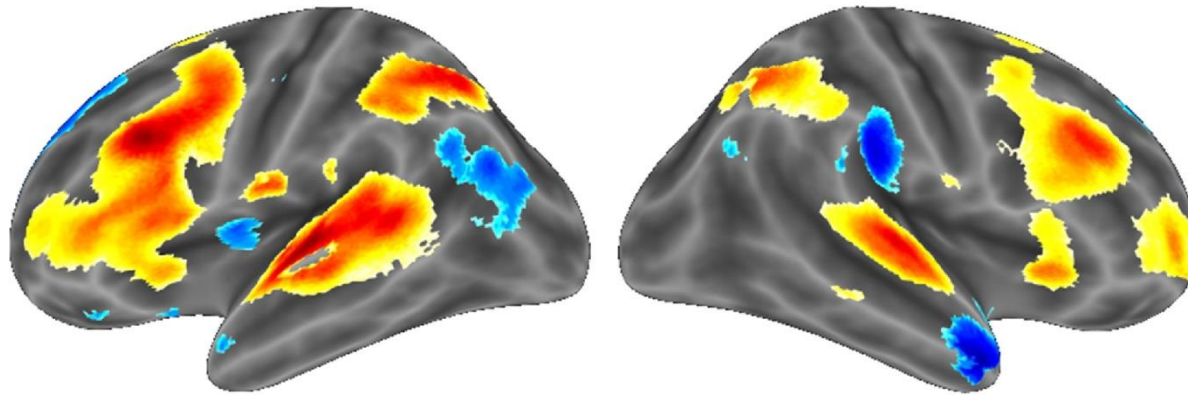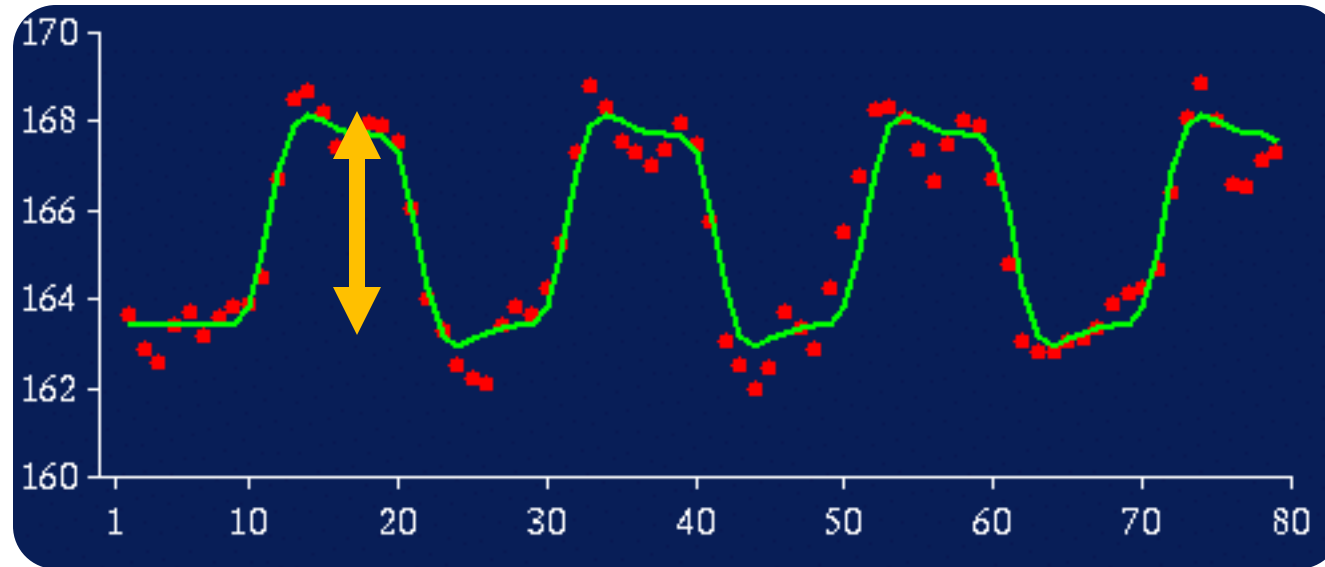# Group Analyses

