# First level fMRI data analysis

Turku PET Centre Brain Imaging Course 2024

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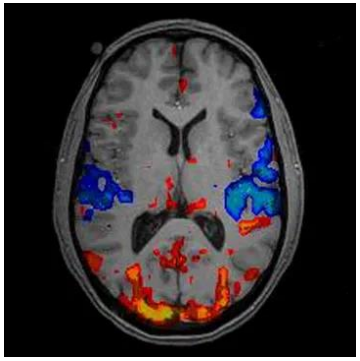
# Outline

- What is 1st level analysis?
- Statistical models
- Contrasts
- Examples for illustration
  - –Operation in SPM12
  - –Reading the results, e.g., the contrasts

# What is 1st level analysis?

- fMRI data analysis has two levels: 1st (within-subject) and 2nd (group-level).

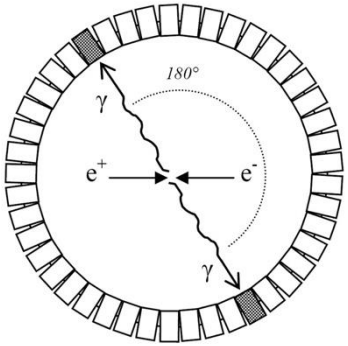
One subject's raw T2* data

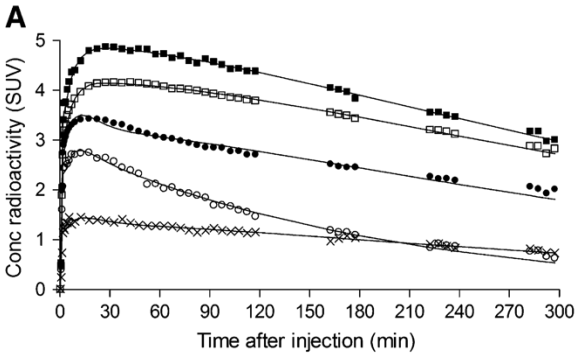


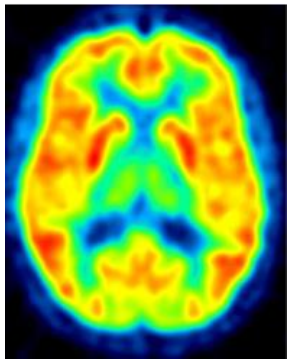
The subject's statistical map

# Within-subject: comparison between PET and fMRI data

## 1. Traditional PET



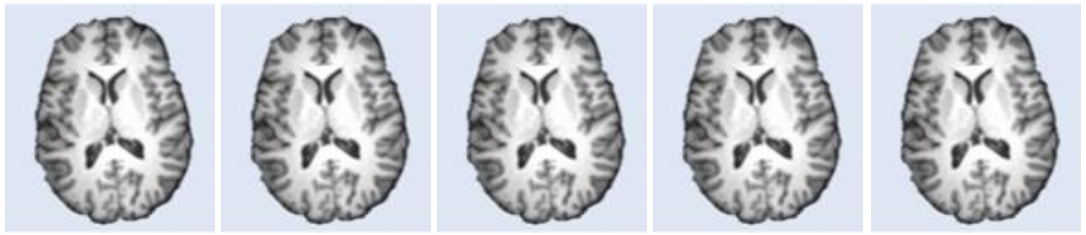



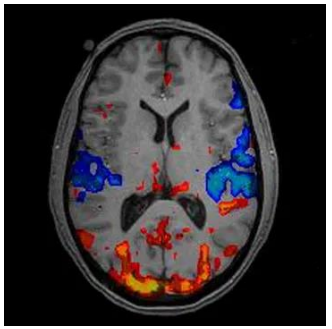
Density
e.g., glucose uptake

## 2. fMRI

Time



Task



Statistical map

# Why is 1st level analysis?

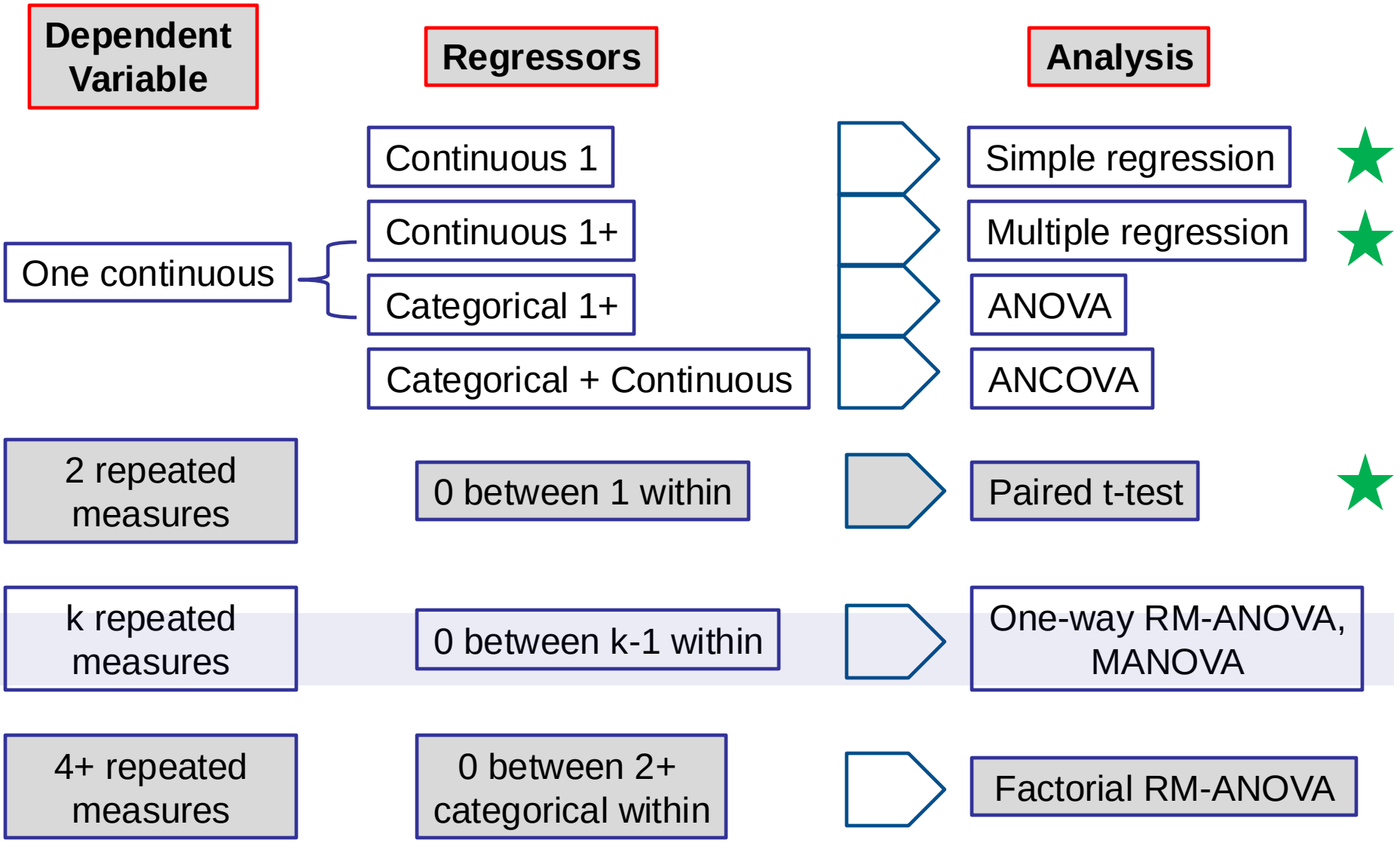
- BOLD signals are dominated by noise:

  physiological factors (breathing, heart rate), head movement, scanner instabilities, magnetic susceptibility artifacts, and neuronal variability, leading to low signal-to-noise ratio

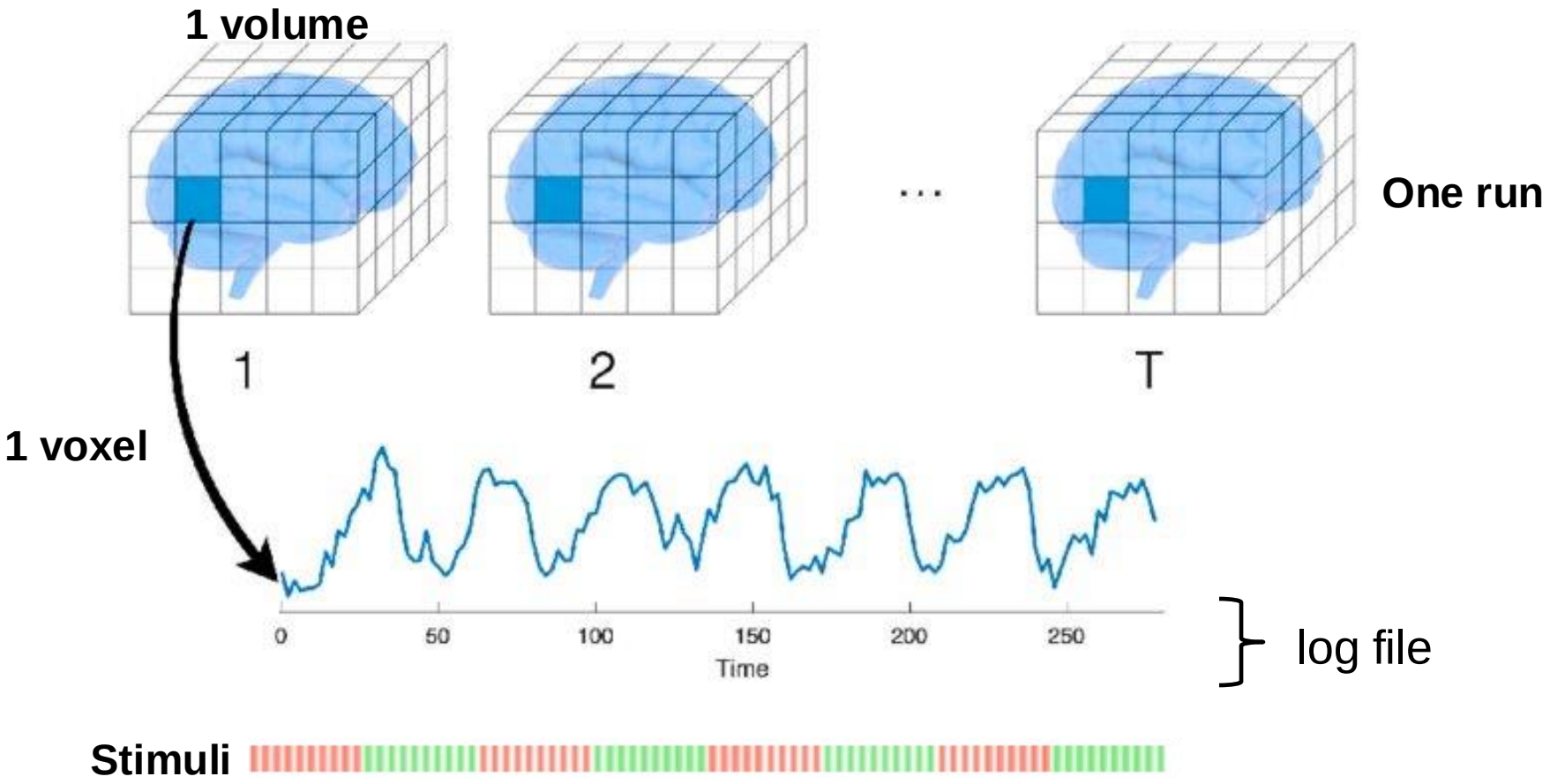
  **>> preprocessing NOT enough!**

- Multiple repeated exposure to stimuli to increase signal-to-noise ratio.
- Statistical analysis to extract the signal-associated brain responses **>> statistical map**

