

Psychophysiological Interactions:

A context dependent functional connectivity

Sunghyon Kyeong

Institute of Behavioural Science in Medicine,
Yonsei University College of Medicine

Contents

- Theoretical backgrounds (standard PPI)
- Generalized PPI
- PPI analysis steps in SPM12
- Useful Matlab functions

Keywords

- Convolution with Hemodynamic Response Function (HRF)
- Deconvolution with HRF
- General Linear Modeling (GLM)
- Interaction term in GLM
- Psychophysiological Interaction (PPI)

Theoretical Background

Understanding an Interaction in GLM

Factor A		
Factor B	A1 / B1	A2 / B1
A1 / B2	A1 / B2	A2 / B2

Example)

A1: Self Face

B1: Positive Word

A2: Other Face

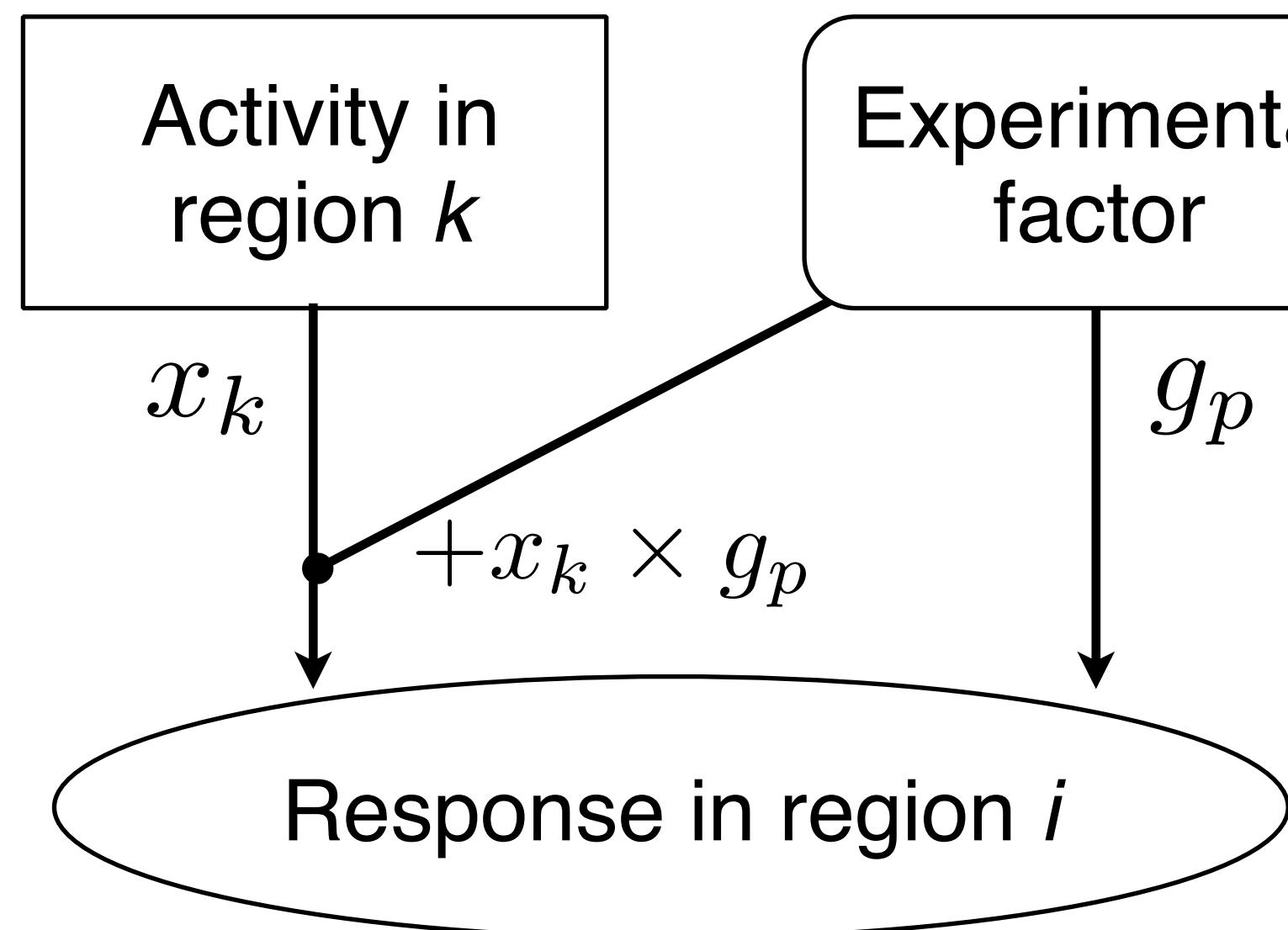
B2: Negative Word

Equation for factorial design

$$y = \underline{(A_2 - A_1)\beta_1} + \underline{(B_2 - B_1)\beta_2} + \underline{(A_2 - A_1)(B_2 - B_1)\beta_3} + \underline{G\beta_4} + \epsilon$$

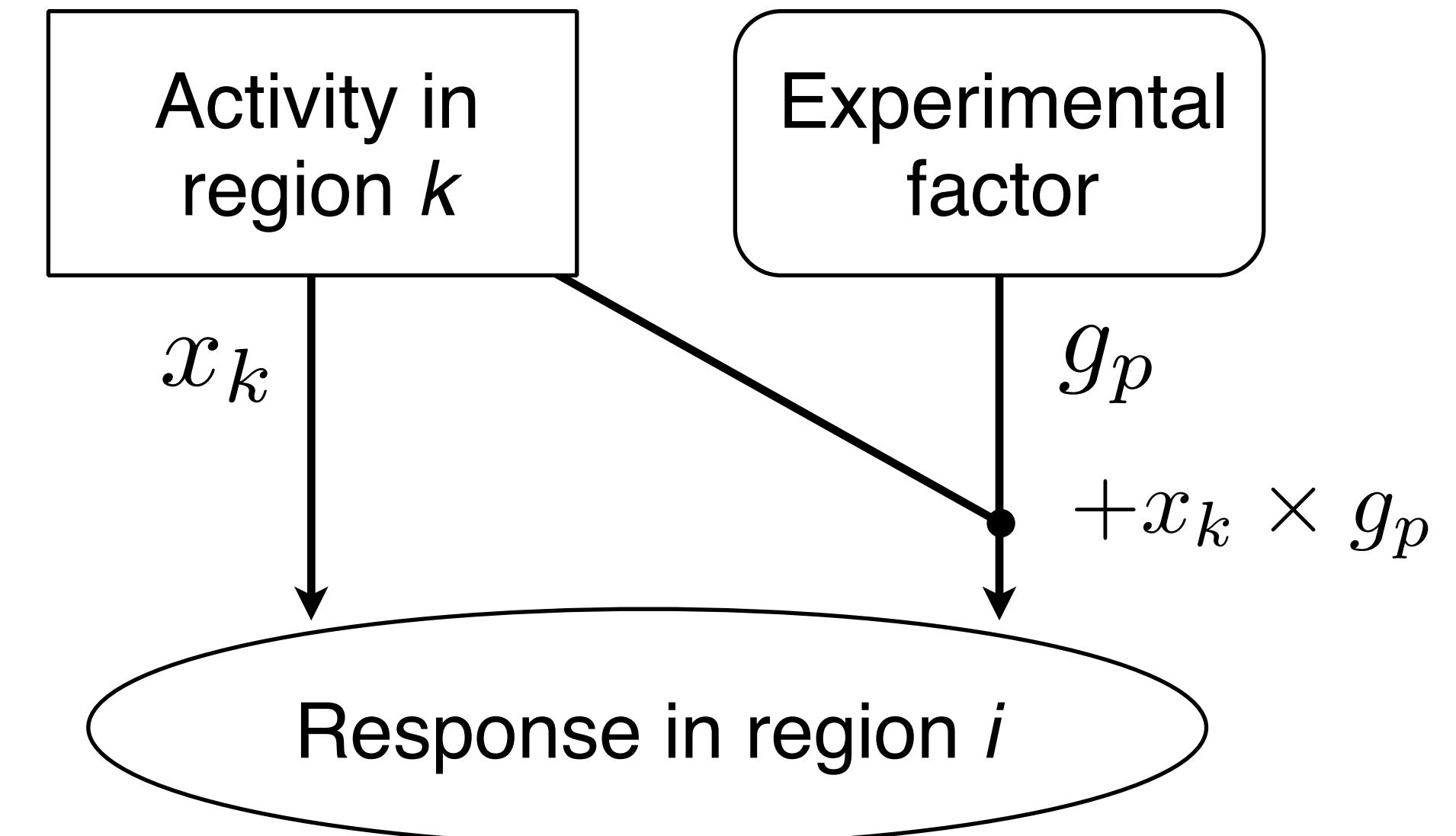
Main effects for A Main effects for B Interaction term Confounding effects

Psychophysiological Interaction



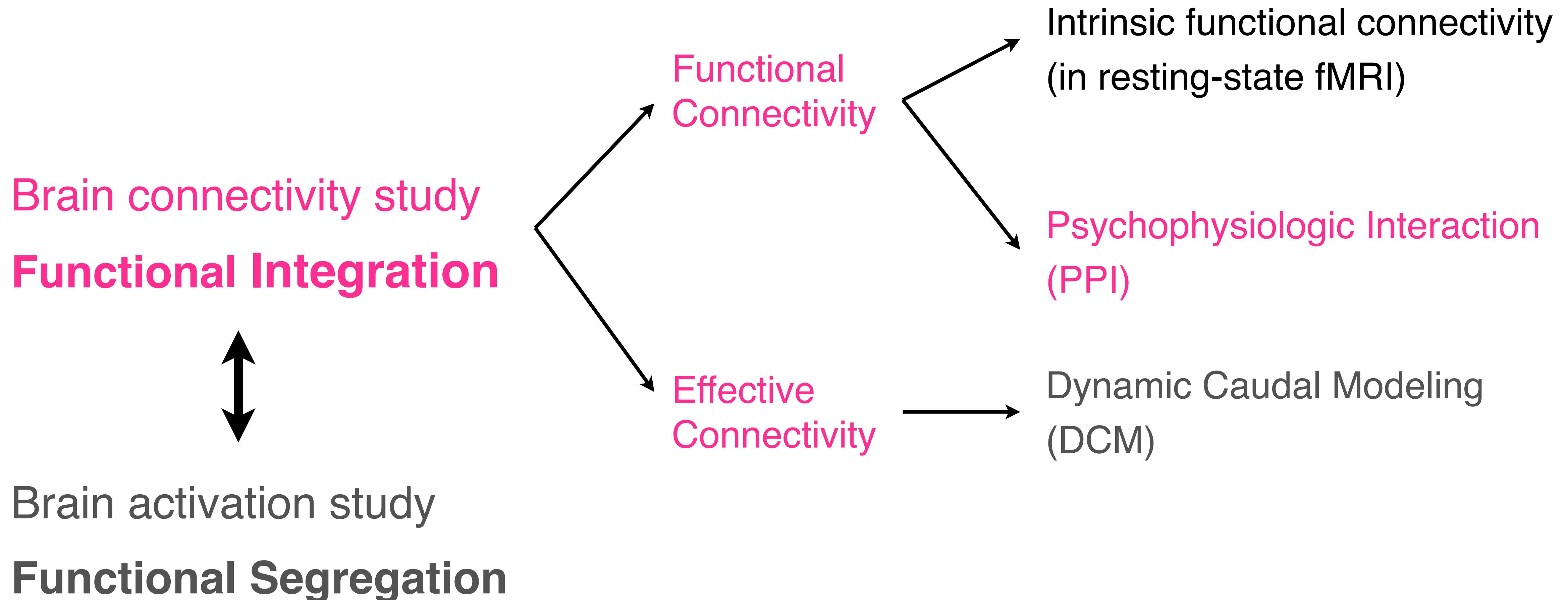
The contribution of one area (k) to another (i) is altered by the experimental context

$$y_i = x_k \beta_1 + g_p \beta_2 + (x_k \times g_p) \beta_3 + \epsilon$$



The responses of an area (i) to an experimental (psychological) context due to the contribution of region (k)

Functional Neuroimaging Study



Functional Connectivity

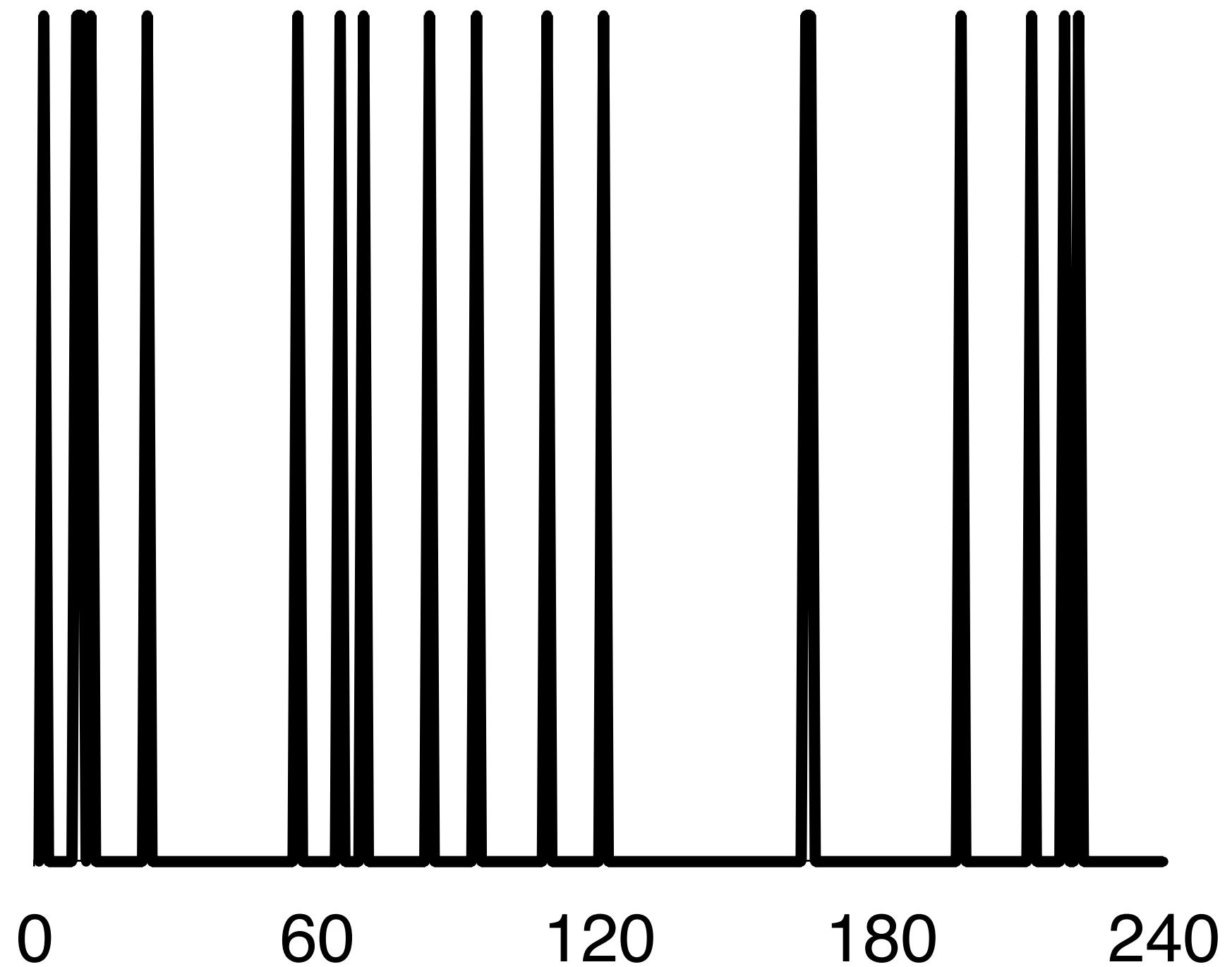
- **Intrinsic functional connectivity**
resting-state (Unconstrained) activity correlations,
interpreted as reflecting intrinsic functional connectivity.
- **Context-dependent functional connectivity**
Physiological correlation as modulated by psychological
variable(s), interpreted as reflecting context-dependent
changes in connectivity.

Psychophysiological Interactions

- Psychophysiological interactions (PPI) model the response in one cortical area as **the influence of another region and its interaction with an experimental treatment.**
- Interactions in the brain take place at the neural and not the hemodynamic level.
- The PPI software (`spm_peb_ppi.m`) was developed in order to provide robust deconvolution of the HRV and the proper derivation of the interaction term.

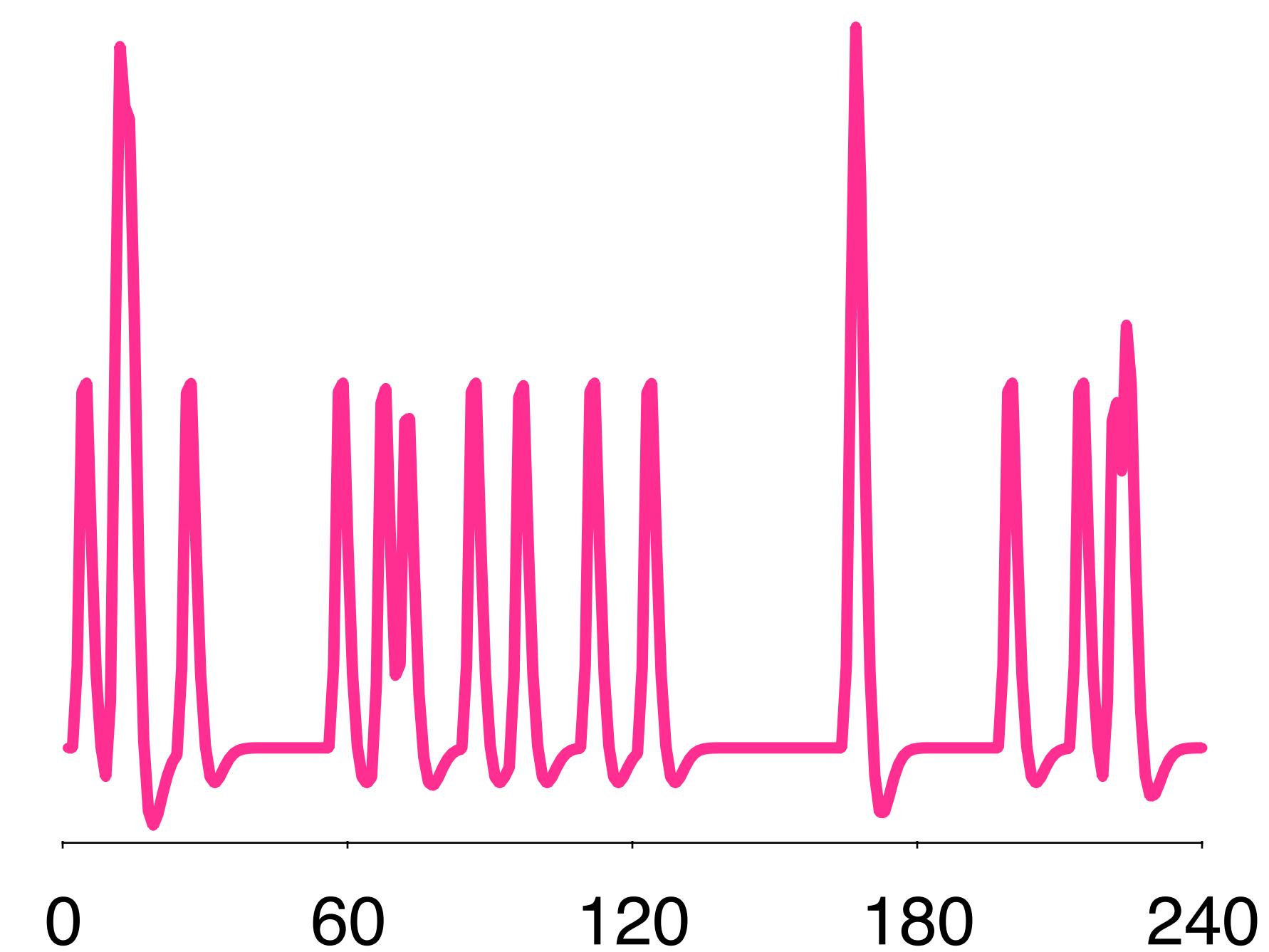
Neural Activity vs. BOLD signal

Experimental Stimulus
(Psychological)