Nadine Dijkstra
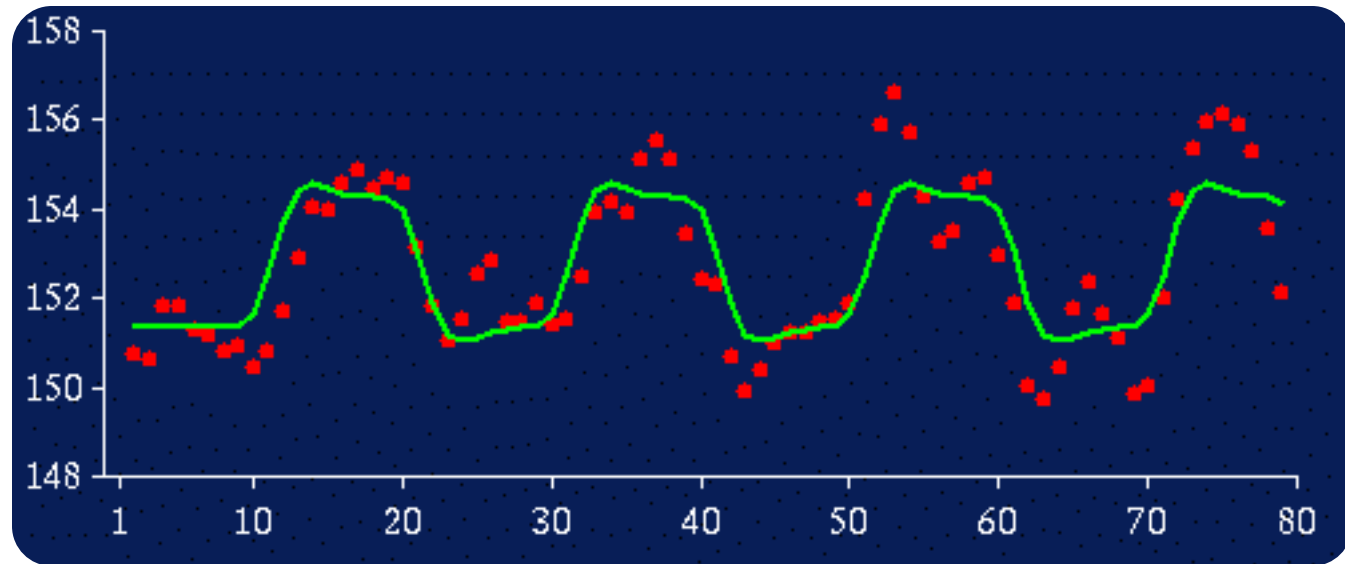
First Level: Subject 1

For voxel *v* in the brain
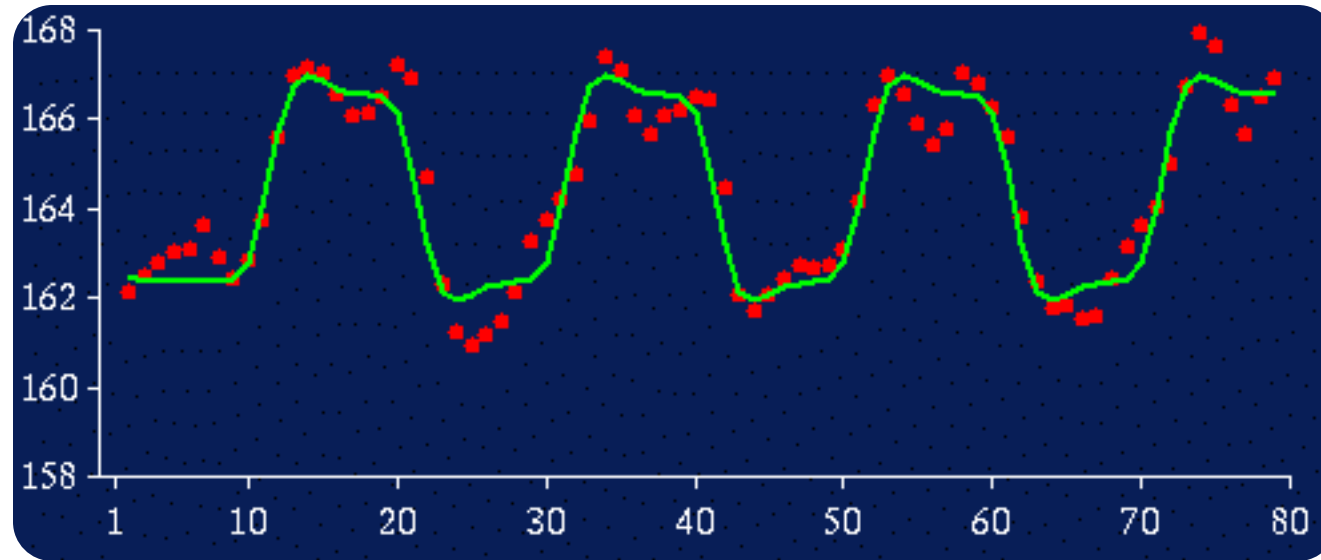

Effect size (c) ≈ 4

First Level: Subject 3

For voxel *v* in the brain

Effect size (c) ≈ 2

First Level: Subject 12

For voxel *v* in the brain

Effect size (c) ≈ 4

Second Level: Group Analysis

	c
Subject 1	4
Subject 2	3
Subject 3	2
Subject 4	1
Subject 5	1
Subject 6	2
Subject 7	3
Subject 8	3
Subject 9	3
Subject 10	2
Subject 11	4
Subject 12	4

Group effect (mean [m])   = 2.67

Between subject variability (stand dev [sb])   = 1.07

Standard error of the mean (SEM)   = sb /sqrt(N)

                                                                                    = 0.31

<u>Is the effect significant at voxel *v*? (one-sample t-test)</u>

t = m/SEM = 2.67/0.31 = 8.61

