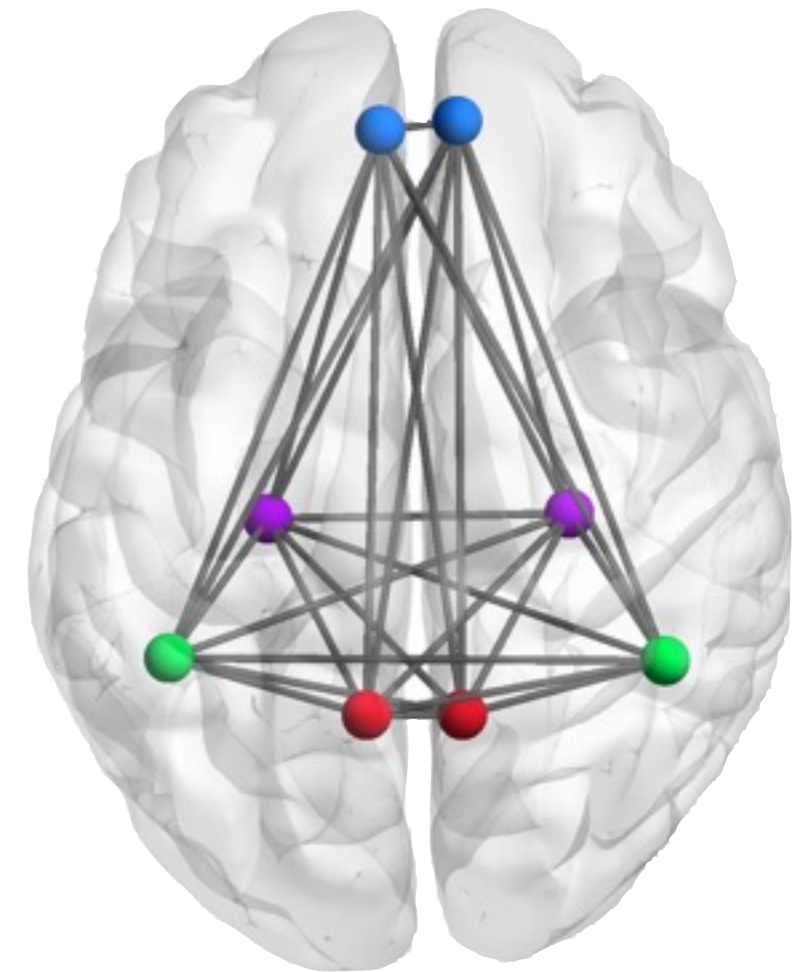


Correlation Analysis between Imaging & Neuropsychological Tests



K.H. Chou, Ph.D (周坤賢)

2016.01.21

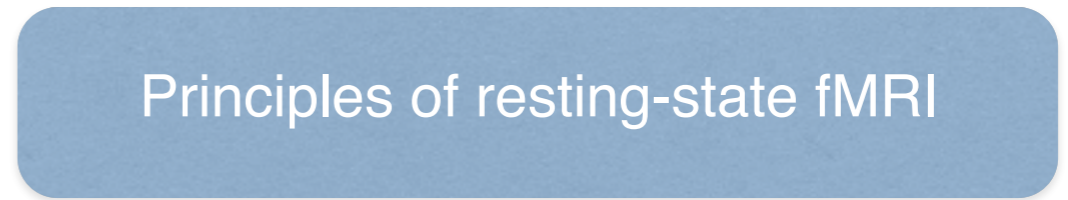
Assistant research fellow / Brain Research Center / National Yang Ming University



Where are we now?



Principles of stimulus-evoked fMRI



Principles of resting-state fMRI



Task-fMRI preprocessing



Resting-state functional connectivity



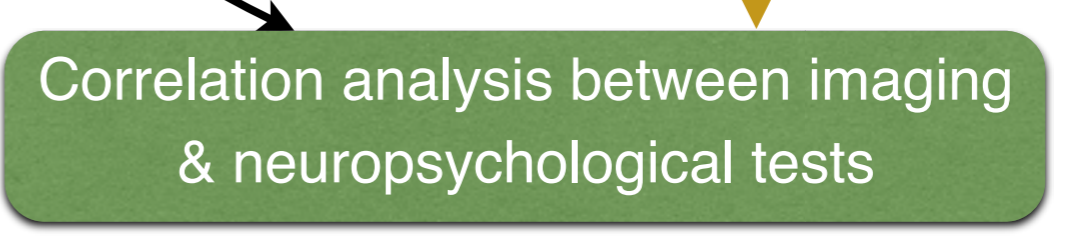
Data modeling & individual analysis
1st



Graph theory & network analysis



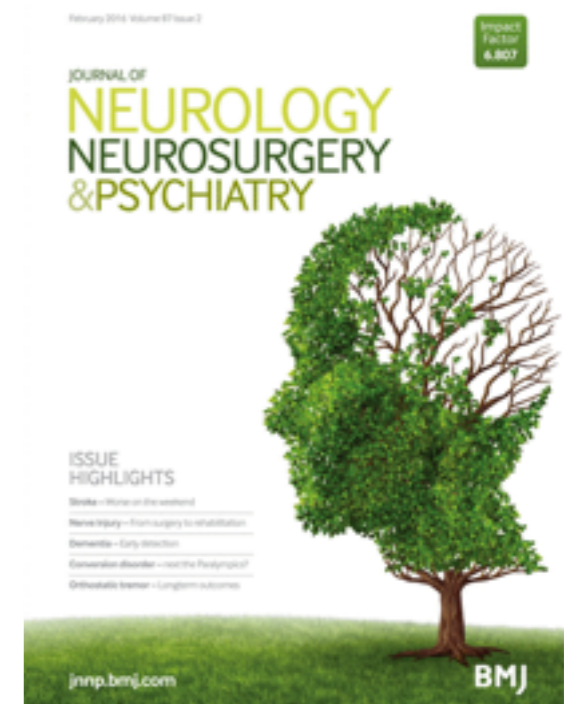
Group analysis to factorial design
2nd level



Correlation analysis between imaging
& neuropsychological tests

Today's mission

My mission today is to teach you how to use **freeware** to perform **basic statistical analysis** of the **imaging journal paper** (**real world example**)



