.mat’ will be created in the folder specified above. Along with this individual DCMs will also be created in each subject’s directories with the names ‘DCM_Full_vs_Self_m0001.mat’ and ‘DCM_Full_vs_Self_m0002.mat’, corresponding to the ‘Full’ and the ‘Self’ models respectively.

Next, we use this definition of model space for model comparison. Open the batch editor, click File → New Batch. Then select SPM → DCM → Second level → Compare / Average PEB models. Fill it out as follows:

• Select PEB file - Double click and choose the file “PEB_Full” we created earlier.

• DCMs - Double click and choose the file “GCM_Full_vs_Self” we created above.

Save the batch, for example as “batch_dcm_peb_bmc”, then click the green play button.

The software will read in the GCM file, which only contains 2 models in this example, and look at which connections should be switched on and off for each candidate PEB model. It produces a file called “BMA_PEB_Full”.

Two windows are also generated. The window titled “BMC” (Figure 14) shows the results of the model comparison. The panels in this window are very similar to Figure 10, except model space only contains 2 models now (full on left, and self-only on right, in top left panel).

The main result is the posterior probabilities of the two models, as shown in middle-left (and top right) panels, which show virtually 100% probability for full model (and 0% for self-only model). In other words, overwhelming evidence that modulation of between-region connections is needed.

The bottom left panel shows the probability for each of the (8) parameters which varied across models. Computed by comparing the evidence for all models which had each parameter switched on vs all models which had the same parameter switched off. All between-region connections have probability close to 1, suggesting all are needed.

The middle and bottom right panels show the parameter sizes for all B parameters in the full model, before and after BMA. Since probability of the full model is close to 1, these are virtually identical to those in middle right panel.

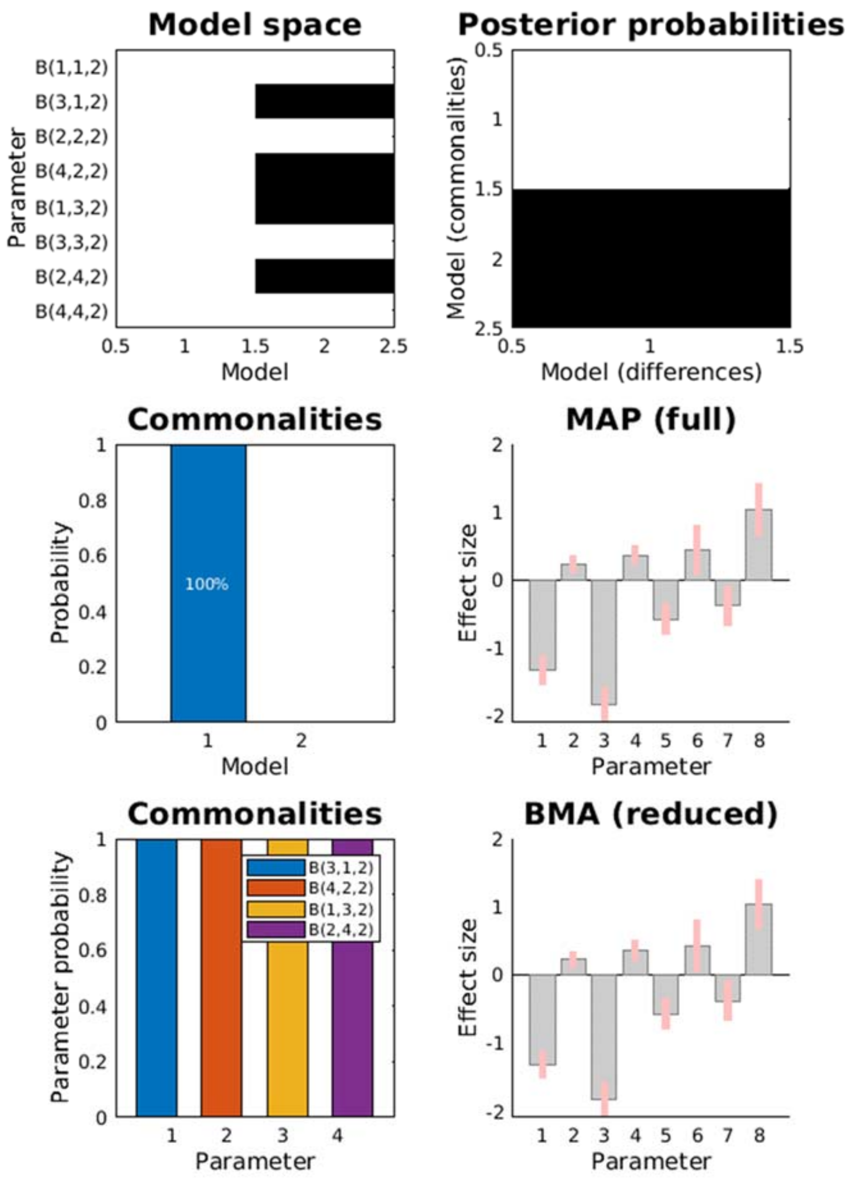


Figure 14 PEB comparison of full and reduced models only: "BMC" window

The second window entitled "PEB – Review Parameters" (Figure 15) is very similar to Figure 11, except that only parameters that varied across models shown (see red text in Figure 14 below). This means that the parameter estimates for the self-connections are not shown. Like in Section 3.6.2, if you select "commonalities", threshold with strong evidence Pp > 0.95, select "Input Faces" for "B matrix", you should get the connectivity matrix shown in Figure 16. Again, note that although the self-connections are white, that does not mean they were not needed; they are just not shown for this particular BMC.