$p = 10^{-6}$

This is called a Random Effects Analysis, because we compare the group effect to the between-subjects variability

Second Level: Group Analysis

	c
Subject 1	4
Subject 2	3
Subject 3	2
Subject 4	1
Subject 5	1
Subject 6	2
Subject 7	3
Subject 8	3
Subject 9	3
Subject 10	2
Subject 11	4
Subject 12	4

Group effect (mean [m]) = 2.67

Between subject variability (stand dev [sb]) = 1.07

Standard error of the mean (SEM) = sb /sqrt(N)

= 0.31

Is the effect significant at voxel v? (one-sample t-test)
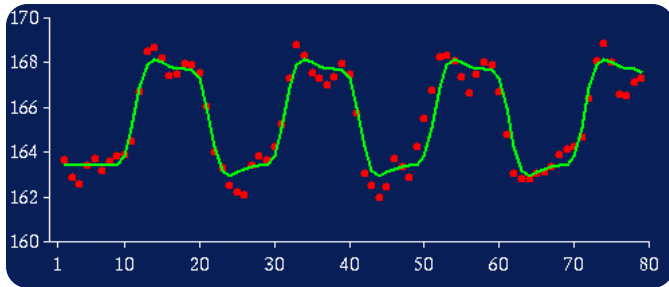
t = m/SEM = 2.67/0.31 = 8.61

$p = 10^{-6}$

...also known as the SUMMARY STATISTIC approach: We summarise the response of each subject by a single statistic (their effect size)
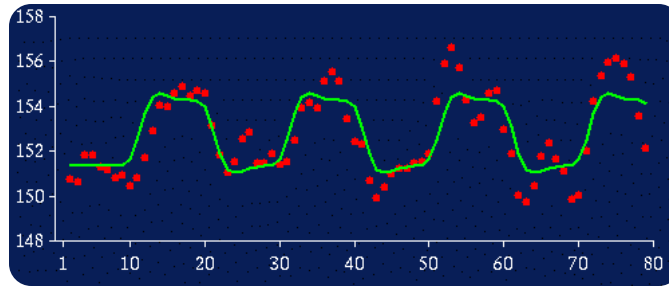
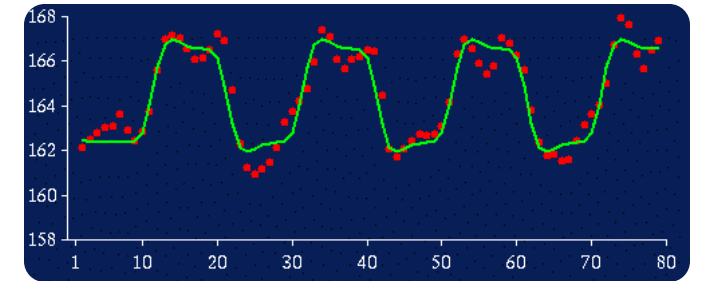# Fixed Effects Analysis