# The general linear model (GLM) family

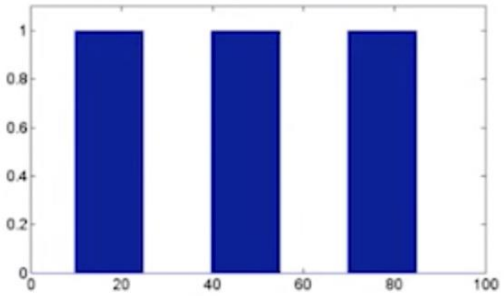


# Voxel-level data modelling

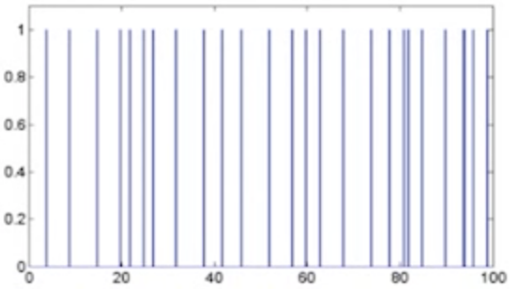


- BOLD responses are delayed: **peak at 4-6 s** and **baseline 20-30 s**.
- Convolved with the hemodynamic response function (**HRF**)
- The linear time-invariant (**LTI)** system

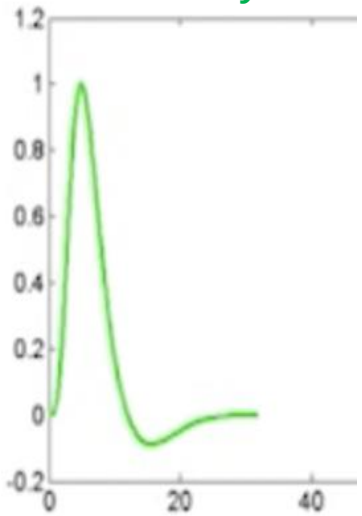
Block design

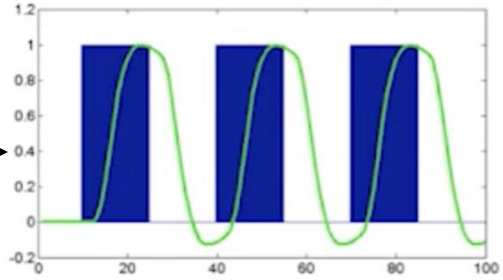


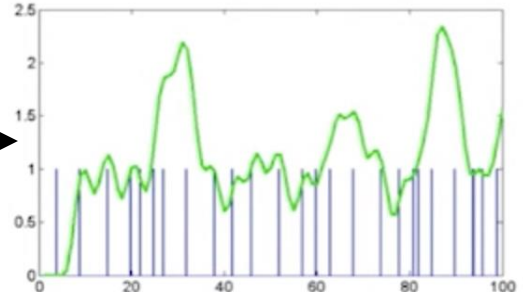
Event-related design



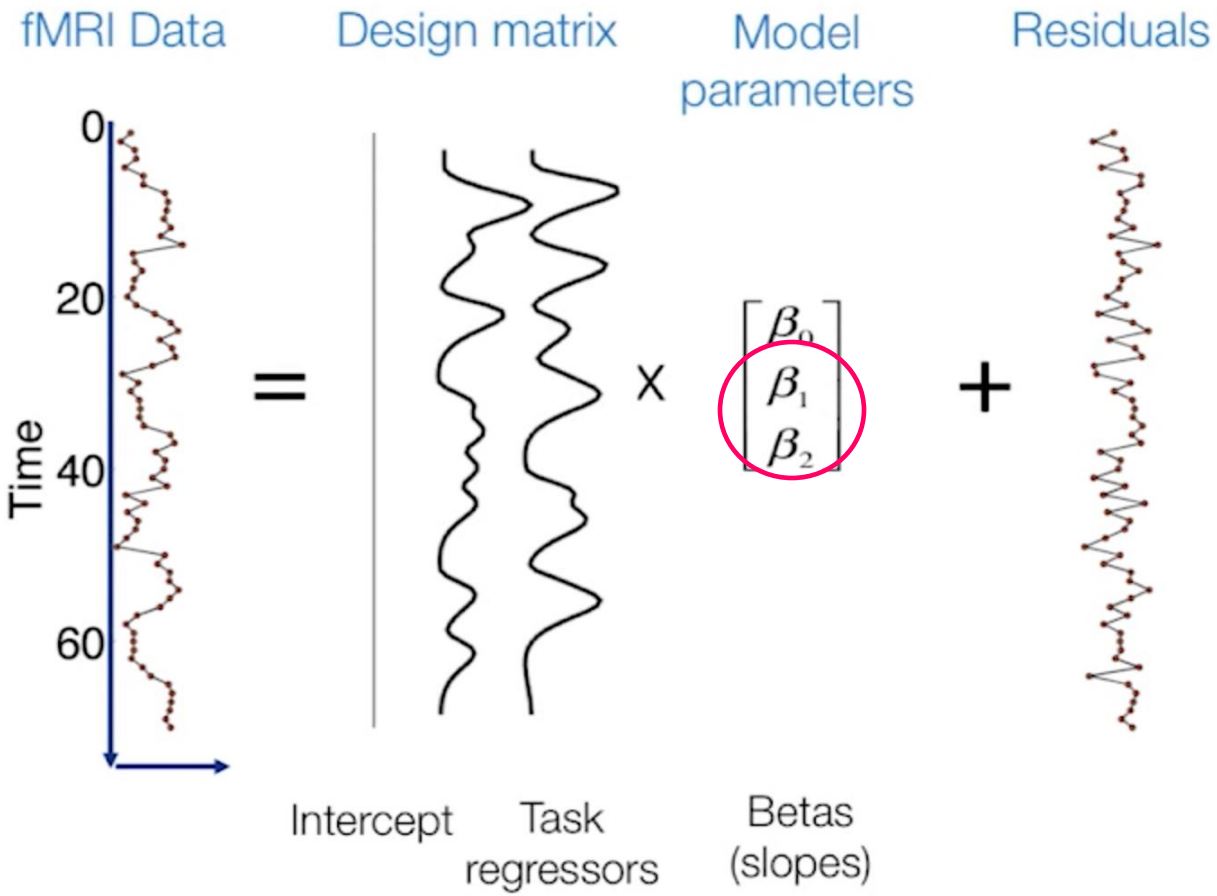
Hemodynamic delay







# Event-related design: two continuous regressors (laughter vs. scrambled laughter regressors)



# Four example studies

1. Social laughter experiment
2. Naturlistic movie stimuli
3. Repeated measure food-reward responses
4. Resting states

# The laughter experiment

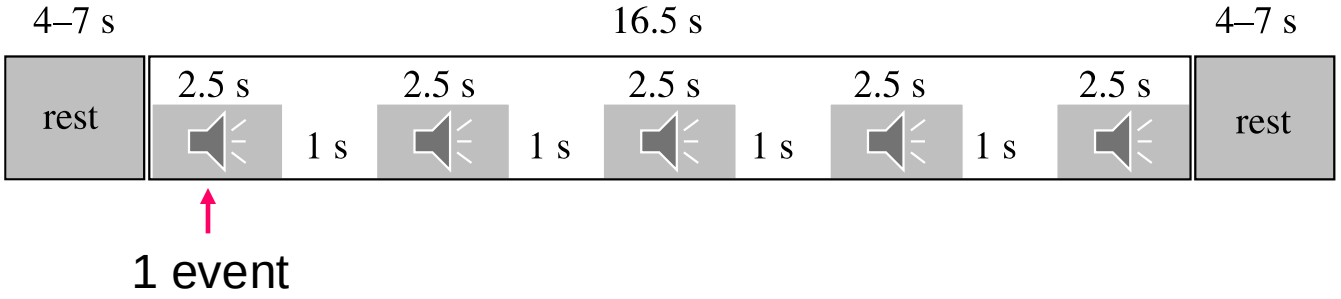
Laughter is a contagious behavioural stimulus that is commonly used to study social brain functions. We have studied the social brain functions of participants with high psychopathy or autism traits.

*>> Sun L., et al., Cerebral Cortex, Volume 33, Issue 2, 15 January 2023*

**Four stimuli types:**

Laughter / Crying vocalization /
Scrambled laughter / Scrambled Crying

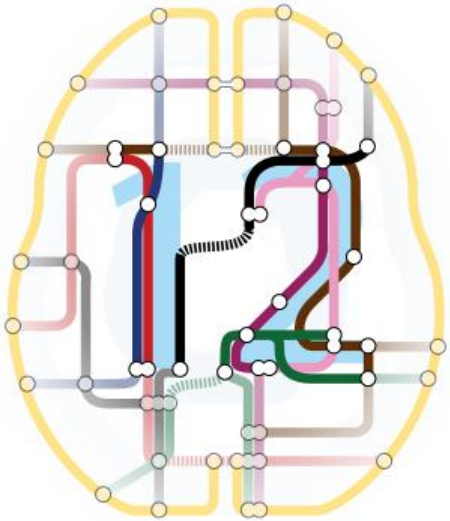
**Block (also event-related) design**



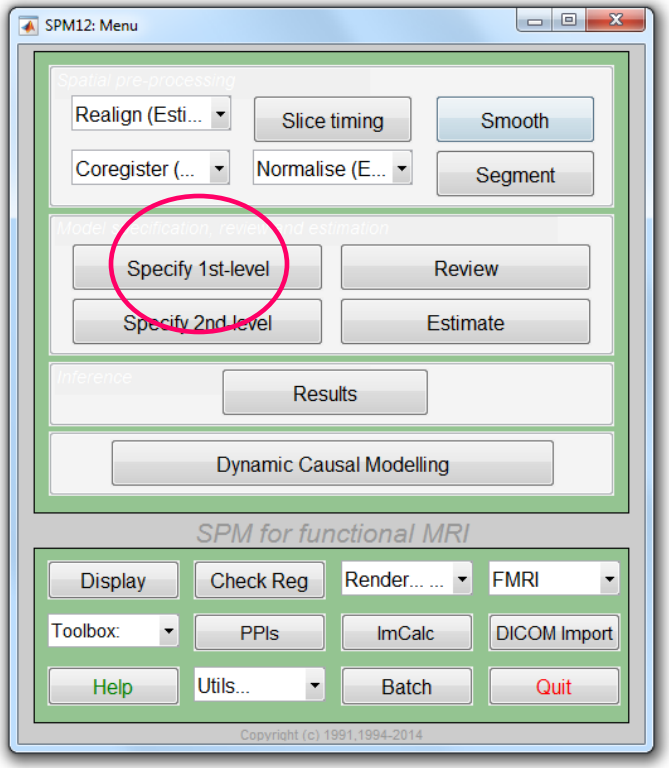

The 16.5 s block contains 5 Laughter, crying, or scrambled sound clips.