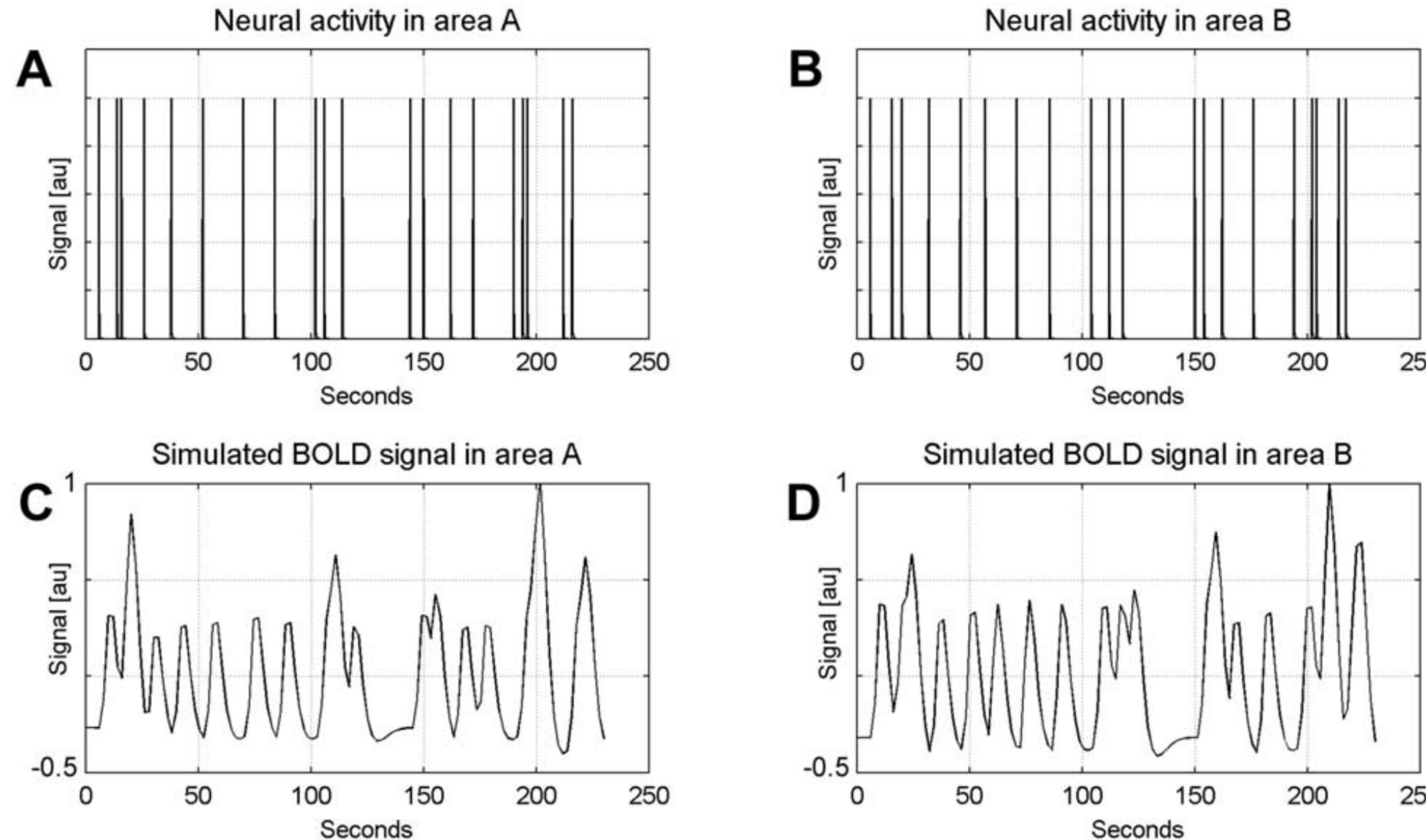


$$\text{Experimental Stimulus} \otimes \text{HRF} = \text{BOLD Response}$$

BOLD Response
(Psychological)



Neural vs BOLD signal



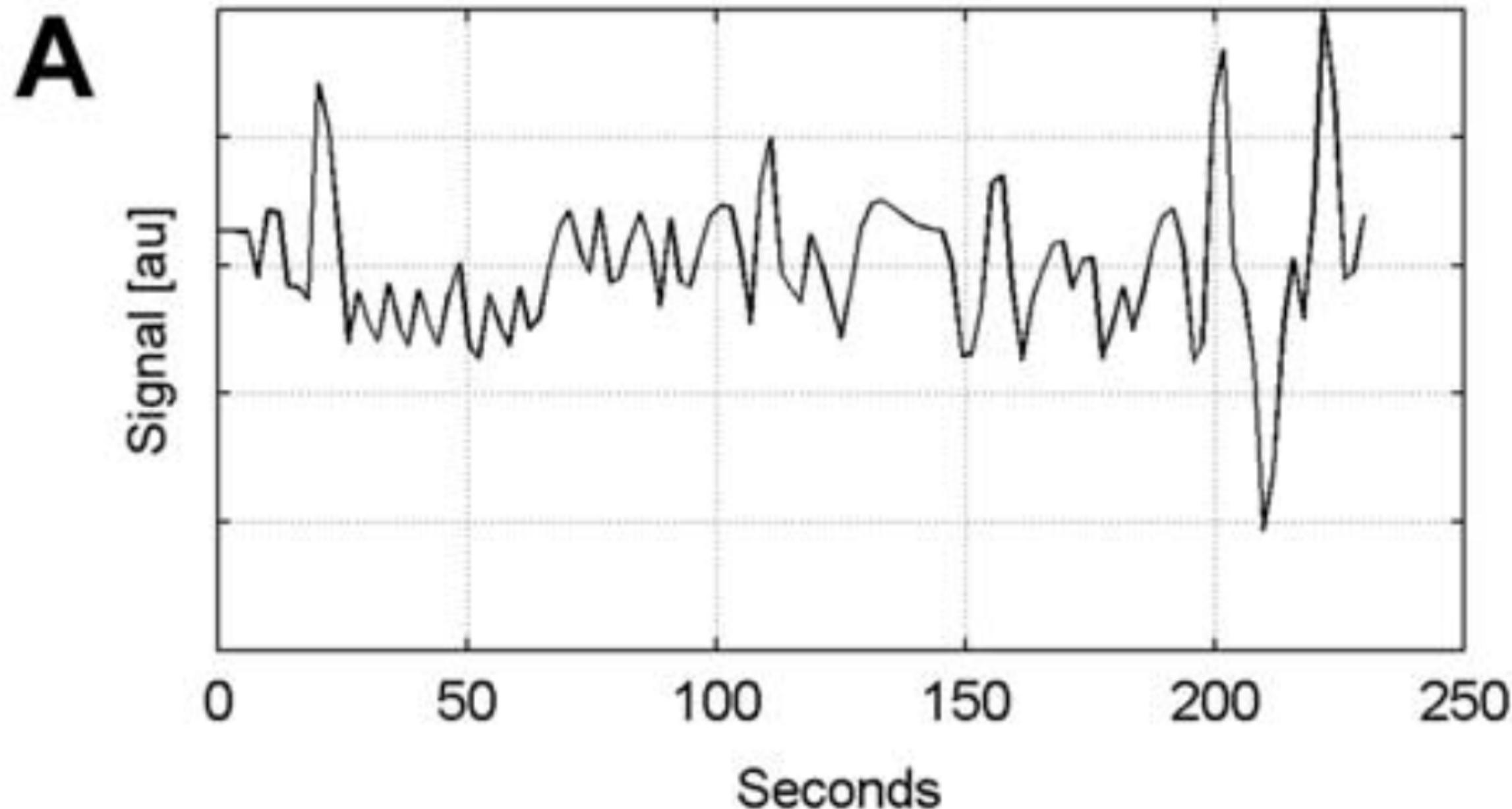
Neural activity from 20 simulated neural events.

Simulated noiseless BOLD signal generated by convolving the neural activity with a HRF.

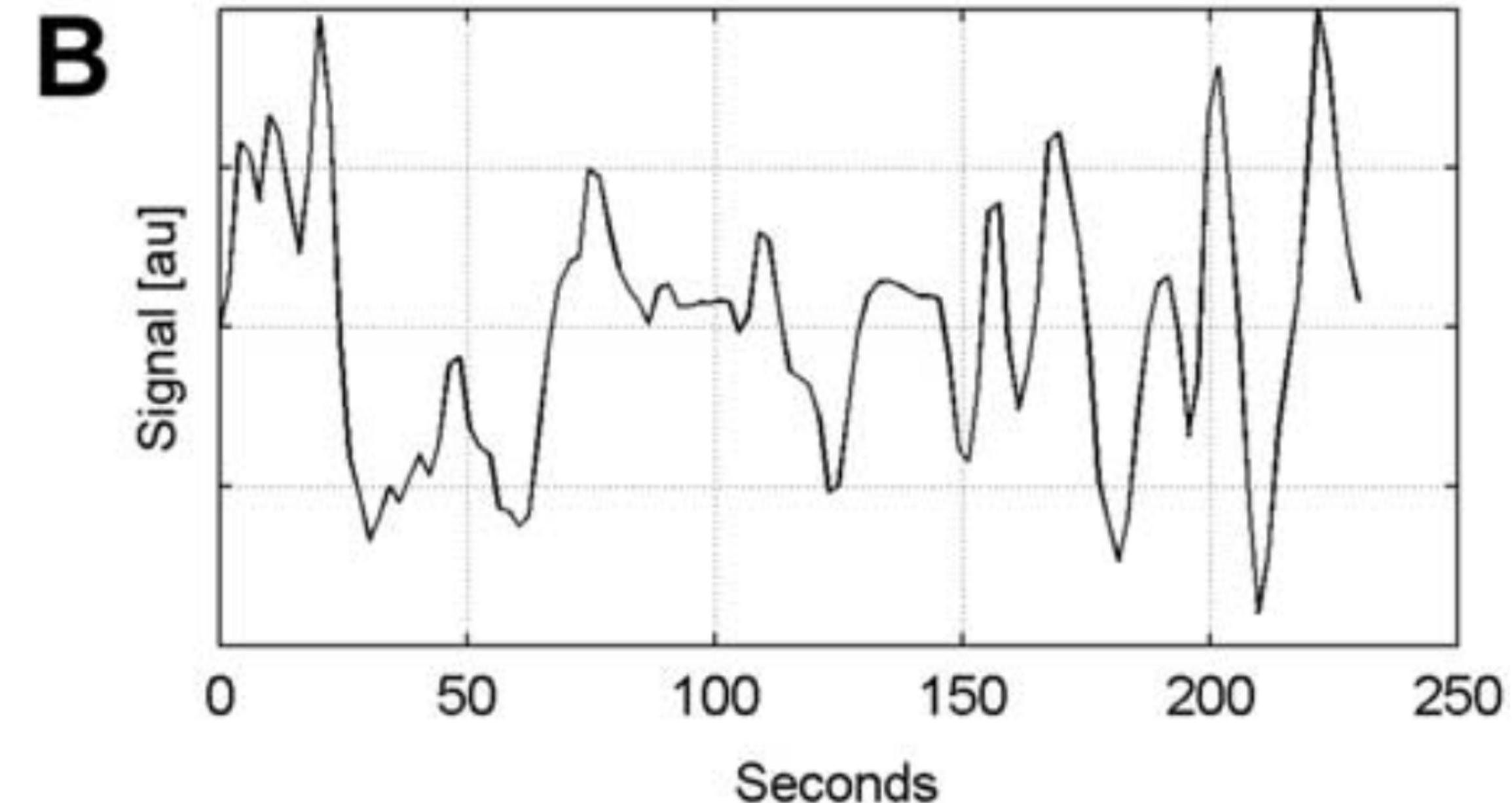
Darren R. Gitelman et al., Modeling regional and psychophysiological interactions in fMRI: the importance of hemodynamic deconvolution, *NeuroImage* **19** (2003) 200-207

Interactions

Interaction term for Bold-A with Bold-B



Interaction term for neural activity-A with neural activity-B, reconolved with a HRF



Darren R. Gitelman et al., Modeling regional and psychophysiological interactions in fMRI: the importance of hemodynamic deconvolution, *NeuroImage* **19** (2003) 200-207

Generalized PPI

Advantages of gPPI

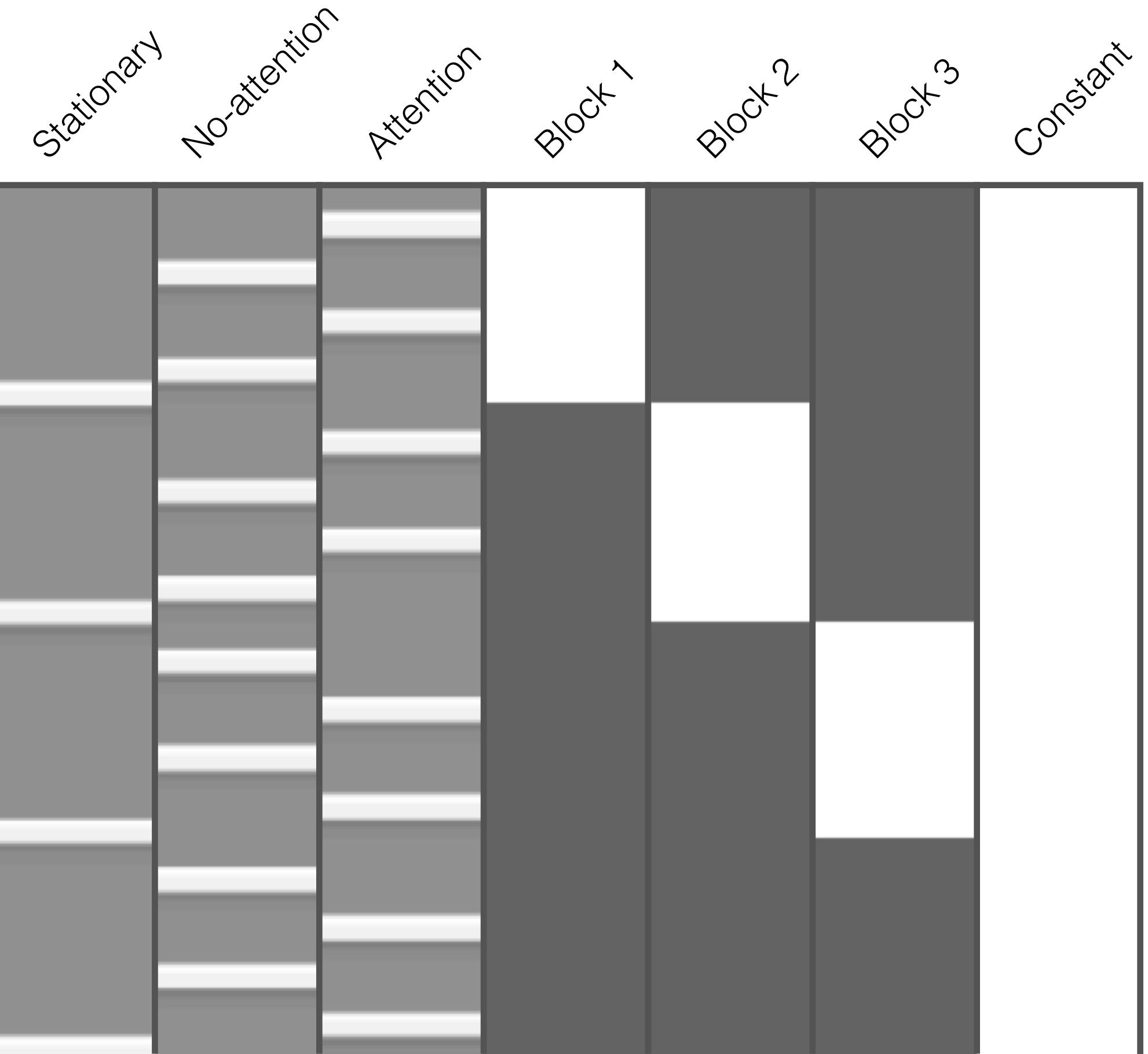
- Generalized PPI (gPPI) accommodate more than two task conditions, and may improve single-subject model fit and the specificity and sensitivity of the analyses.
- More flexible than standard PPI, as it allows for examinations of connectivity in individual conditions or a combination of individual conditions relative to baseline rather than a contrast between two conditions.

References

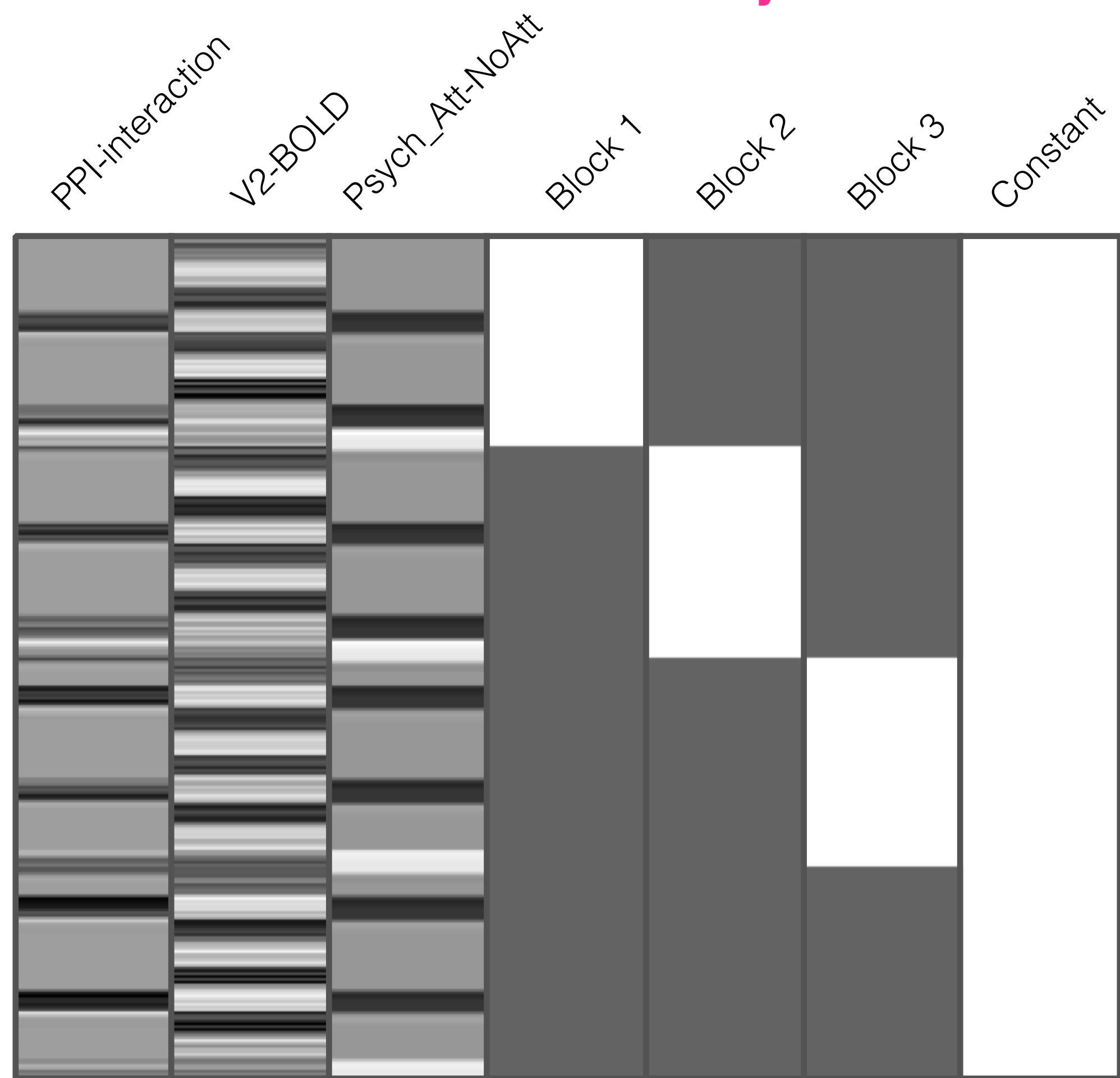
1. Donald G. McLeren *et al.*, A generalized form of context-dependent psychophysiological interactions (gPPI): A comparison to standard approaches, **NeuroImage**, 61: 1277-86 (2012)
2. Josh M. Cisler *et al.*, A comparison of statistical methods for detecting context-modulated functional connectivity in fMRI, **NeuroImage**, 84: 1042-52 (2014)