The three basic roles of this course



Don't think any shortcut solutions

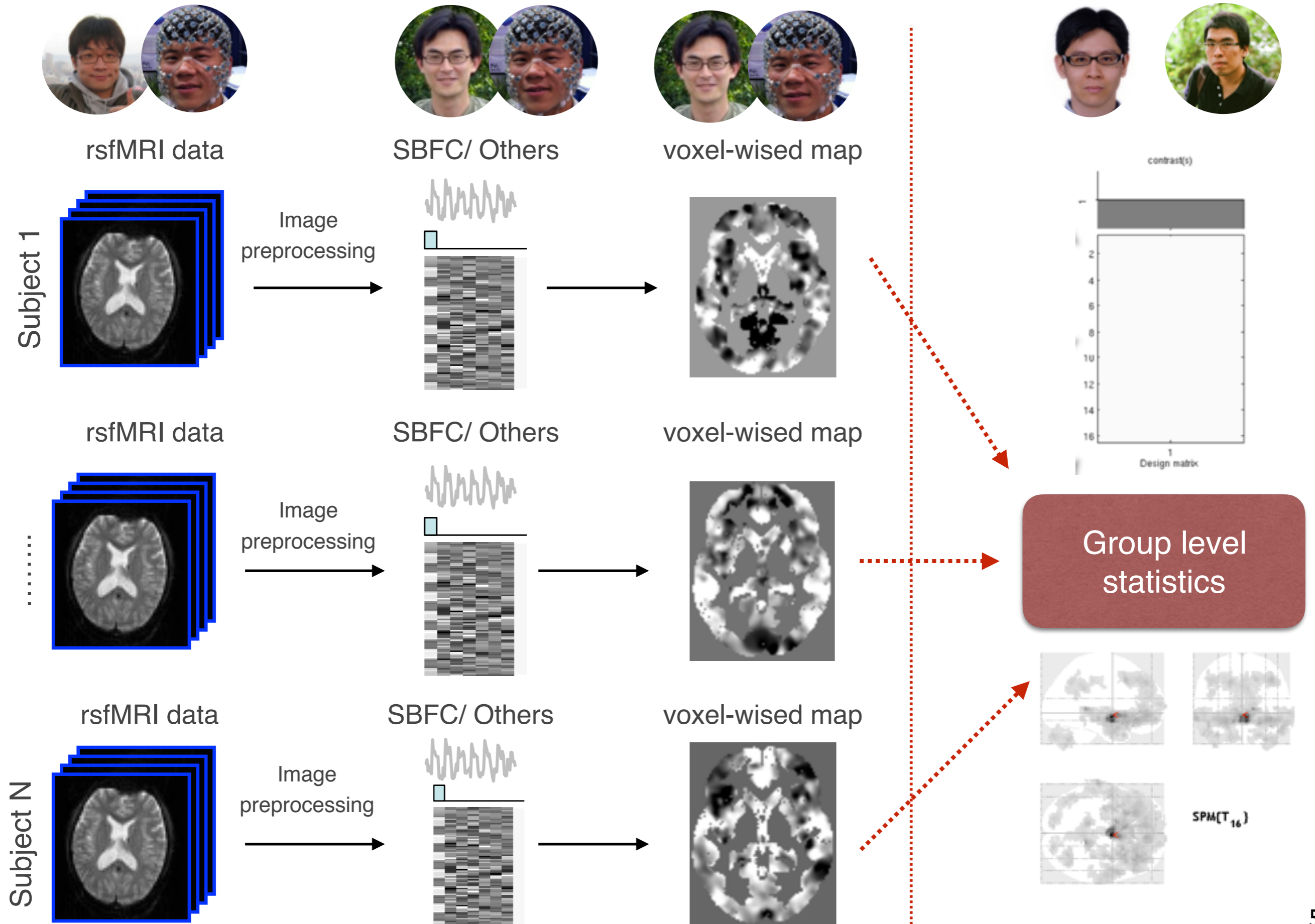


Practice, practice and practice

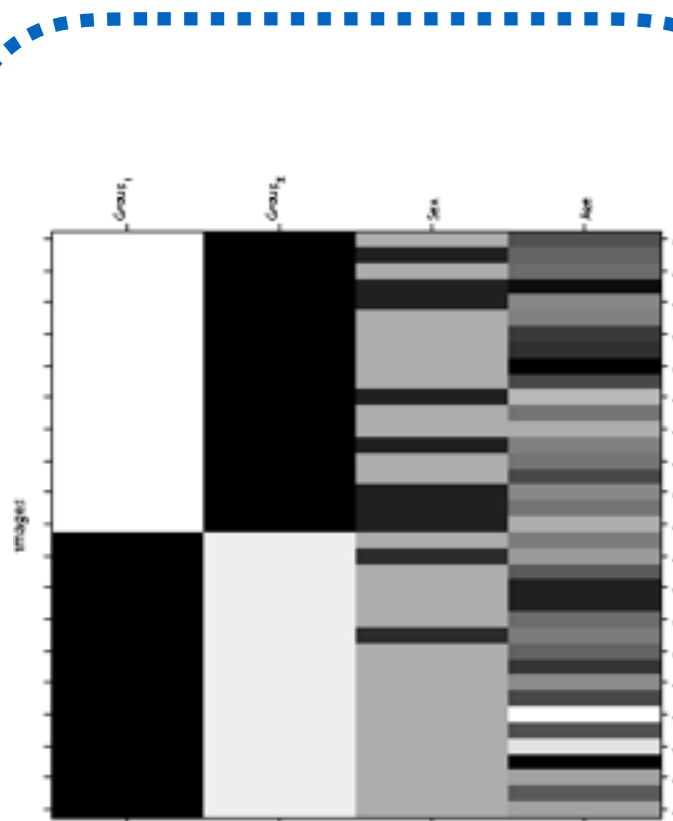


Ask me why when we have free time

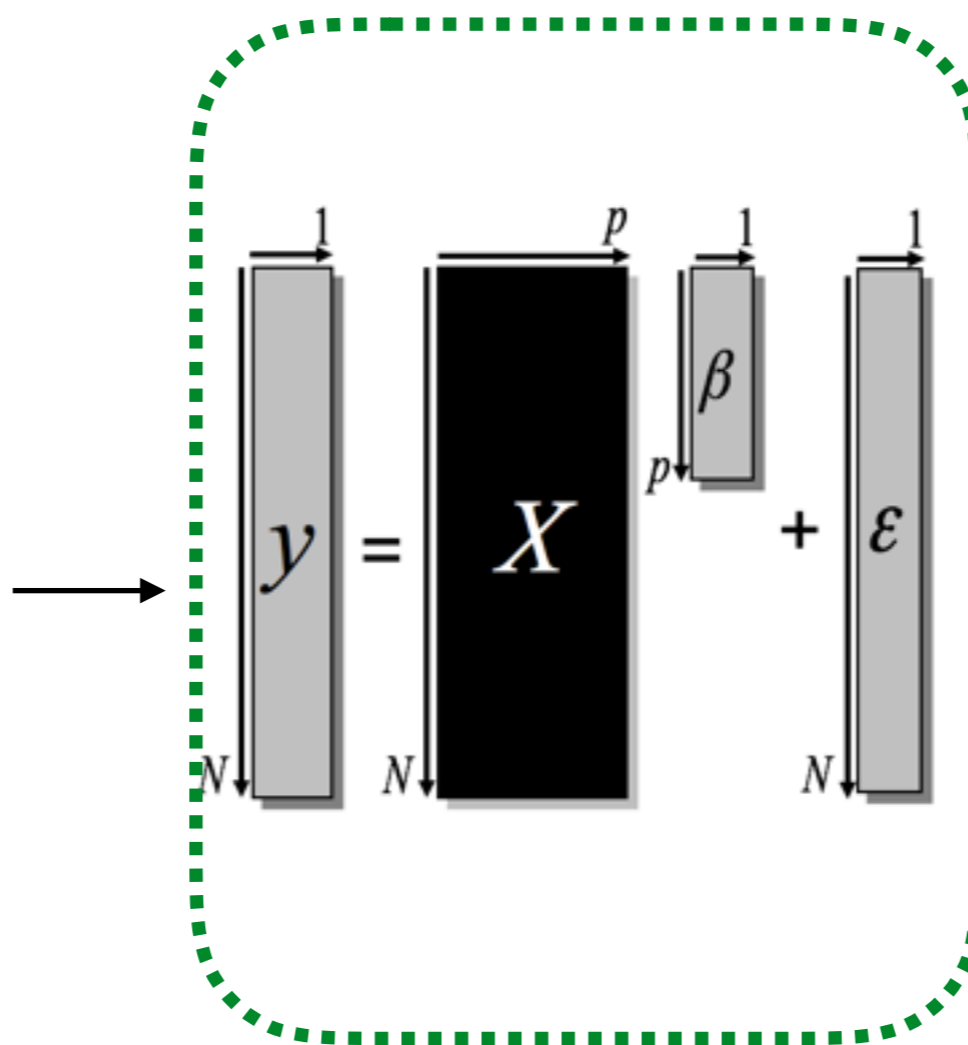
From individual pattern to group representation



The basic statistical pipeline of **S**tatistical **P**arametric **M**apping

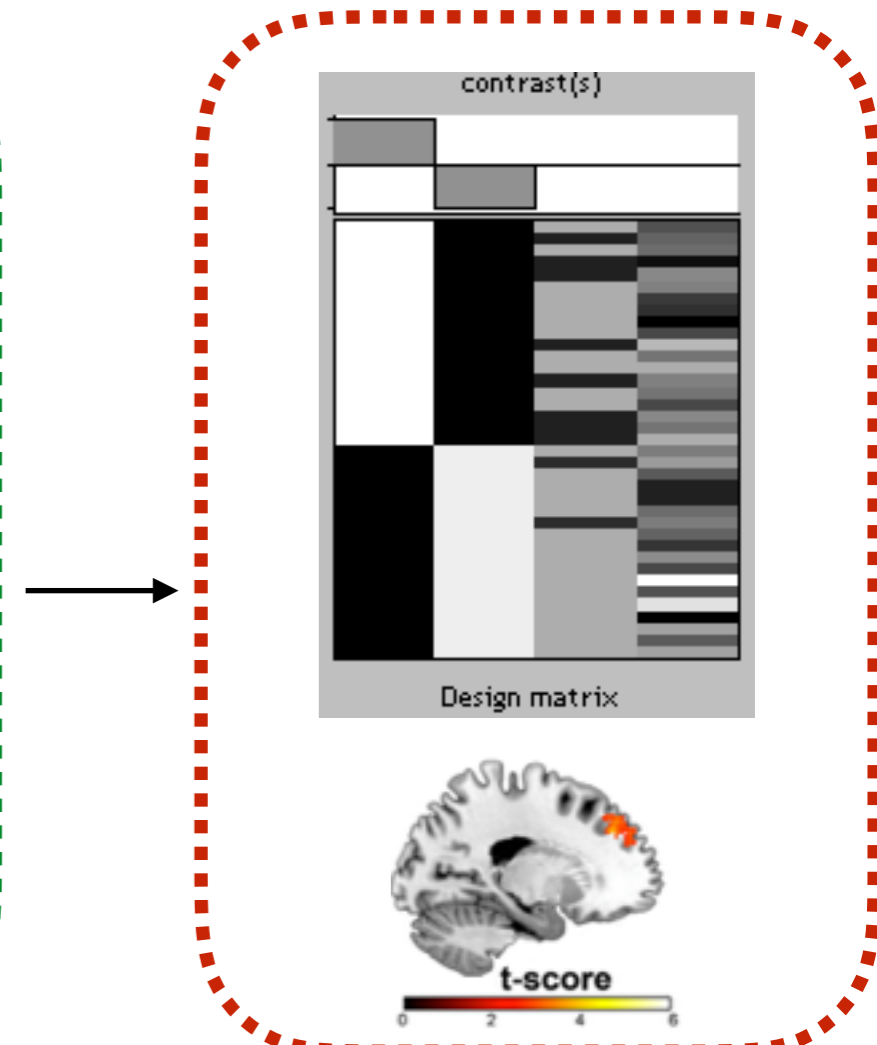


Model construction



A diagram illustrating the model estimation phase. It shows the linear model equation: $y = X\beta + \epsilon$. The vector y has dimension N and width 1. The matrix X has dimension N and width p . The vector β has dimension p and width 1. The vector ϵ has dimension N and width 1. The entire diagram is enclosed in a green dashed border.

Model estimation



Statistical inference

General Linear Model - Modeling the measured signal

Why? Make inferences about effects of interest

How?

- Decompose data into effects and error
- Form statistic using estimates of effects and error

$$Y = X \beta + E$$

Dependent Variable

(What you are measuring)

Independent Variable

(What you are manipulating)

Relative Contribution

(These need to be estimated)

Error

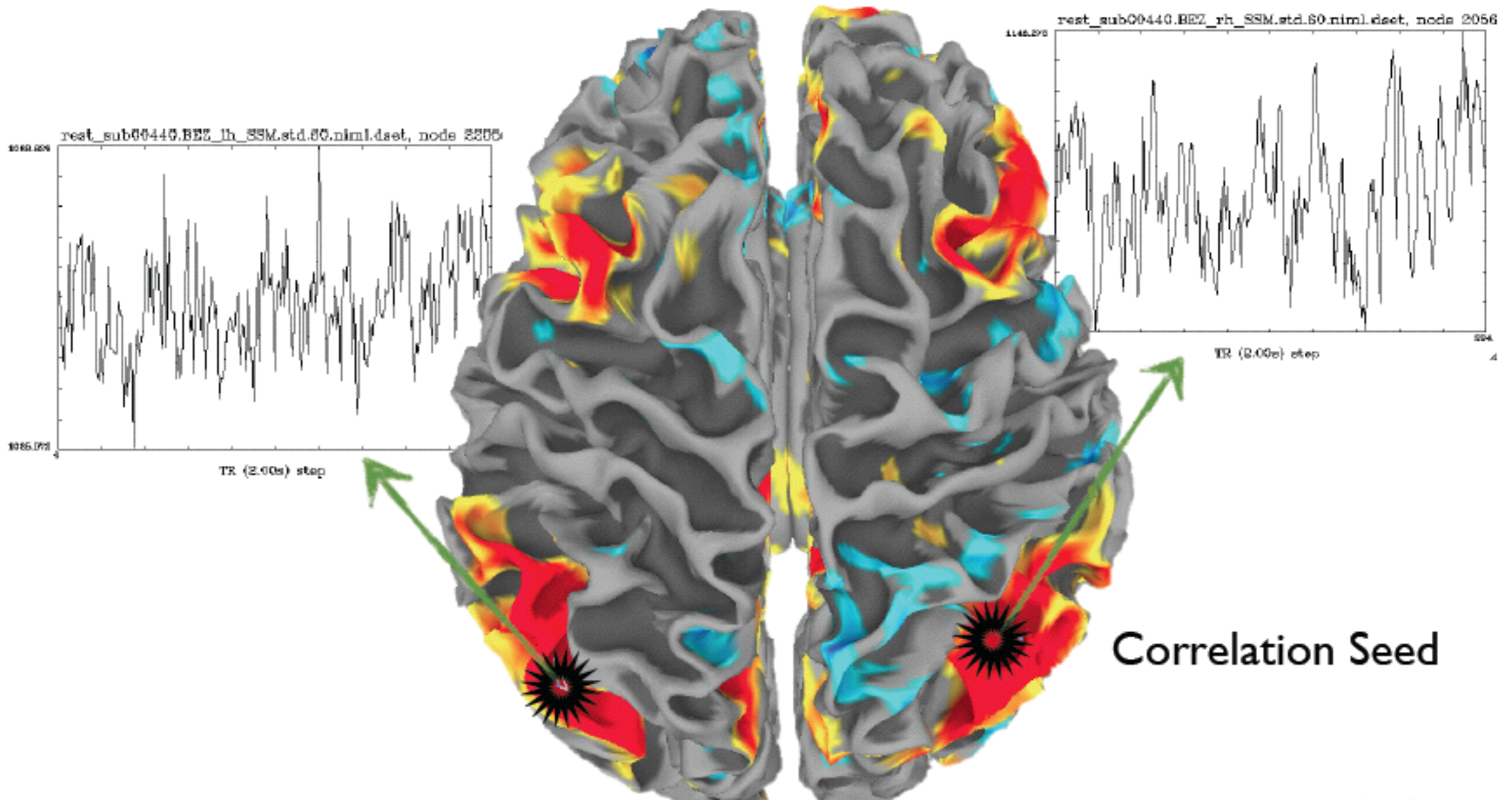
(The difference between the observed data and that which is predicted by the model)

Aim: To explain as much of the variance in Y by using X, and thus reducing E

More than 1 EV ? $Y = X_1\beta_1 + X_2\beta_2 + \dots X_n \beta_n \dots + E$

Univariate analysis !!