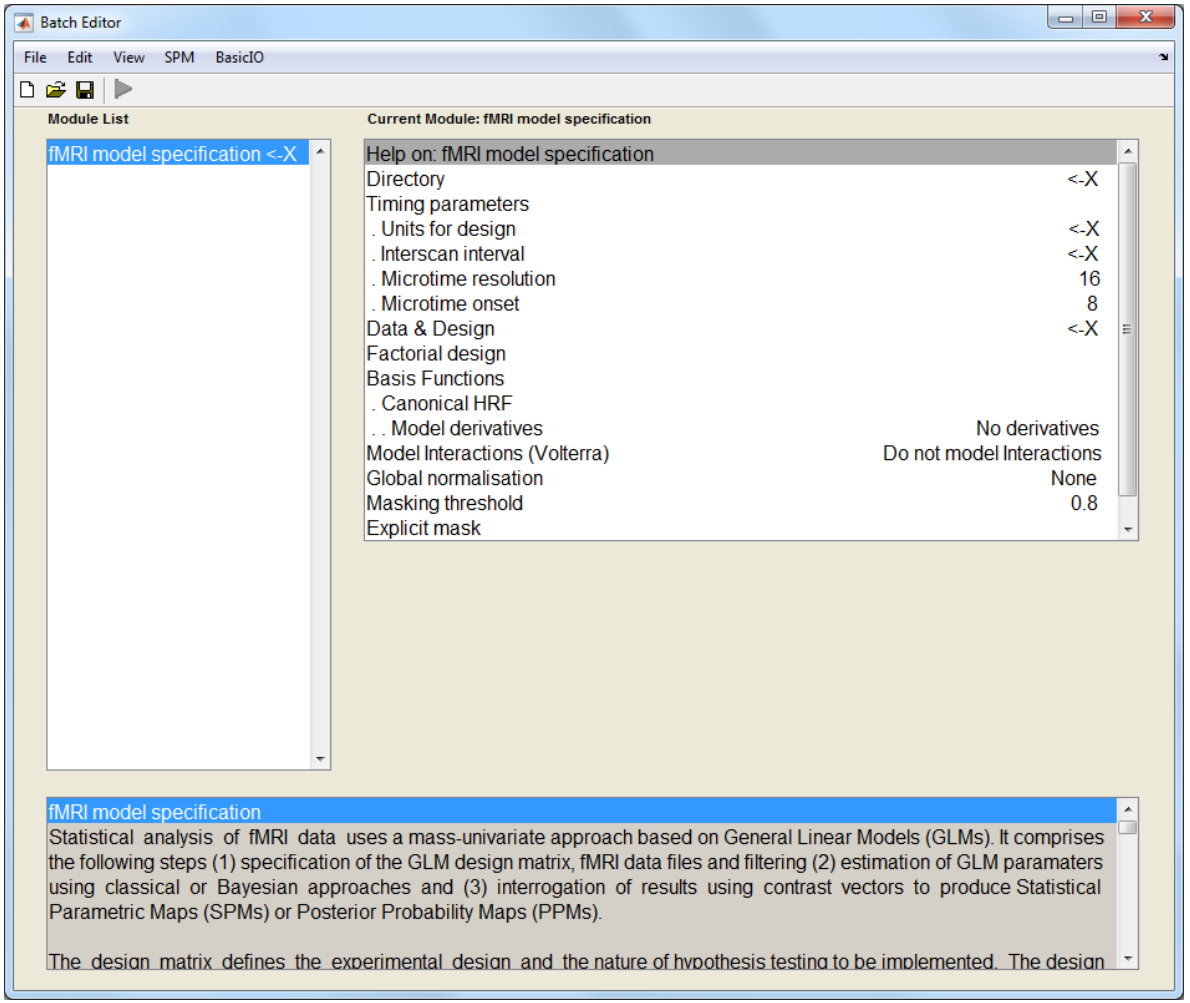
# SPM12

- SPM - theoretical concepts of Statistical Parametric Mapping in a complete analysis package.
- Run in matlab
- See more information: https://www.fil.ion.ucl.ac.uk/spm/software/spm12/

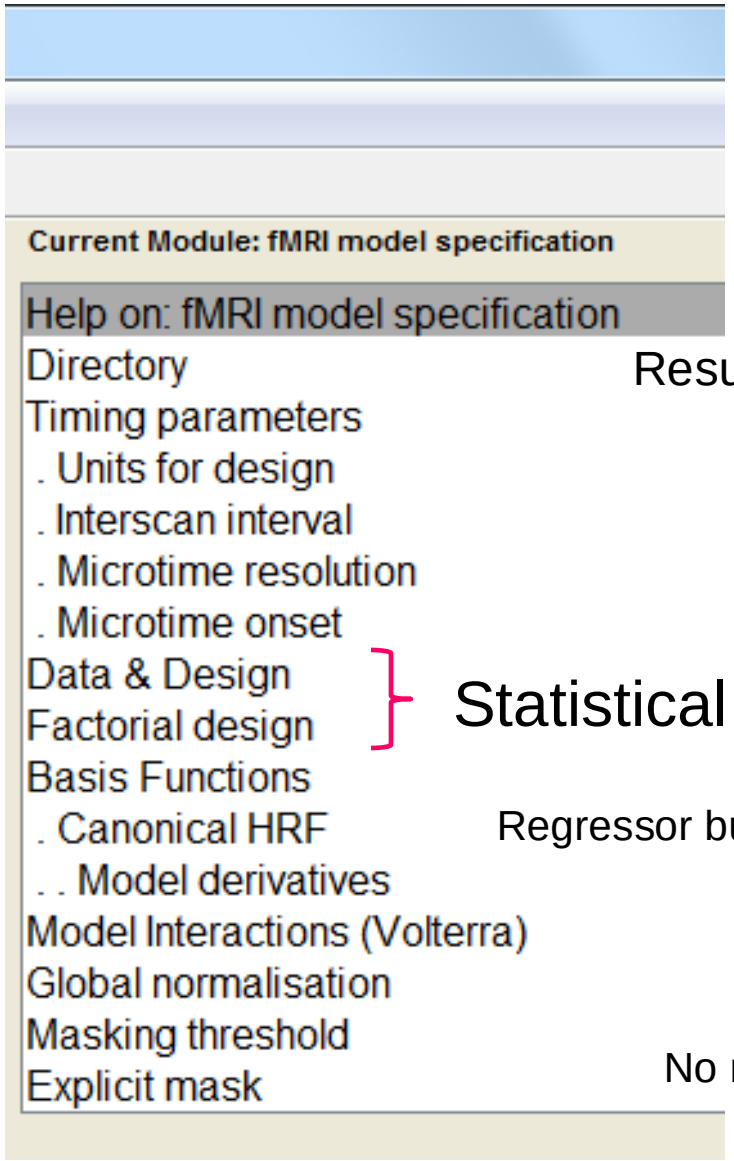


# Operation in SPM12



# SPM12: parameter setting




Result to store

seconds
2.6

Basic settings

Statistical model

Regressor building

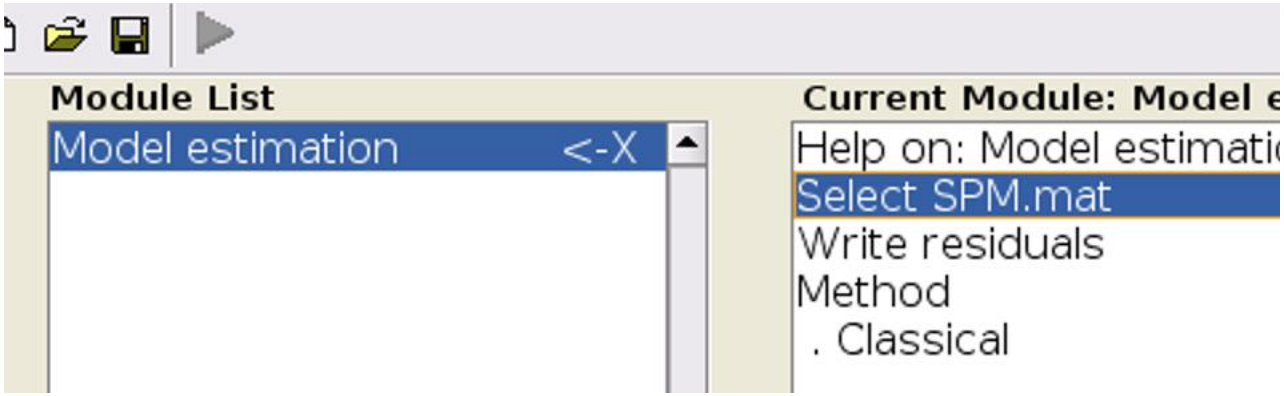
Leave as default,
or specify if necessary

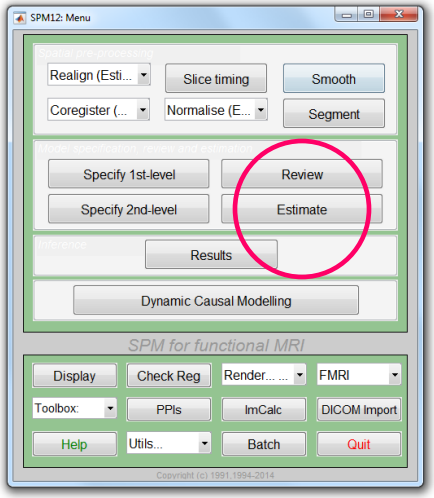
No masks

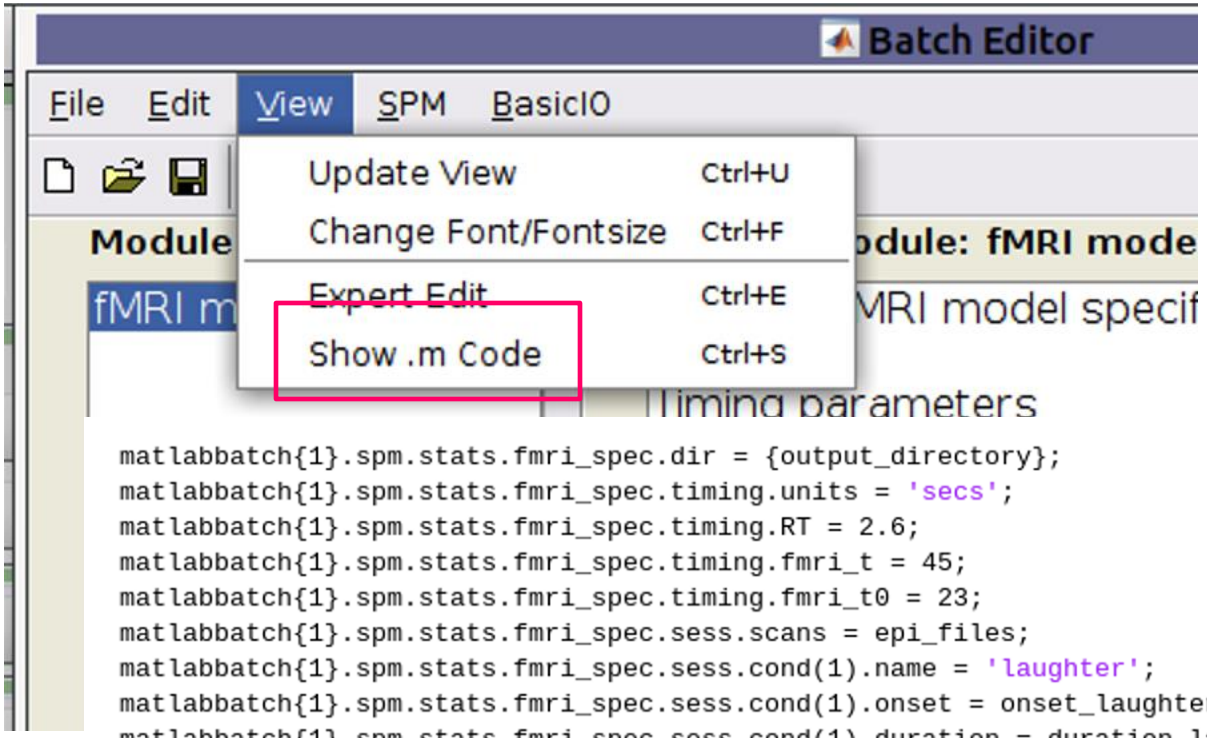
Current Module: fMRI model specification