Design Matrices - Task vs. sPPI

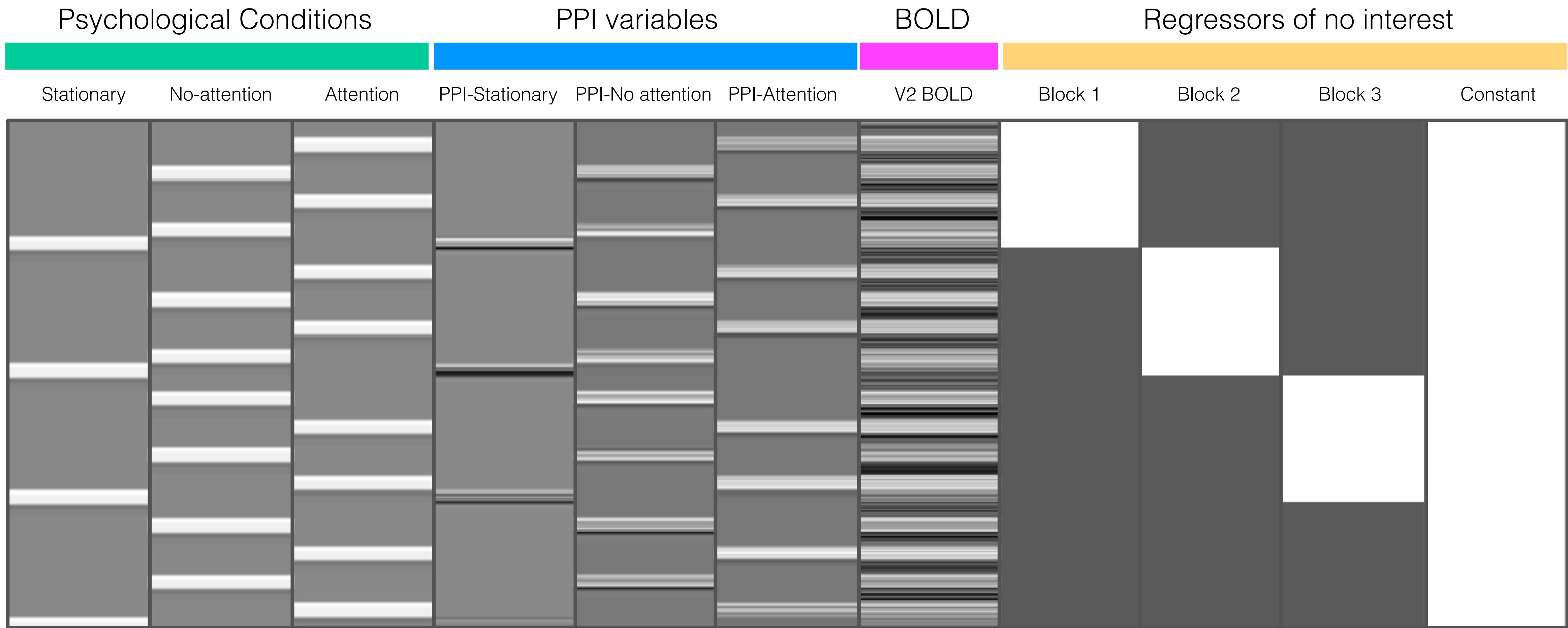
GLM for Task Related Activation



Standard PPI Analysis



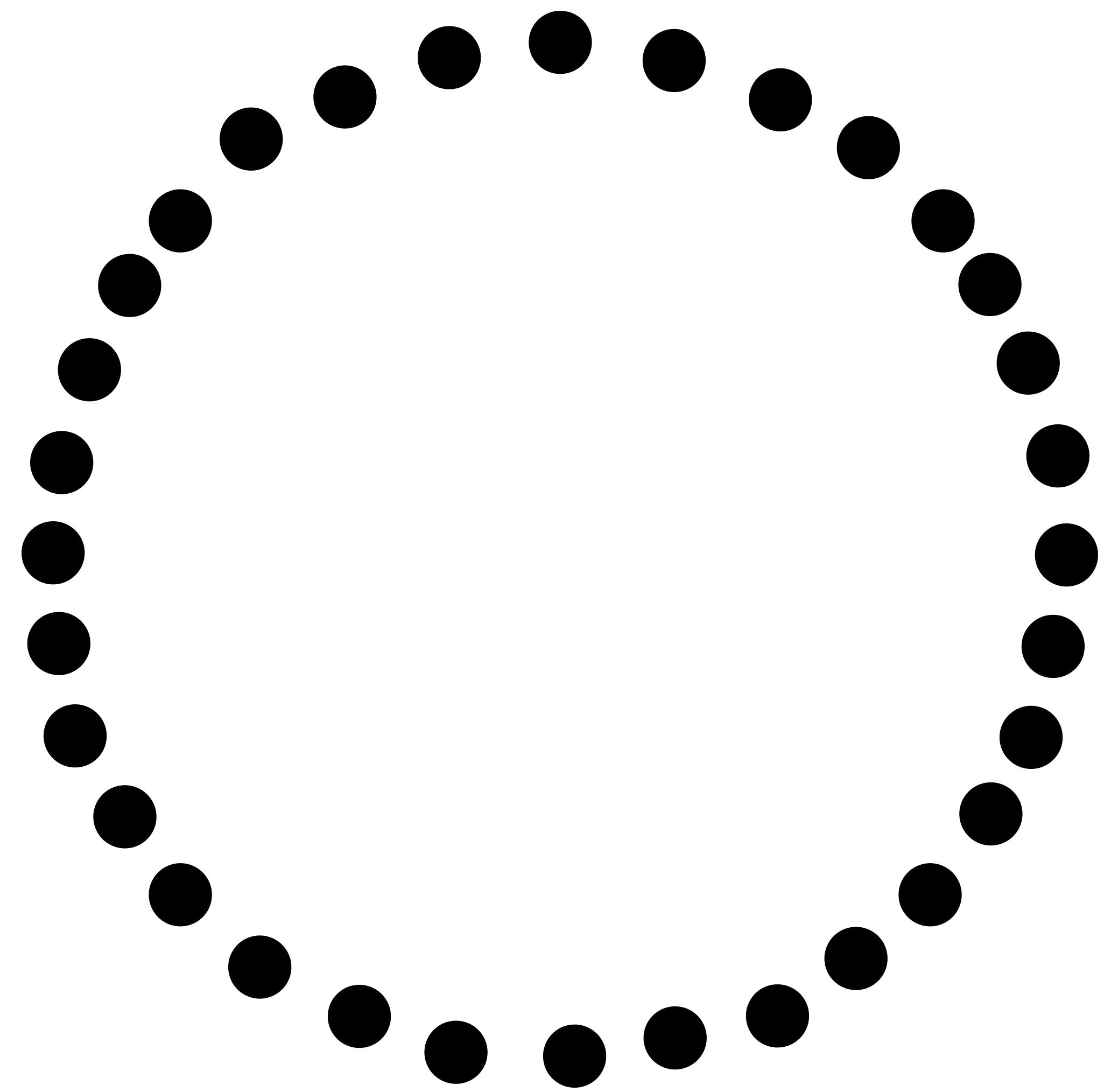
Design Matrices - gPPI



PPI Steps in SPM12

Dataset and Experiment Design

- Preprocessed example fMRI dataset can be downloaded from
<http://www.fil.ion.ucl.ac.uk/spm/download/data/attention/attention.zip>
- Interscan interval (TR) = 3.22 second
- In **Attention** condition, the subject viewed 250 dots moving radially from the center at 4.7° per second and were asked to detect changes in radial velocity.
- In **No-attention** condition, the subjects were asked simply to view the moving dots.
- In **Stationary** condition, the subjects viewed stationary dots.
- In all conditions, the subject fixated the center of the screen. In a prescanning session, the subjects were given five trials with five speed changes (reducing to 1%).



A goal of this practice

- Examining the change in **functional connectivity** between V2 and V5 while the subject observes visual motion (radially moving dots) under the **experimental treatments of attending vs. not attending** to the speed of the dots.
- Psychophysiological interaction conceived of as looking for a significant difference in the regression slopes of V1 vs. V5 activity under the influence of attentional states.

PPI Analysis Steps

- Performing a standard GLM analysis (*i.e.*, 1st level analysis)
- Extracting BOLD signal from a source region identified in the GLM analysis
- Forming the interaction term as:
psycho (experimental treatment) × **physiological** (neural signal)
- Performing a second GLM analysis that includes the interaction term, the source region's extracted signal and the experimental vector in the design.

PPI Analysis in SPM12

Step 1: GLM analysis (*i.e.*, 1st level analysis)

실습 데이터 다운로드

Raw data:

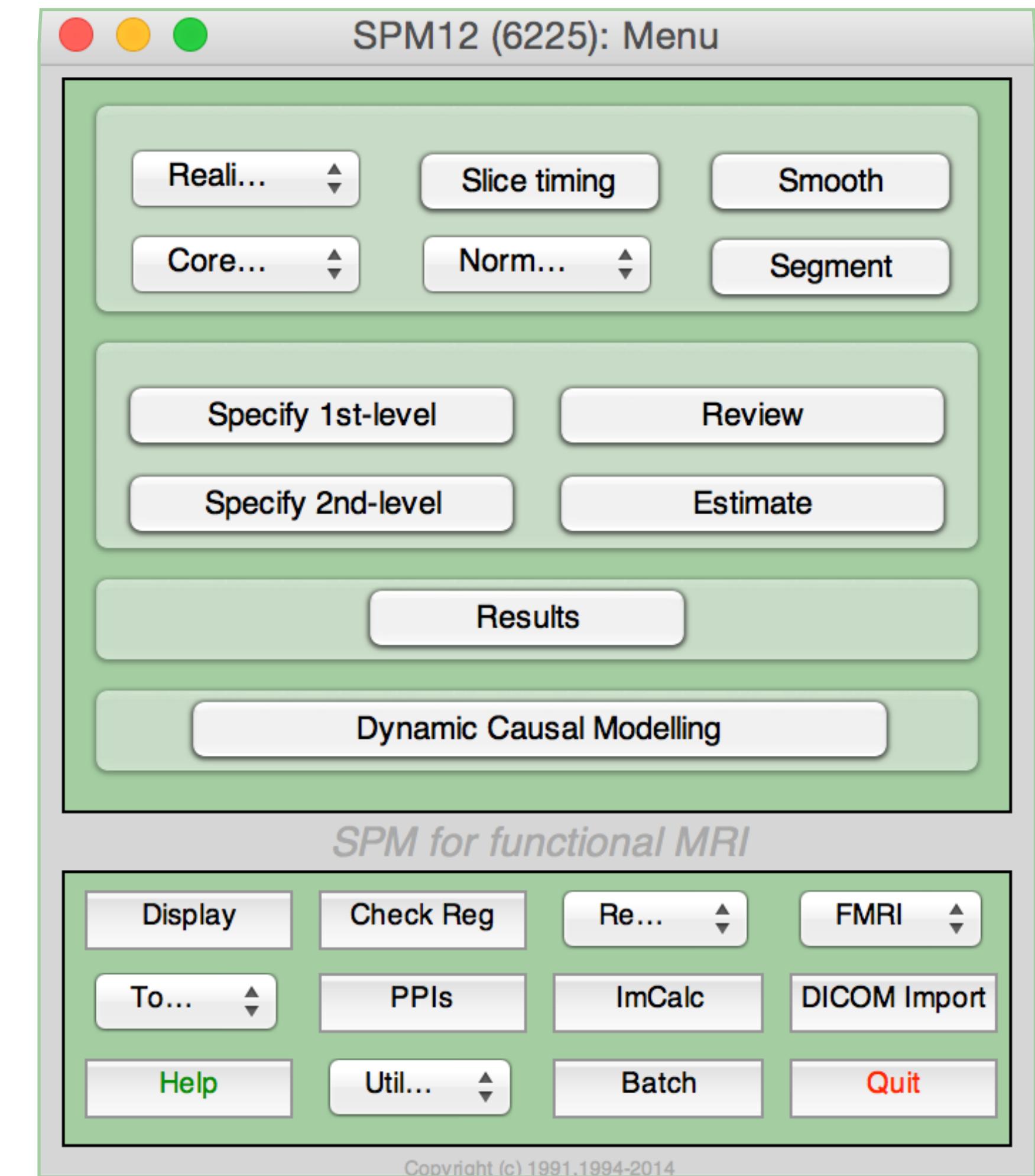
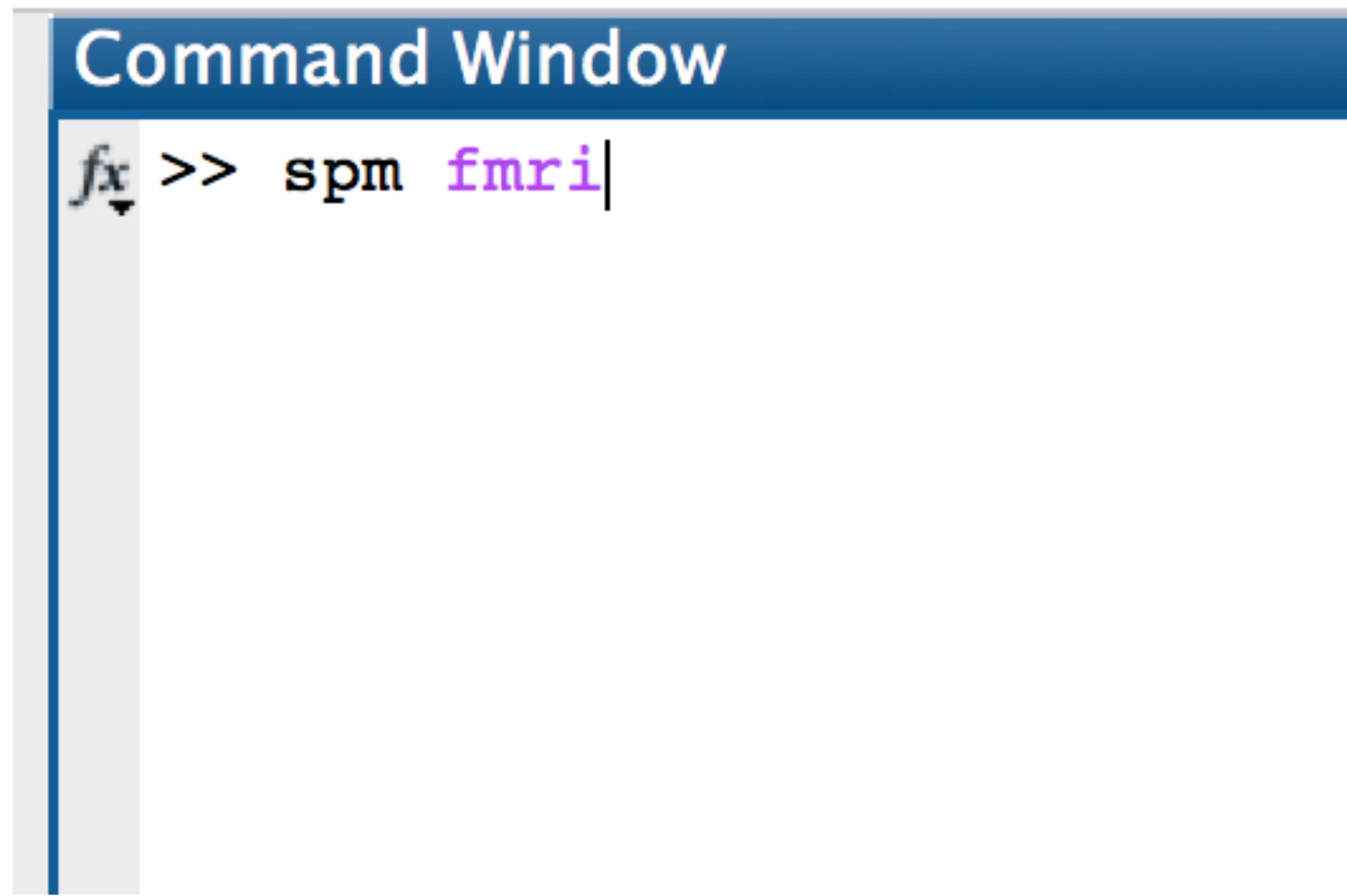
<http://www.fil.ion.ucl.ac.uk/spm/download/data/attention/attention.zip>

First-level 분석이 완료된 data:

https://drive.google.com/drive/folders/0B6863JbB_YV-MDIJcjRKTkxjV1k

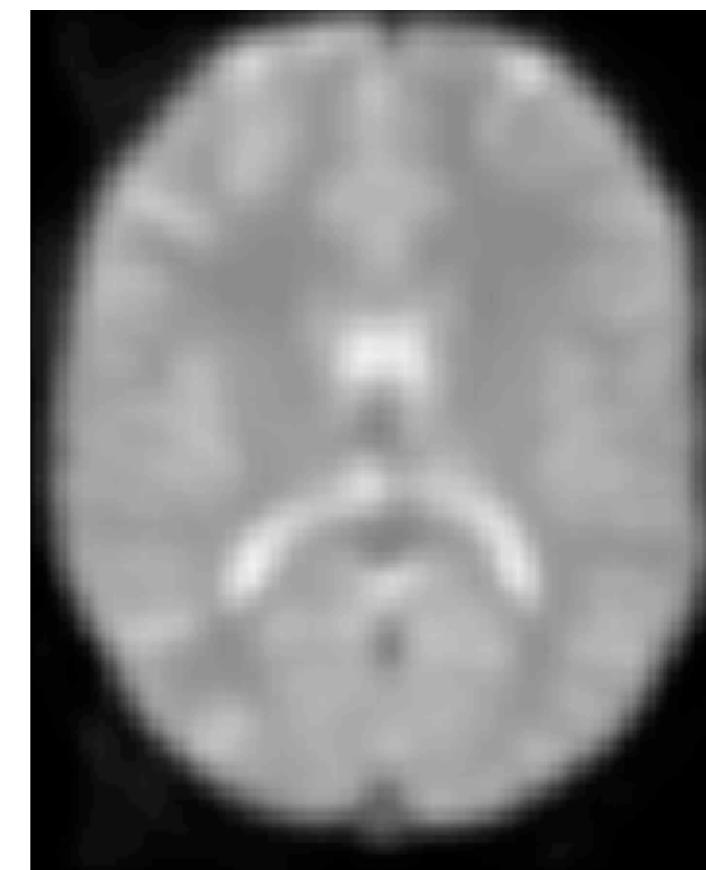
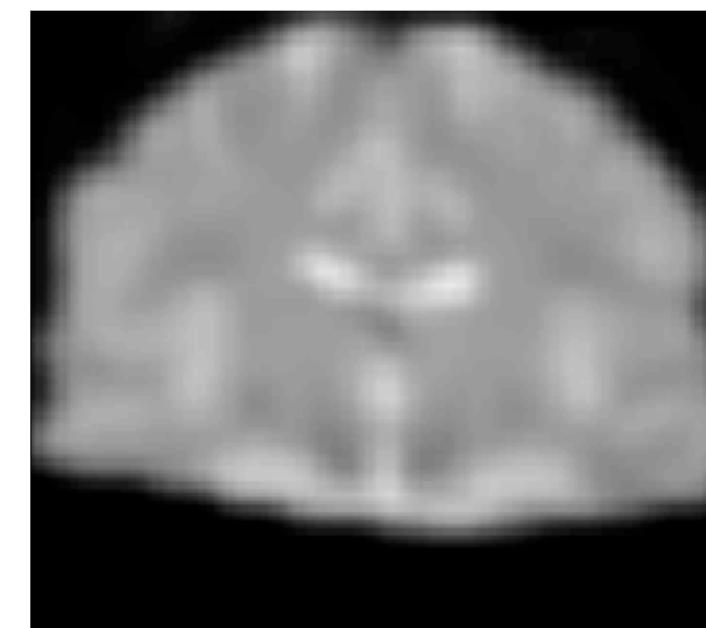
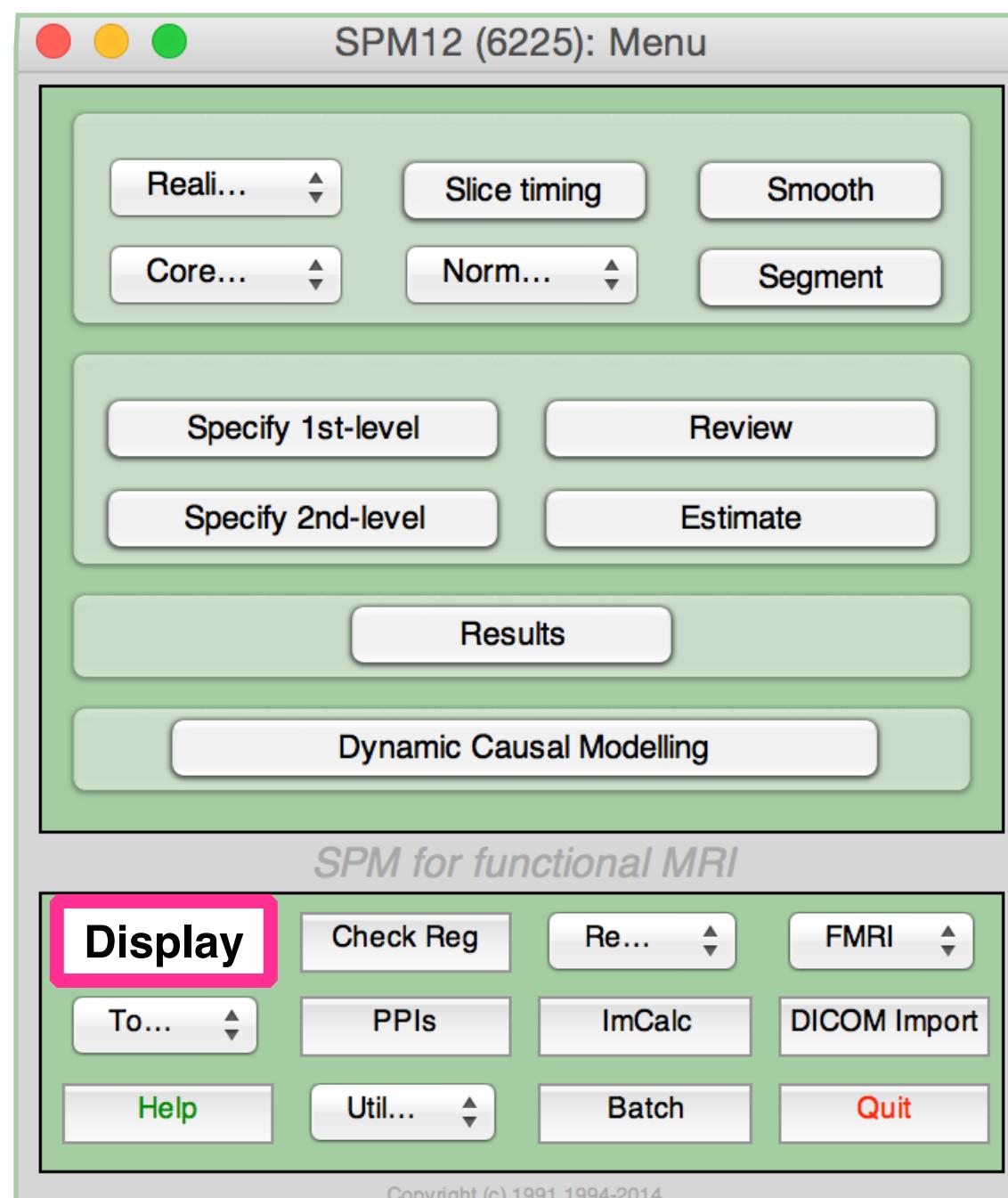
Execute SPM ('fMRI')

type '**spm fmri**'
in command window



Explore Image Files

A smoothed & normalised fMRI Image



snffM00587_0016.img

...