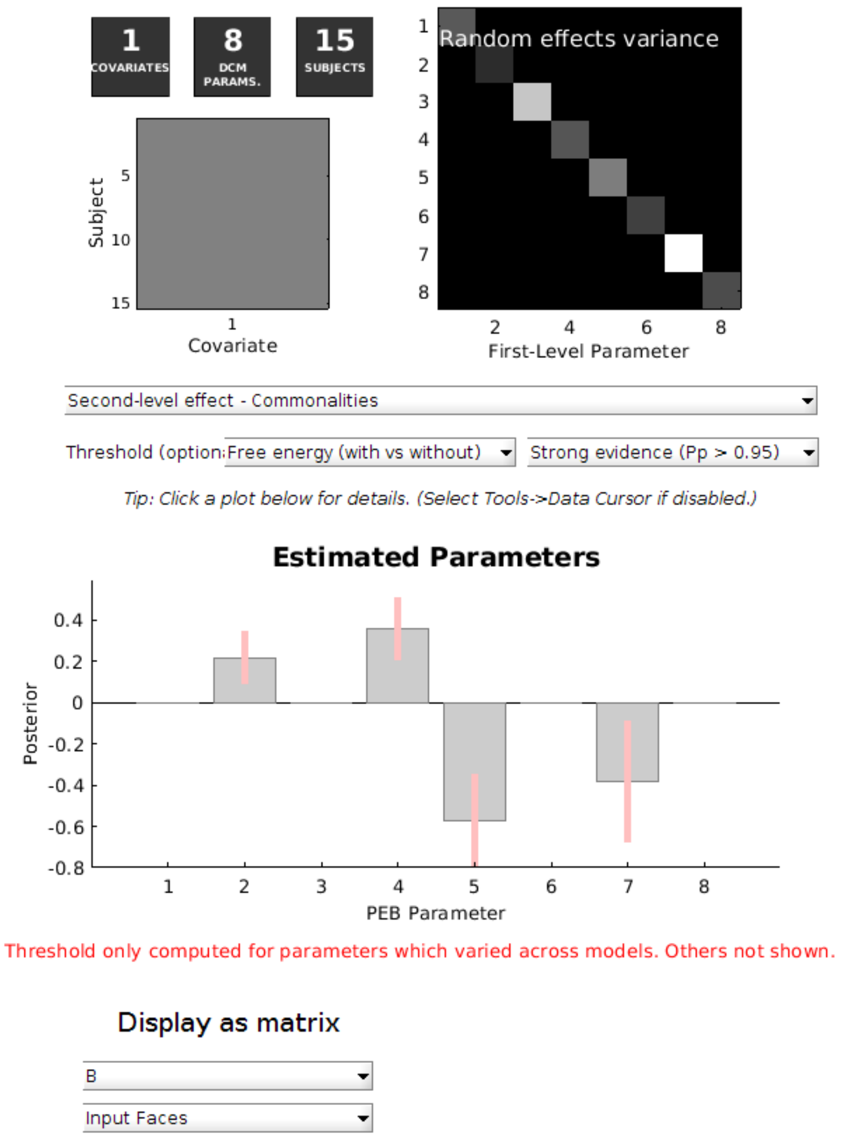

1
COVARIATES
8
DCM PARAMS.
15
SUBJECTS
Subject
5
10
15
1
Covariate
Random effects variance
1
2
3
4
5
6
7
8
2
4
6
8
First-Level Parameter
Second-level effect - Commonalities
Threshold (option: Free energy (with vs without)
Strong evidence (Pp > 0.95)
Tip: Click a plot below for details. (Select Tools->Data Cursor if disabled.)
Estimated Parameters
Posterior
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
1
2
3
4
5
6
7
8
PEB Parameter
Threshold only computed for parameters which varied across models. Others not shown.
Display as matrix
B
Input Faces

Figure 15 PEB comparison of full and reduced models only: "Parameter Review" window

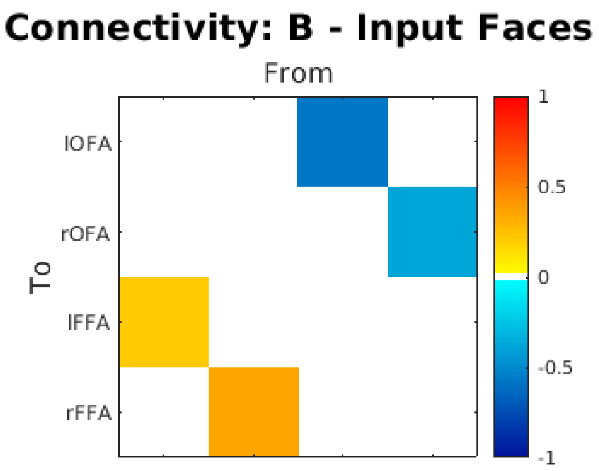


Figure 16 PEB comparison of full and reduced models only: Thresholded B connectivity matrix. Note self-connections not shown, because shared in both models.

The results are similar to in Figure 12 (from BMA across all possible reduced models), except for the positive connection from lOFA to lFFA, and negative connections from rFFA to rOFA. Note that the reason for the differences between the B matrices in Figure 16 and Figure 12 is that BMA has been applied over different model spaces, i.e. the all 2^8 reduced models in Figure 12, but only 2 models in Figure 16. Because the BMA estimates are weighted by the evidence for each model, and there are some reduced models with evidence (and posterior probabilities) not too dissimilar to the full model (see top right panel of Figure 10), these comparable models will influence the BMA estimates in Figure 12, but not in Figure 16, where they were not included.

4.7.4 Model comparison: families

Instead of testing for modulation of all between-region connections versus none, we could alternatively ask whether one or more combinations of between-region connections are modulated. This involves multiple models with different combinations of between-region connections being modulated, i.e. switched ‘off’ or ‘on’ in the B-matrix. The model space therefore expands from just 2 models, like the previous BMC, to a larger number of models, which can be divided into different “families” (sets) according to which types of modulation are enabled. Below, we will distinguish models according to whether they contain self-modulations, modulations of “forward” connections (from OFA to FFA) or modulations of “backward” connections (from FFA to OFA).[6] This entails 8 models in total:

1. Modulation of forward, backward and self-connections
2. Modulation of forward and self, but not backward connections
3. Modulation of backward and self, but not forward connections
4. Modulation of self, but neither forward nor backward connections
5. Modulation of forward and backward, but not self-connections
6. Modulation of forward, but neither backward nor self-connections
7. Modulation of backward, but neither forward or self-connections
8. Modulation of neither forward, backward, or self-connections

By comparing the family of 6 models (models 1, 2, 3, 5, 6, 7) that include modulation of forward and/or backward connections with the family of 2 models (models 4 and 8) that do not contain forward or backward modulations (only with or without self-modulations), we can test a similar hypothesis to the previous section i.e., whether between-region connections are needed. The subtle difference is that the precise question now being asked is no longer whether all between-region connections are needed, but whether at least one type of between-region connection (forward and/or backward) is needed, and furthermore, whether this holds regardless of whether self-connections are also modulated.

4.7.4.1 Family-BMC for between-region connections

The first step involves creation of the eight template models for each model in the list above, which correspond to the matrices shown in Figure 17.

[6] Note we are always combining across hemispheres, though one could of course expand the model space to ask whether forward, backward or self-connections are needed in specific hemispheres. However, if one does not care about hemispheric differences, we are reducing the problem of model dilution by not considering models that differ in modulations between hemispheres.