Data & Design
. Subject/Session
. . Scans → All scan volumes <-X
. . Conditions
. . . Condition
. . . . Name → Laughter humans
. . . . Onsets <-X
. . . . Durations <-X
. . . . Time Modulation No Time Modulation
. . . . Parametric Modulations
. . . . Orthogonalise modulations Yes
. . . Condition
. . . . Name Crying
. . . . Onsets <-X

⇩ Data estimation






```
matlabbatch{1}.spm.stats.fmri_spec.dir = {output_directory};
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matlabbatch{1}.spm.stats.fmri_spec.timing.fmri_t = 45;
matlabbatch{1}.spm.stats.fmri_spec.timing.fmri_t0 = 23;
matlabbatch{1}.spm.stats.fmri_spec.sess.scans = epi_files;
matlabbatch{1}.spm.stats.fmri_spec.sess.cond(1).name = 'laughter';
matlabbatch{1}.spm.stats.fmri_spec.sess.cond(1).onset = onset_laughter;
matlabbatch{1}.spm.stats.fmri_spec.sess.cond(1).duration = duration_laughter;
matlabbatch{1}.spm.stats.fmri_spec.sess.cond(1).tmod = 0;
matlabbatch{1}.spm.stats.fmri_spec.sess.cond(1).pmod = struct('name', {}, 'param', {}, 'poly', {});
matlabbatch{1}.spm.stats.fmri_spec.sess.cond(1).orth = 1;

matlabbatch{1}.spm.stats.fmri_spec.sess.cond(2).name = 'crying';
matlabbatch{1}.spm.stats.fmri_spec.sess.cond(2).onset = onset_crying;
matlabbatch{1}.spm.stats.fmri_spec.sess.cond(2).duration = duration_crying;
matlabbatch{1}.spm.stats.fmri_spec.sess.cond(2).tmod = 0;
matlabbatch{1}.spm.stats.fmri_spec.sess.cond(2).pmod = struct('name', {}, 'param', {}, 'poly', {});
matlabbatch{1}.spm.stats.fmri_spec.sess.cond(2).orth = 1;

matlabbatch{1}.spm.stats.fmri_spec.sess.cond(3).name = 'scramble';
```
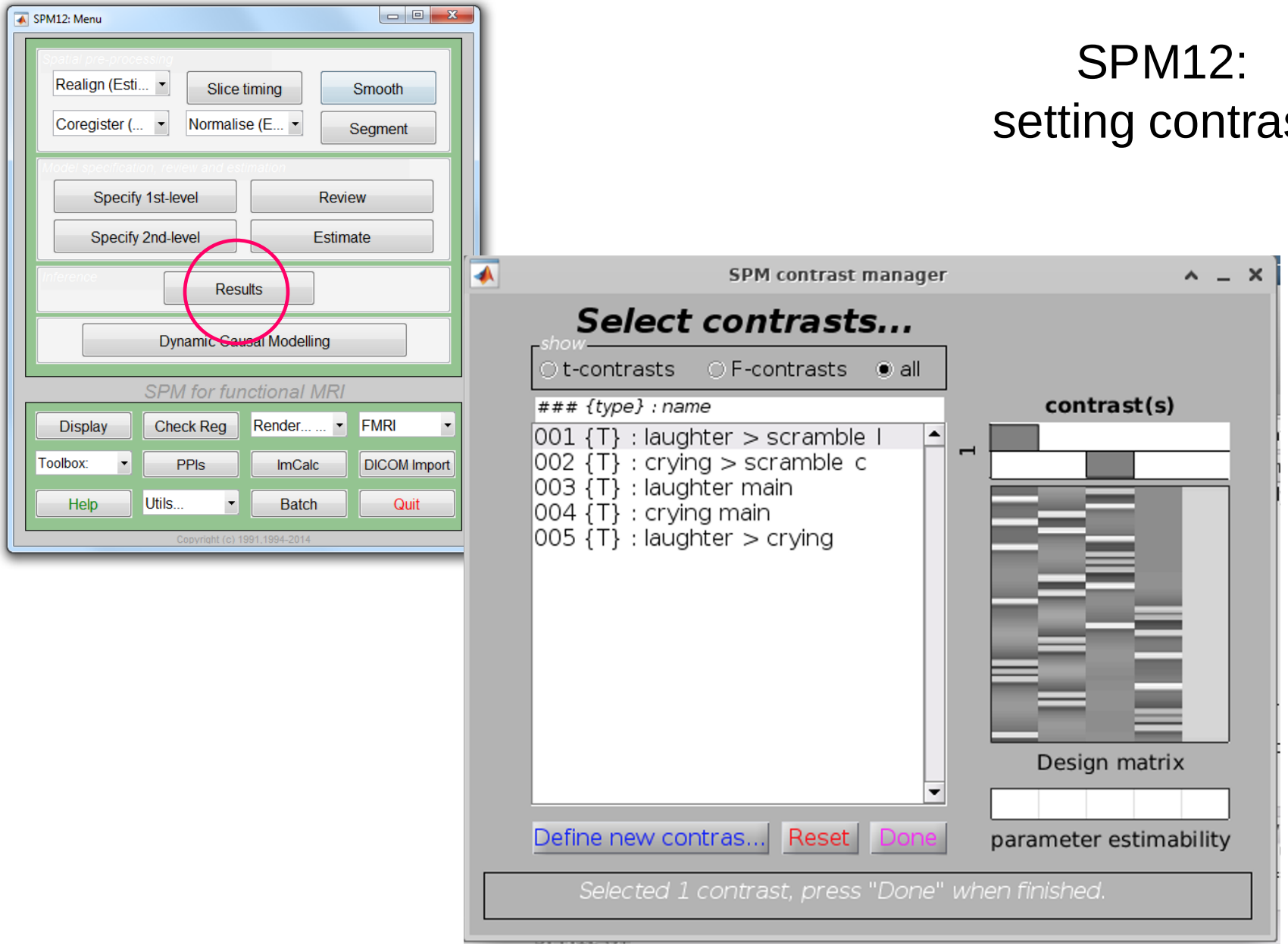

# SPM12: setting contrasts

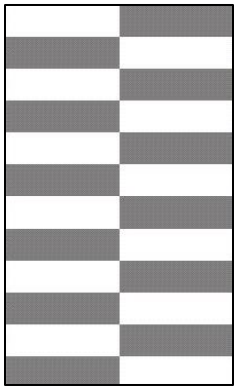


# Contrasts

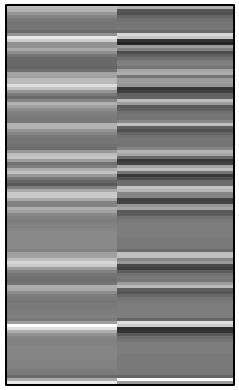
Experimental conditions: stimuli or interest vs. control stimuli

- Your interest is often the difference between the two conditions, which is "contrast"
- You can calculate the difference, sum or separately each conditions, which are calculated by different linear contrasts.

- We only introduce T contrast in this lecture ! !




Block design




Event-related design

Design matrix in SPM 12

## Difference between conditions

[ 1 -1] = “Con1 > Con2”

[ -1 1] = “Con1 < Con2”

## Separately

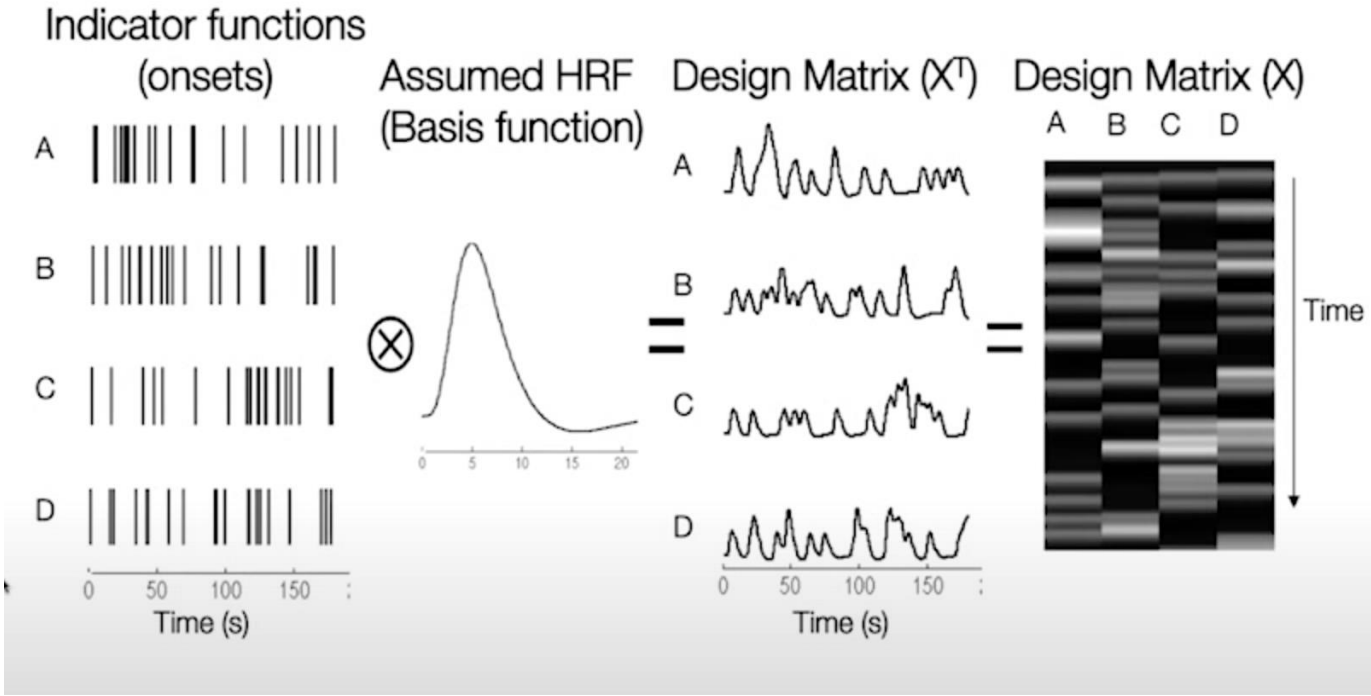
[ 1 0] or [ -1 0] = “main effect Con1”

[ 0 1] or [ 0 -1] = “main effect Con2”

## Sum

[ 1 1] or [ -1 -1]