<u>Concatenate timeseries</u>
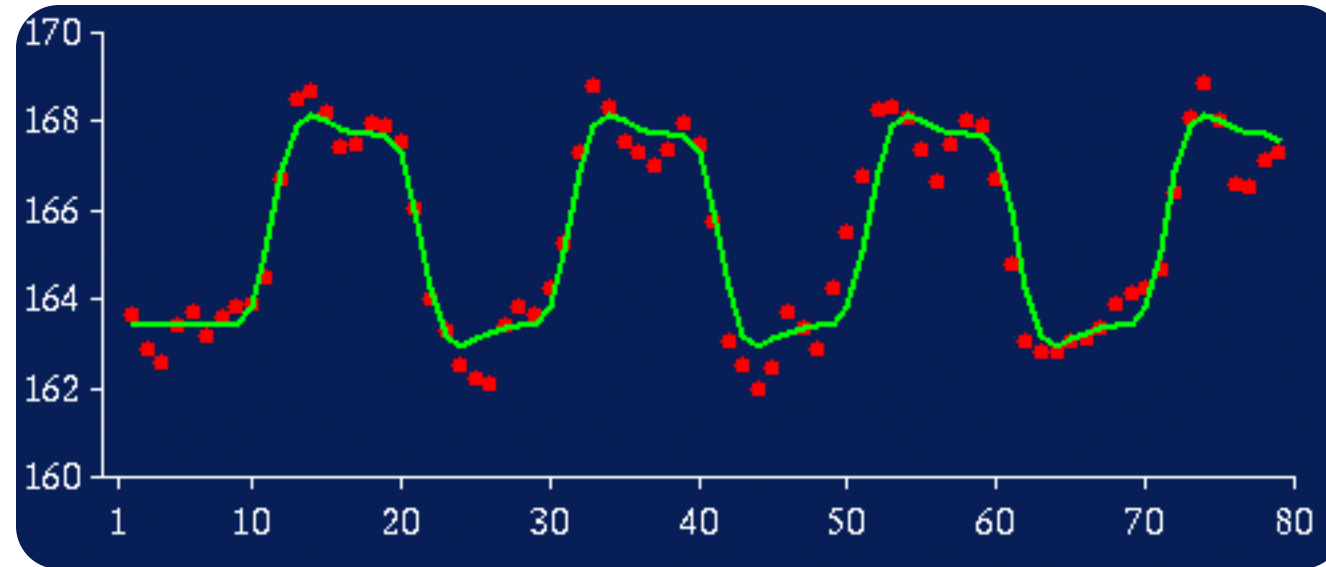

Subject 1 ... Subject 3 ... ... Subject 12

Each measurement is one scan from one subject
... we now have 600 scans (50 scans in each of 12 subjects)