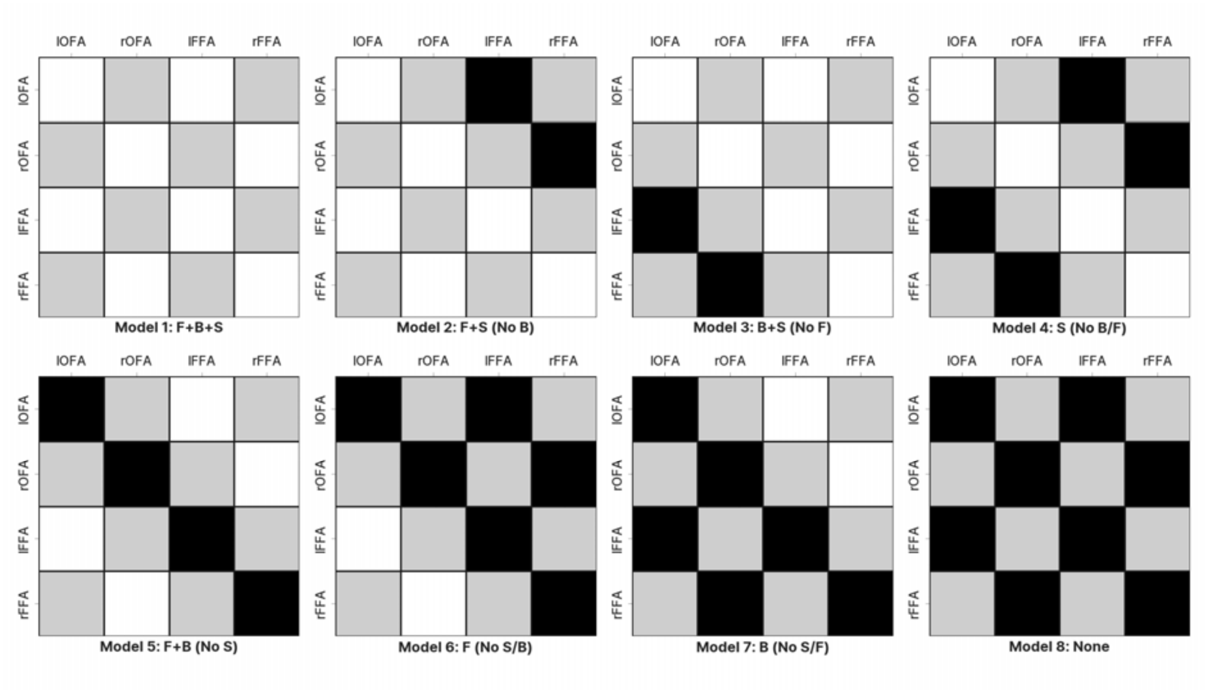


Figure 17: Model space for family-wise comparisons. White squares are connections that can be modulated (have value 1); grey and black squares cannot be modulated (both have value 0, but are distinguished here simply according to whether they never existed in the full model (grey) or need to be explicitly turned off (black)).

This can be done through the GUI by loading the full model (for one subject), switching corresponding B-matrix connections off, and saving as a new file in the directory 'fits/batch_gui/fmri/templates/GCMs/families', as done for the "Self" model in Section 4.7.3. Or this can also be done more efficiently using simple MATLAB functions through the scripting interface, as illustrated on lines 867-1012 in the scripts spm_master_script_dcm_fmri_peb_batch.m.

Either way, the resulting DCM definition files needed to be loaded into a GCM cell array, which now contains only one row, but eight columns, each column corresponding to one of the models (in same order as above). Note that because we will re-use the PEB that we estimated in the previous section, which already contains the full model for all subjects, we do not need to specify the alternative models for every subject; SPM will realise that the GCM now just contains the model space (for one subject), which is sufficient to use BMR to estimate all the nested (alternative) models for all subjects.

Once you have the GCM cell array in the MATLAB workspace, load the PEB model we fit earlier, and reduce the model space using direct calls to the following underlying SPM functions:

```
load('fits/batch_gui/fmri/PEB_Full.mat');

[BMA, BMR] = spm_dcm_peb_bmc(PEB, GCM);
```

Running this will show a window with BMC for all 8 models, along with parameter estimates. The model space in the top-left panel reflects the 8 models we defined earlier. Based on the middle left panel, model 1 with modulation of all specified connections in the B-matrix appears to be the 'winning' model with overwhelming evidence (~100%). This is also reflected in the parameter estimates in the BMA, where estimates of all parameters have a posterior probability greater than 95%. While this could be used as sufficient evidence to choose model 1 over the rest, we proceed to demonstrate partitioning of model space into families for inference.