Recall your memory - The definition of functional connectivity



- Functional connectivity in rsfMRI

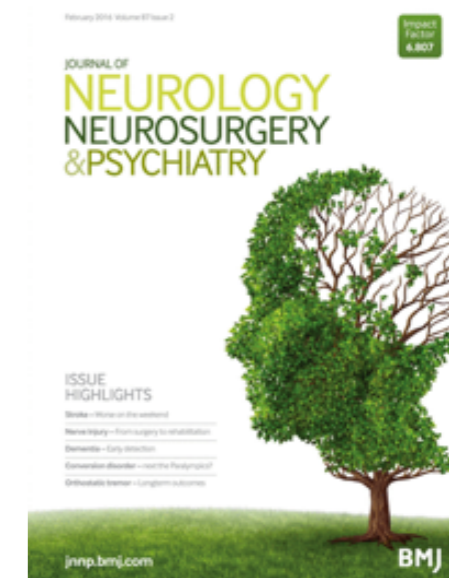
Temporal correlation of biophysical signal measured in distributed brain areas

The material of today's course

RESEARCH PAPER

Altered hypothalamic functional connectivity in cluster headache: a longitudinal resting-state functional MRI study

Fu-Chi Yang,^{1,2} Kun-Hsien Chou,^{3,4} Jong-Ling Fuh,^{5,6} Pei-Lin Lee,⁷
Jiing-Feng Lin,^{8,9} Yung-Yang Lin,^{1,4,5,6} Ching-Po Lin,^{1,3,4,7} Shuu-Jiun Wang^{1,4,5,6}



Subjects:

19 HCs ; 18 CH-In-bout (baseline) ; 18 CH-out-bout (follow-up)

Hypothesis:

- (1) Alteration of hypothalamic functional connectivity in CH
- (2) Bout associated alteration in hypothalamic functional connectivity
- (3) The relationship between clinical evaluation and hypothalamic functional connectivity

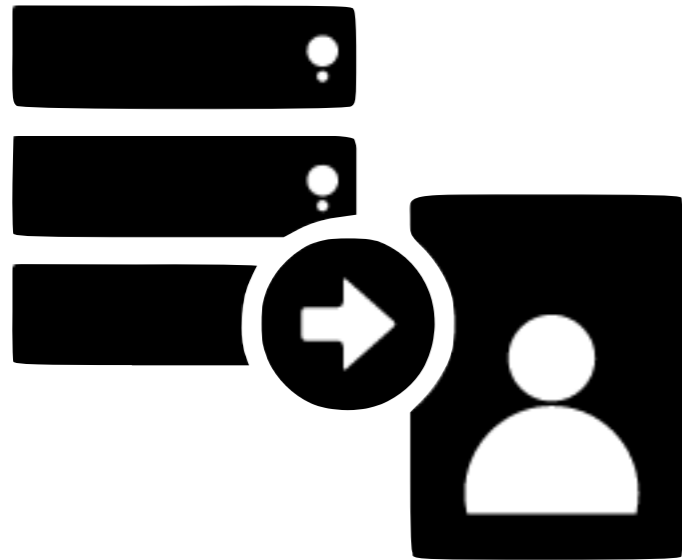
Image approach:

Whole brain voxel-wise seed based functional connectivity analysis

Statistical approach: (General Linear Model)

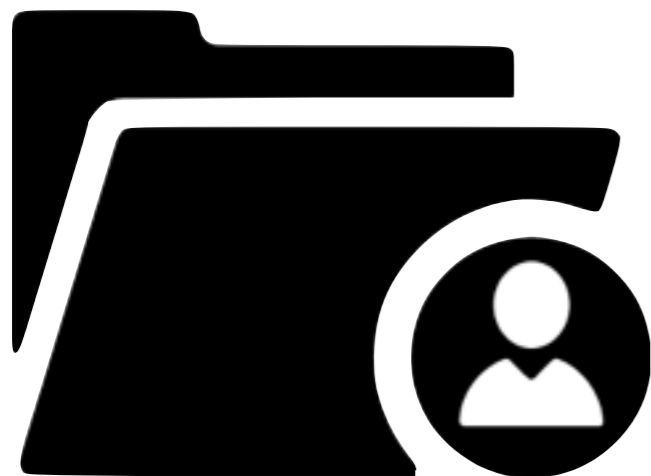
- (1) **Two-sample T-test** (Analysis of covariance ; ANCOVA test)
- (2) **Pair T-test**
- (3) **Multiple regression** (Partial correlation)

Before playing data



Copy “Image dataset” to your personal folder

Right_Hypothalamus_FC



Make three new folder for following practice

Two_Sample_T_NC_Baseline

Pair_T_Baseline_Followup

Multiple_Regression

The interface of Statistical Parametric Mapping

The image displays the SPM8 software interface, divided into two main windows: 'SPM8 (PaulSmith): Menu' and 'SPM8 (PaulSmith): Graphics'.

SPM8 (PaulSmith): Menu

- Spatial pre-processing:** Includes dropdown menus for 'Reali...', 'Norm...', and 'Coreg...', and buttons for 'Smooth' and 'Segment'.
- Model specification, review and estimation:** Contains buttons for 'Basic models', 'Estimate', 'Review', and 'Bayesian'. The 'Basic models' and 'Estimate' buttons are highlighted with dashed blue and green borders, respectively.
- Inference:** Features a 'Results' button highlighted with a dashed red border.
- Dynamic Causal Modelling:** A button located below the inference section.
- SPM for PET/SPECT:** A section containing buttons for 'Display', 'Check Reg', 'Re...', 'PET', 'Too...', 'PPIs', 'ImCalc', 'DICOM Import', 'Help', 'Utils...', 'Batch', and 'Quit'.

SPM8 (PaulSmith): Graphics

SPM8
Welcome to SPM8

Please refer to this version as "SPM8" in papers and communications.

SPM is developed under the auspices of Functional Imaging Laboratory (FIL), The Wellcome Trust Centre for NeuroImaging, in the Institute of Neurology at University College London (UCL), UK.

Although SPM8 will read image files from previous versions of SPM, there are differences in the algorithms, templates and models used. Therefore, we recommend you use a single SPM version for any given project.

The SPM8 Release Notes can be found online:
<http://www.fil.ion.ucl.ac.uk/spm/software/spm8/>

Further information may be found at the SPMweb site:
<http://www.fil.ion.ucl.ac.uk/spm/>
where details of the SPM email discussion list can be found:
<http://www.fil.ion.ucl.ac.uk/spm/support/>
& PDF manual is also available in the 'man' folder of SPM and online:
<http://www.fil.ion.ucl.ac.uk/spm/doc/manual.pdf>

SPM is free but copyright software, distributed under the terms of the GNU General Public Licence as published by the Free Software Foundation (either version 2, as given in file `spm_LICENCE.man`, or at your option, any later version). Further details on "copyleft" can be found at <http://www.gnu.org/copyleft/>.

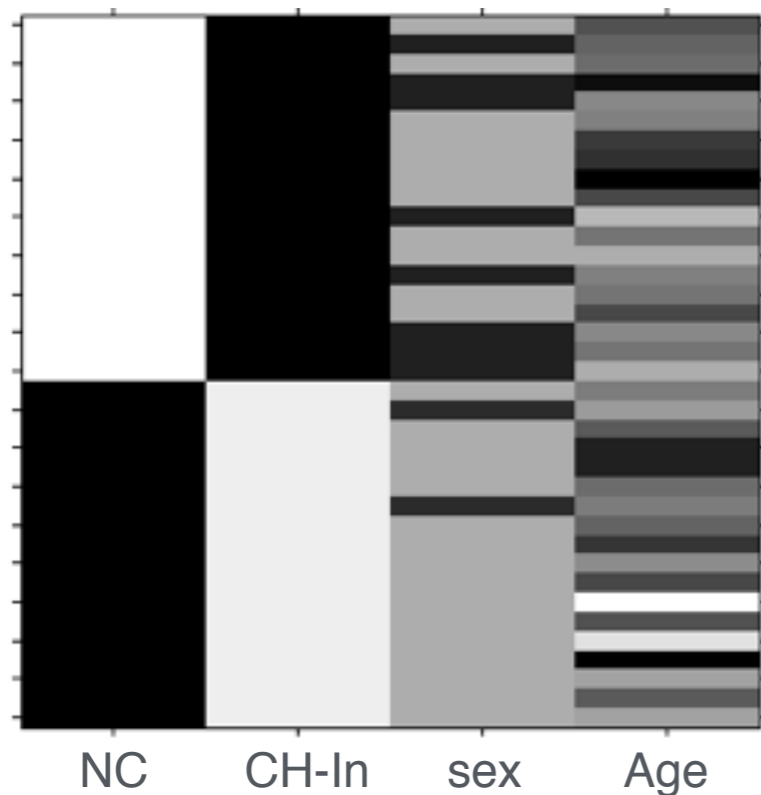
Copyright (C) 1991,1994-2015 Wellcome Trust Centre for Neuroimaging

Alteration of hypothalamic functional connectivity in CH

“For hypothalamic functional connectivity, is there significantly higher FC in the healthy controls than in the patient with cluster headache after adjusting age and gender effect ? (two sample T-test)”

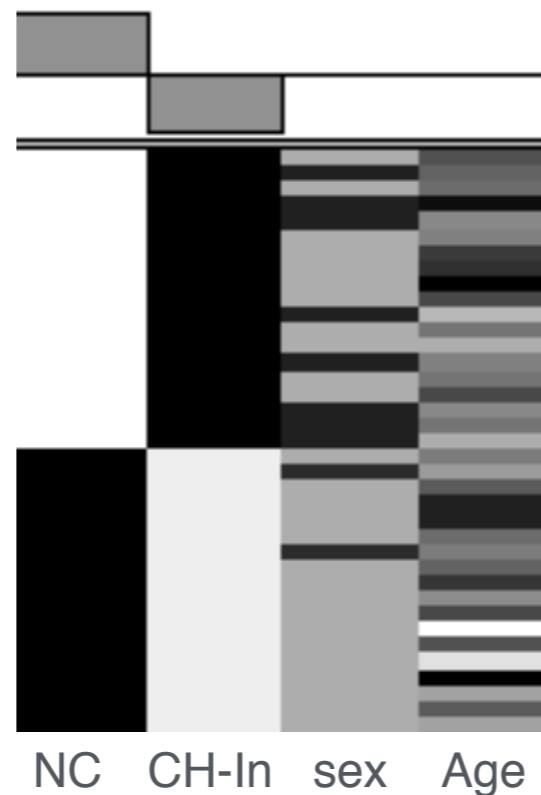
$$Y = \beta_1(\text{NC}) + \beta_2(\text{CH-In-bout}) + \beta_3(\text{sex}) + \beta_4(\text{age}) + \varepsilon$$