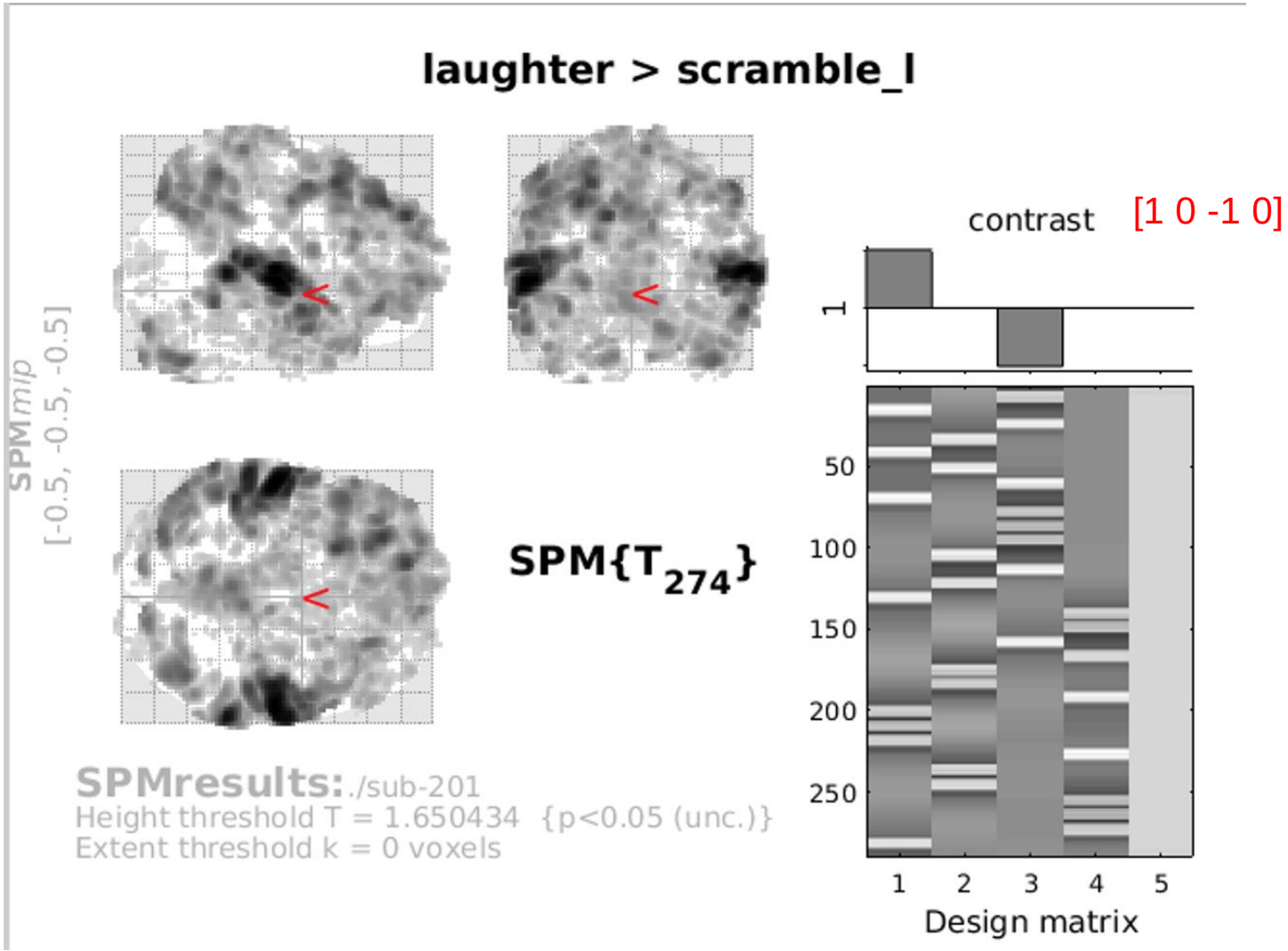
# More regressors




- [ 1 1 -1 -1] : (A+B) > (C+D)
- [ 1 -1 1 -1] : (A+C) > (B+D)
- [ 1 0 0 0 ] : main effect of A
- [ 1 1 0 0] : Sum of (A+B) vs the mean of the signal

  ….

# SPM12: result



# Example 2: Naturalistic stimuli

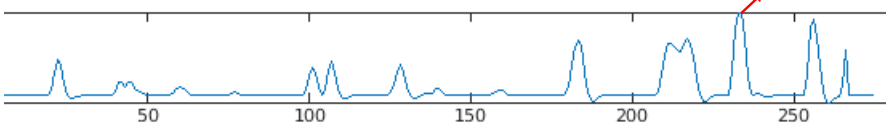
Naturalistic fMRI offers **ecological validity**, engages **complex brain functions**, **richer data**, **better participant engagement**, etc.

*>> Santavirta S. et al., NeuroImage, Volume 272, 15 May 2023, 120025*
*>> Nummenmaa L., et al., Cerebral Cortex, Volume 31, Issue 9, September 2021, Pages 4104–4114*

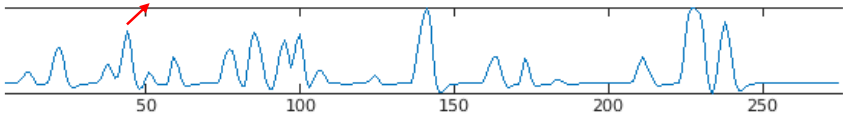
# Movie-based fMRI

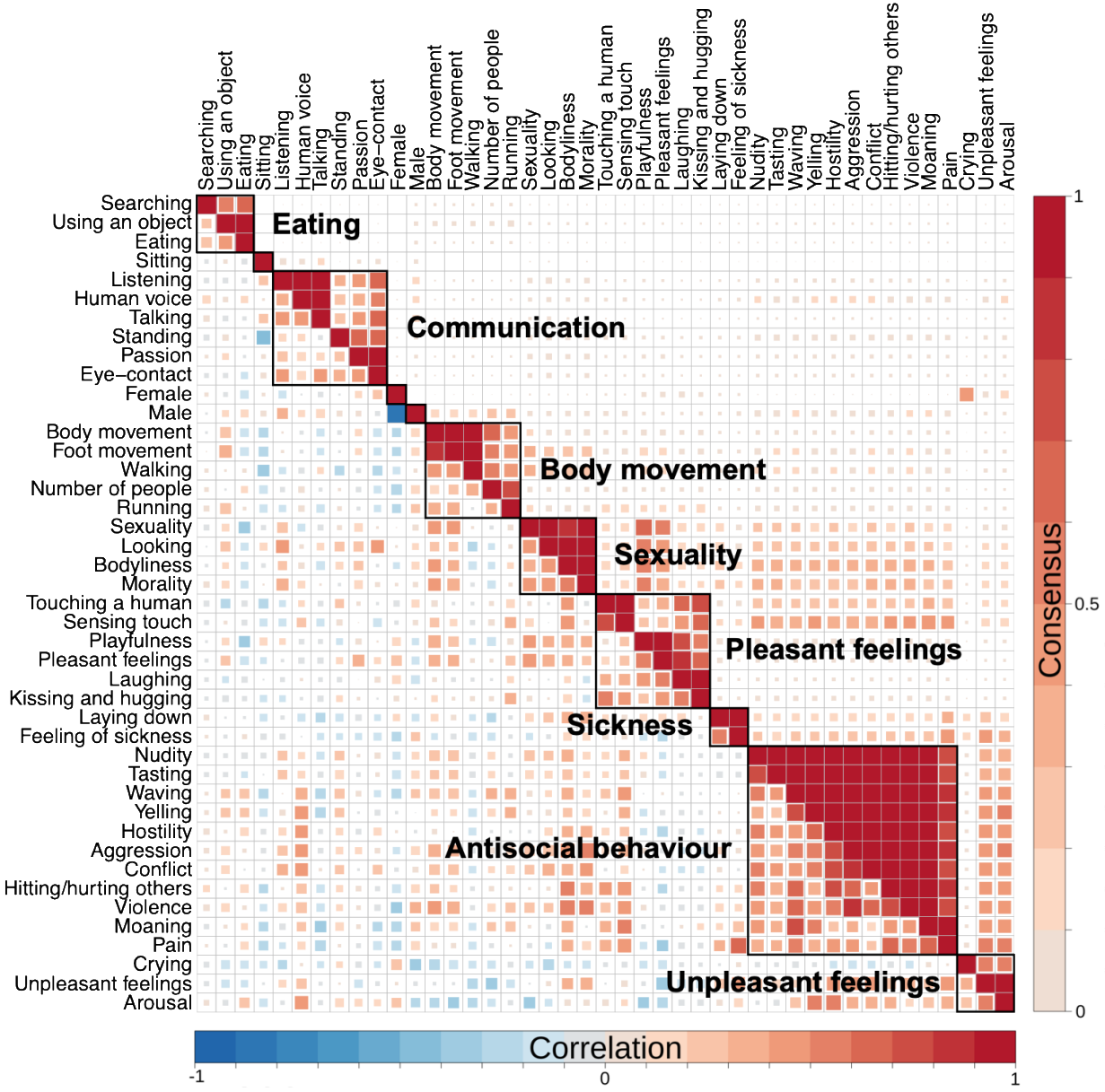
- ✓ Ratings of different dimensions (social, emotional, neutral, objective…)
- ✓ Each regressor should contain certain number of stimuli. CAN NOT be too small number!