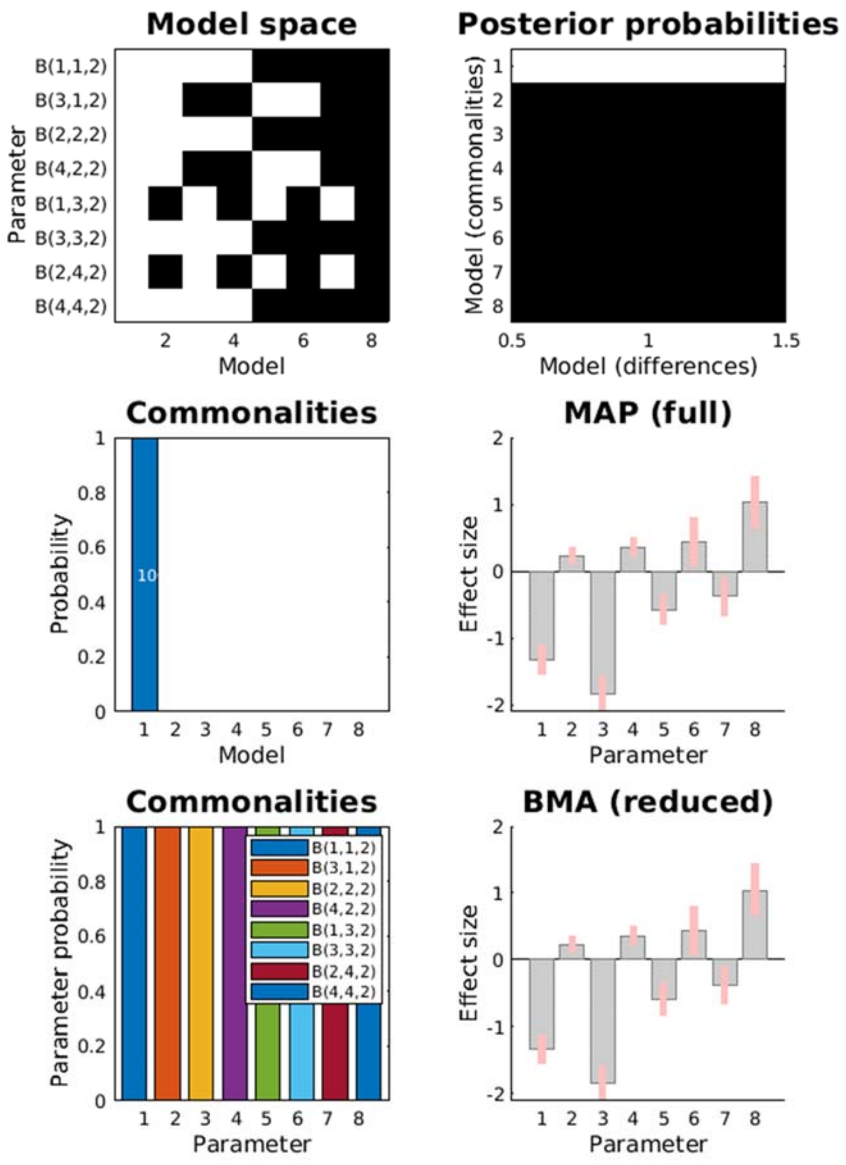


Figure 18: BMR for the 8 models in model space

Lastly, we group these models into families by specifying an integer for each of the models in our model space defined in the GCM above. Models with the same integer belong to the same family, which can be done by running this line of code:

```
families = [1, 1, 1, 2, 1, 1, 1, 2];
```

We can then perform inference at the level of families by running:

```
[~, fam] = spm_dcm_peb_bmc_fam(BMA, BMR, families, 'NONE');
```

where, BMA and BMR are variables obtained from the BMR step earlier.[7] Running this produces Figure 19, with three panels.

[7] Note we are assuming that each model is equally likely a priori. Note also that spm_dcm_peb_bmc_fam can return an updated BMA structure if needed, but we have ignored this output (using the "~" symbol in Matlab and passing in the argument 'NONE'), because we want to re-use the original BMA for further family comparisons

The top left panel shows posterior probability of each family, where the family with modulation of at least one between-region connection has overwhelming probability (~1) compared to the family with no modulation of between-region connections (consistent with the binary comparison in Section 4.7.3). The top right panel shows posterior probabilities of each model conditioned by the probability of each family. Comparing this panel to the middle left panel from the previous figure shows how the probabilities have reduced after conditioning. The bottom left plot shows the grouping of models under each family.

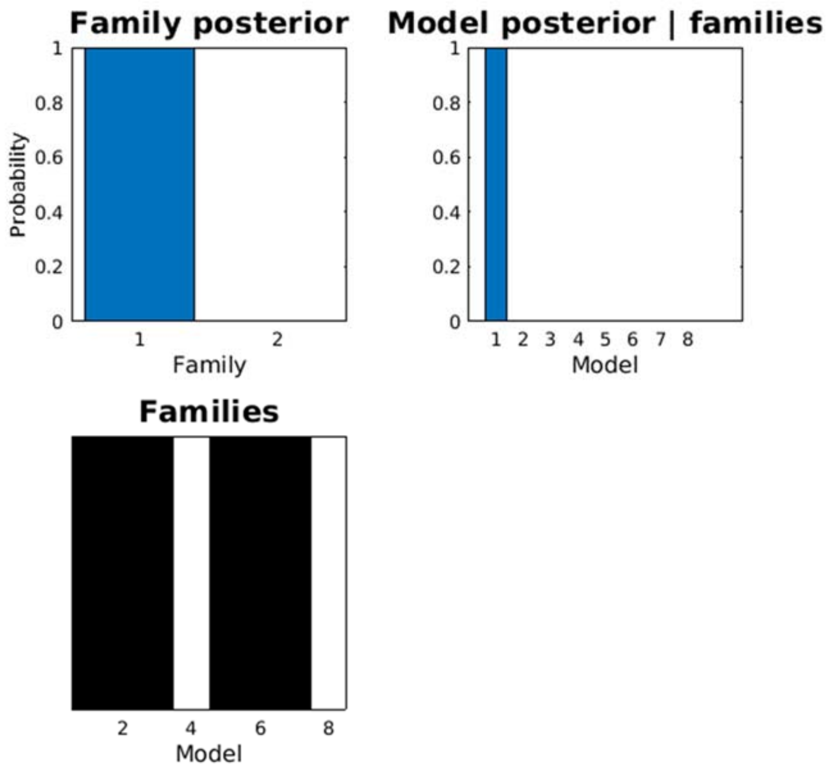


Figure 19: Family-wise comparison for modulation of between-region connections due to faces.

4.7.4.2. Family-BMC for forward connections

Since we have evidence for modulation of between-region connections, we can now test whether a sub-group of between-region connections is modulated by Faces. We do this for both forward connections and backward connections, by specifying families for each of them.

Repeat the last step in the previous section, except with the 'families' variable now re-defined to [1, 1, 2, 2, 1, 1, 2, 2], and run again:

```
[~, fam] = spm_dcm_peb_bmc_fam(BMA, BMR, families, 'NONE');
```

This will produce results for the family-wise comparison showing overwhelming evidence (~1) for the family with at least one forward connection, as in Figure 20.

below (or else you could specify the output as, e.g., "BMAf", so it does not overwrite the "BMA" from the full PEB that we will re-use below).