Two sample T-test

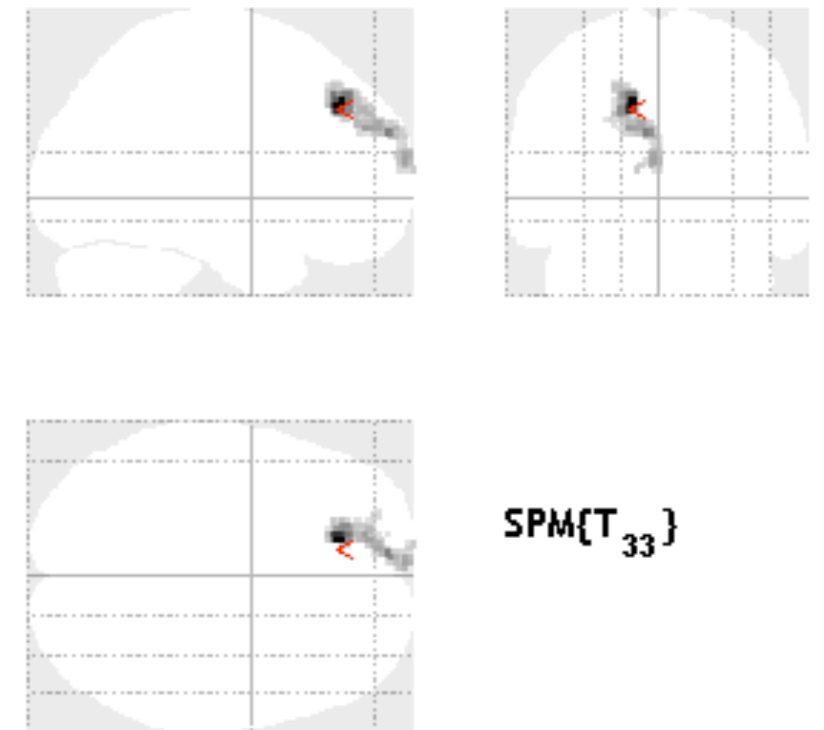


Model construction

Contrast



Statistical inference



Result visualization

Demo - Two Sample T-test (Model construction)

Current Module: Factorial design specification

Help on: Factorial design specification

Directory	/Volumes/Data HD/NTU_Course_Material/Statistical/Two_Sample_T_NC_Baseline/
Design	
. Two-sample t-test	
. Group 1 scans	19 files
. Group 2 scans	18 files
.. Independence	Yes
.. Variance	Unequal
.. Grand mean scaling	No
ANCOVA	No
Covariates	
. Covariate	
.. Vector	37x1 double
.. Name	Sex
.. Interactions	None
.. Centering	Overall mean
. Covariate	
.. Vector	37x1 double
.. Name	Age
.. Interactions	None
.. Centering	Overall mean
Masking	
. Threshold masking	
.. None	
. Implicit Mask	
. Explicit Mask	No
Global calculation	
. Omit	
Global normalisation	
. Overall grand mean scaling	

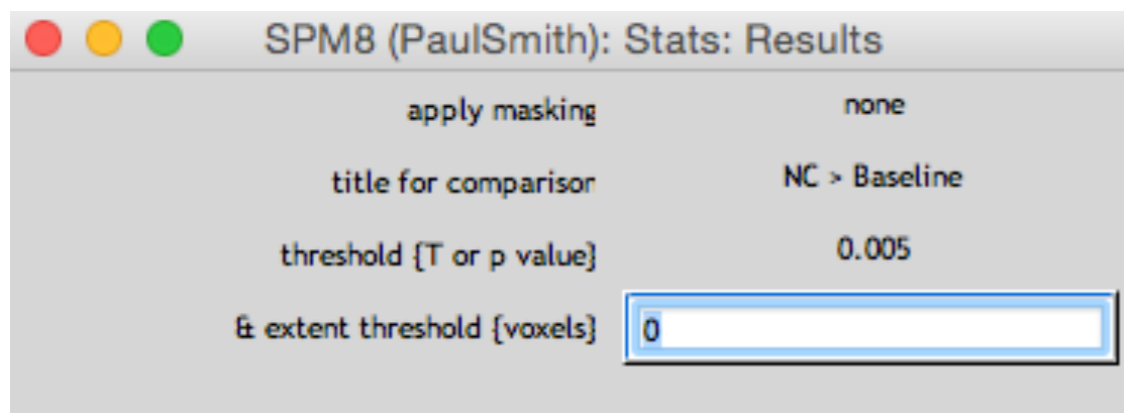
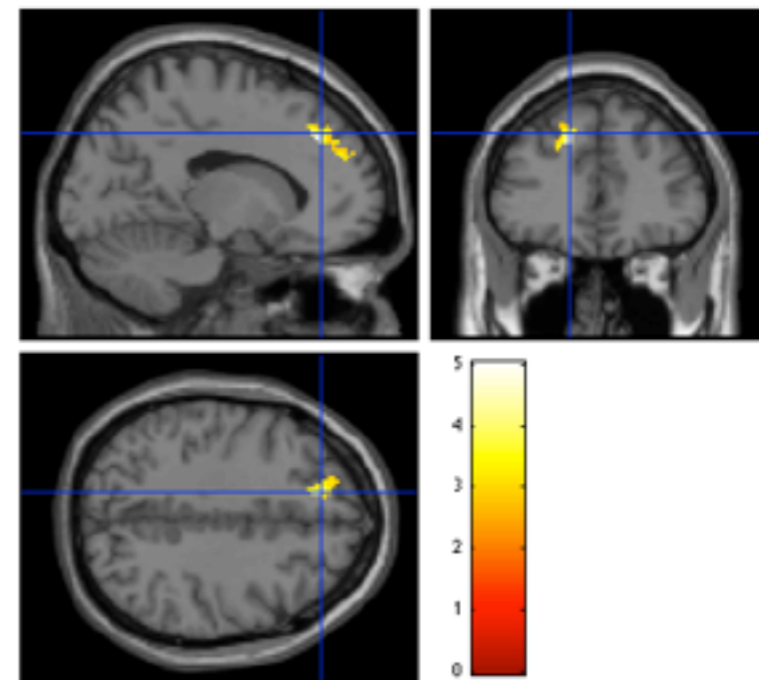
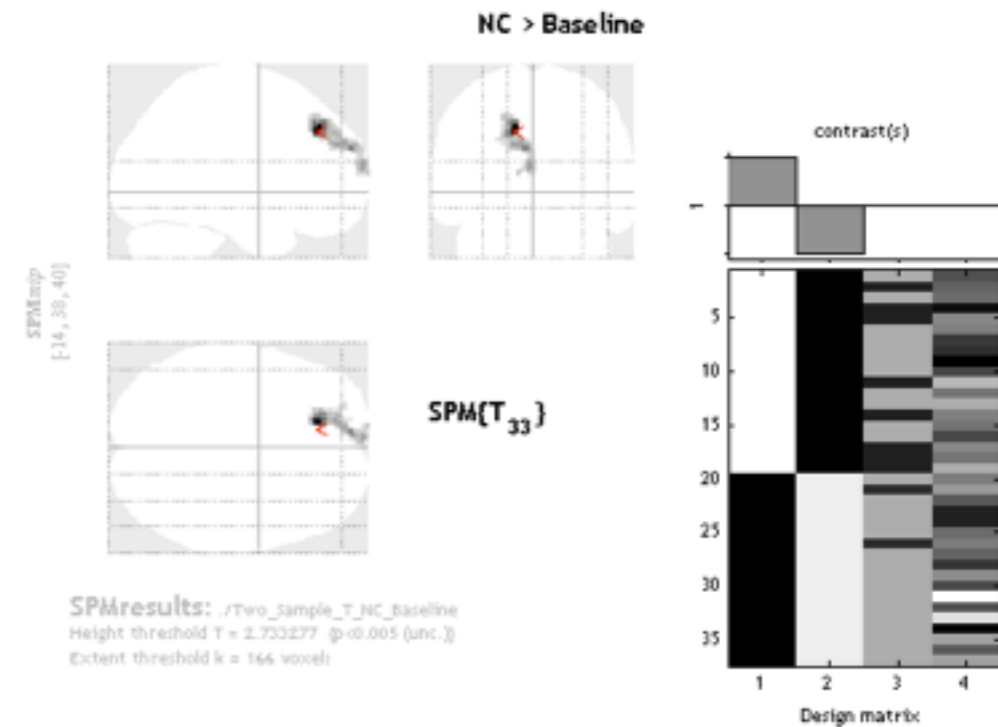
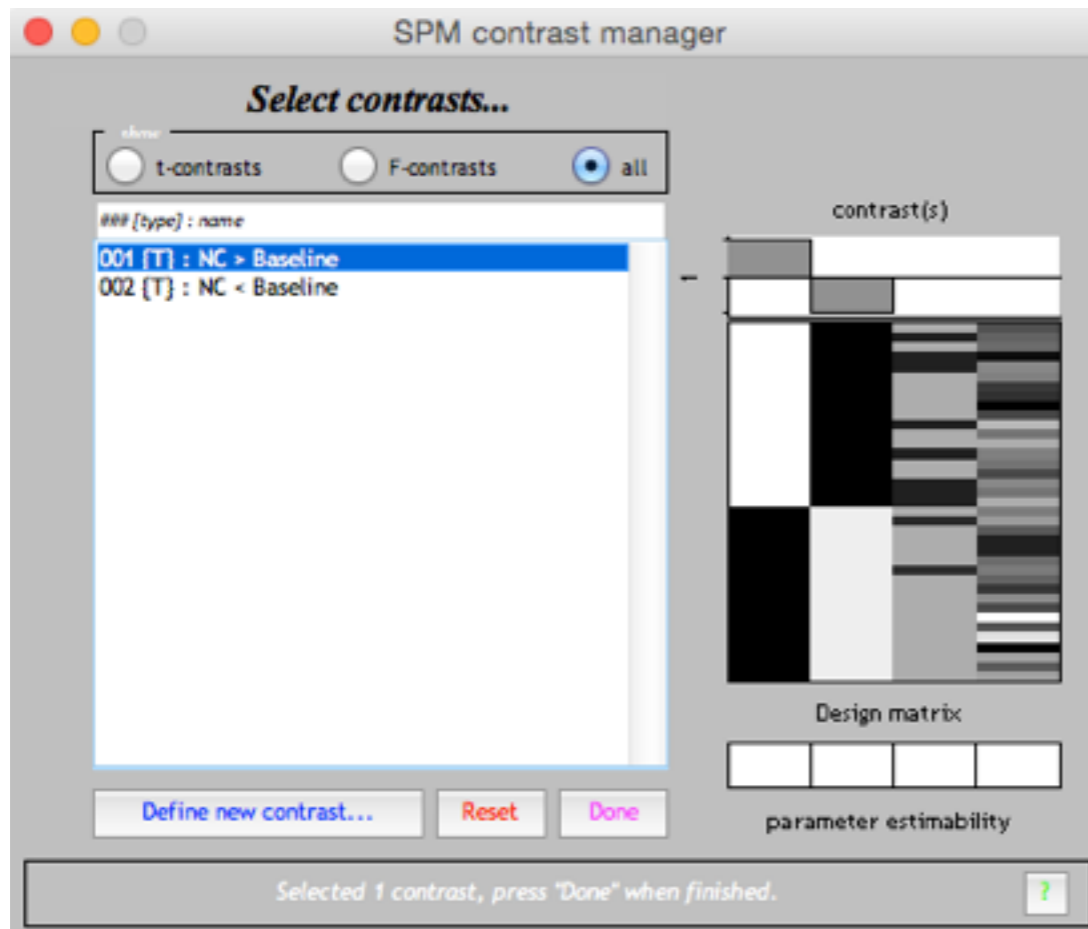
Directory: The output directory of your statistical model

Design: The statistical model you want to use (**Two sample T-test**)

Covariates: The effect you want to adjust (sex and age)