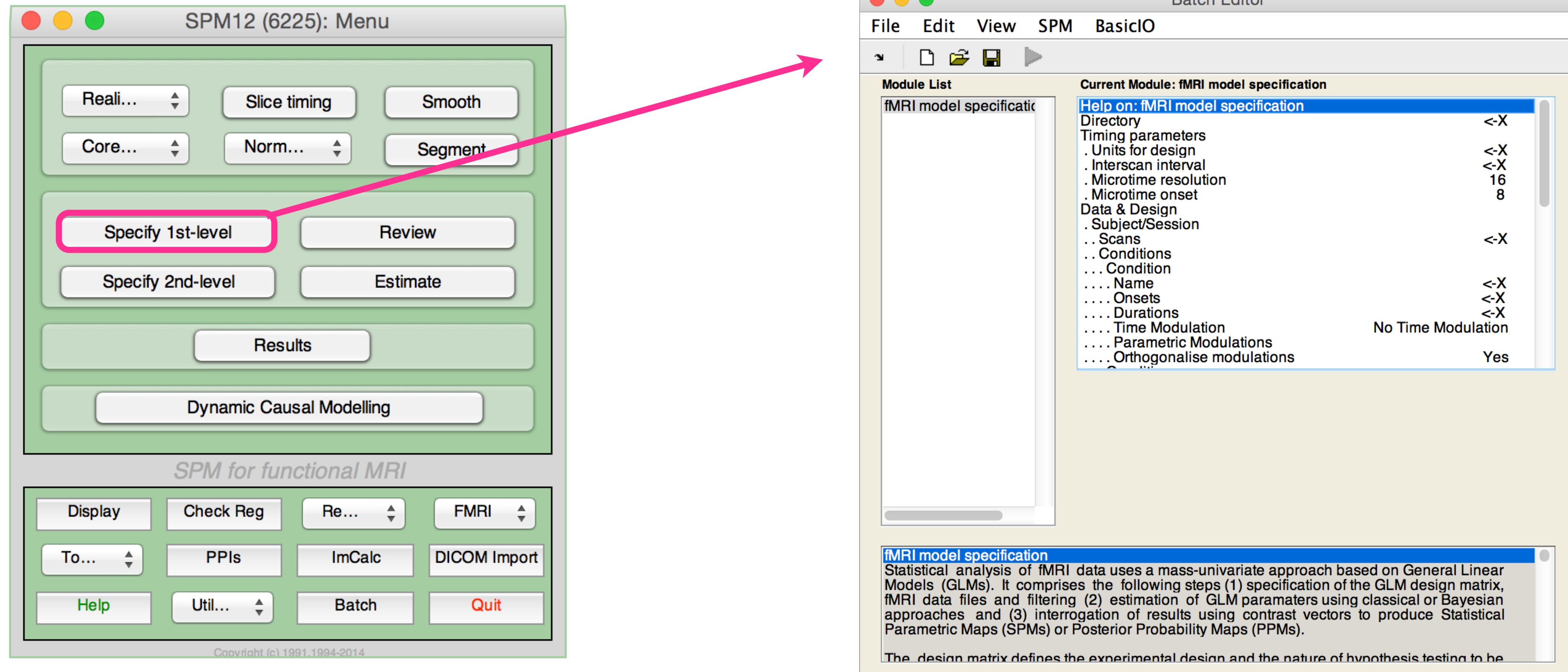


A normalised T1 Image



nsM00587_0002.img

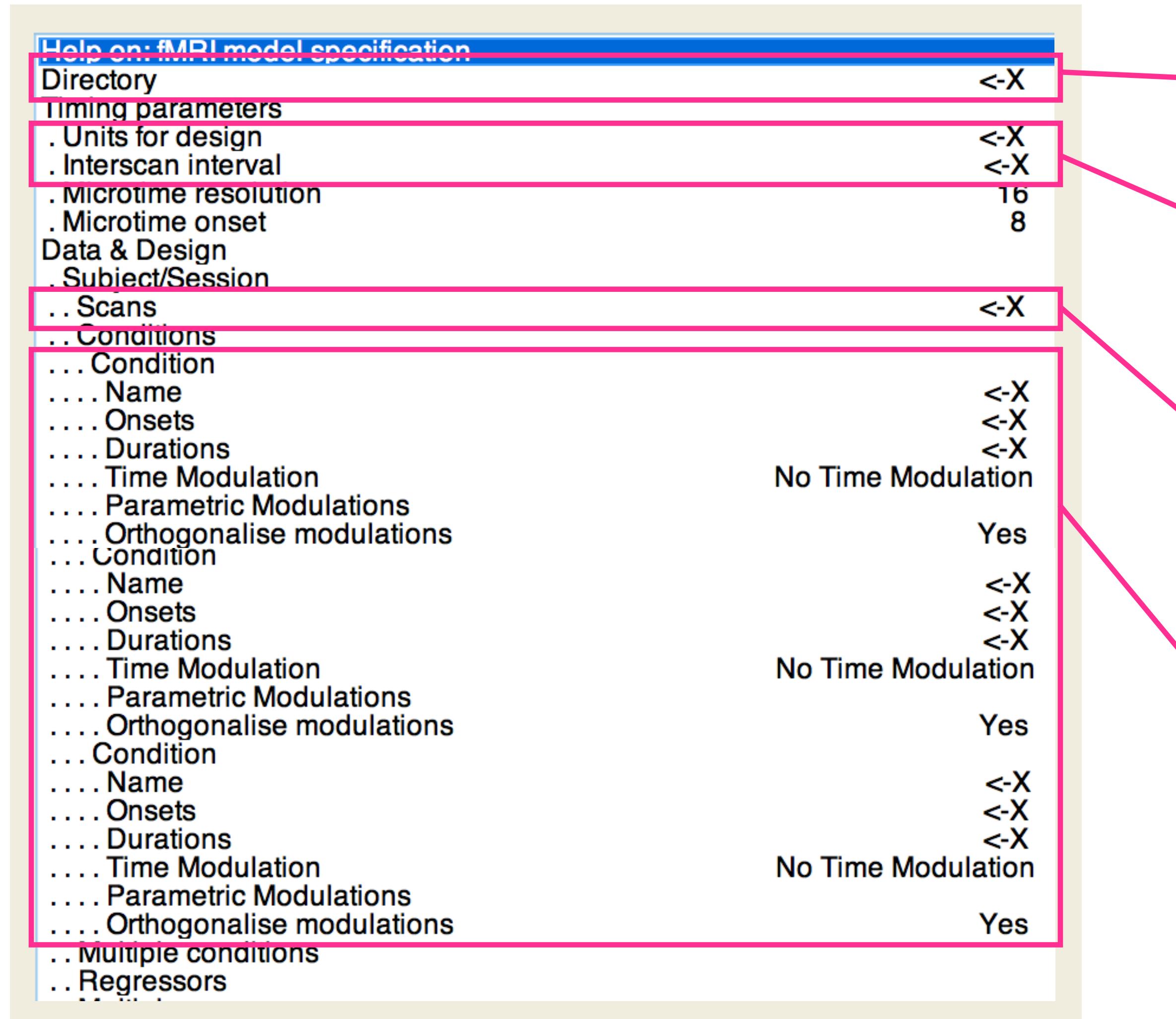
GLM analysis - 1st level (1/3)



Load Condition Parameters

```
Command Window
>> load factors.mat % same information with multi_condition.mat
>> whos
  Name      Size            Bytes  Class     Attributes
  att       1x8              64    double
  natt      1x8              64    double
  stat      1x4              32    double
>> att
att =
    10    50   100   140   210   250   300   340
>> natt
natt =
    30    70   120   160   190   230   280   320
>> stat
stat =
    80   170   260   350
```

GLM analysis - 1st level (2/3)



Directory: Select a directory to save outputs

Timing parameters

- Units for design: scans
- Interscan interval: 3.22

Subject/Session

- Scans: select all functional images (snff*.img)

Condition 1:

- Name=Stationary, Onset=stat, Durations=10

Condition 2:

- Name=No-attention, Onset=natt, Durations=10

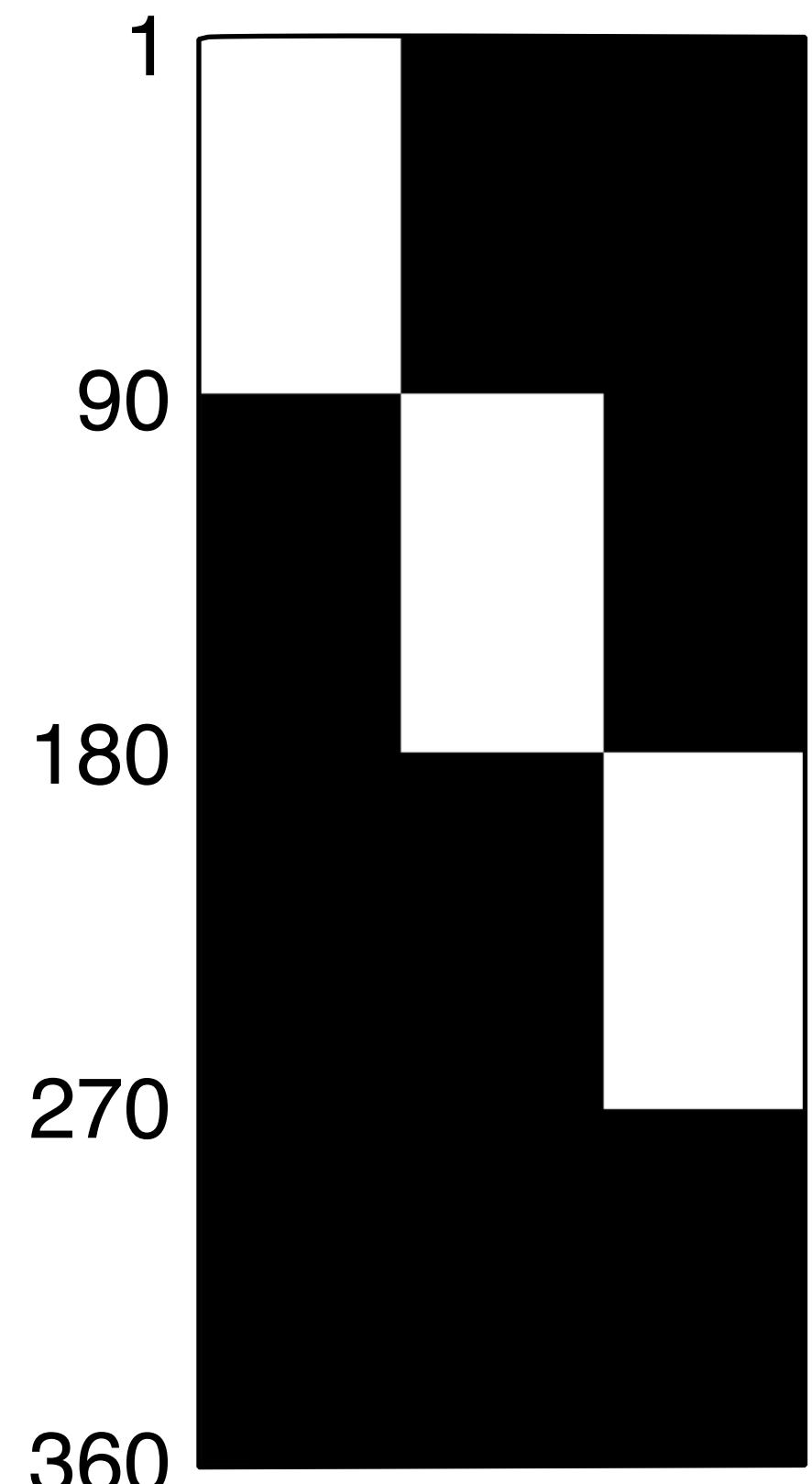
Condition 3:

- Name=Attention, Onset=att, Durations=10

Load Regressor Parameters

Command Window

```
>> load block_regressors.mat  
  
>> whos  
  
Name          Size            Bytes  Class      Attributes  
  
block1        360x1           2880  double  
block2        360x1           2880  double  
block3        360x1           2880  double  
  
>> figure;  
  
>> imagesc([block1, block2, block3]);  
  
>> load multi_block_regressors  
  
>> R    % the same as [block1, block2, block3]
```



GLM analysis - 1st level (3/3)

.... Time Modulation	No Time Modulation
.... Parametric Modulations	Yes
.... Orthogonalise modulations	Attention 8x1 double 10
.... Condition	No Time Modulation
.... Name	Yes
.... Onsets	Attention 8x1 double 10
.... Durations	No Time Modulation
.... Time Modulation	Yes
.... Parametric Modulations	Attention 8x1 double 10
.... Orthogonalise modulations	No Time Modulation
... Multiple conditions	Yes
.. Regressors	
.... Regressor	<-X
.... Name	<-X
.... Value	<-X
.... Regressor	<-X
.... Name	<-X
.... Value	<-X
.... Regressor	<-X
.... Name	<-X
.... Value	<-X
.. Multiple regressors	
.. High-pass filter	128
Editorial decision	

Regressor 1:

- Name=Block 1, Value=block1

Regressor 2:

- Name=Block 2, Value=block2

Regressor 3:

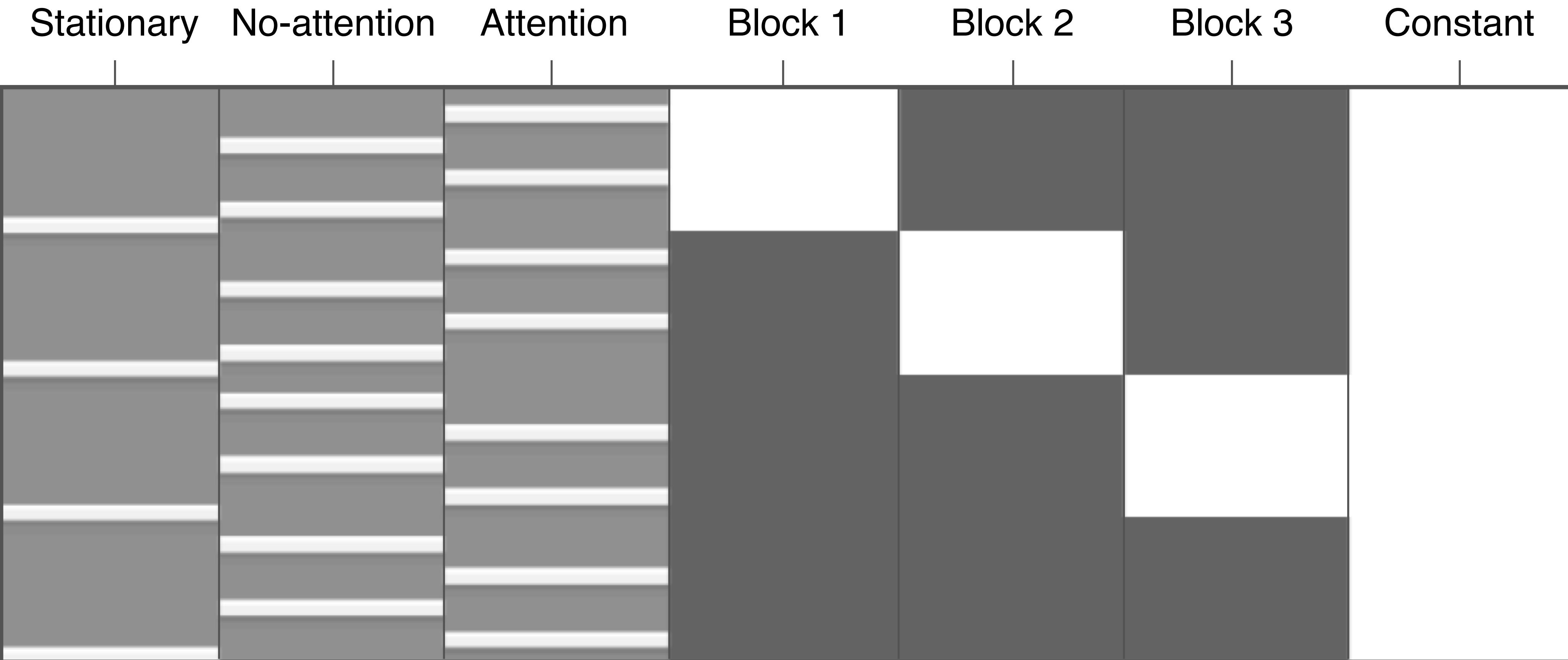
- Name=Block 3, Value=block3

High-pass filter:

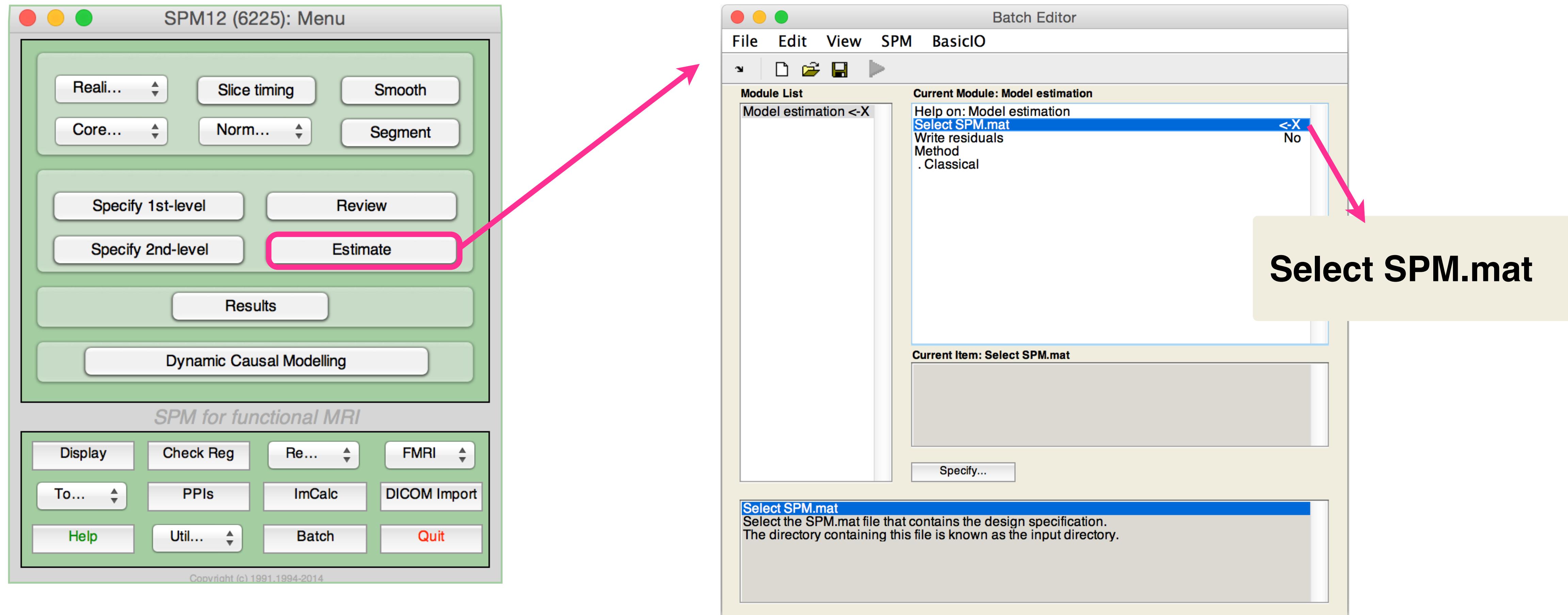
- 192 (in second, i.e., freq. >1/192 Hz)

Note) Most designs will use a high-pass filter value of 128 (default value). However, this dataset requires a longer high-pass filter in order not to lose the low frequency components of the design.