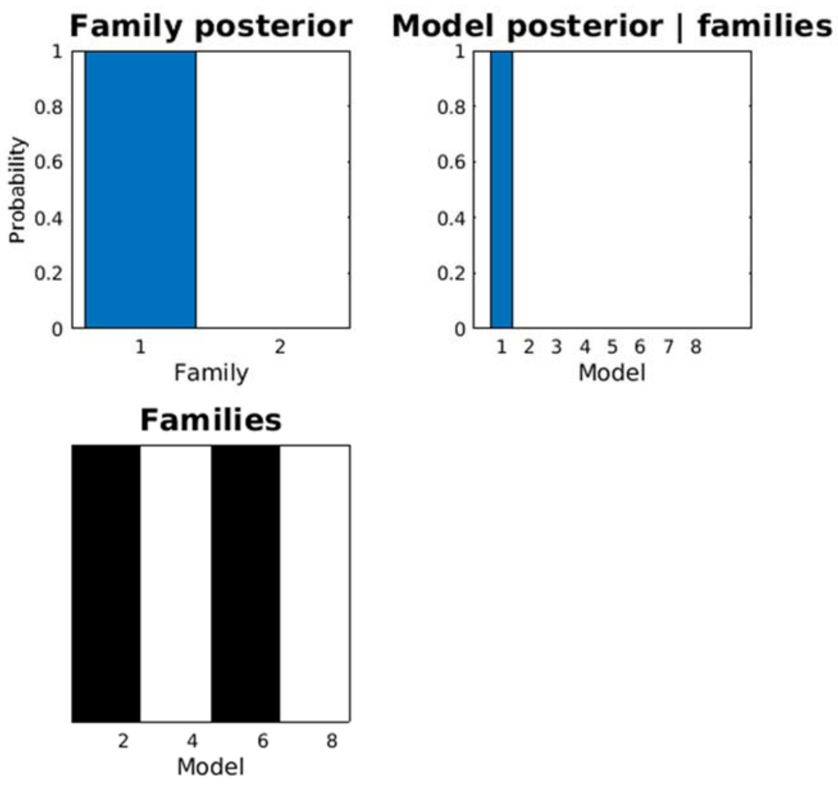


Figure 20: Family-wise comparison for modulation of forward connections due to faces

4.7.4.3. Family-BMC for backward connections

Similarly, to test backward connections, set the 'families' variable to [1, 2, 1, 2, 1, 2, 1, 2], re-run the spm_dcm_peb_bmc_fam command, and this should produce overwhelming evidence (probability ~1) for the family with backward connections, as in Figure 21.

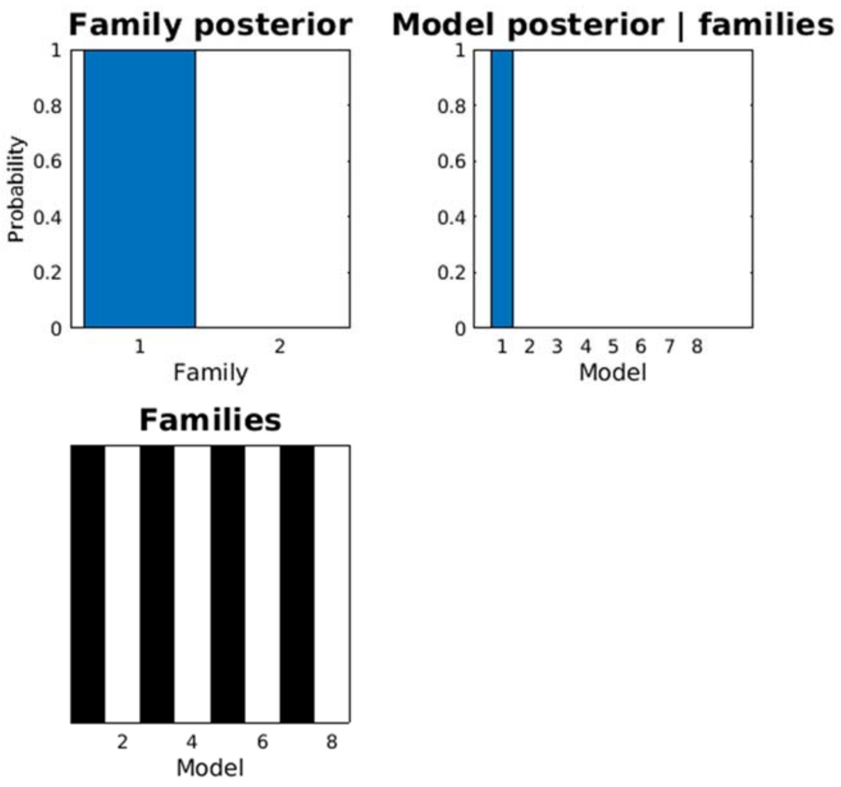


Figure 21: Family-wise comparison for modulation of backward connections due to faces.

4.7.4.4. Family-BMC for self-connections

Lastly, we can test whether self-connections are modulated by faces, by defining the 'families' as [1, 1, 1, 1, 2, 2, 2, 2]. Re-running the spm_dcm_peb_bmc_fam call should produce the results in Figure 22, showing overwhelming evidence for the family with self-connections.

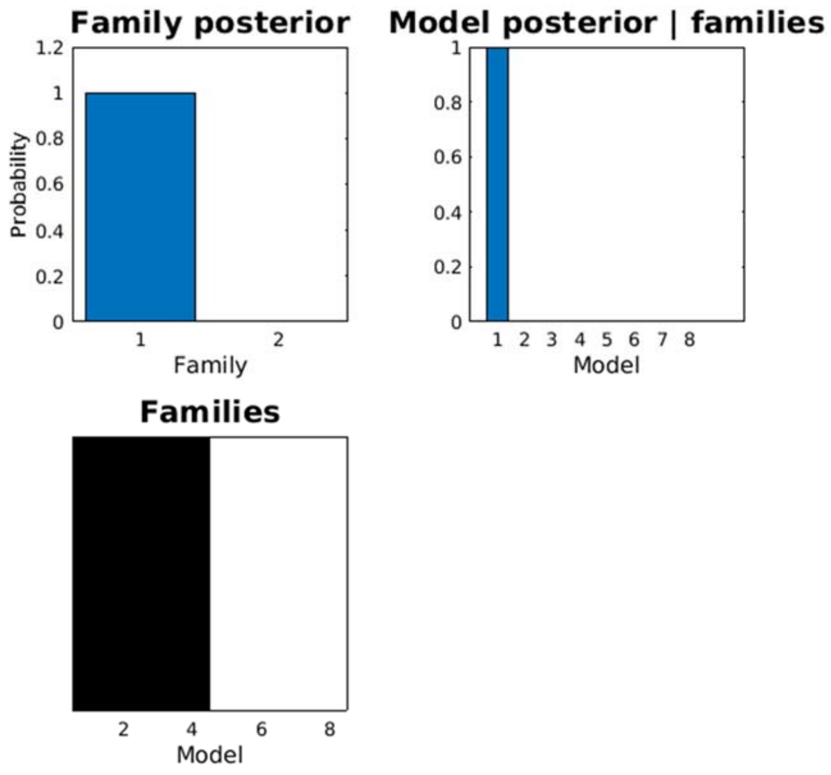


Figure 22: Family-wise comparison for modulation of self-connections due to faces

4.7.5 PEB with subject-level covariates

In this section, we demonstrate the addition of an age covariate for 2nd-level PEB estimation. Although we do not expect any effect of age on modulation of connections in these data (given the narrow range of adult participants from 23 to 31), we conduct this exercise to highlight the key steps involved, since PEB was designed for testing differences between subjects (e.g, patients versus controls).