Masking: The region you want to do statistical inference

Demo - Two Sample T-test (Statistical inference & Result visualization)



Statistical criteria:

Uncorrected voxel $p < 0.005$ with 166 extended voxels

(Page 3)

Cluster location:

$(x,y,z) = (-14, 38, 40)$

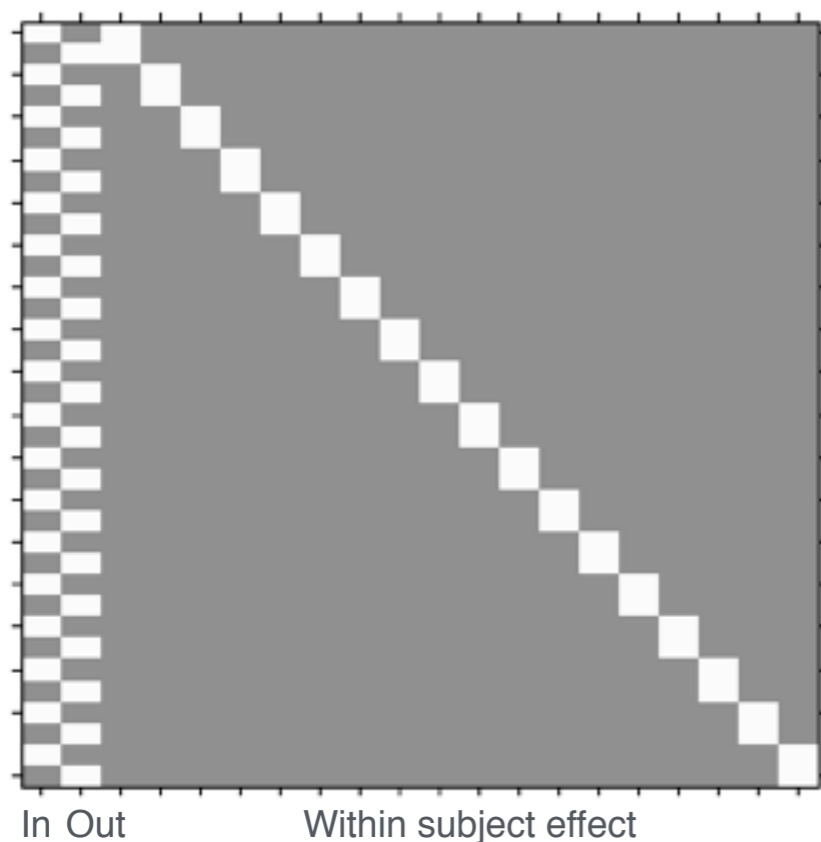
(Page 6, Table 2)

Bout associated alteration in hypothalamic functional connectivity

“For hypothalamic functional connectivity, is there significantly higher FC in the follow-up scan than in the baseline scan of the patient with cluster headache ? (pair T-test)”

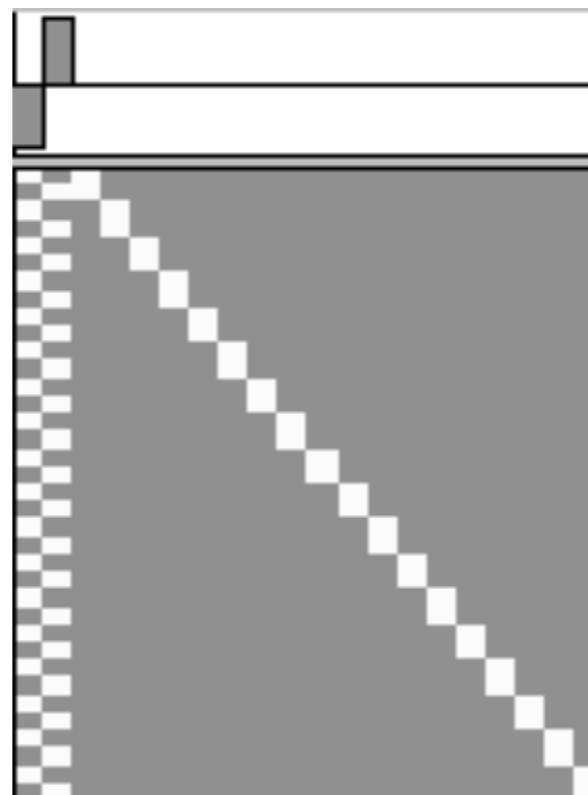
$$Y = \beta_1(\text{baseline}) + \beta_2(\text{follow-up}) + \beta_3(\text{within-subject 1 effect}) + \dots + \beta_n(\text{within-subject n effect}) + \varepsilon$$

Pair T-test

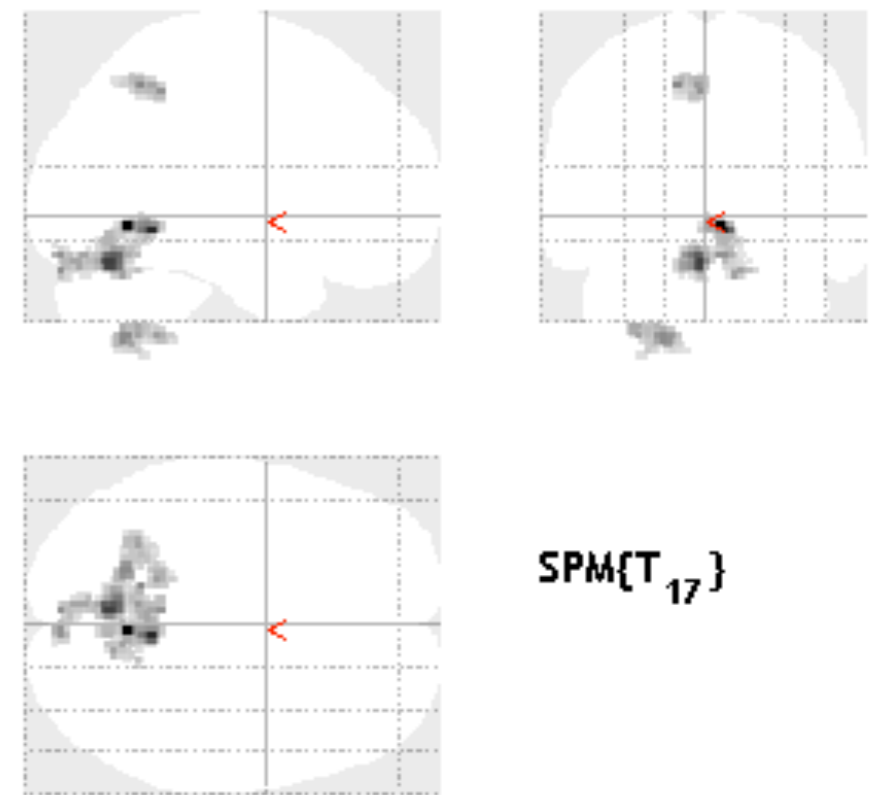


Model construction

Contrast



Statistical inference



Result visualization

Demo - Pair T-test (Model construction)

Current Module: Factorial design specification

Help on: Factorial design specification

Directory /Volumes/Data HD/NTU_Course_Material/Statistical/Pair_T_Baseline_Followup/