We use this to calculate the average effect

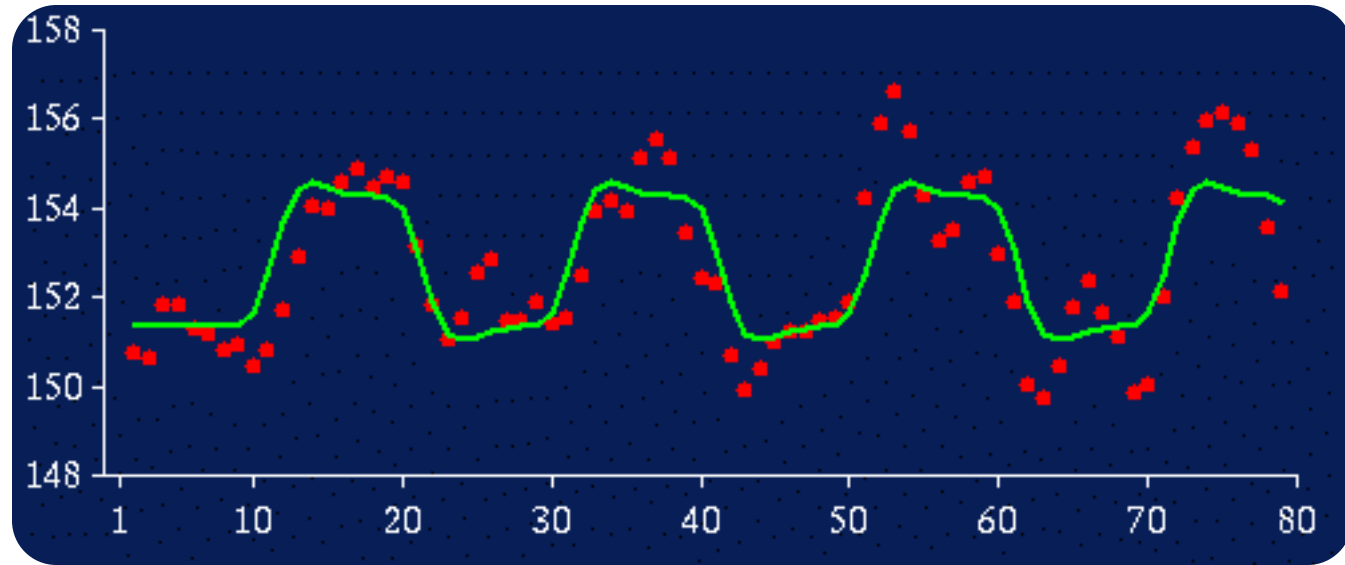# First Level: Subject 1

For voxel *v* in the brain

Effect size (c) ≈ 4

Within subject variability (s_w) ≈ 0.9

Root mean square error (GLM fit)
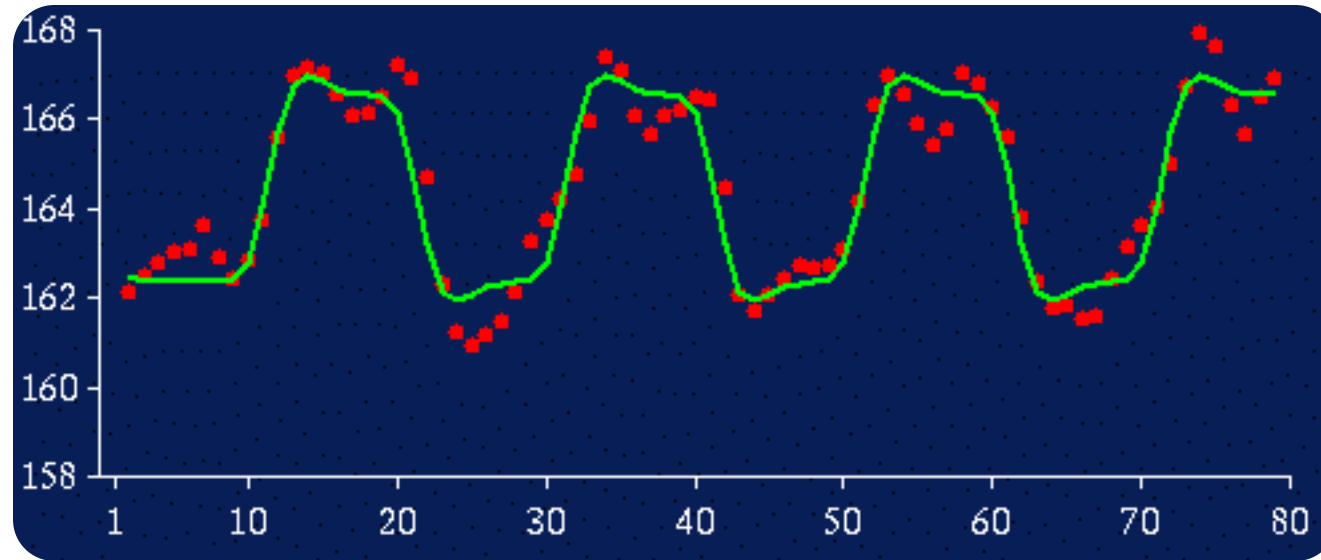
First Level: Subject 3

For voxel *v* in the brain

Effect size (c) ≈ 2

Within subject variability (s_w) ≈ 1.5

First Level: Subject 12

For voxel *v* in the brain

Effect size (c) ≈ 4

Within subject variability (s_w) ≈ 1.1

Group Analysis: Fixed Effects

	s_w
Subject 1	0.9
Subject 2	1.2
Subject 3	1.5
Subject 4	0.5
Subject 5	0.4
Subject 6	0.7
Subject 7	0.8
Subject 8	2.1
Subject 9	1.8
Subject 10	0.8
Subject 11	0.7
Subject 12	1.1

Group effect (mean [m])   = 2.67

Average within subject variability (sw)   = 1.07

Standard error of the mean (SEMW)   = sw /sqrt(N)

= 0.04

Is the effect significant at voxel v?

t = m/SEMW = **62.7**

p = **10^{-51}**   Overconfident?

Number of data points is now total number of scans (i.e. 600)

Random Effects vs. Fixed Effects

Fixed Effects Analysis (FFX)

• We compare the group effect to the within-subject variability.

• It an inference about this specific sample of subjects.

• Statistics are often inflated relative to random effects analysis.

Random Effects Analysis (RFX)

• We compare the group effect to the between-subject variability.