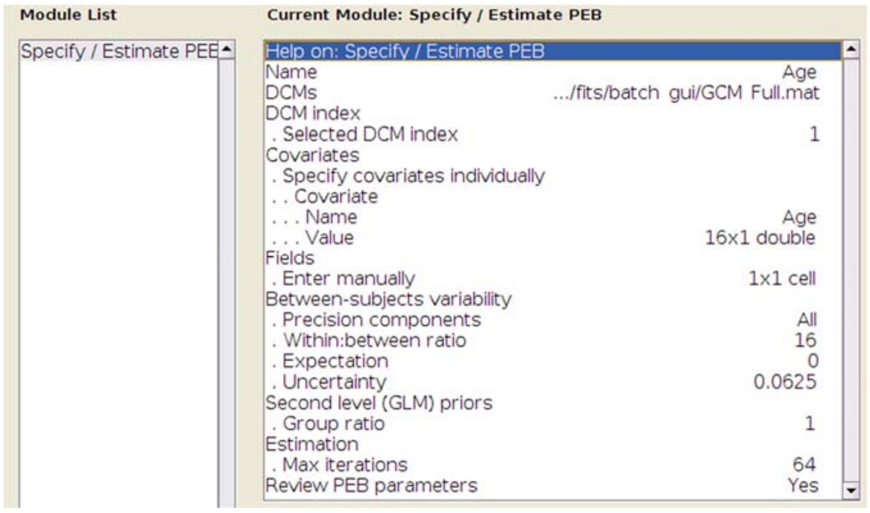
In a new batch, add a module to specify PEB by selecting ‘SPM’ → ‘DCM’ → ‘Second level’ → ‘Specify / Estimate PEB’. In the options for this module, set ‘Name’ to ‘Age’ and select ‘GCM_Full.mat’ estimated earlier from ‘fits/batch_gui/fmri’ for ‘DCMs’. Leave the ‘DCM index’ option as is.

For ‘Covariates’, select the option ‘Specify covariates individually’ from the grey box below. (Alternatively, a full design matrix with all covariates can be passed via this option). Then click on ‘New: Covariate’ in the grey box to create a pair of options – ‘Name’ and ‘Value’ for the covariate. Set ‘Name’ to ‘Age’. For ‘Value’, enter the following numbers, one on each line in the text box that pops open on clicking ‘Specify’:

```
4.6, -1.4, 3.6, -0.4, -3.4, -0.4, 4.6, -0.4, 2.6, -3.4, -2.4, -2.4, -1.4, -2.4,
3.6, -1.4
```

These numbers are the ages of the 15 subjects taken from the BIDS ‘participants.tsv’ file (available here: https://openneuro.org/datasets/ds000117/versions/1.0.5/file-display/participants.tsv), after subtracting the mean age (and to one decimal place).

This age covariate adds a second column to the design matrix (with the default first column still representing the group mean, and the mean correction of ages ensuring the two regressors are orthogonal, to ease interpretation).



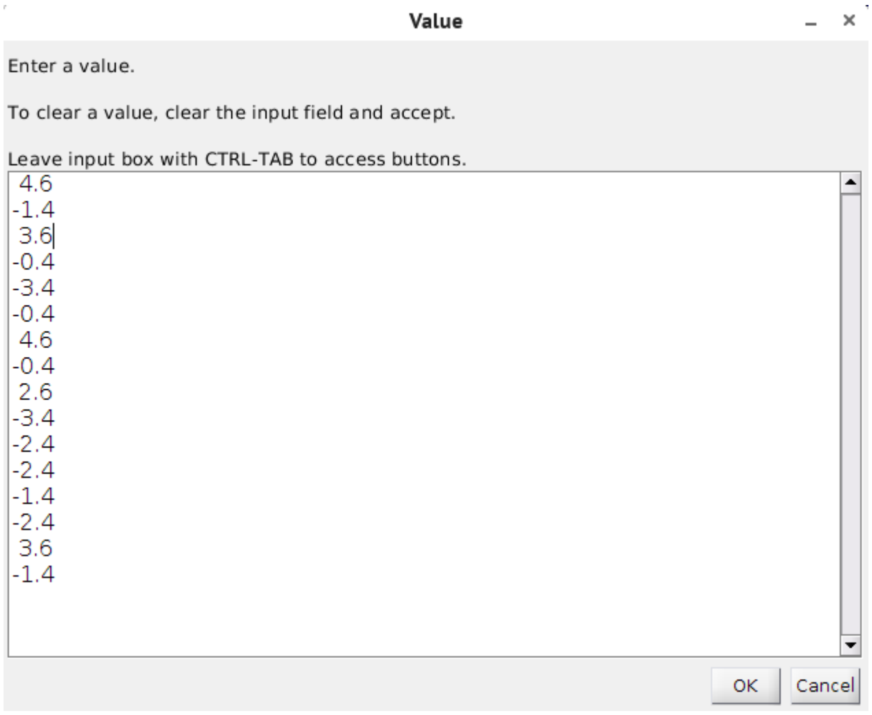
Module List

Specify / Estimate PEB

Current Module: Specify / Estimate PEB

Help on: Specify / Estimate PEB	
Name	Age
DCMs	.../fits/batch_gui/GCM_Full.mat
DCM index	
. Selected DCM index	1
Covariates	
. Specify covariates individually	
. . Covariate	
. . . Name	Age
. . . Value	16x1 double
Fields	
. Enter manually	1x1 cell
Between-subjects variability	
. Precision components	All
. Within:between ratio	16
. Expectation	0
. Uncertainty	0.0625
Second level (GLM) priors	
. Group ratio	1
Estimation	
. Max iterations	64
Review PEB parameters	Yes

Figure 23: Specification of Covariates in PEB



Value

Enter a value.

To clear a value, clear the input field and accept.