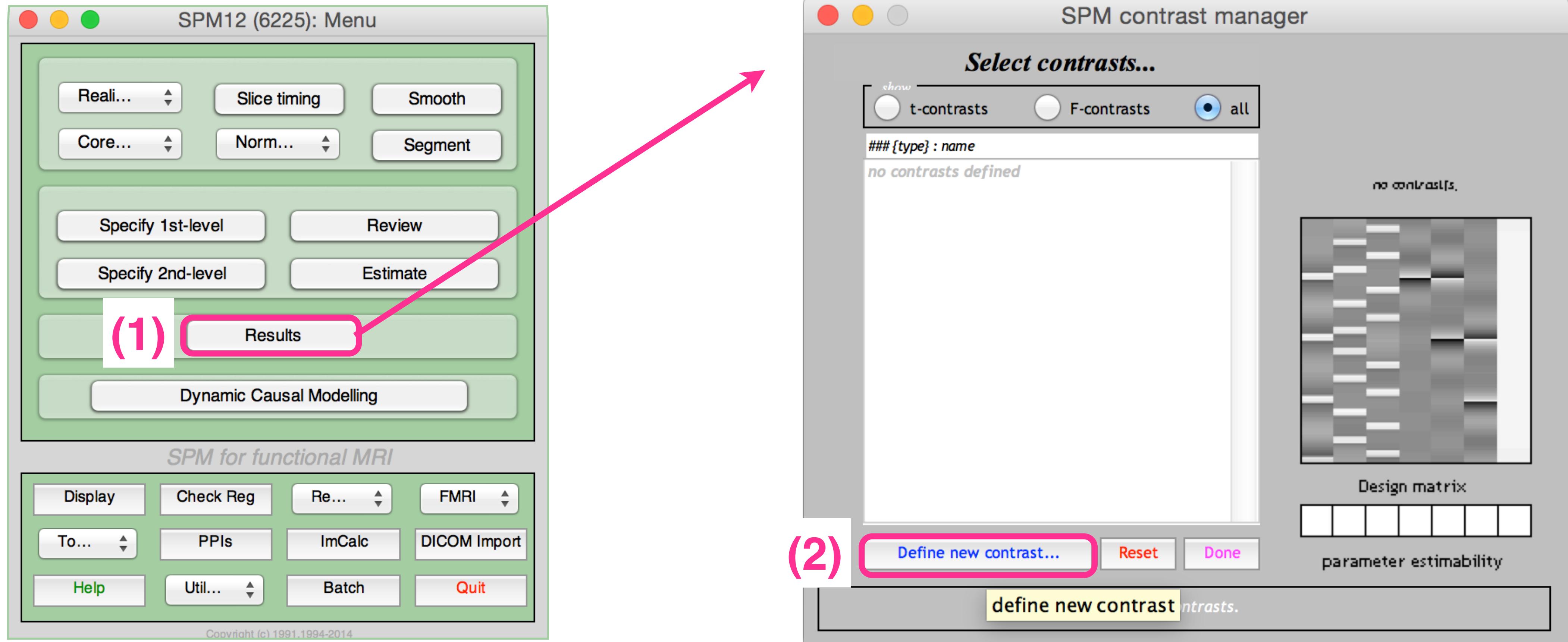
Design Matrix



GLM analysis - Estimate

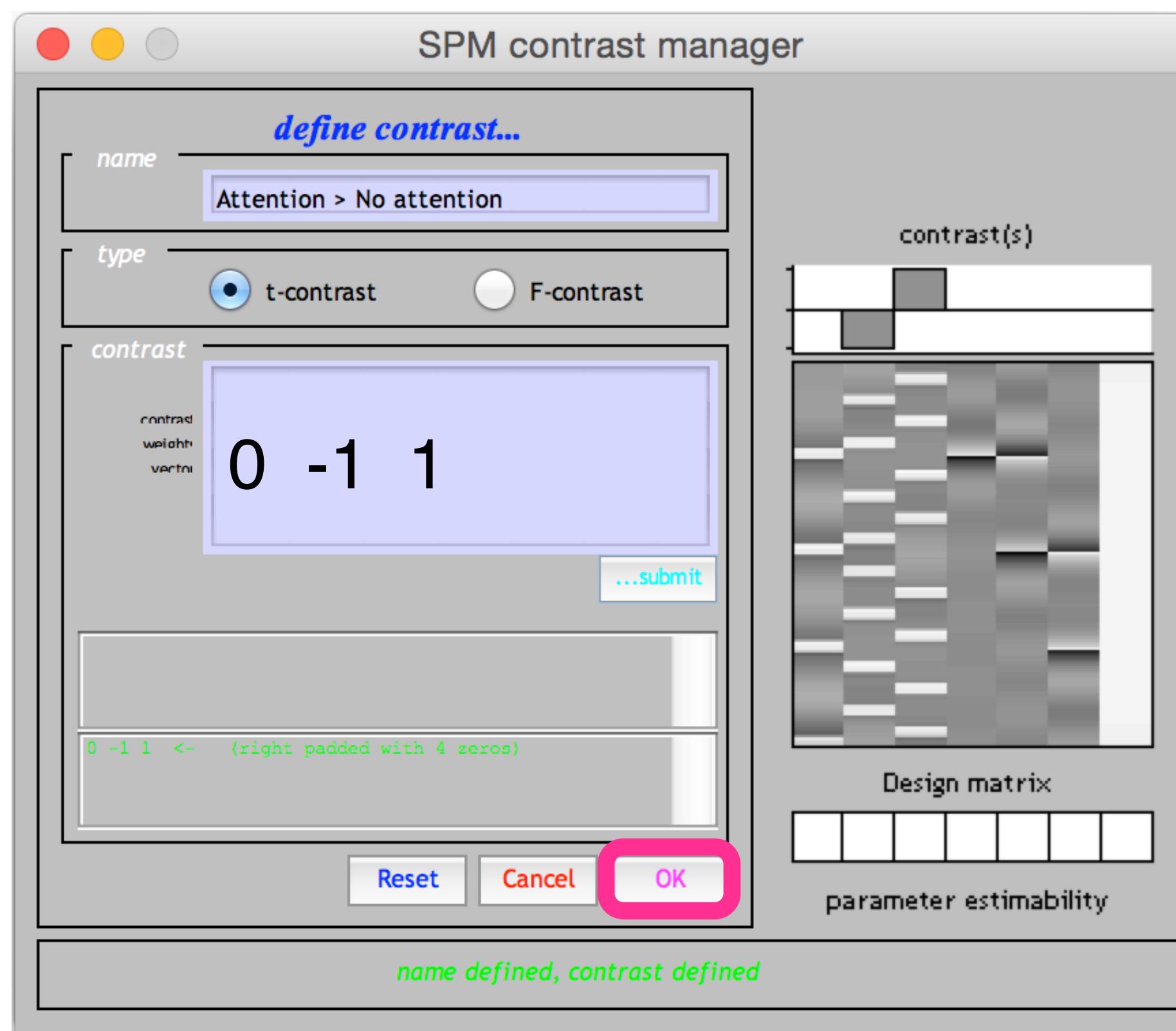


GLM analysis - SPM Results

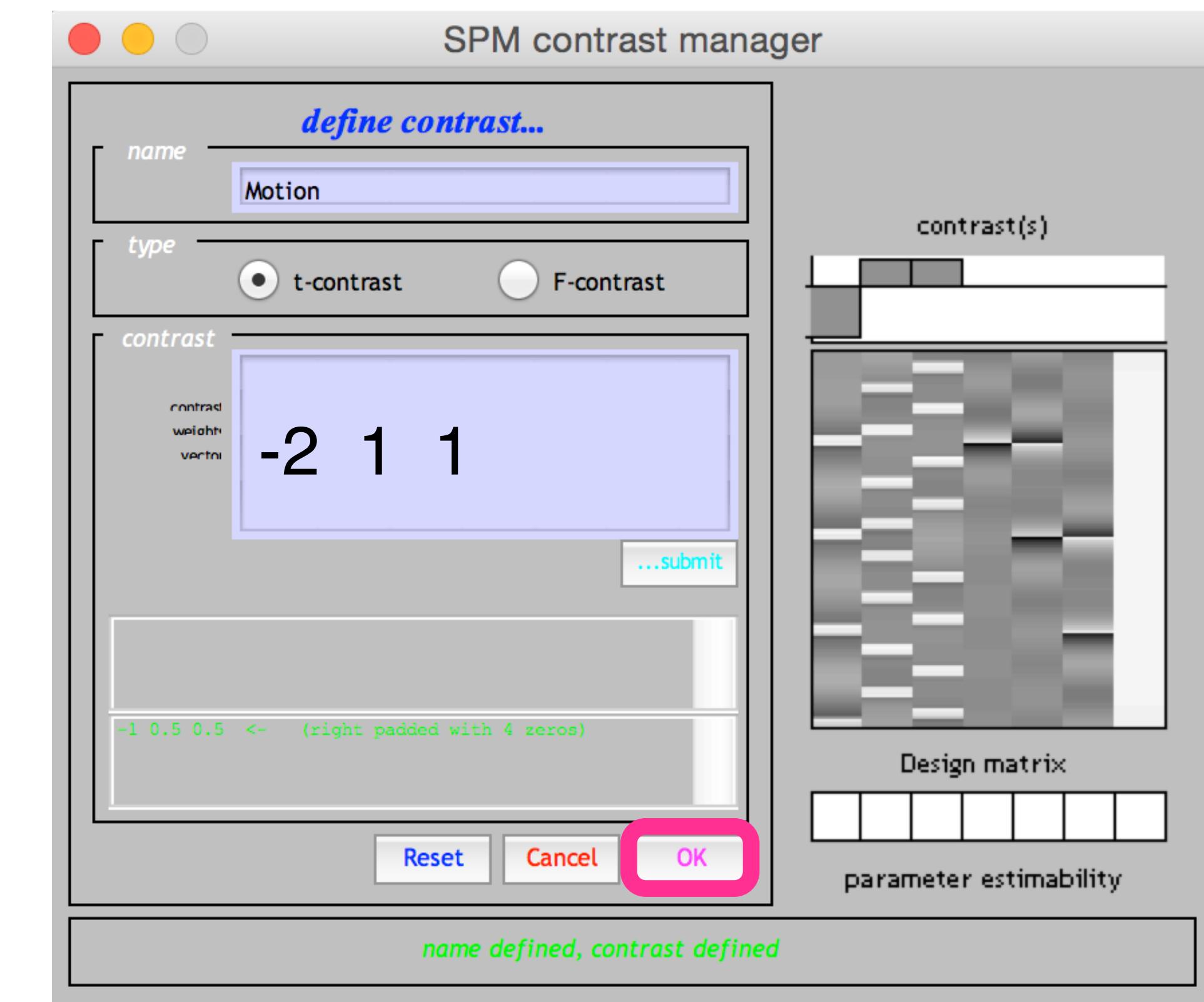


GLM analysis - Contrast

Contrast for “Attention > No Attention”



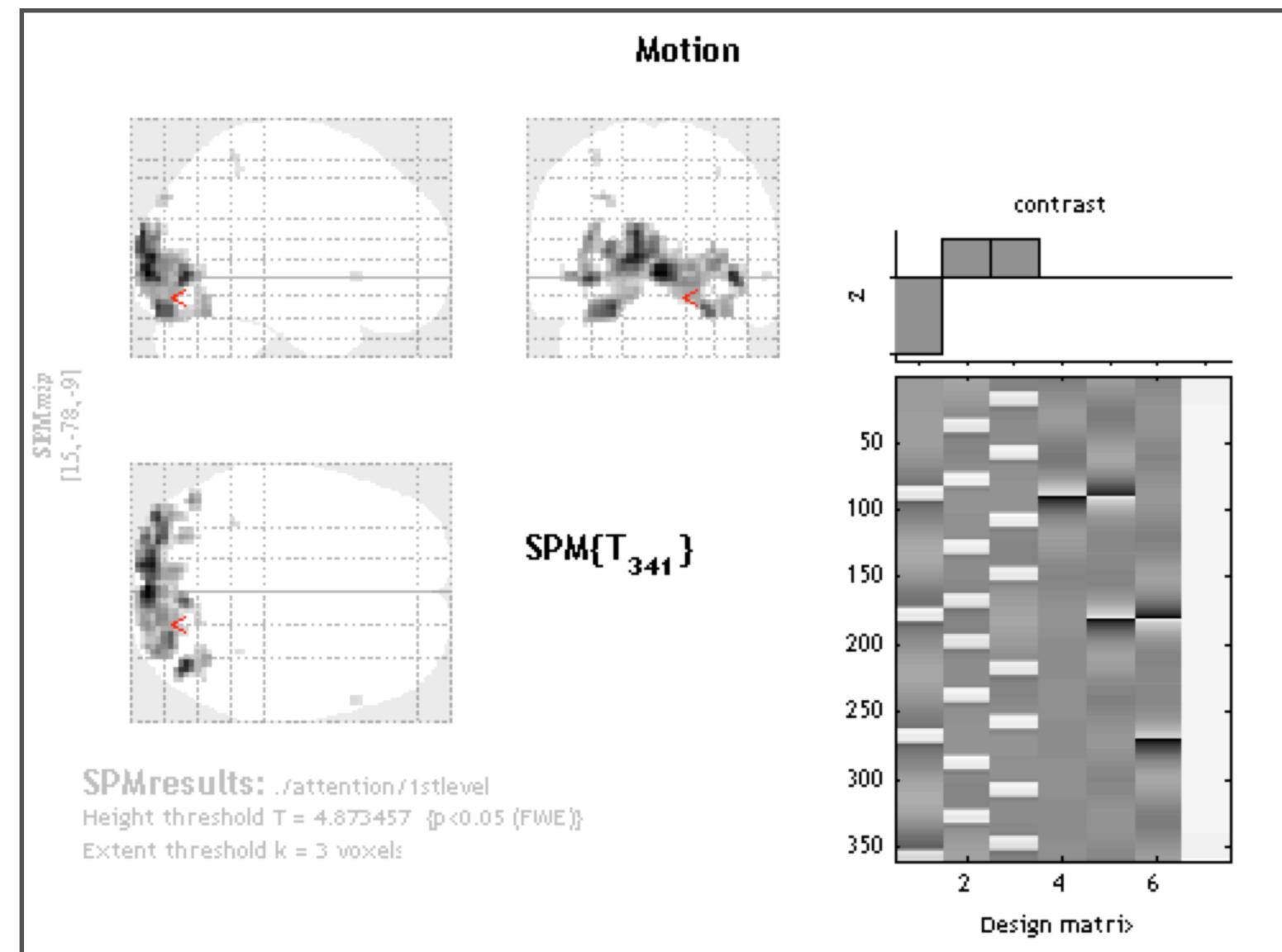
Contrast for Motion (“Moving > Stationary”)



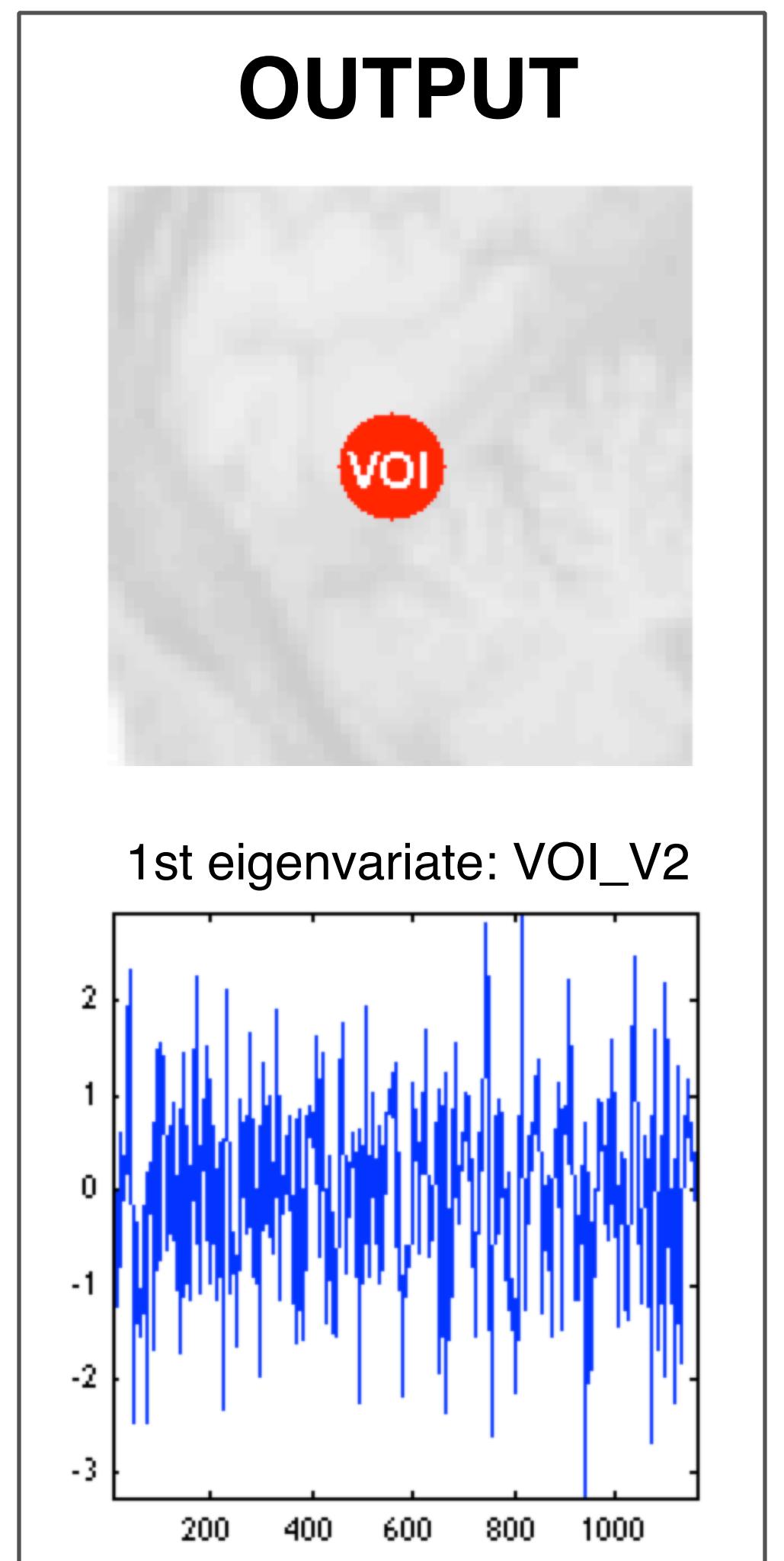
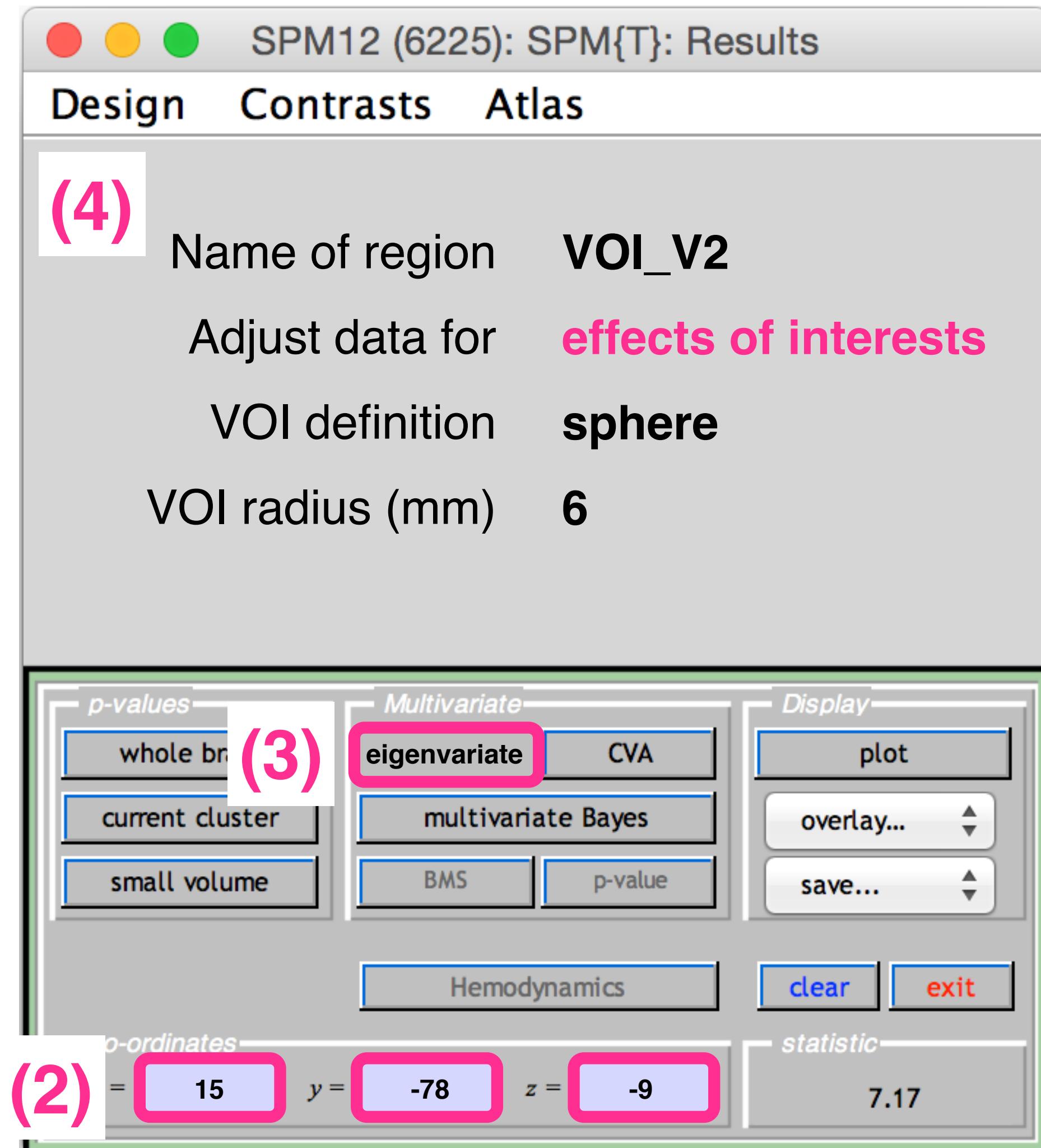
PPI Analysis in SPM12