Self-control



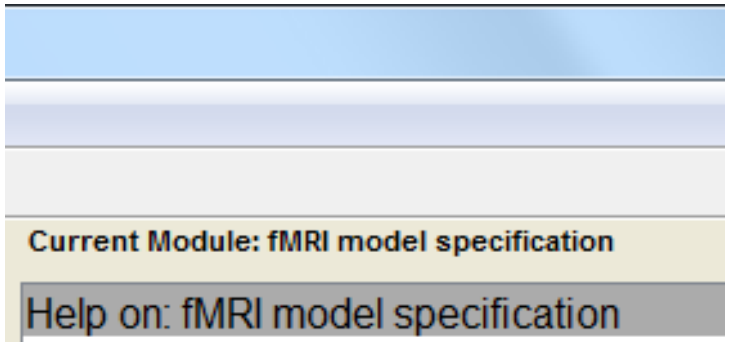

Wanting





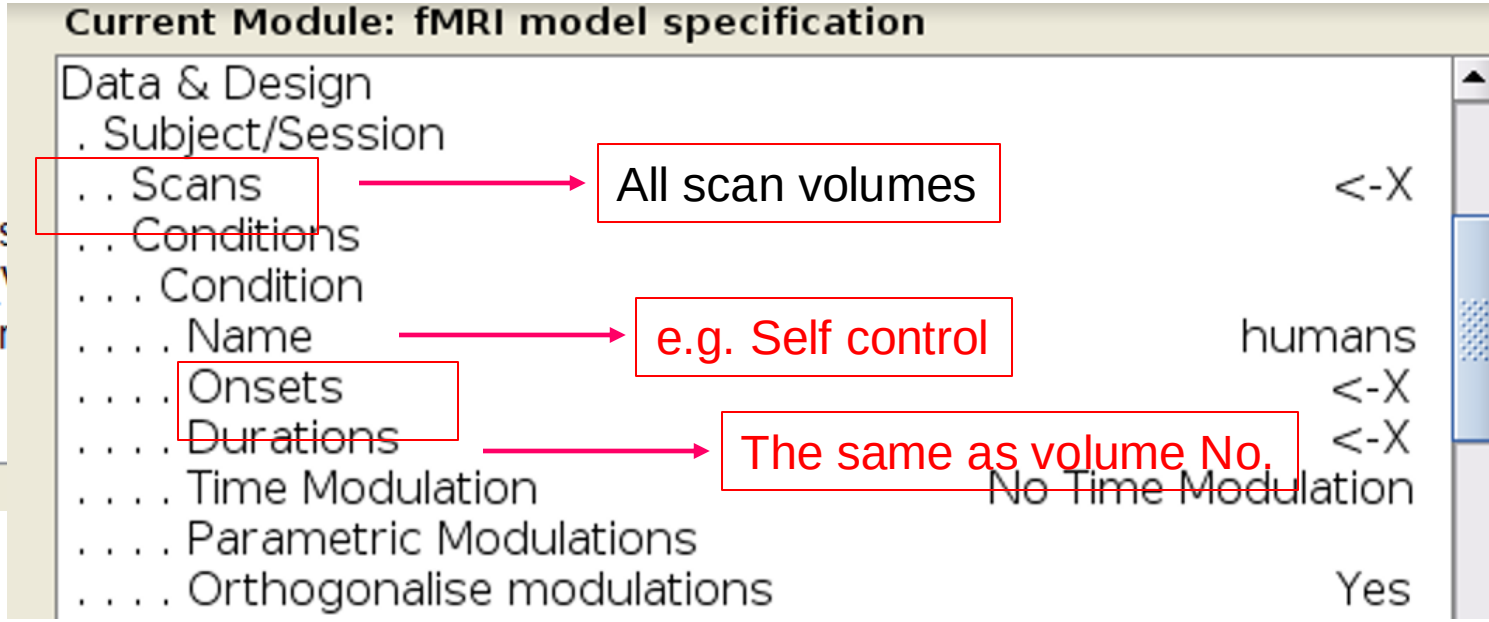

PCA analysis

# SPM12: parameter setting

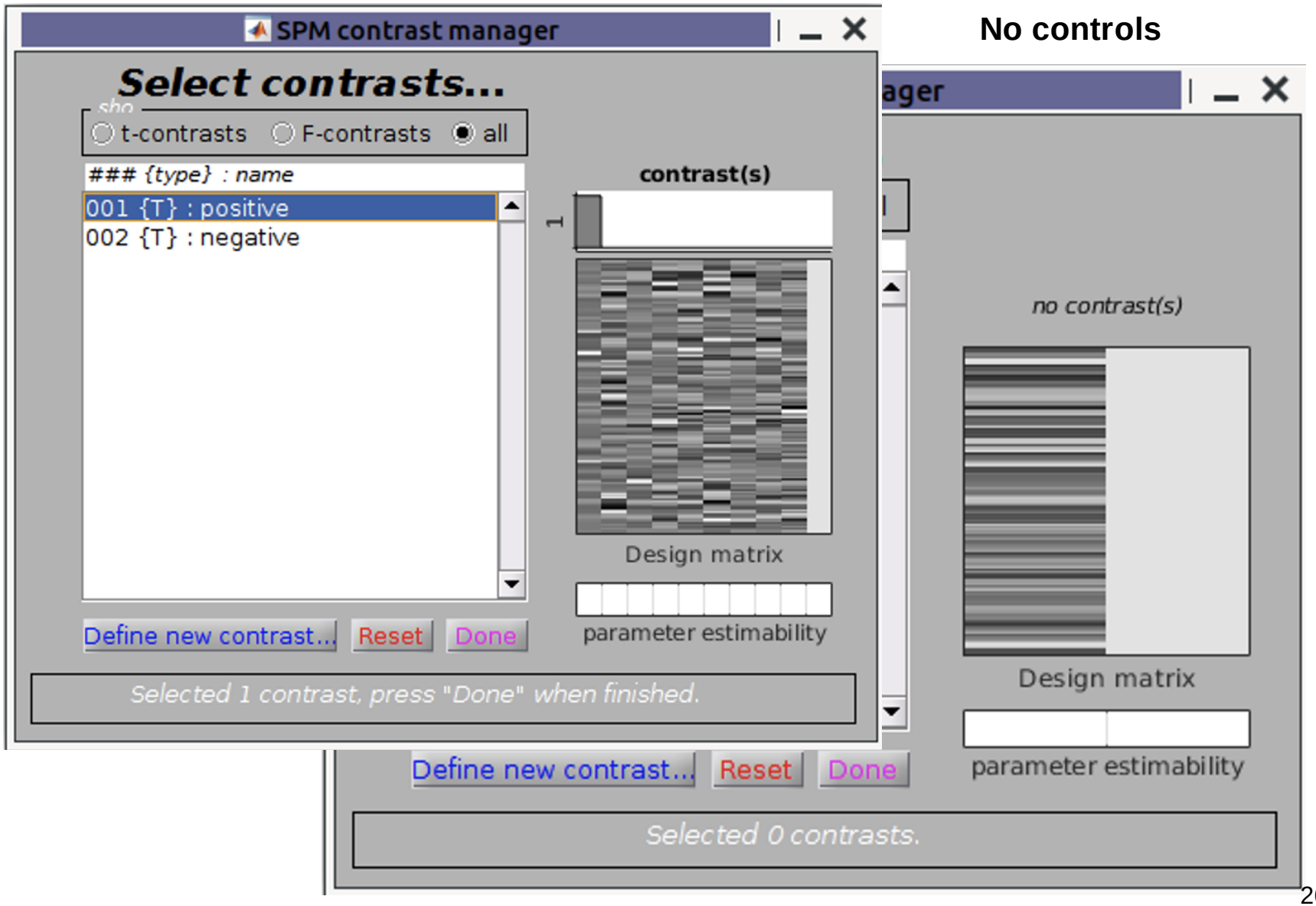


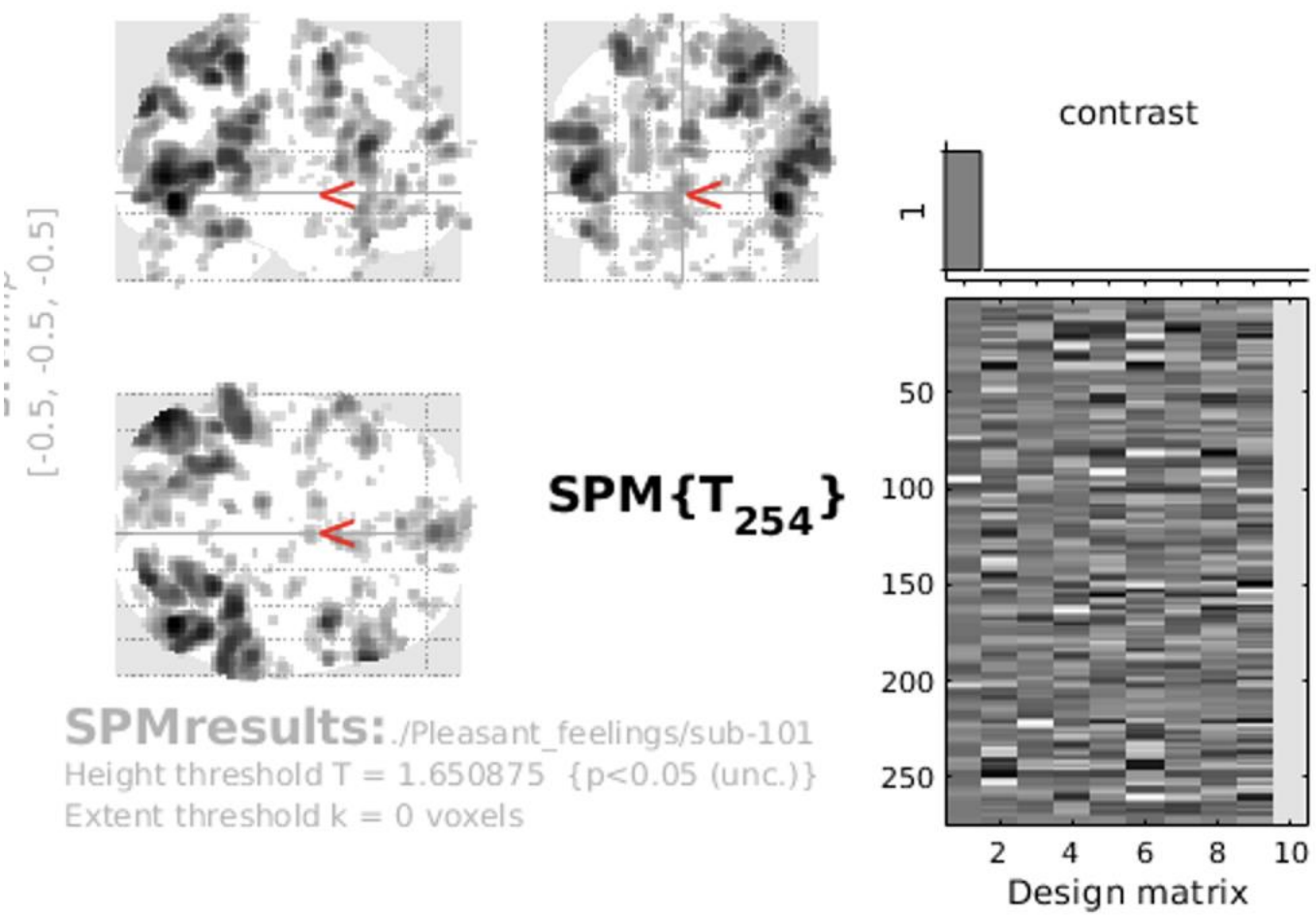

Result to store

scan } Dependent variables



## Controlling for low-level regressors





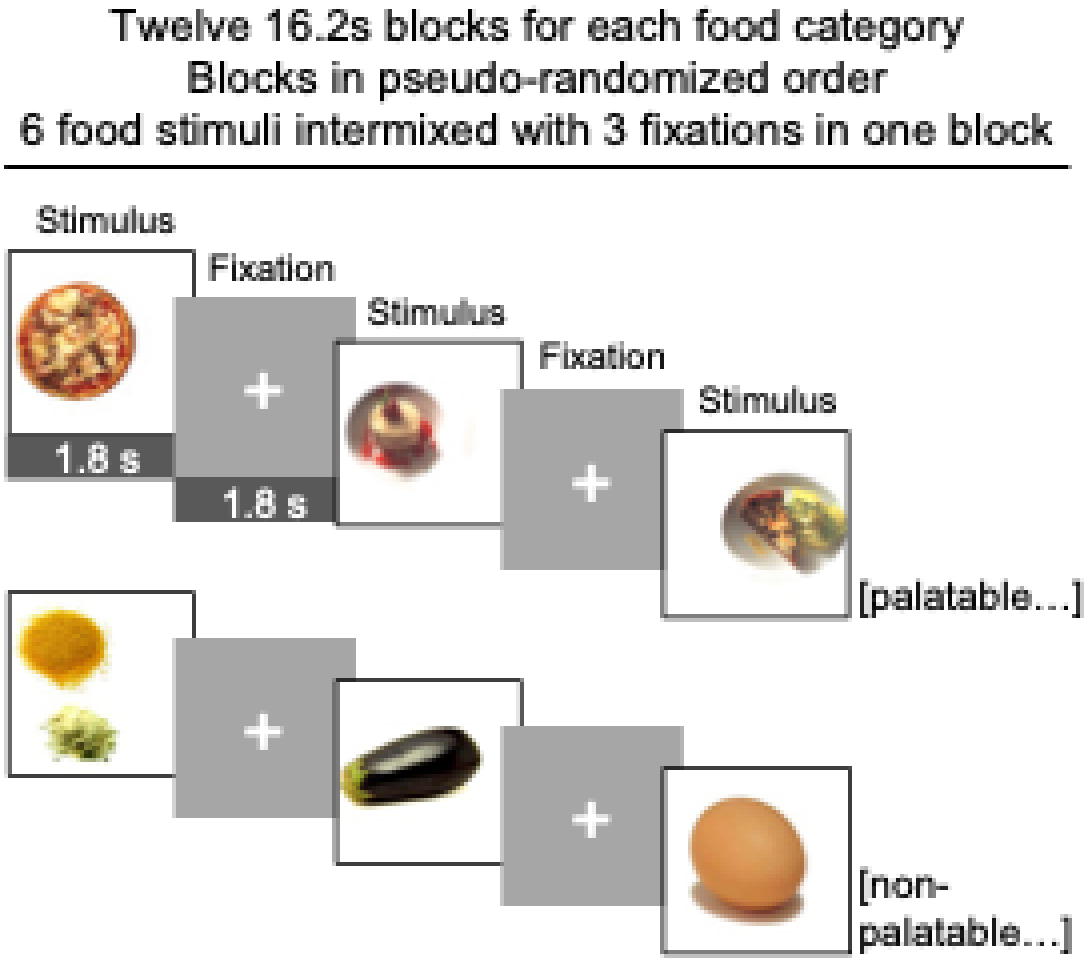

**Statistics:** ***p-values adjusted for search volume***

| set-level | | cluster-level | | | | peak-level | | | | | mm | mm | mm |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $p$ | $c$ | $p_{FWE\text{-}corr}$ | $q_{FDR\text{-}corr}$ | $k_E$ | $p_{uncorr}$ | $p_{FWE\text{-}corr}$ | $q_{FDR\text{-}corr}$ | $T$ | $(Z_{=})$ | $p_{uncorr}$ | | | |
| **1.000** | **100** | **0.009** | **0.002** | **1576** | **0.000** | **0.026** | **0.025** | **5.21** | **5.07** | **0.000** | **46** | **-72** | **-6** |
| | | | | | | 0.211 | 0.055 | 4.67 | 4.57 | 0.000 | 48 | -56 | 8 |
| | | | | | | 0.701 | 0.100 | 4.23 | 4.15 | 0.000 | 54 | -66 | 6 |
| | | **0.034** | **0.005** | **1272** | **0.000** | **0.070** | **0.034** | **4.97** | **4.85** | **0.000** | **-52** | **-76** | **6** |

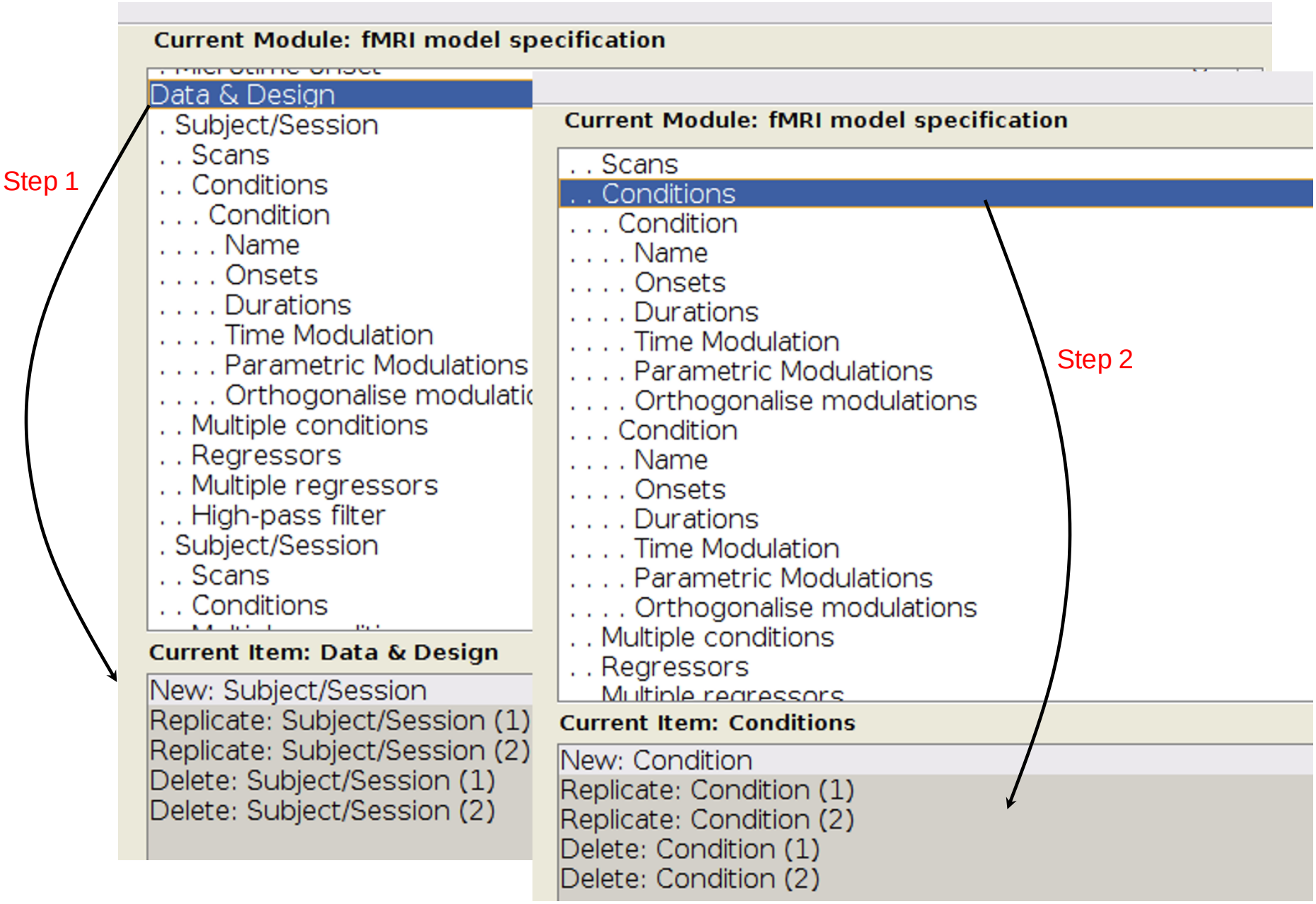
# Example 3: Repeated measure food-reward

Food reward experiment has been used in decoding the brain conceptualizeion of satiation as induced by secretin hormone.

*>> Lauri S., Sun L., et al., Nature Metabolism, volume 3, pages 798–809 (2021)*




- Control condition vs. condition with infusion of secretin.
- Each subject **scanned twice** with fMRI: one in control condition, the other under intervention (secretin infusion).


Current Module: fMRI model specification
Data & Design
. Subject/Session
. . Scans