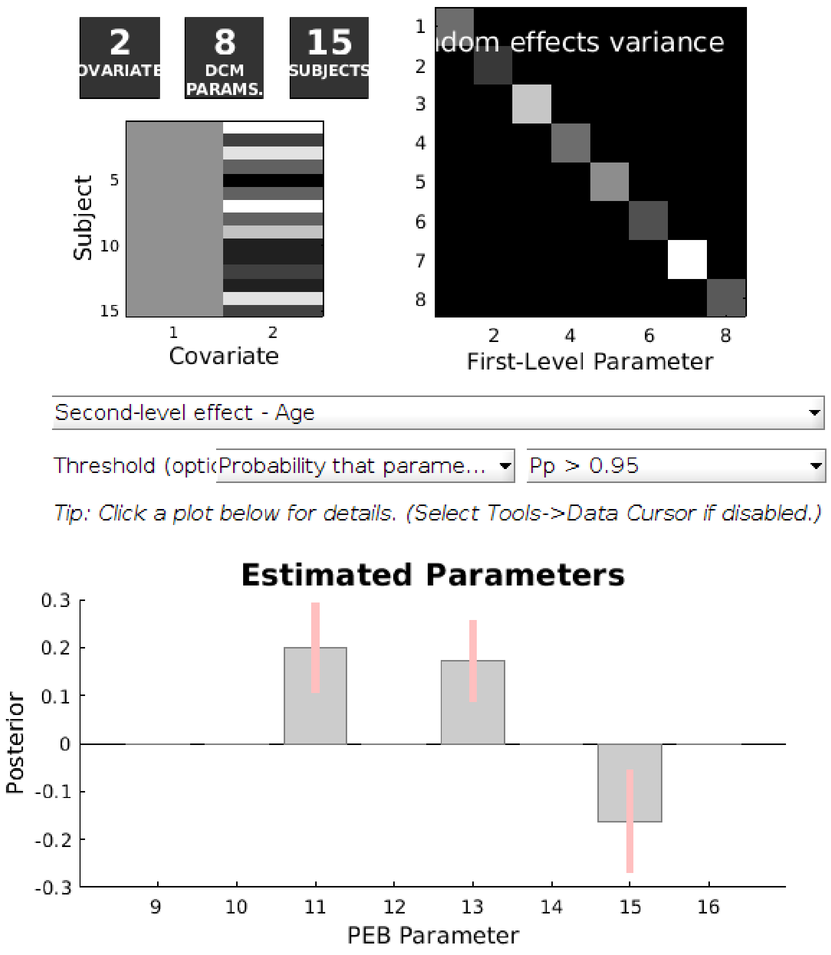
Leave input box with CTRL-TAB to access buttons.

```
 4.6
-1.4
 3.6
-0.4
-3.4
-0.4
 4.6
-0.4
 2.6
-3.4
-2.4
-2.4
-1.4
-2.4
 3.6
-1.4
```

Figure 24: Entry of Age covariate values

In 'Fields', select 'Enter manually' and specify the field as "{'B'}", including curly braces. Lastly, set 'Review PEB parameters' to 'Yes', and press the green play button to estimate this PEB. This will generate the file 'PEB_Age.mat' in the folder 'fits/batch_gui/fmri' and open the review window with estimates of group-level PEB parameters (Figure 23).

The review window now shows our design matrix in the top-left corner, with age as the second covariate. Since age was mean-centred, the first covariate represents mean modulation of connections across subjects. In addition to these common effects estimated at the group level ('Second-level effect – Commonalities'), the review window now has an additional option of viewing the effect of age by selecting 'Second-level effect – Age' from the drop-down menu. Thresholding these parameters based on posterior probabilities shows a subset of modulations were influenced by the age of participants. We do not have any hypotheses about these age effects, so do not discuss further. in order to carry out further inference and principled hypothesis testing based on model comparisons, any of the approaches illustrated earlier in section 4.7 can be applied to this group-level PEB estimate.



Second-level effect - Age

Threshold (opti Probability that parame... Pp > 0.95

Tip: Click a plot below for details. (Select Tools->Data Cursor if disabled.)

Figure 23: Review of PEB Parameters: 2nd level effect of Age

5. Discussion

We have demonstrated workflows for estimating group DCMs and PEB models for inference on connectivity parameters from fMRI data. These workflows make use of SPM's graphical batch interface, and illustrate a systematic pipeline that begins with processed multimodal data for multiple subjects and ends with model-comparison based group-level inference about modulation of connections. We also show how to translate all steps of this pipeline from the graphical interface to batch scripts which allow for greater flexibility and easier chaining of multiple dependent steps. This tutorial accompanies a similar one for M/EEG, for which notable differences exist in specifying individual DCMs, but the workflow for group-level PEB inference (i.e, once a GCM array has been specified) is identical.

Using our pipeline, we performed model comparisons at the group level on DCMs estimated from 15 subjects to test our hypotheses about effective connectivity of OFA and FFA during face perception. We first carried out a binary model comparison between a 'Full' model, in which we modelled the modulation of both between-region connections and self-connections due to faces, and a 'self-only' model in which only self-connections but not between-region connections were modulated by faces. We observed greater evidence for the 'Full' model, suggesting that modulation of between-region connections is needed to explain the data better.

Next, instead of testing for modulation of all between-region connections versus none, we focused on specific groups of connections and tested whether one or more combinations of between-region connections are modulated. We created multiple models with different combinations of connections, grouped them under 'families' and then compared families of models. Each way of grouping models into families corresponded to a hypothesis. For the hypothesis of at least one between-region connection modulated by faces, we grouped all models with at least one forward or backward connection being modulated by faces into one family, and all models without into another. On comparison, we observed greater evidence in favour of the family with at least one between-region connection, in agreement with the binary comparison of 'all' between-region connections versus 'none'. We then zoomed in, and reassigned models into families for testing whether at least one forward connection was modulated, and found higher evidence in favour of modulation of at least one forward connection, regardless of other connections. Similarly, we reassigned models into different families for testing modulation of backward connections and self-connections, and found evidence in favour of modulation of those connections. In other words, at least one of all these types of modulatory connections is needed to fit the fMRI data.

These findings from our DCM analysis support the key role of OFA-FFA connectivity during face processing, in agreement with extensive experimental findings in humans and non-human primates. The results differ somewhat from the companion tutorial on DCM for ERPs (using M/EEG data), where modulation of only backward connections were needed, but the underlying neuronal models and timescales are quite different, such that there are good reasons why the connectivity captures different aspects of true neuronal interactions. Note we do not make strong scientific claims from these results, and other work has shown the importance of considering other ROIs, such as input to both OFA and FFA from early visual cortex (Lee et al., 2022).

6. Appendix

6.1 Re-parametrising the SPM model

In the Supplementary Section 2 of our previous tutorial (Henson et al., 2019), we fit a GLM to each subject in which there were 3 conditions: famous faces, unfamiliar faces and scrambled faces. In the present tutorial, we ignore the distinction between famous and unfamiliar faces, simply to make the tutorial simpler. More importantly, DCM normally assumes a common driving input (the "C" matrix in DCM), plus one or more modulatory inputs according to different conditions (the "B" matrix or matrices). To define the driving input, we need to define a new condition which contains all trials (i.e, onsets for all famous faces, unfamiliar faces and scrambled faces). Then the second condition will be faces only (i.e, onsets for famous and unfamiliar faces), and this will be used as the only modulatory input for DCM.