Step 2: Extracting eigenvariate in V2 region

Extracting Eigenvariates



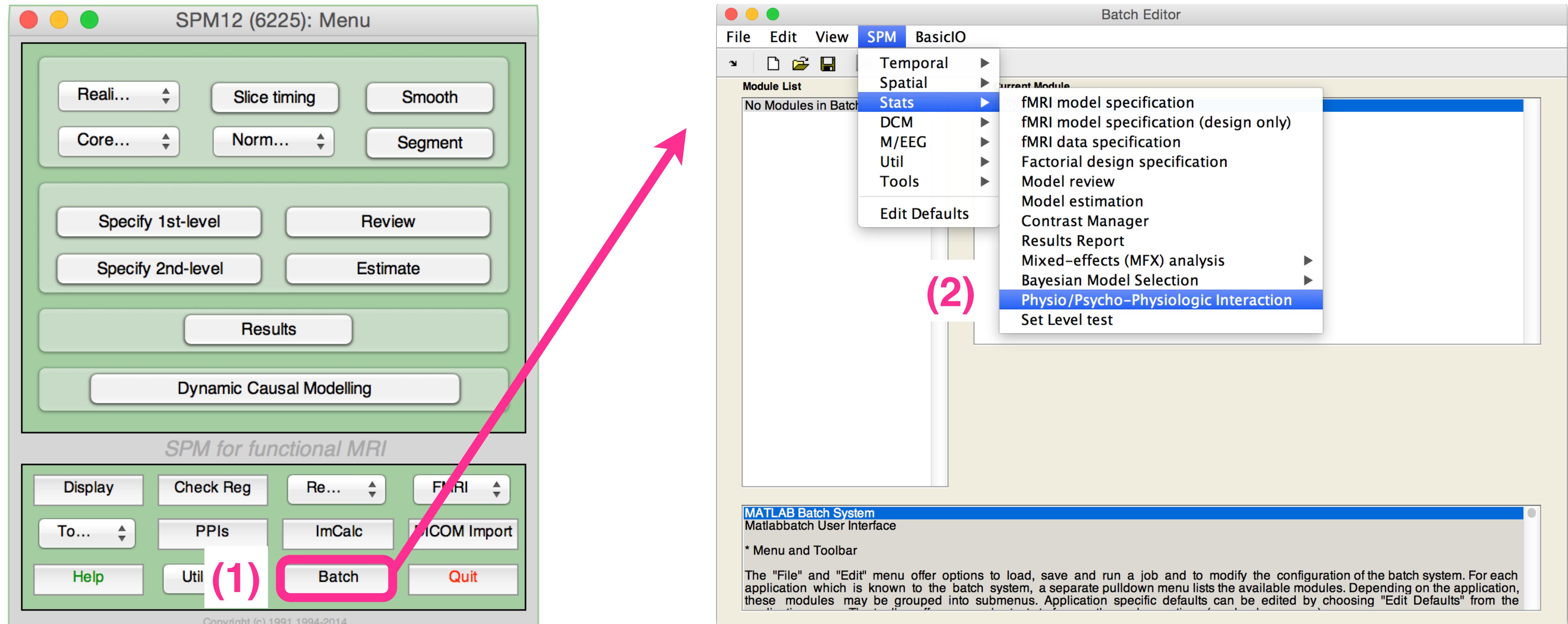
(1)
Select the Motion contrast,
- do not include masking
- FWE p<0.05
- cluster size threshold of 3



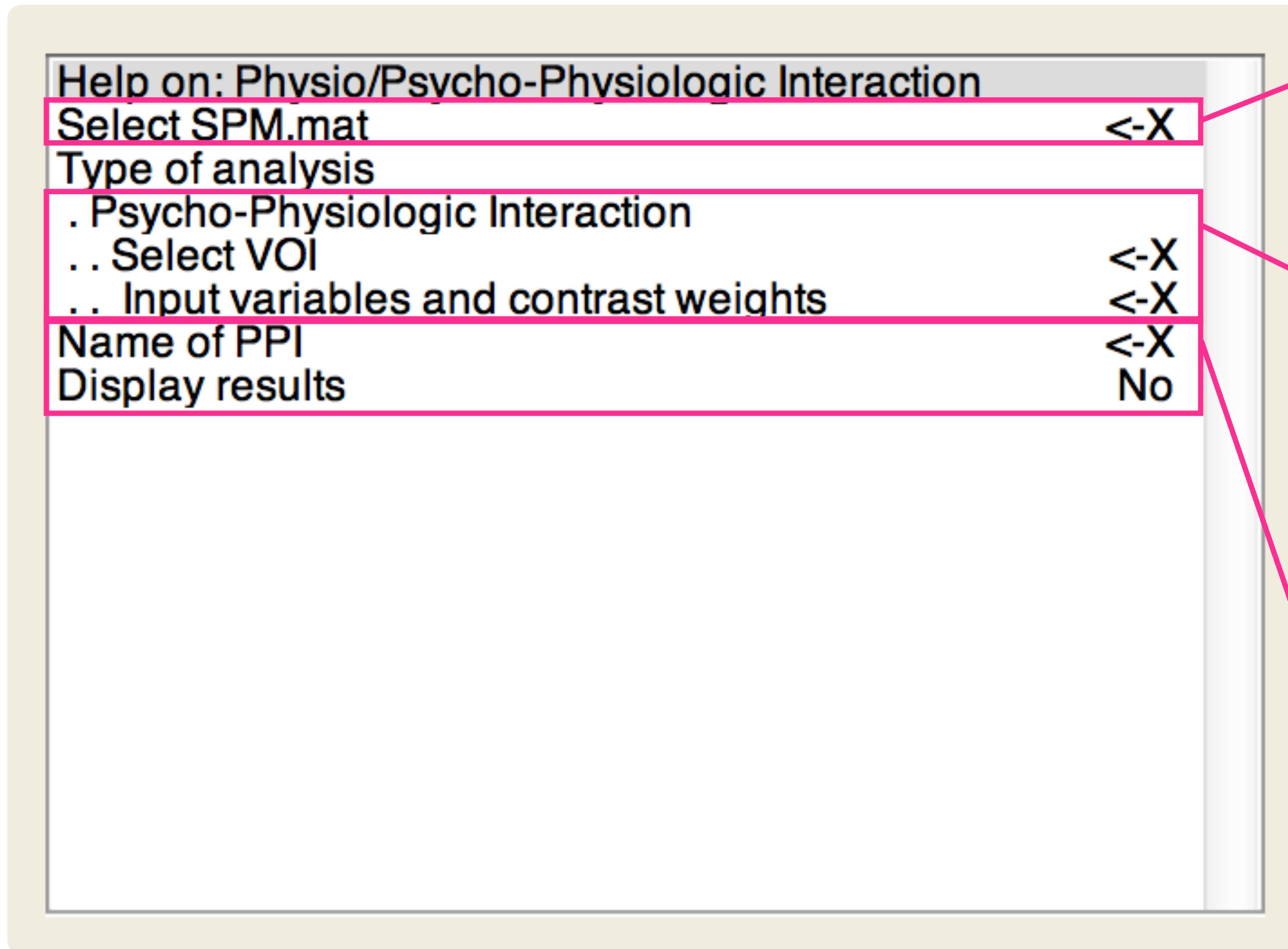
PPI Analysis in SPM12

Step 3: Create PPI variables

PPI analysis - Create PPI variable



PPI analysis - Create PPI variable



Select SPM.mat

- Select 1st level analysis result file

Type of analysis:

- Psycho-Physiologic Interaction

Select VOI: VOI_VOI_V2_1.mat

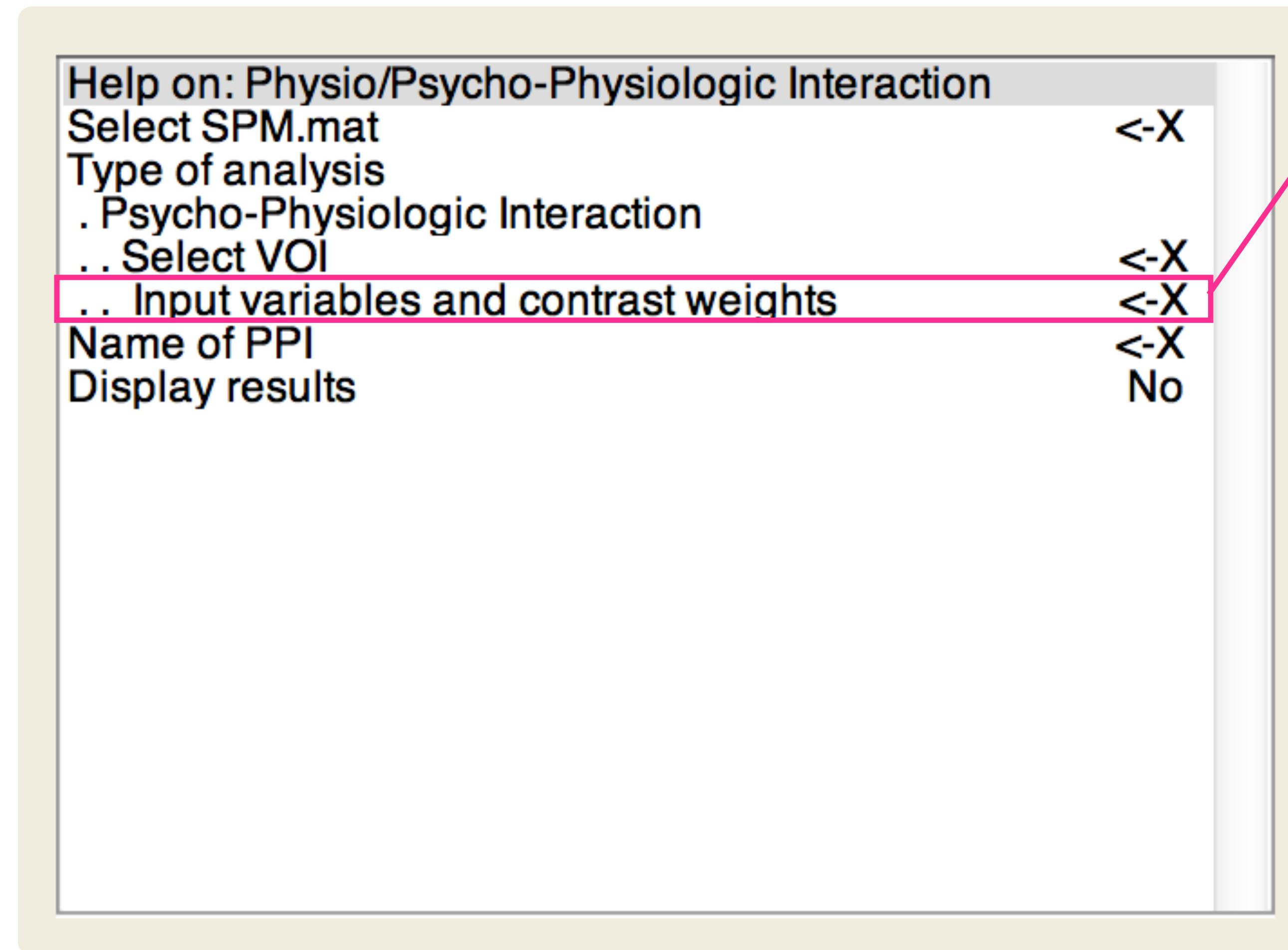
Input variables and contrast

weights: [2 1 -1; 3 1 1]

Name of PPI: V2x(Att-NoAtt)

Display results: Yes

Continued ...



Input variables and contrast weights: [2 1 -1; 3 1 1]

The number of conditions included in the PPI

A diagram illustrating the mapping of conditions to contrast weights. Three conditions are listed on the left: 1: Stationary, 2: No attention, and 3: Attention. Blue arrows point from these labels to the corresponding columns in the contrast weight matrix below.

1: Stationary	2	1	-1
2: No attention	3	1	1

- 1: Stationary
2: No attention
3: Attention

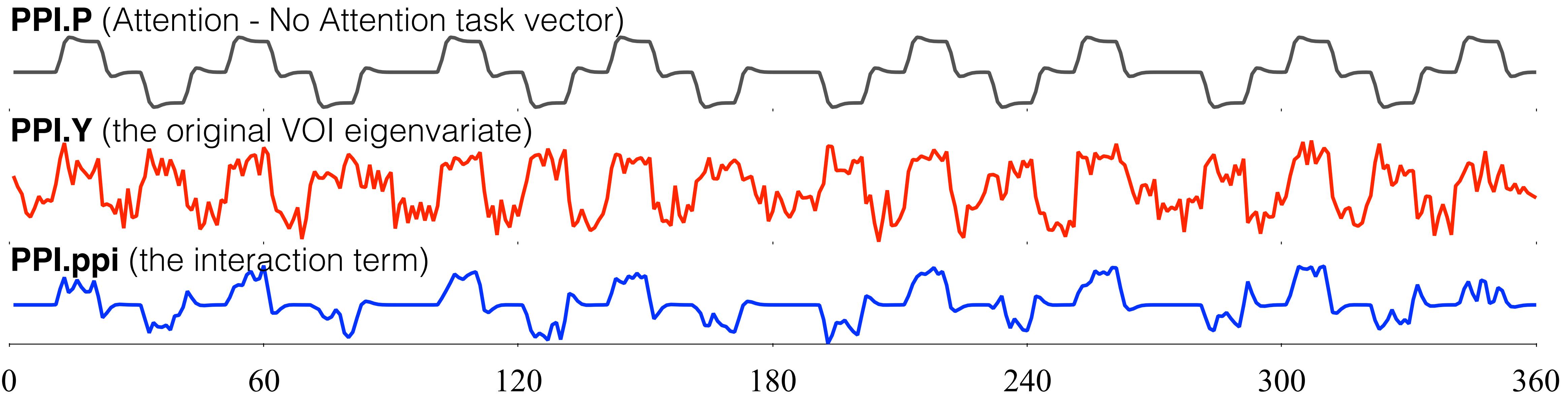
Generally be a 1 unless there are parametric effects

Contrast Weight

Load PPI Output Parameters

Command Window

```
fx >> load PPI_V2x(Att-NoAtt).mat  
  
>> figure; plot(PPI.P) % PSY convolved with HRF for psychophysiological interactions  
  
>> figure; plot(PPI.Y) % Original BOLD eigenvariate.  
  
>> figure; plot(PPI.ppi) % PSY*(neural level activity at V2) convolved with the HRF
```



PPI Structure

PPI.ppi	= (PSY*xn or xn1*xn2) convolved with the HRF
PPI.y	= Original BOLD eigenvariate. Use as covariate of no interest.
PPI.P	= PSY convolved with HRF for psychophysiological interactions, or in the case of physiophysiological interactions contains the eigenvariate of the second region.
PPI.name	= Name of PPI
PPI.xY	= Original VOI information
PPI.xn	= Deconvolved neural signal(s)
PPI.U.u	= Psychological variable or input function (PPIs only)
PPI.U.w	= Contrast weights for psychological variable (PPIs only)
PPI.U.name	= Names of psychological conditions (PPIs only)

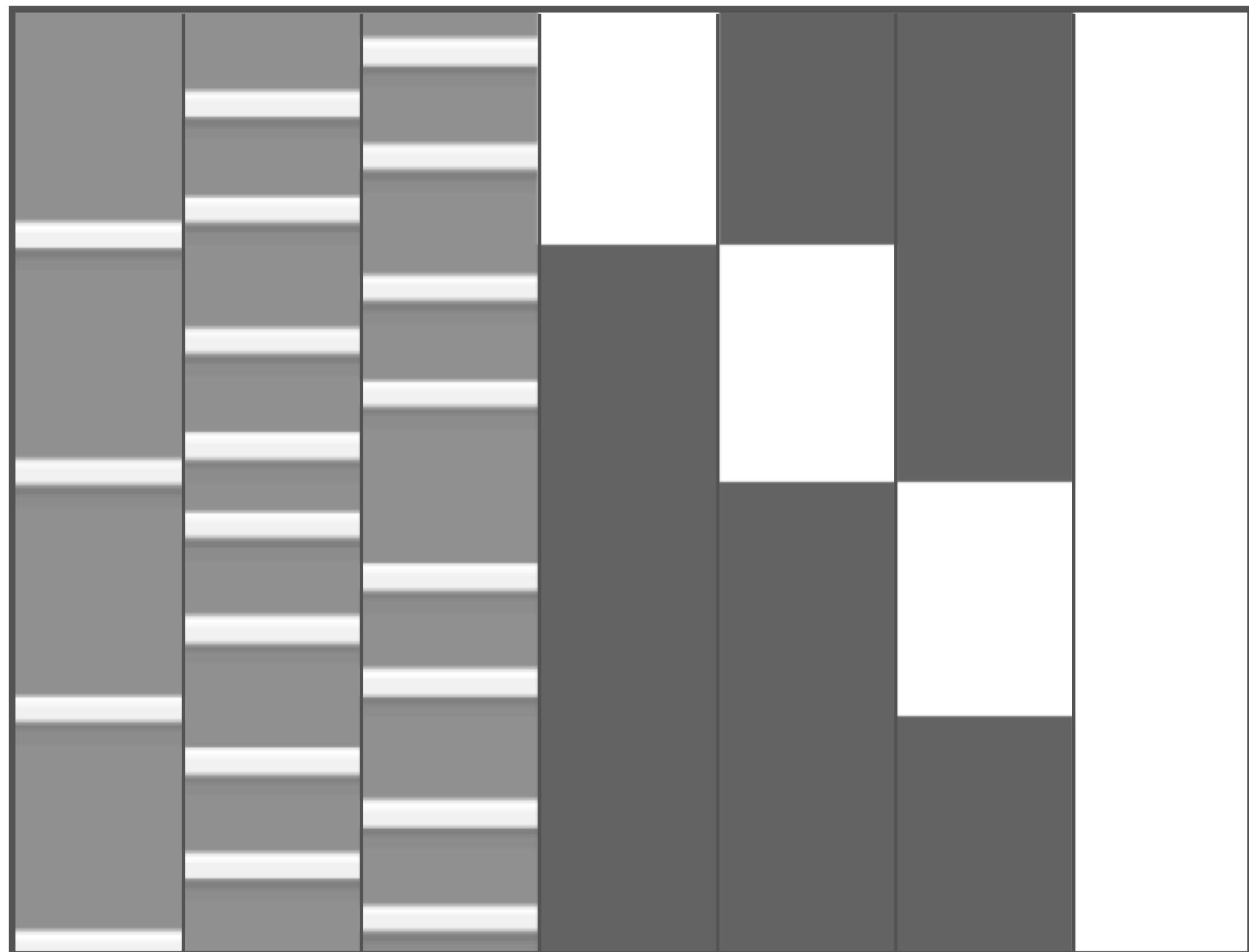
PPI Analysis in SPM12

Step 4: GLM Analysis for PPI

Design Matrices - Task vs. PPI

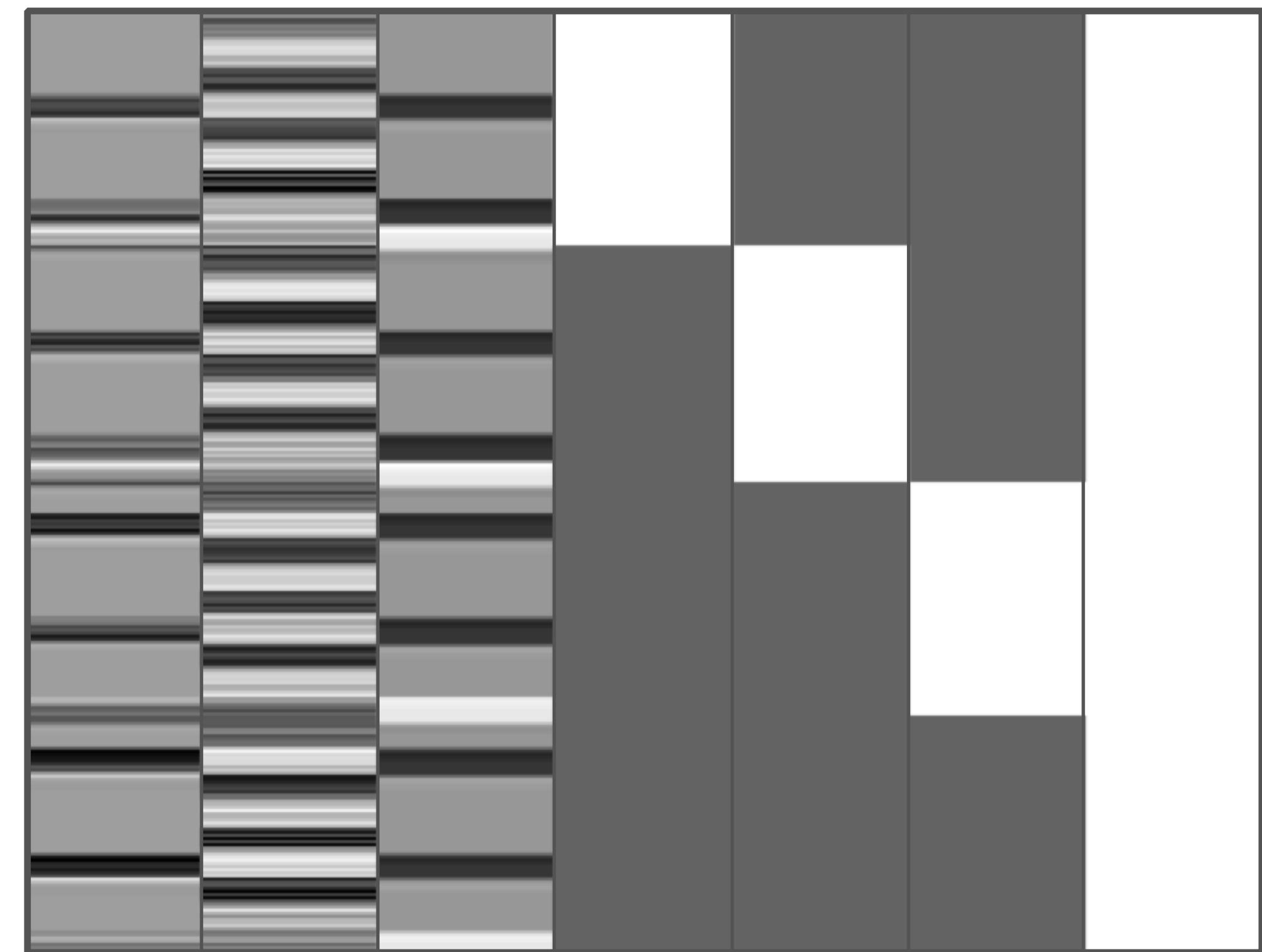
GLM for Task Related Activation

Stationary
No-attention
Attention
Block 1
Block 2
Block 3
Constant



GLM for PPI Analysis

PPI-interaction
V2-BOLD
Psych_Att-NoAtt
Block 1
Block 2
Block 3
Constant



How GLM works in PPI analysis

$$Y = (\text{PPI_interaction}) * b_1 + V2_BOLD * b_2 + (\text{Psych_Att-NoAtt}) * b_3 + e$$