Design

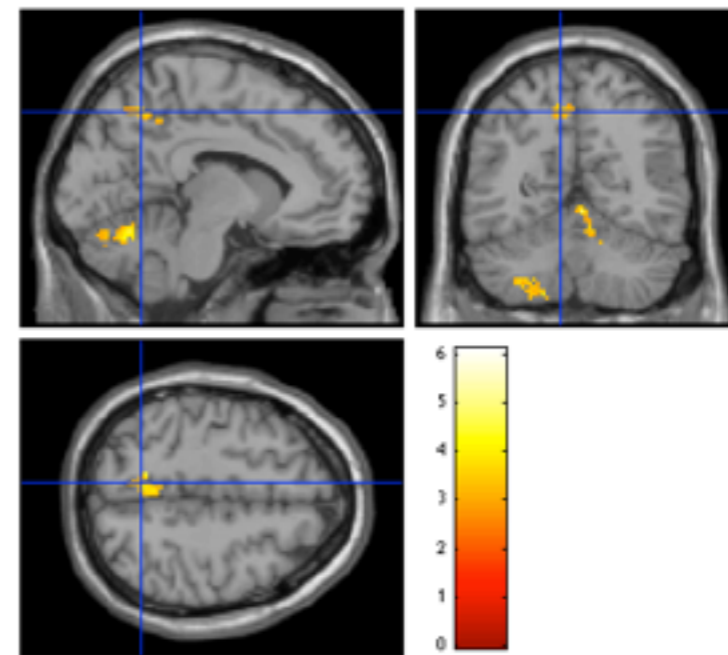
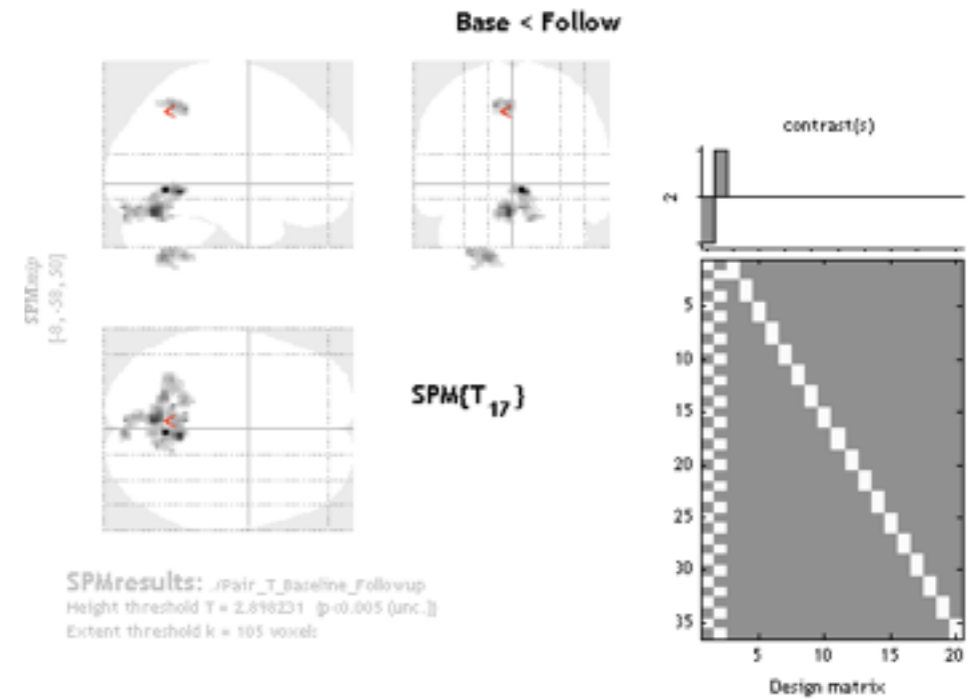
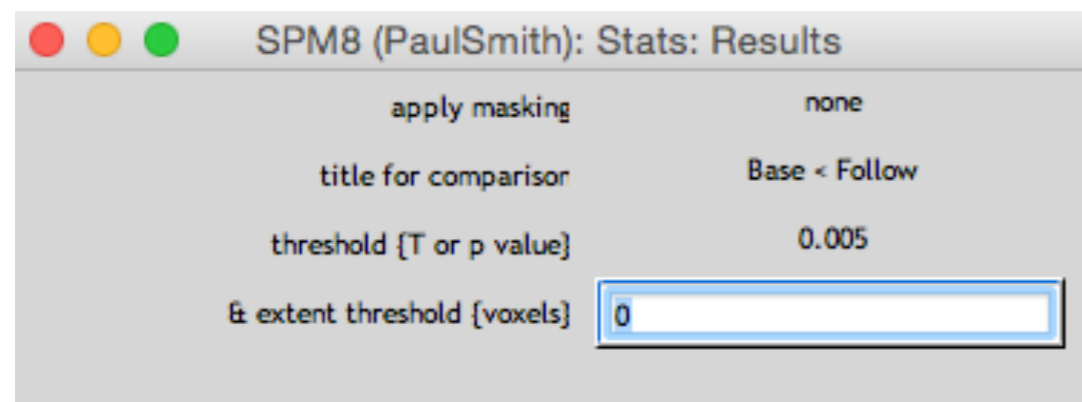
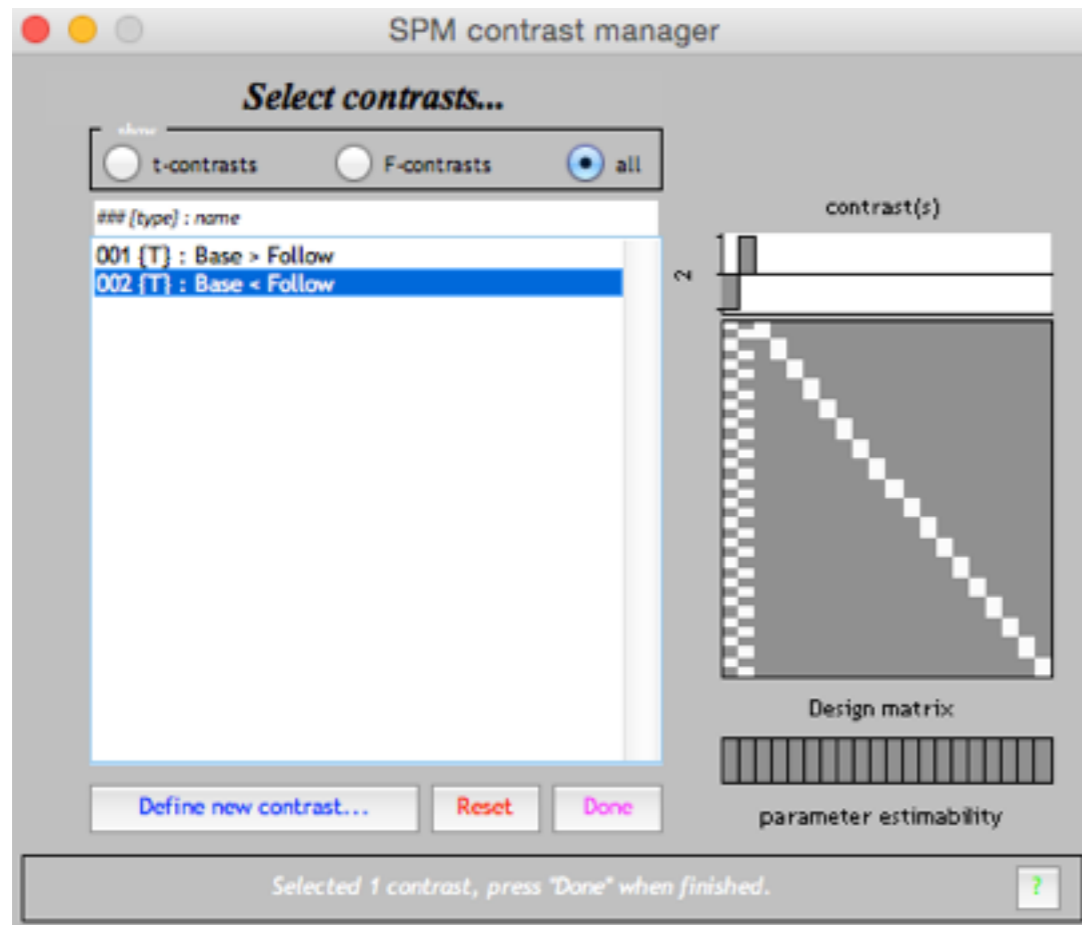
. Paired t-test	
. Pairs	
.. Pair	
... Scans [1,2]	2 files
.. Pair	
... Scans [1,2]	2 files
.. Pair	
... Scans [1,2]	2 files
.. Pair	
... Scans [1,2]	2 files
.. Pair	
... Scans [1,2]	2 files
.. Grand mean scaling	No
.. ANCOVA	No
Covariates	
Masking	
. Threshold masking	
.. None	
. Implicit Mask	No
. Explicit Mask	
Global calculation	
. Omit	
Global normalisation	
. Overall grand mean scaling	
.. No	
. Normalisation	None

Directory: The output directory of your statistical model

Design: The statistical model you want to use (**Pair T-test**)

Masking: The region you want to do statistical inference

Demo - Pair T-test (Statistical inference & Result visualization)



Statistical criteria:

Uncorrected voxel $p < 0.005$ with 105 extended voxels

(Page 3)

Cluster location:

$(x,y,z) = (-8, -58, 50)$

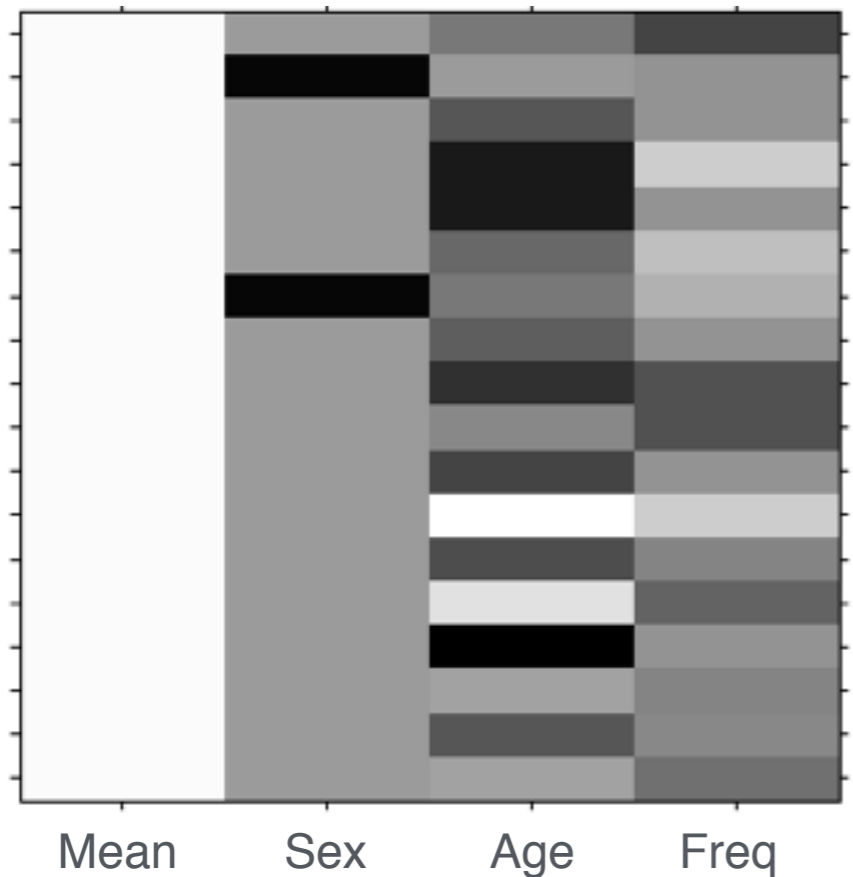
(Page 7, Table 3)

The relationship between clinical evaluation and hypothalamic functional connectivity

“Is there any significantly negative correlation between headache frequency and hypothalamic functional connectivity after adjusting age and sex effect in patient with cluster headache ? (multiple regression test)”

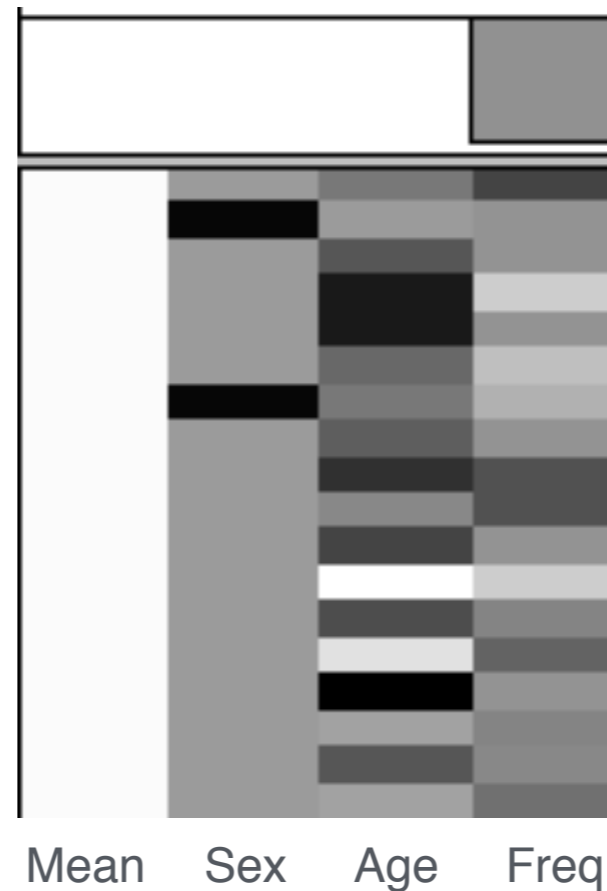
$$Y = \text{Mean} + \beta_1(\text{sex}) + \beta_2(\text{age}) + \beta_3(\text{headache frequency}) + \varepsilon$$

Multiple regression

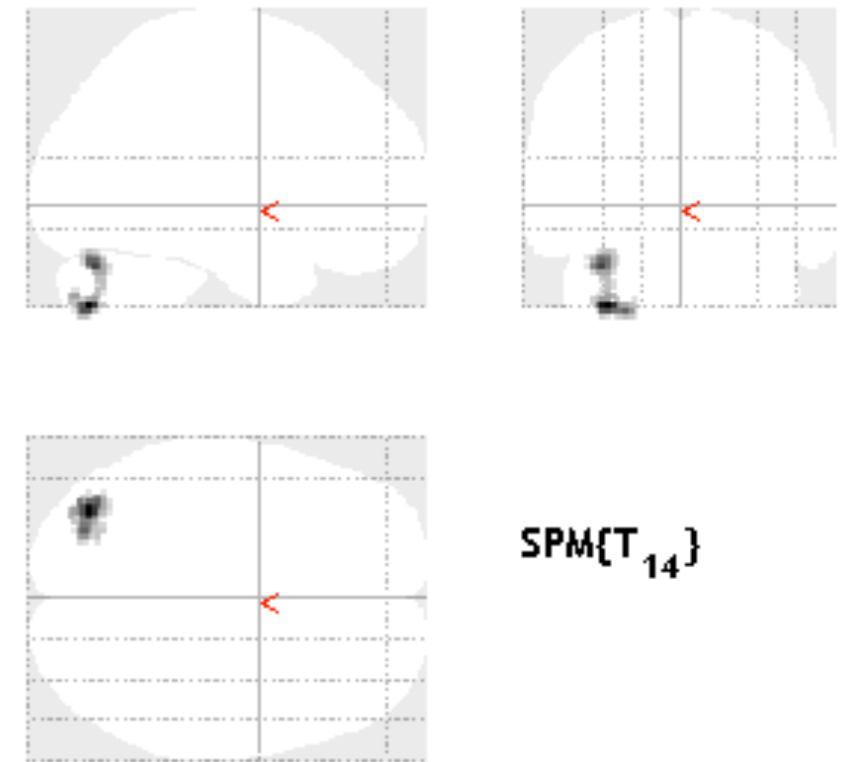


Model construction

Contrast



Statistical inference



Result visualization

Demo - Multiple regression analysis (Model construction)