A second change to the GLM is to concatenate data across all 9 runs. In principle, DCM could be estimated for each run separately (and combined with 3-level PEB model across runs and subjects), but it is easier (and more typical) to concatenate runs within each subject. This requires concatenating volumes, onsets and motion parameters across runs, and creating a new SPM.mat file that contains only a single run, while maintaining the temporal filtering from the original run-specific design matrix (using 'spm_fmri_concatenate' function below).

These steps can be achieved in two ways.

6.1.1 Updating existing SPM.mat files using MATLAB

The first approach is to run lines 173 to 268 from the section 'Combine' in the provided script spm_master_script_dcm_fmri_peb_direct.m, which extracts the information from the SPM.mat files assumed present if you have run Supplementary Section 2 of Henson et al (2019). This code aggregates volumes, movement parameters and trial information across all runs for each subject, specifies a concatenated GLM with new conditions 'All' and 'Faces', and then estimates this model to an updated SPM.mat file. This last step involves a function called 'spm_fmri_concatenate', which maintains run-specific highpass filtering and prewhitening by the estimated temporal autocorrelation.

6.1.2 Recreating SPM.mat files using SPM's Batch

The second is to use SPM's batch script. This creates new SPM.mat files from scratch (like in Henson et al., 2019), assuming you have the preprocessed fMRI volumes (either from Henson et al., 2019, or from Figshare link in main paper). This uses two batch jobs, batch_stats_fmri_concatenated_specify_job.m and batch_stats_fmri_concatenated_estimate_job.m in "code/fmri".[8]

Unfortunately spm_fmri_concatenate.m is not batched, so see lines 271 to 283 of the supplied script 'spm_master_script_dcm_fmri_peb_batch.m', which shows how to integrate this step as a part of the batch scripting pipeline.

[8] Alternatively, the batch job for specification can be created by editing "batch_stats_fmri_job.m" in https://figshare.com/collections/Multimodal_integration_of_M_EEG_and_f_MRI_data_in_SPM12/4367120 in the code/scripted folder, as follows:

1. Delete lines 17-64, ie from "matlabbatch{1}.spm.stats.fmri_spec.sess(2).scans = '<UNDEFINED>';" to "matlabbatch{1}.spm.stats.fmri_spec.sess(9).hpf = 128;", because we only want one session (run)
2. Delete lines 72 onwards, ie from "matlabbatch{2}.spm.stats.fmri_est.spmmat(1) = cfg_dep('fMRI model specification: SPM.mat File', substruct('.','val', '{}',{1}, '.','val', '{}',{1}, '.','val', '{}',{1}), substruct('.','spmmat'));"
3. Save as "batch_stats_fmri_concatenated_specify_job.m" in "code/fmri" directory

The batch job for estimation can be created by starting SPM (eg “spm fmri” once SPM12 on Matlabpath), open Batch and create a new batch job to estimate this new concatenated SPM and evaluate a basic effects of interest contrast:

From batch interface, select SPM:Stats:Model Estimation, and then SPM:Stats:Contrast Manager. For “Select SPM.mat” from Contrast Manager, select “Dependency” and SPM.mat file that (will be) produced by Model estimation.

In Contrast Sessions, select new F-contrast, call “Effects of Interest”, and for “Weights matrix”, enter “eye(2)”, which is a MATLAB function for creating the identity matrix [1 0; 0 1].

Then call batch in (par)for loop for each subject as per lines 169 to 284 of the section ‘Combine’ in the script ‘spm_master_script_dcm_fmri_peb_batch.m’

While the onsets and regressors in the GLM have been concatened, “underneath the hood”, SPM has kept separate highpass filters and separate autocorrelation estimation for each run (since not really a continuous timeseries; small discontinuities across run boundaries might remain in the GLM (eg if HRF for one run overlaps next, so good idea to have ~30 seconds of rest at end of each run if planning to concatenate)).

Finally, if you don’t wish to use either step above, you can download re-parametrised SPM.mat files from:
https://figshare.com/articles/dataset/Face_processing_M_EEG_data_for_Dynamic_Causal_Modelling/21333996

6.2 VOI creation

As stated in main paper, our ROIs are bilateral OFA and FFA. They are defined by 10-mm radius of spheres centred on group-level results, thresholded (*p* < .001) by individual SPM results. You’ll need to have re-parametrised the SPM.mat files as explained in Appendix 6.1.

From batch interface, press SPM:Util:Volume of Interest, enter “1” for “Adjust data” (since only one contrast in above SPM.mat files), enter “1” for “Which session”, select “New: Sphere” for “Region(s) or Interest”, enter “10” for Radius, leave Centre undefined.

- In “Region(s) or Interest” again, select “New: Thresholded SPM”, and set Contrast to “1”
- For Expression, enter “i1&i2”.[9]
- So empty fields are SPM.mat file, Name of VOI, and Centre (which we provide in script).
- Save and script as “batch_VOI”
- Coordinates come from 2nd-level group analysis described in Section A2.9 of Supplementary Material of Henson et al. (2019):

lOFA	[-38, -86, -14]
rOFA	[+36, -86, -10]
lFFA	[-42, -56, -20]
rFFA	[+42, -52, -14]

[9] This is the same format as SPM’s ImCalc function to do basic operations on every voxel across a set of images indicated by i1, i2, i3, etc. Here the use of “&” restricts voxels to those that are non-zero in both images i1 and i2 (where those images are the sphere and the set of voxels showing p<.001 uncorrected).

Then call batch in (par)for loop for each subject as in lines 300 to 342 from the section 'VOI' of the script 'spm_master_script_dcm_fmri_peb_batch.m'. This will produce several graphical outputs that you can examine, but focus here is on DCM, and more details on VOI extraction can be found in SPM12 manual.

This saves several files in each subject's directory for each ROI (VOI), the most important of which are called "VOI_lOFA_1.mat", "VOI_rOFA_1.mat", "VOI_lFFA_1.mat" and "VOI_rFFA_1.mat". These contain the fMRI timeseries (first singular temporal vector) for each ROI that DCM will fit below (plus some other parameters needed for DCM). The other files are images, e.g, "VOI_lOFA_mask.nii", which contains a binary image defining voxels within an ROI, and "VOI_lOFA_1_eigen.nii", where voxels contain the spatial weights instead (first singular spatial vector).

7. References

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