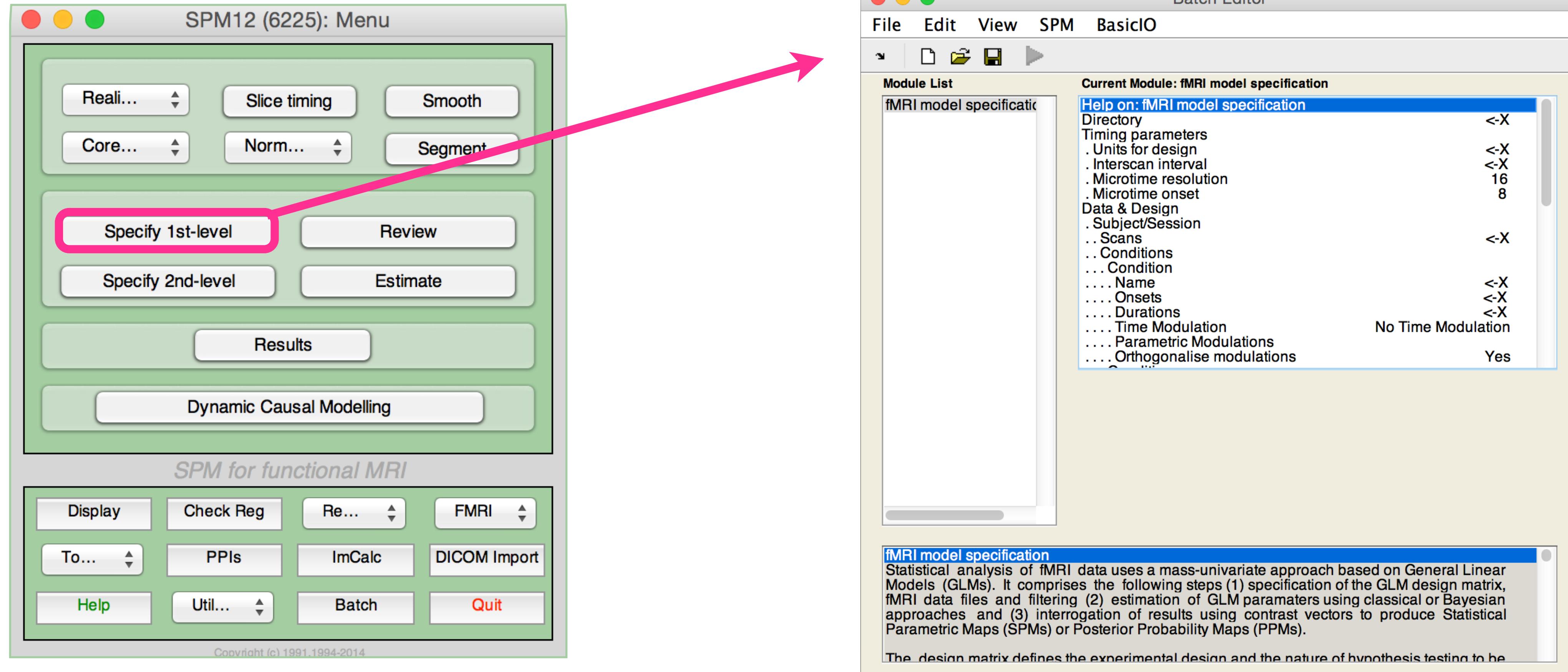
where

$$\begin{aligned} \text{PPI_interaction} &= \text{HRF} \otimes (\text{V2_neural} \times \text{Att-NoAtt}) \\ &\neq (\text{HRF} \otimes \text{V2_neural}) \times (\text{HRF} \otimes \text{Att-NoAtt}) \end{aligned}$$

$$V2_BOLD = \text{HRF} \otimes \text{V2_neural}$$

$$\text{Psych_Att-NoAtt} = \text{HRF} \otimes \text{Att-NoAtt}$$

PPI GLM analysis - Design (1/3)



PPI GLM analysis - Design (2/3)

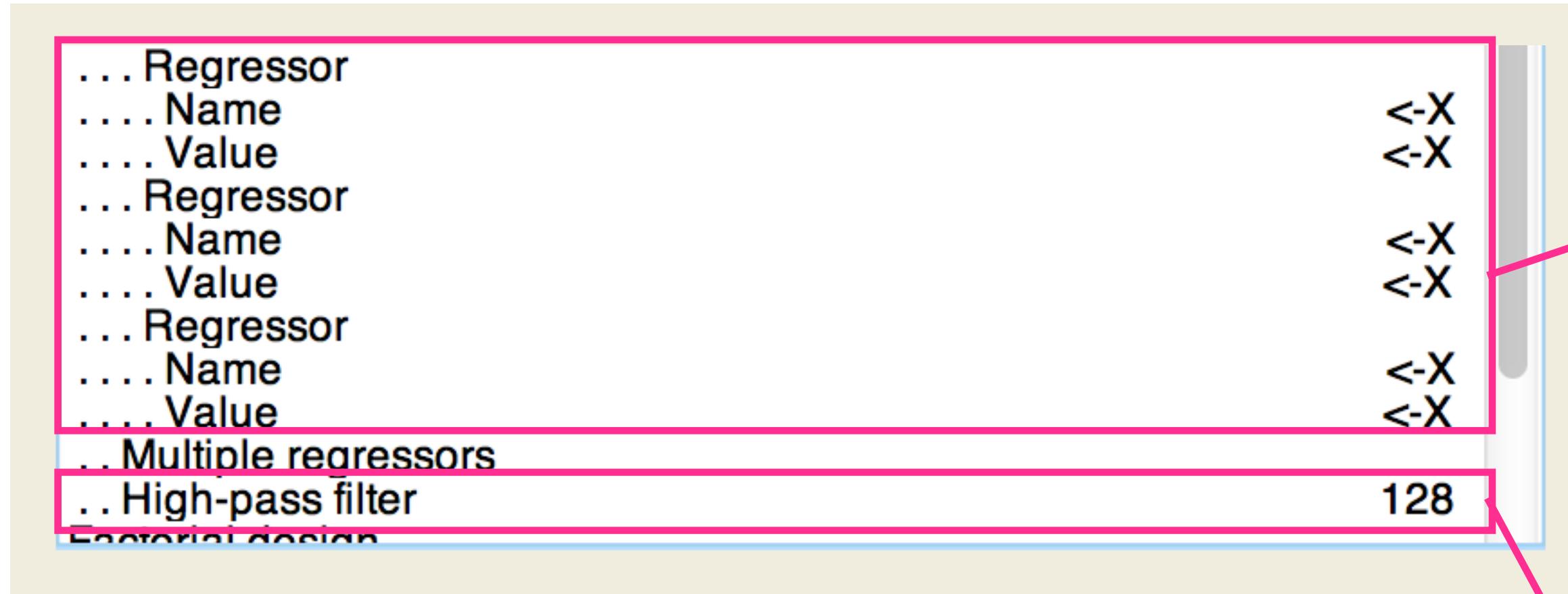
The screenshot shows a software interface for PPI GLM analysis. On the left, a tree view displays various parameters:

- Help on: fMRI model specification
- Directory: /Users/skyeong/Desktop/ppi_example/ppi
- Timing parameters
 - . Units for design
 - . Interscan interval
 - . Microtime resolution
 - . Microtime onset
- Data & Design
 - . Subject/Session
 - .. Scans: 360 files
 - .. Conditions
 - .. Multiple conditions
- Regressors
 - ... Regressor
 - Name
 - Value
 - ... Regressor
 - Name
 - Value
 - ... Regressor
 - Name
 - Value

On the right, four boxes explain the corresponding parameters:

- Select OUTPUT directory**: Points to the Directory path.
- Timing parameters**: Points to the Interscan interval parameter. It includes:
 - Units for design [**Scans**]
 - Interscan interval [**3.22**]
- Subject/Session**: Points to the Subject/Session section. It includes:
 - Scans: select all functional images (snff*.img)
- Regressors**: Points to the Regressors section. It includes:
 - Name = PPI-interaction, Value = PPI.ppi
 - Name = V2-BOLD, Value = PPI.Y
 - Name = Psych_Att-NoAtt, Value = PPI.P

PPI GLM analysis - Design (3/3)



Regressor 1:

- Name=Block 1, Value=block1

Regressor 2:

- Name=Block 2, Value=block2

Regressor 3:

- Name=Block 3, Value=block3

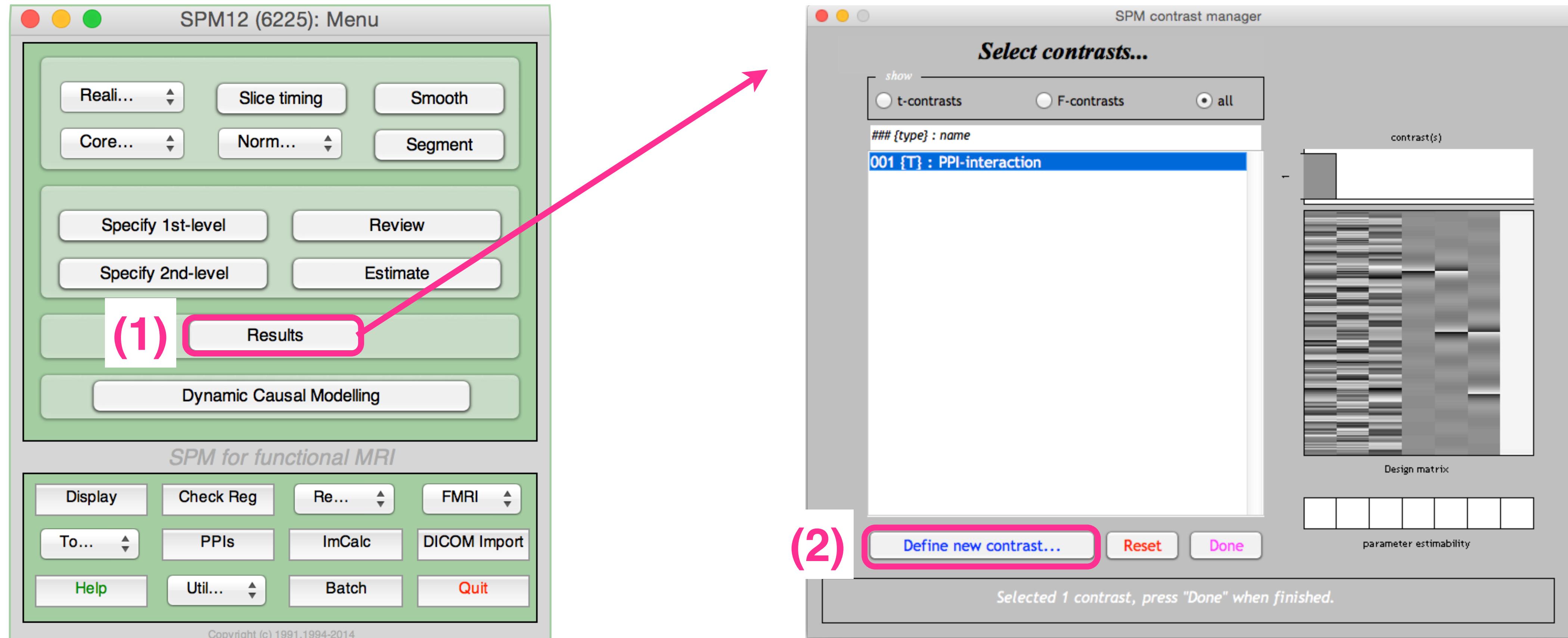
High-pass filter:

- 192 (in second, i.e., freq. >1/192 Hz)

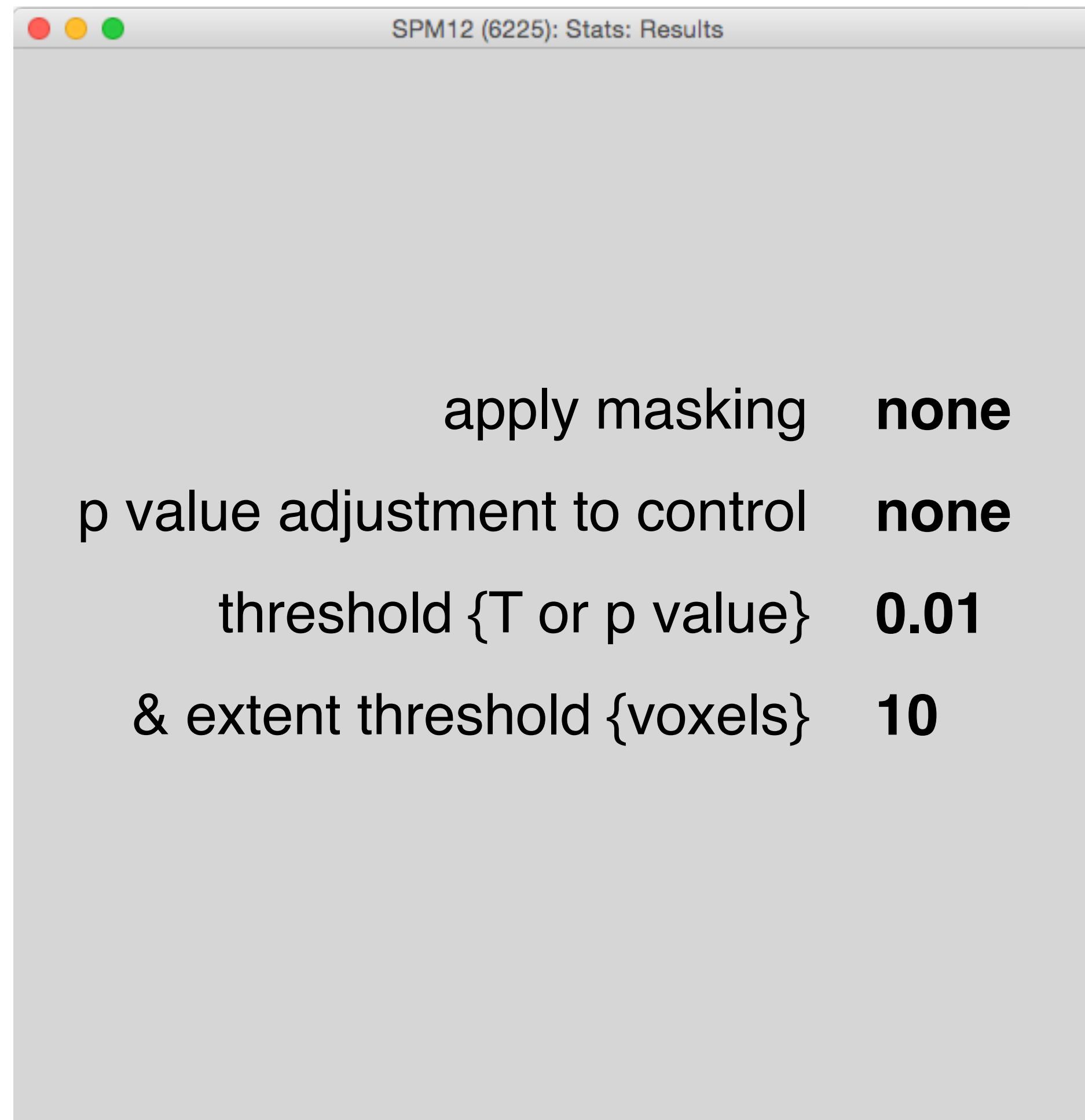
PPI Analysis in SPM12

Step 5: PPI results

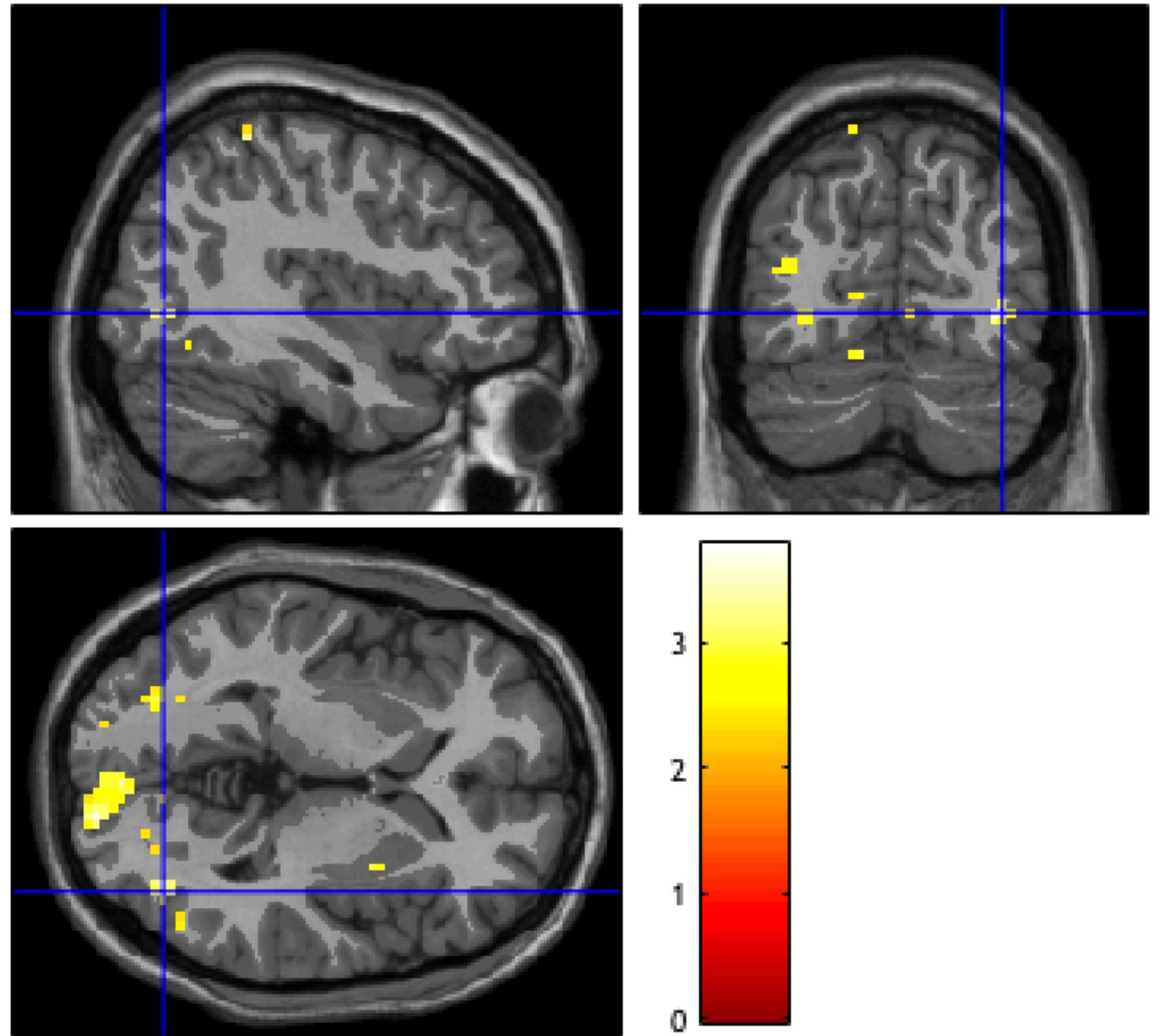
PPI analysis - Results



PPI analysis - Results



Go to MNI coordinate: [39 -72 0]