. . Conditions
. . . Condition
. . . . Name
. . . . Onsets
. . . . Durations
. . . . Time Modulation
. . . . Parametric Modulations
. . . . Orthogonalise modulatic
. . Multiple conditions
. . Regressors
. . Multiple regressors
. . High-pass filter
. Subject/Session
. . Scans
. . Conditions
Current Item: Data & Design
New: Subject/Session
Replicate: Subject/Session (1)
Replicate: Subject/Session (2)
Delete: Subject/Session (1)
Delete: Subject/Session (2)
Step 1
Current Module: fMRI model specification
. . Scans
. . Conditions
. . . Condition
. . . . Name
. . . . Onsets
. . . . Durations
. . . . Time Modulation
. . . . Parametric Modulations
. . . . Orthogonalise modulations
. . . Condition
. . . . Name
. . . . Onsets
. . . . Durations
. . . . Time Modulation
. . . . Parametric Modulations
. . . . Orthogonalise modulations
. . Multiple conditions
. . Regressors
Current Item: Conditions
New: Condition
Replicate: Condition (1)
Replicate: Condition (2)
Delete: Condition (1)
Delete: Condition (2)
Step 2

```
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matlabbatch{1}.spm.stats.fmri_spec.sess(1).cond(1).duration = duration_apep;
matlabbatch{1}.spm.stats.fmri_spec.sess(1).cond(1).tmod = 0;
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matlabbatch{1}.spm.stats.fmri_spec.sess(1).cond(1).orth = 1;
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matlabbatch{1}.spm.stats.fmri_spec.sess(2).cond(1).name = 'appetite';
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matlabbatch{1}.spm.stats.fmri_spec.sess(2).cond(1).duration = s2_duration_apep;
matlabbatch{1}.spm.stats.fmri_spec.sess(2).cond(1).tmod = 0;
matlabbatch{1}.spm.stats.fmri_spec.sess(2).cond(1).pmod = struct('name', {}, 'p
```