Current Module: Factorial design specification

Help on: Factorial design specification

Directory /Volumes/Data HD/NTU_Course_Material/Statistical/Correlation_Baseline_Frequency/

Design	
Multiple regression	
Scans	18 files
Covariates	
Covariate	
Vector	18x1 double
Name	Frequency
Centering	Overall mean
Intercept	Include Intercept
Covariates	
Covariate	
Vector	18x1 double
Name	Sex
Interactions	None
Centering	Overall mean
Covariate	
Vector	18x1 double
Name	Age
Interactions	None
Centering	Overall mean
Masking	
Threshold masking	
None	
Implicit Mask	No
Explicit Mask	
Global calculation	
Omit	
Global normalisation	

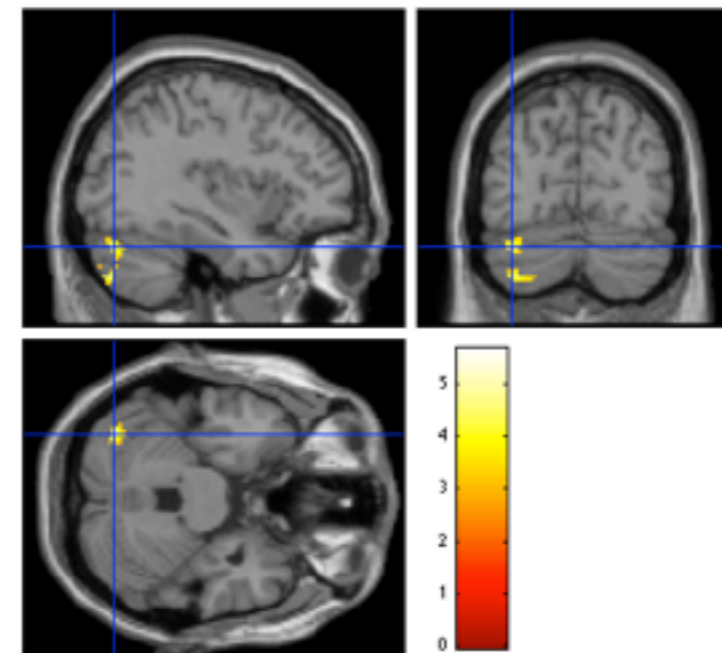
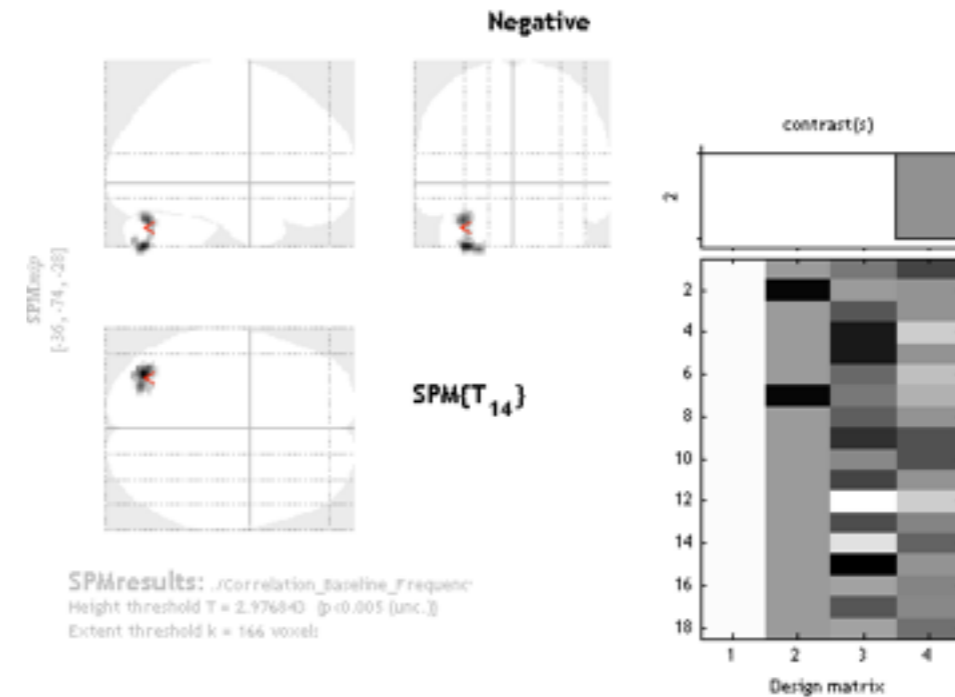
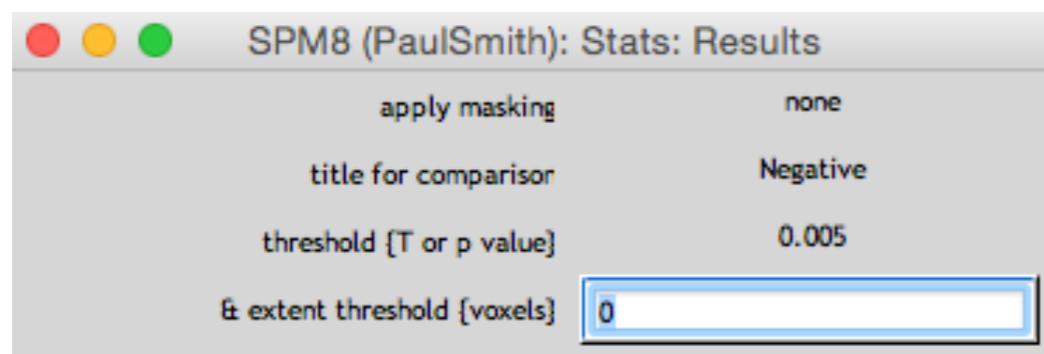
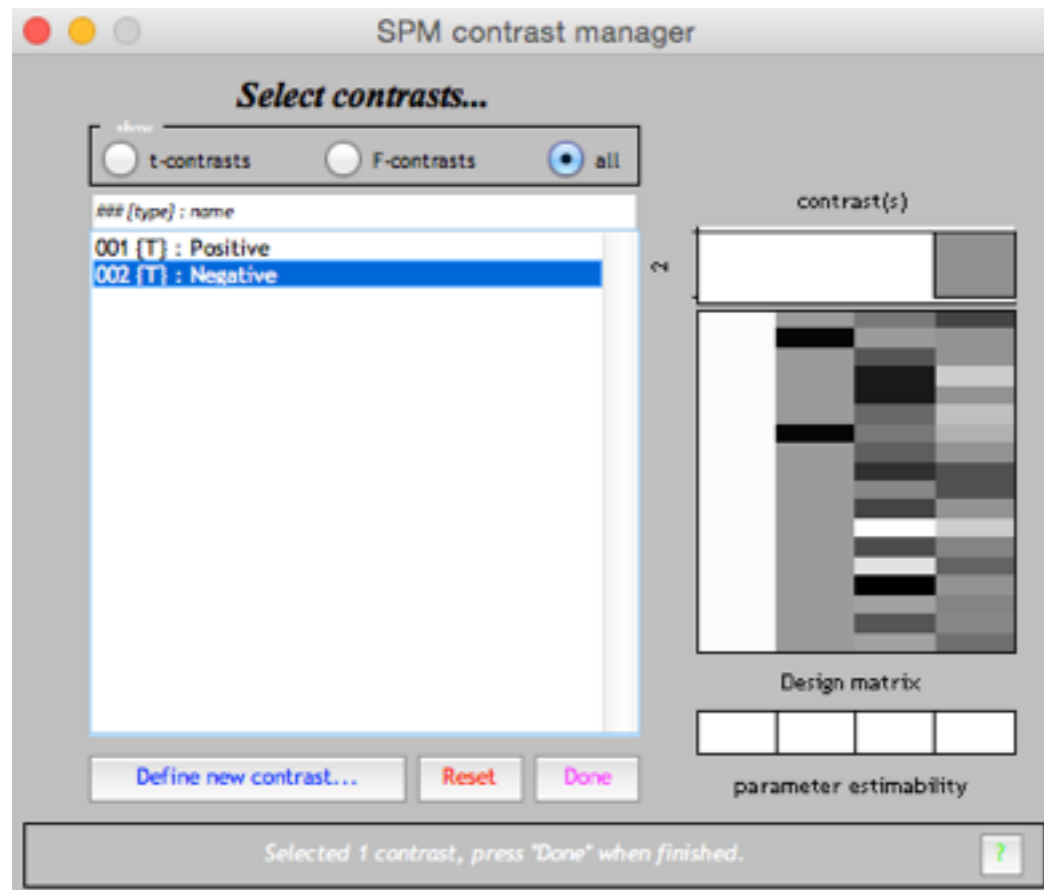
Directory: The output directory of your statistical model

Design: The statistical model you want to use (**Multiple regression**)

Covariates: Covariate of **interest** (headache frequency) and **non-interest** (sex & age)

Masking: The region you want to do statistical inference

Demo - Multiple regression analysis (Statistical inference & Result visualization)



Statistical criteria:

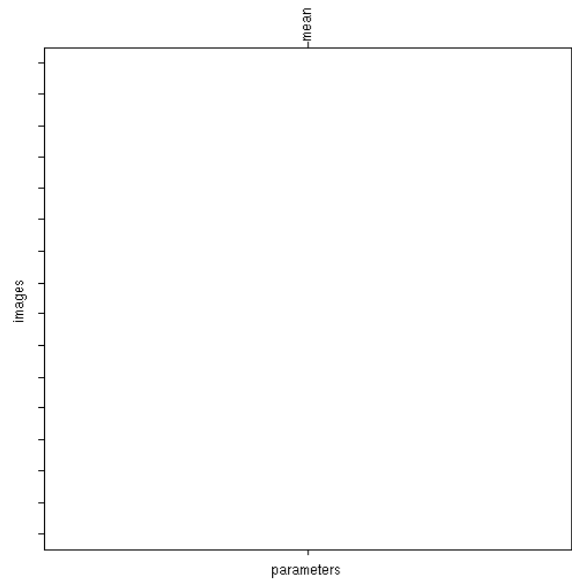
Uncorrected voxel $p < 0.005$ with 166 extended voxels

Cluster location:

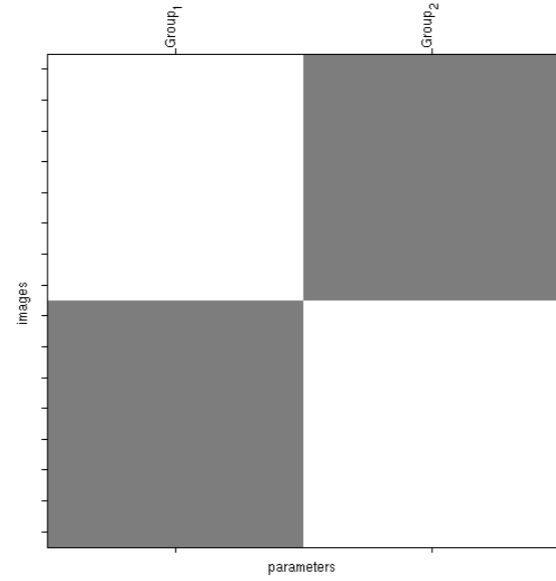
$(x,y,z) = (-36, -74, -28)$ [Page 4]