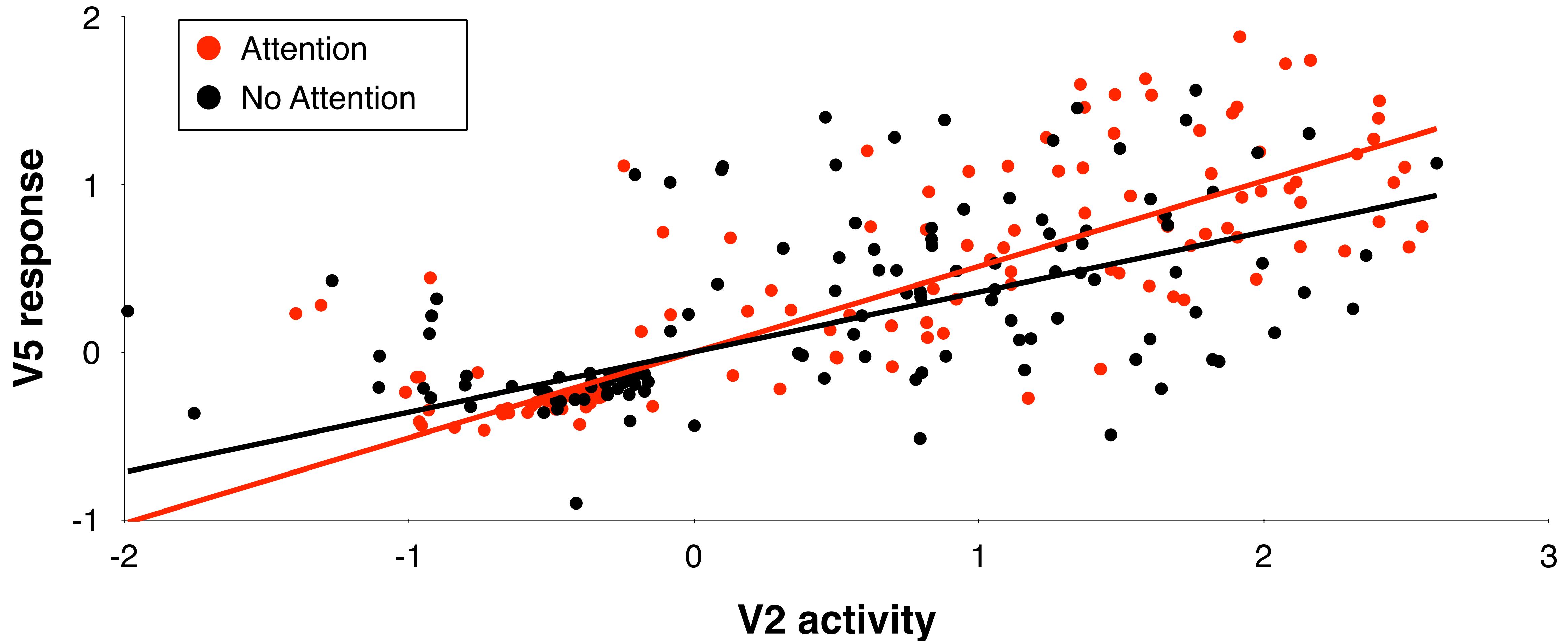
Group Statistics

- Collecting all con_0001.nii (*i.e.*, PPI-interaction contrast)
- Insert them into 2nd level specify in SPM12
- Model Parameter Estimation

PPI Analysis in SPM12

Extra step: Demonstrating PPI interaction

Demonstrating PPI interaction



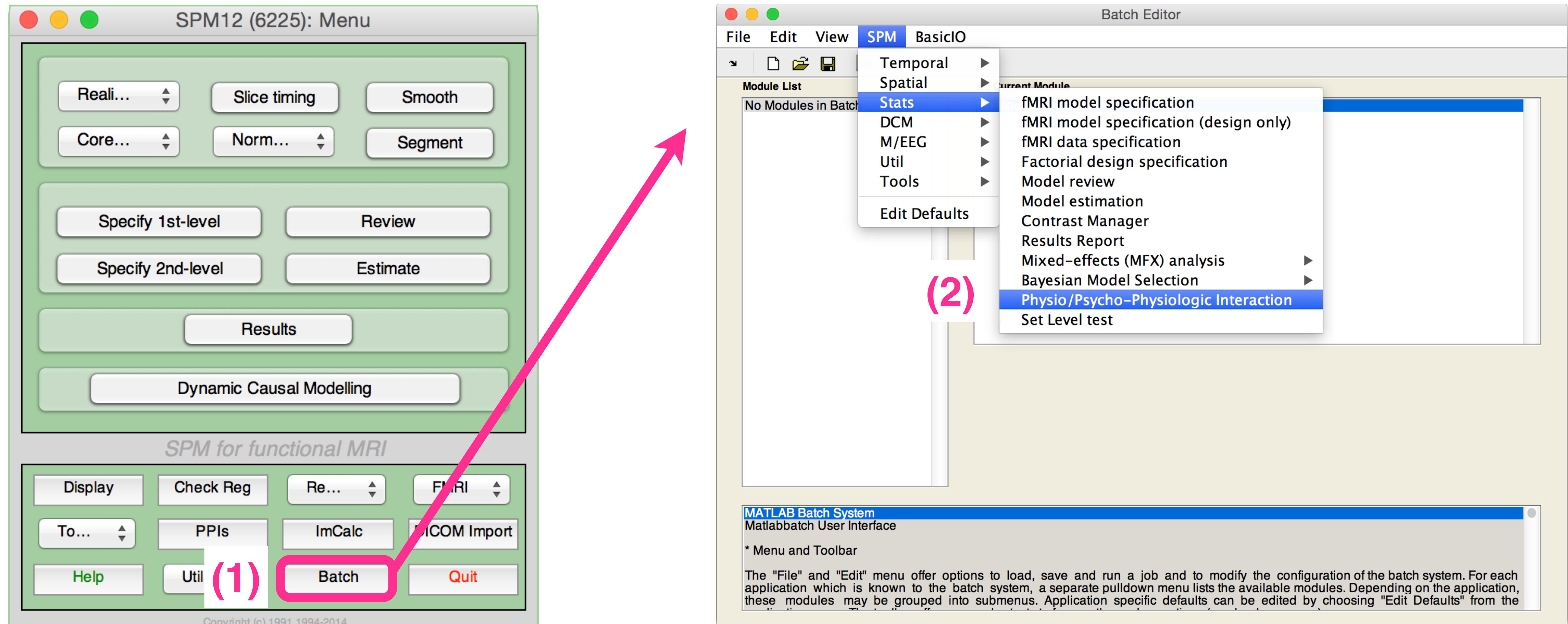
Create four PPI variables

VOI of **V2**: MNI=[15 -78 -9], sphere with radius 6mm

VOI of **V5**: MNI=[39 -72 0], sphere with radius of 6mm

- **V2xNoAttention**: Use the V2 VOI and include No-Attention with a contrast weight of 1, do not include Stationary, No-Attention
- **V2xAttention**: Use the V2 VOI and include Attention with a contrast weight of 1, do not include Stationary, Attention
- **V5xNoAttention**: Use the V5 VOI and include No-Attention with a contrast weight of 1, do not include Stationary, No-Attention
- **V5xAttention**: Use the V5 VOI and include Attention with a contrast weight of 1, do not include Stationary, Attention

PPI analysis - Create PPI variable



Create PPI - V2xNoAttention

The screenshot shows the PPI software interface with the following parameters:

- Help on: Physio/Psycho-Physiologic Interaction**
- Select SPM.mat**
- Type of analysis**:
 - . Psycho-Physiologic Interaction
 - . . Select VOI
 - . . Input variables and contrast weights
- Name of PPI**
- Display results**

Arrows point from specific parameters to their corresponding configuration details:

- An arrow points from **Select SPM.mat** to the text: **Select SPM.mat** - Select 1st level analysis result file
- An arrow points from **Type of analysis** to the text: **Type of analysis:** - Psycho-Physiologic Interaction
- An arrow points from **Input variables and contrast weights** to the text: **Select VOI:** VOI_VOI_V2_1.mat
Input variables and contrast weights: [2 1 1]
- An arrow points from **Display results** to the text: **Name of PPI:** V2xNoAttention
Display results: Yes

Create PPI - V2xAttention

The screenshot shows a software window with the following configuration:

- Help on: Physio/Psycho-Physiologic Interaction**: No arrow.
- Select SPM.mat**: Points to a callout box labeled **Select SPM.mat**.
 - Select 1st level analysis result file
- Type of analysis**: Points to a callout box labeled **Type of analysis:**
 - Psycho-Physiologic Interaction
 - Select VOI
 - Input variables and contrast weights
- Name of PPI**: No arrow.
- Display results**: Points to a callout box labeled **Display results**: Yes

Create PPI - V5xNoAttention

The screenshot shows a software window with the following options:

- Help on: Physio/Psycho-Physiologic Interaction
- Select SPM.mat
- Type of analysis
 - . Psycho-Physiologic Interaction
 - . . Select VOI
 - . . Input variables and contrast weights
- Name of PPI
- Display results

Arrows point from the following fields to callout boxes:

- An arrow points from the "Select SPM.mat" field to a box labeled "Select SPM.mat".
- An arrow points from the "Type of analysis" section to a box labeled "Type of analysis:".
- An arrow points from the "Input variables and contrast weights" field to a box labeled "Input variables and contrast weights".
- An arrow points from the "Display results" field to a box labeled "Display results".

Select SPM.mat

- Select 1st level analysis result file

Type of analysis:

- Psycho-Physiologic Interaction

Select VOI: VOI_VOI_V5_1.mat

Input variables and contrast weights: [2 1 1]

Name of PPI: V5xNoAttention

Display results: Yes

Create PPI - V5xAttention

Select SPM.mat
- Select 1st level analysis result file

Type of analysis:
- Psycho-Physiologic Interaction
 .. Select VOI
 .. Input variables and contrast weights

Name of PPI: V5xAttention
Display results: Yes

Help on: Physio/Psycho-Physiologic Interaction

Select SPM.mat <-X

Type of analysis:
. Psycho-Physiologic Interaction
. . Select VOI
. . Input variables and contrast weights

<-X
<-X
<-X
No

Name of PPI

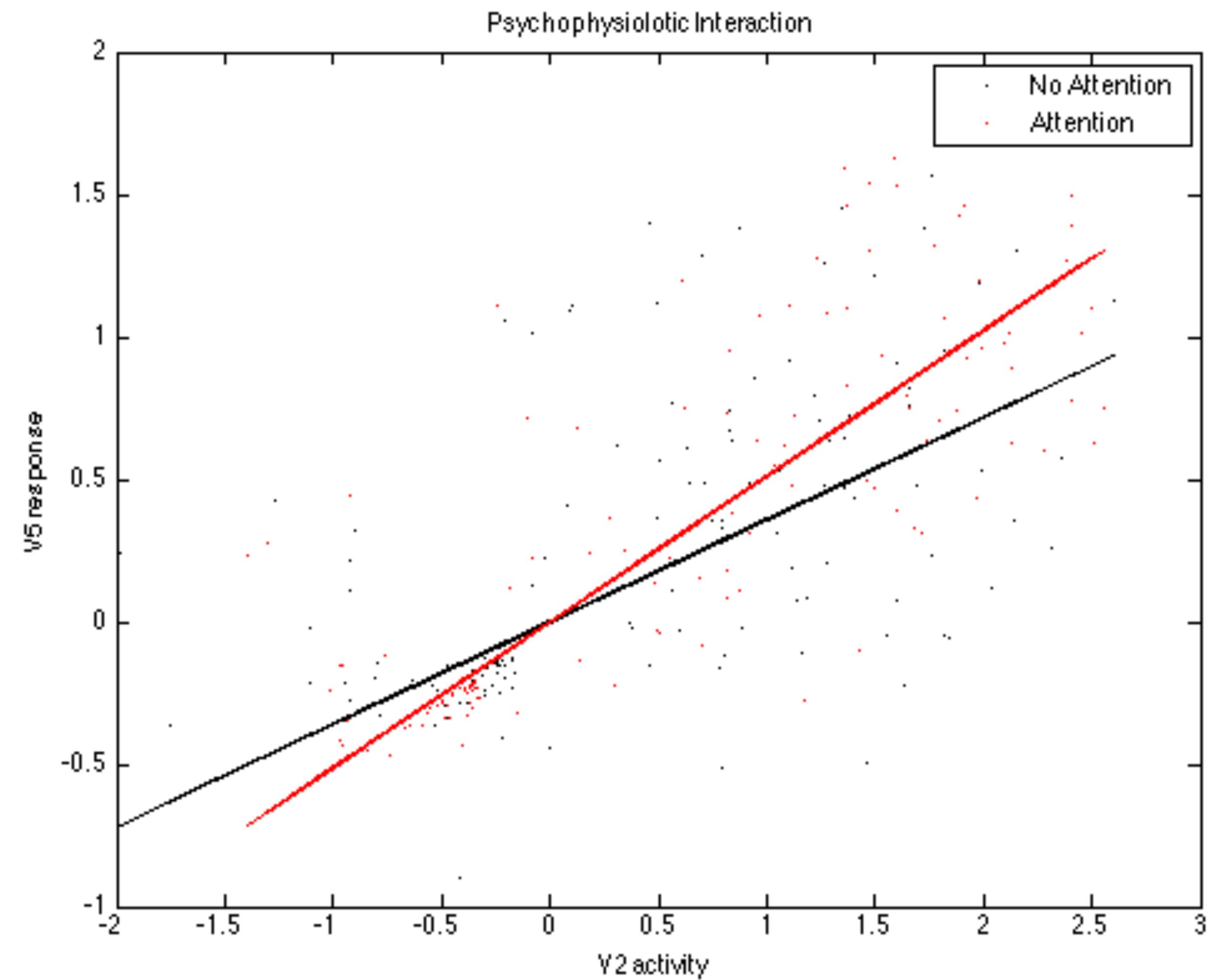
Display results

Matlab Codes (1/2)

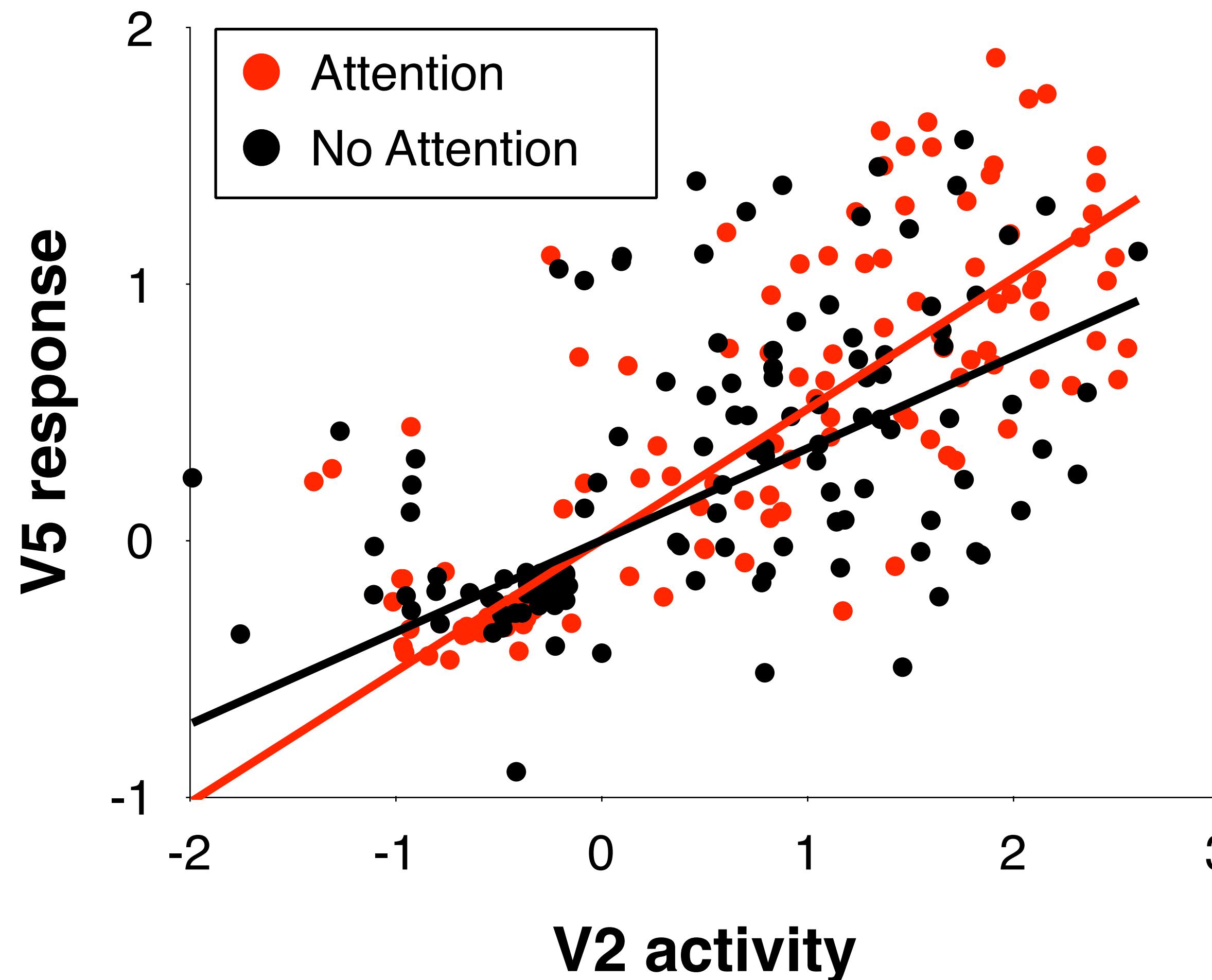
```
>> % Load PPI files
>> v2noatt = load('PPI_V2xNoAttention.mat');
>> v2att = load('PPI_V2xAttention.mat');
>> v5noatt = load('PPI_V5xNoAttention.mat');
>> v5att = load('PPI_V5xAttention.mat');
>>
>>
>> % Plot the PPI data points with the following commands at the Matlab
>> figure;
>> plot(v2noatt.PPI.ppi, v5noatt.PPI.ppi, 'k.');
>> hold on
>> plot(v2att.PPI.ppi, v5att.PPI.ppi, 'r.');
```

Matlab Codes (2/2)

```
>> % Plot the best fit lines for NoAttention  
>> x = v2noatt.PPI.ppi(:);  
>> x = [x, ones(size(x))];  
>> y = v5noatt.PPI.ppi(:);  
>> B = pinv(x)*y; % Linear Regression  
>> y1 = B(1)*x(:,1)+B(2);  
>> plot(x(:,1), y1, 'k-');  
>  
>  
>> % Plot the best fit lines for Attention  
>> x = v2att.PPI.ppi(:);  
>> x = [x, ones(size(x))];  
>> y = v5att.PPI.ppi(:);  
>> B = pinv(x)*y; % Linear Regression  
>  
> y1 = B(1)*x(:,1)+B(2);  
>> plot(x(:,1), y1, 'r-');  
>  
>> legend('No Attention', 'Attention');  
>> xlabel('V2 activity');  
>> ylabel('V5 response');  
>> title('Psychophysiolotic Interaction');
```



Demonstrating PPI interaction



Linear Regression Model

$$V5_response = V2_activity * b1 + b2 + e$$

Estimated Parameters

	Attention	No Attention
b1	0.5112	0.3585
b2	0.0000	0.0000

gPPI Analysis using PPPI toolbox

gPPI Toolbox (PPPI)

1. DOWNLOAD

The gPPI toolbox can be downloaded from: www.nitrc.org/projects/gppi

The file will be in the form: PPPI*.tar

2. INSTALLATION

Untar the downloaded file and move the files to the toolbox directory in **SPM8**.

This will create a folder called path to SPM8/toolbox/PPPI.

In MATLAB, make sure path to SPM8/toolbox/PPPI is in the search path.

This can be set by using the addpath command or from File Set Path.

The toolbox also requires SPM8 to be in the MATLAB path.

gPPI Matlab Codes

```
>> addpath(genpath('/Users/skyeong/matlabwork/spm12/toolbox/PPPI/'));
>>
>> % Initialise SPM
>> %-----
>> spm('Defaults','fMRI');
>> spm_jobman('initcfg');
>>
>>
>> % Create volume of interest
>> %-----
>> proj_path = '/Volumes/JetDrive/workshops/Neuroimaging/Lecture11-PPI';
>> GLMdir = fullfile(proj_path,'Analysis','attention_GLM');
>> VOI = struct('name','V2','center',[15 -78 -9],'radius',6);
>> create_sphere_image(GLMdir,VOI); % this create VOI_V2_mask.nii
>>
>>
>> % Configure the PPPI Parameter structure
>> %-----
>> clear P;
>> P.subject='gPPI';
>> P.directory=GLMdir;
>> P.VOI=fullfile(GLMdir, 'VOI_V2_mask.nii');
>> P.Estimate=1;
>> P.contrast=0;
>> P.extract='eig';
>> P.Tasks={'1' 'Stationary' 'No-Attention' 'Attention'};
```



```
>> P.Weights=[];
>> P.analysis='psy';
>> P.method='cond';
>> P.CompContrasts=1;
>> P.Weighted=0;
>> P.Contrasts(1).left={'Attention'};
>> P.Contrasts(1).right={'No-Attention'};
>> P.Contrasts(1).STAT='T';
>> P.Contrasts(1).Weighted=0;
>> P.Contrasts(1).MinEvents=5;
>> P.Contrasts(1).name='Attention_minus_No-Attention';
>> P.Contrasts(2).left={'No-Attention'};
>> P.Contrasts(2).right={'Attention'};
>> P.Contrasts(2).STAT='T';
>> P.Contrasts(2).Weighted=0;
>> P.Contrasts(2).MinEvents=5;
>> P.Contrasts(2).name='No-Attention_minus_Attention';
>> P.Contrasts(3).left={'Attention'};
>> P.Contrasts(3).right={'Stationary'};
>> P.Contrasts(3).STAT='T';
>> P.Contrasts(3).Weighted=0;
>> P.Contrasts(3).MinEvents=5;
>> P.Contrasts(3).name='Attention_minus_Stationary';
>>
>>
>> % Run PPPI with the command:
>> %-----
>> PPPI(P);
```

References

- Chapter 36 (Psychophysiological Interaction) of the SPM12 manual
<http://www.fil.ion.ucl.ac.uk/spm/data/>
- K. J. Friston *et al.*, Psychophysiological and Modulatory Interactions in Neuroimaging, *NeuroImage*, 6, 218-229 (1997)
- Darren R. Gitelman *et al.*, Modeling regional and psychophysiological interactions in fMRI: the importance of hemodynamic deconvolution, *NeuroImage*, 19, 2000-207 (2003)