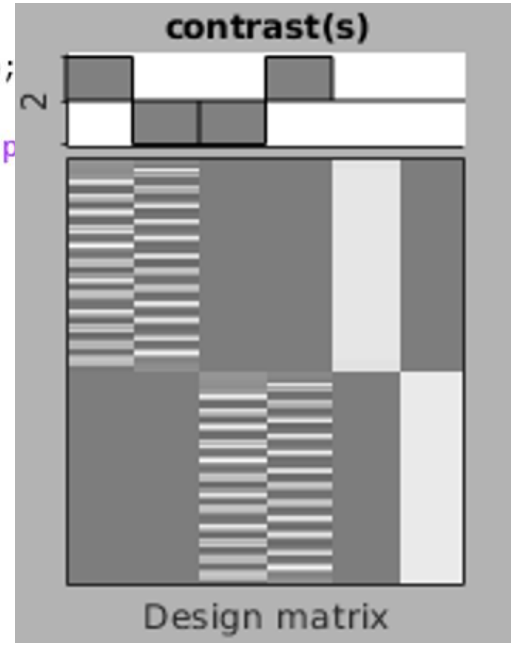

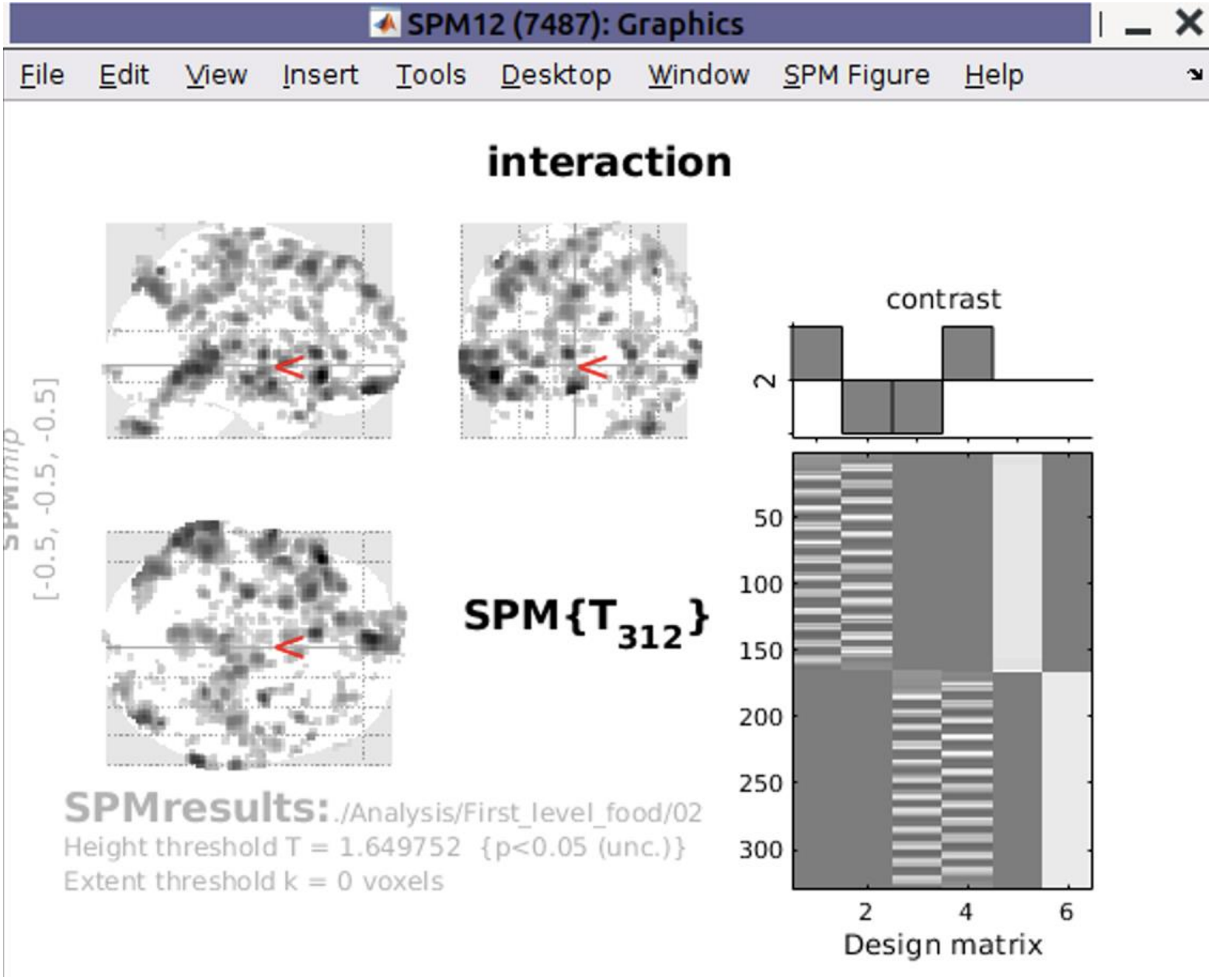
SPM12 (7487): Graphics
File Edit View Insert Tools Desktop Window SPM Figure Help
interaction
SPMmip
[-0.5, -0.5, -0.5]
SPM{T312}
contrast
2
50
100
150
200
250
300
2
4
6
Design matrix
SPMresults: ./Analysis/First_level_food/02
Height threshold T = 1.649752 {p<0.05 (unc.)}
Extent threshold k = 0 voxels

# Example 4: resting state fMRI

- ReHo = regional homogeneity: larger value indicates a higher regional synchronization.
- ALFF = amplitude of low-frequency fluctuation: indicate the magnitude of neural activity
- **FC = functional connectivity (between ROIs): inter-regional correlations**

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DPARSF: a MATLAB toolbox for "pipeline" data analysis of resting-state fMRI

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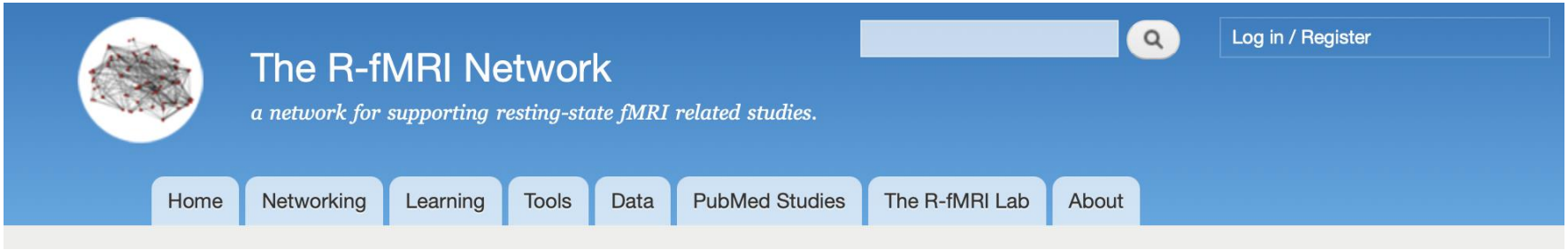
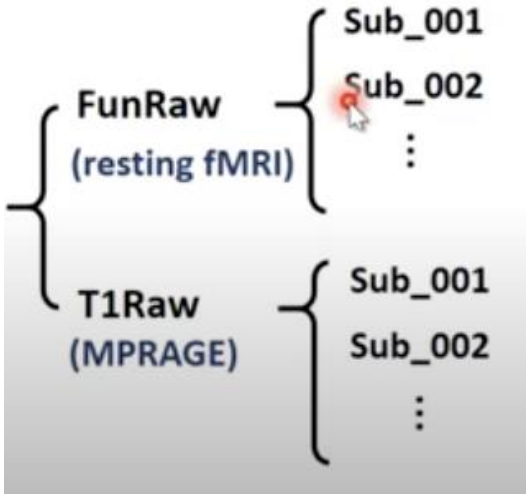
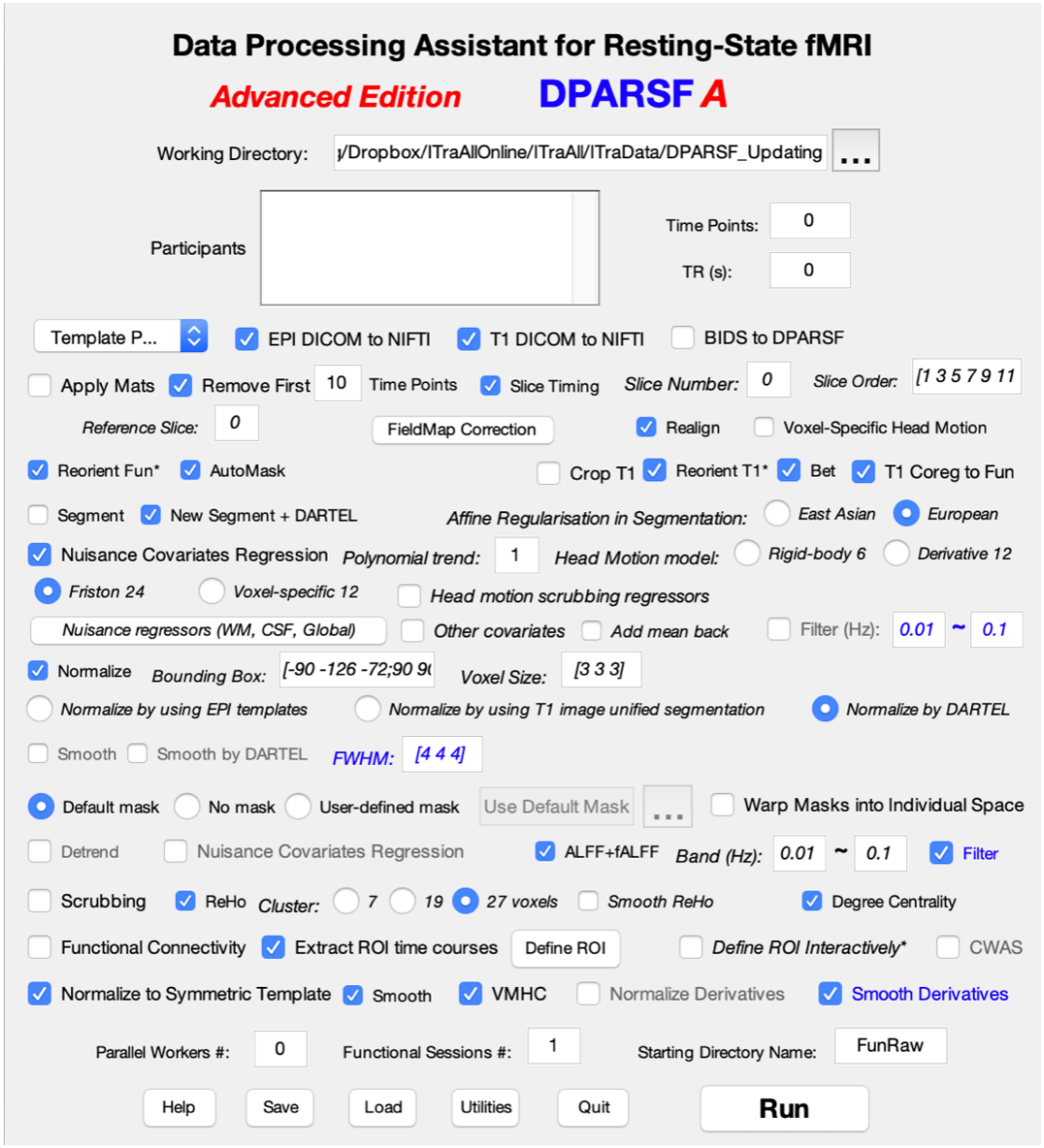
# Toolbox for rs-fMRI analysis

- Matlab based
- Download DPARSF from: http://rfmri.org/DPARSF



Data folder


FunRaw
(resting fMRI)
Sub_001
Sub_002
T1Raw
(MPRAGE)
Sub_001
Sub_002


Data Processing Assistant for Resting-State fMRI
Advanced Edition
DPARSF A
Working Directory:
Participants
Time Points:
TR (s):
Template P...
EPI DICOM to NIFTI
T1 DICOM to NIFTI
BIDS to DPARSF
Apply Mats
Remove First
Time Points
Slice Timing
Slice Number:
Slice Order:
Reference Slice:
FieldMap Correction
Realign
Voxel-Specific Head Motion
Reorient Fun*
AutoMask
Crop T1
Reorient T1*
Bet
T1 Coreg to Fun
Segment
New Segment + DARTEL
Affine Regularisation in Segmentation:
East Asian
European
Nuisance Covariates Regression
Polynomial trend:
Head Motion model:
Rigid-body 6
Derivative 12
Friston 24
Voxel-specific 12
Head motion scrubbing regressors
Nuisance regressors (WM, CSF, Global)
Other covariates
Add mean back
Filter (Hz):
Normalize
Bounding Box:
Voxel Size:
Normalize by using EPI templates
Normalize by using T1 image unified segmentation
Normalize by DARTEL
Smooth
Smooth by DARTEL
FWHM:
Default mask
No mask
User-defined mask
Use Default Mask
Warp Masks into Individual Space
Detrend
Nuisance Covariates Regression
ALFF+fALFF
Band (Hz):
Filter
Scrubbing
ReHo
Cluster:
7
19
27 voxels
Smooth ReHo
Degree Centrality
Functional Connectivity
Extract ROI time courses
Define ROI
Define ROI Interactively*
CWAS
Normalize to Symmetric Template
Smooth
VMHC
Normalize Derivatives
Smooth Derivatives
Parallel Workers #:
Functional Sessions #:
Starting Directory Name:
FunRaw
Help
Save
Load
Utilities
Quit
Run

# Summary

- The first level analysis is **a within-subject analysis, necessary due to the low signal-noise ratios**.
- **Experimental design decides the statistical model**.
- We have showed 4 example studies on how to conduct the first level analysis.
- Using **Contrasts** to view the results
- Contrast images are ready for second level analysis.

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# Thanks!

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