Using different design matrices to answer different scientific questions

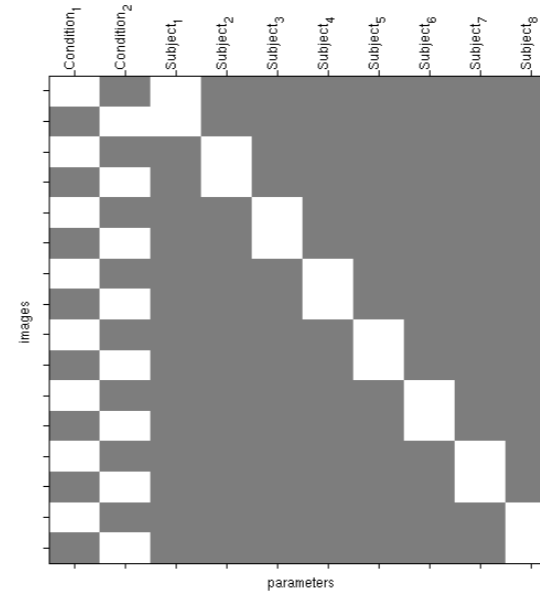
One-sample t-test



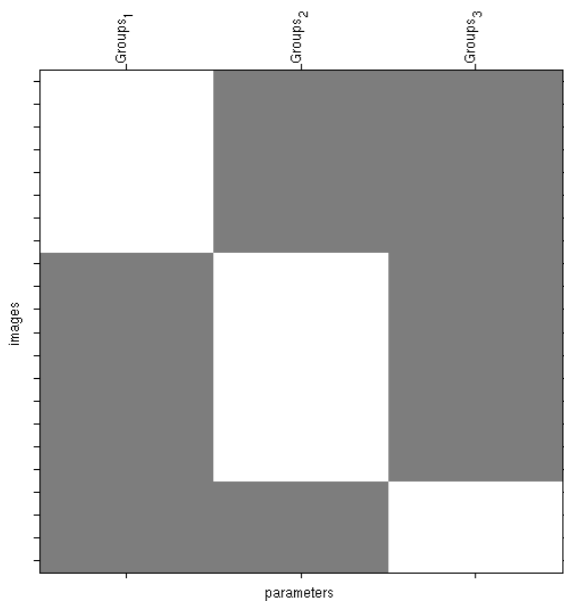
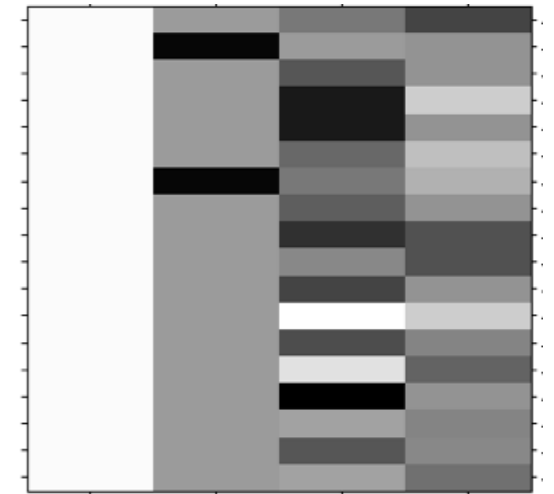
Two-sample t-test



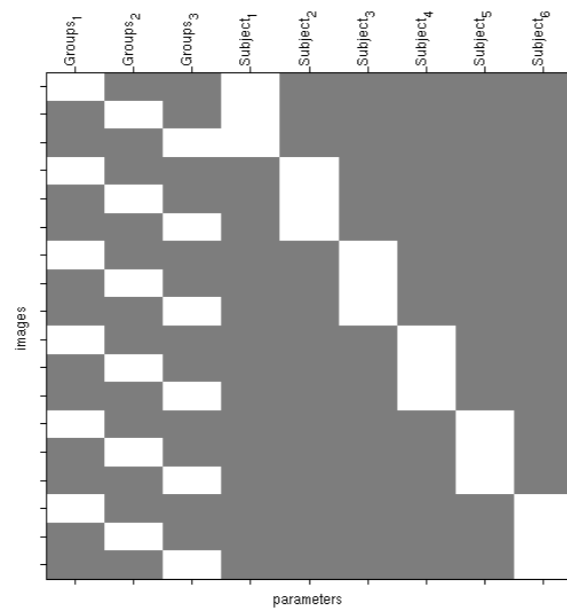
Pair t-test



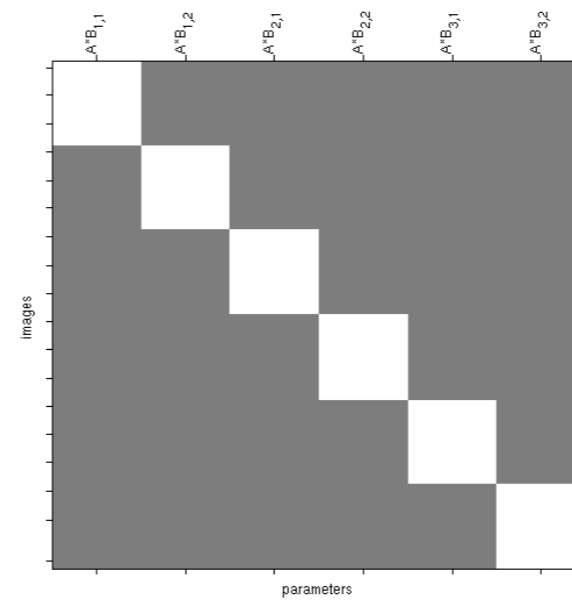
Multiple regression



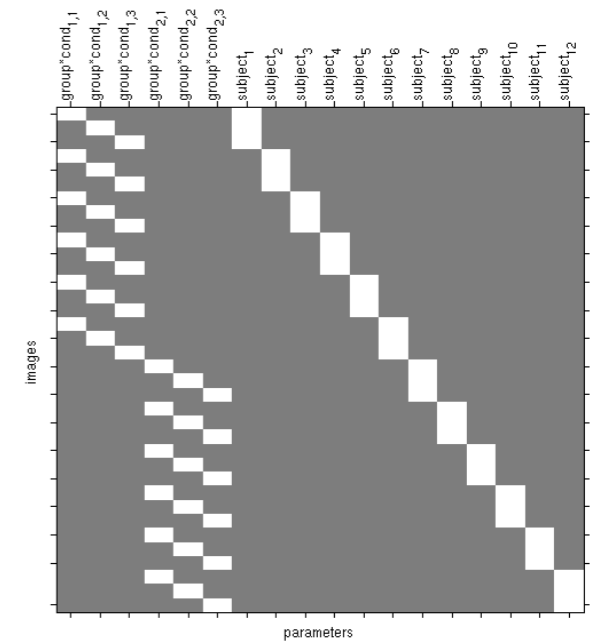
One-way ANOVA (1F3L)



One-way ANOVA
within-subject (1F3L)



Full factorial

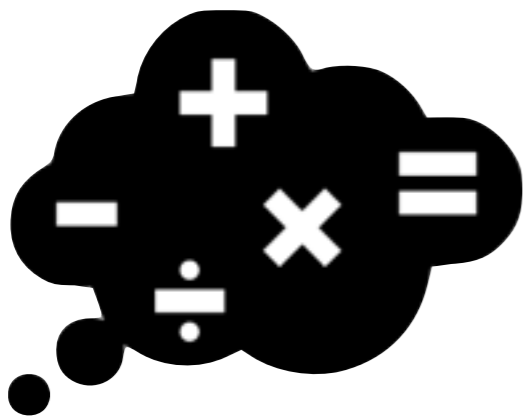


Flexible factorial

Take home message



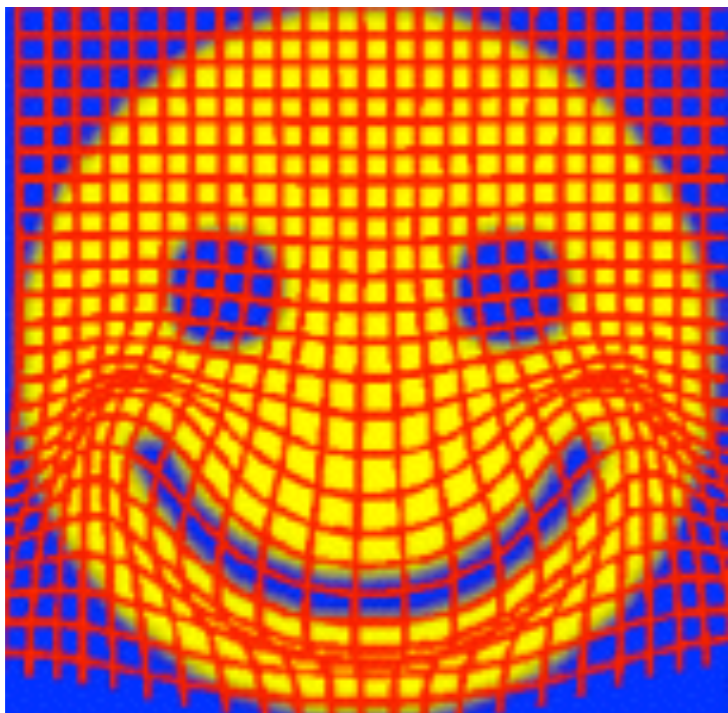
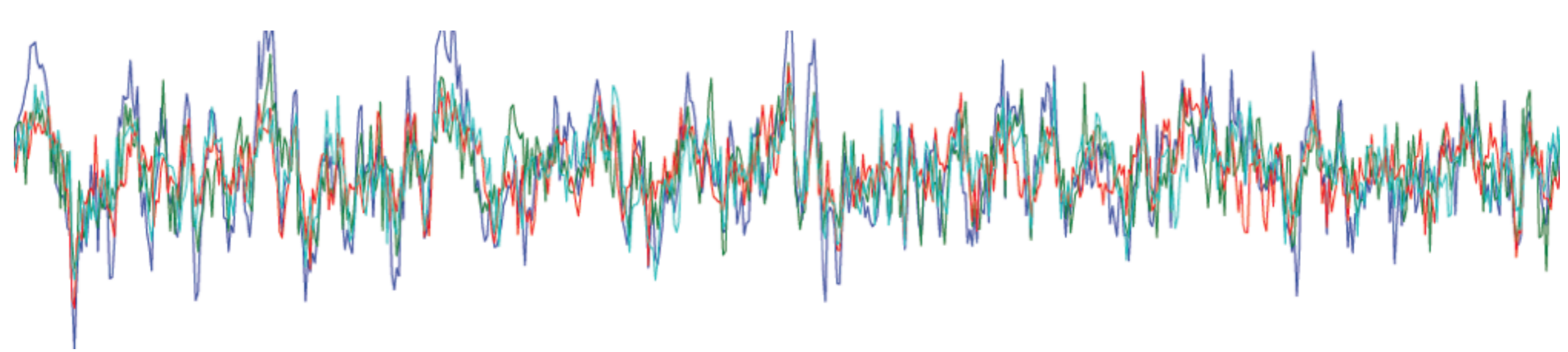
What's your scientific question ?



Redefine your question
using statistical language



Practice, practice and practice



Analyzing your data for fun !!

dargonchow1@gmail.com