• It is an inference about the population from which the subjects were drawn: If you had a new subject from that population, you could be confident they would also show the effect.
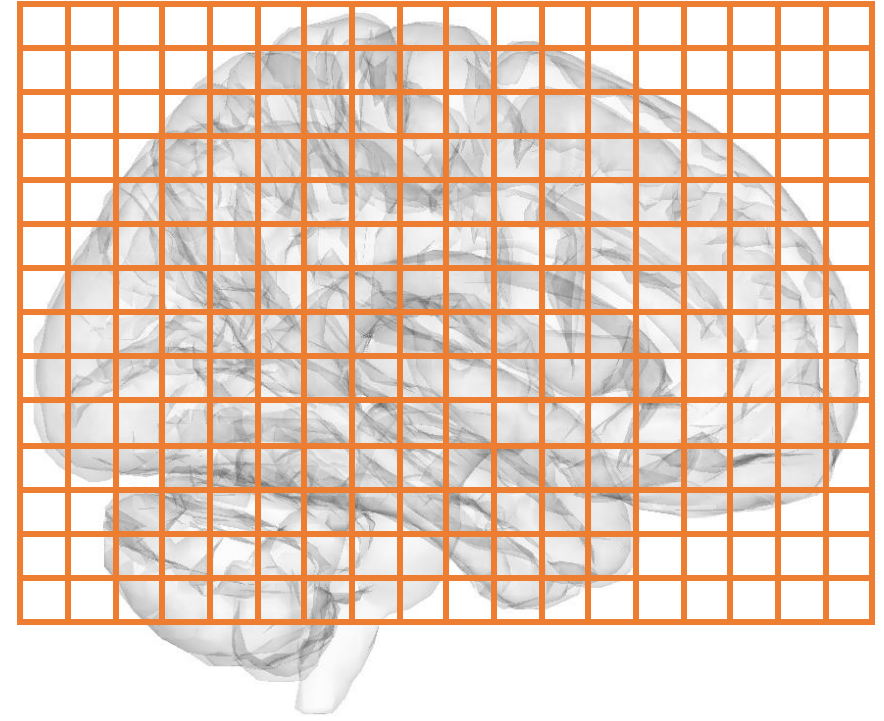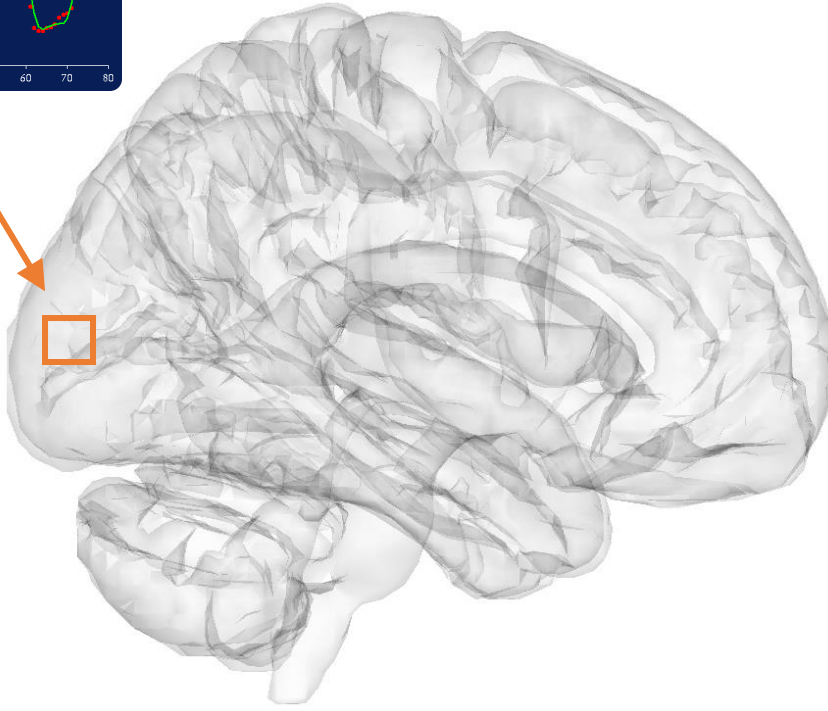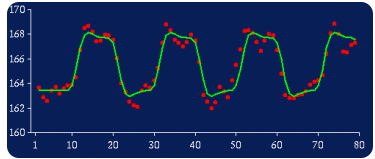
Random Effects vs. Fixed Effects

Mixed Effects Analysis (MFX)

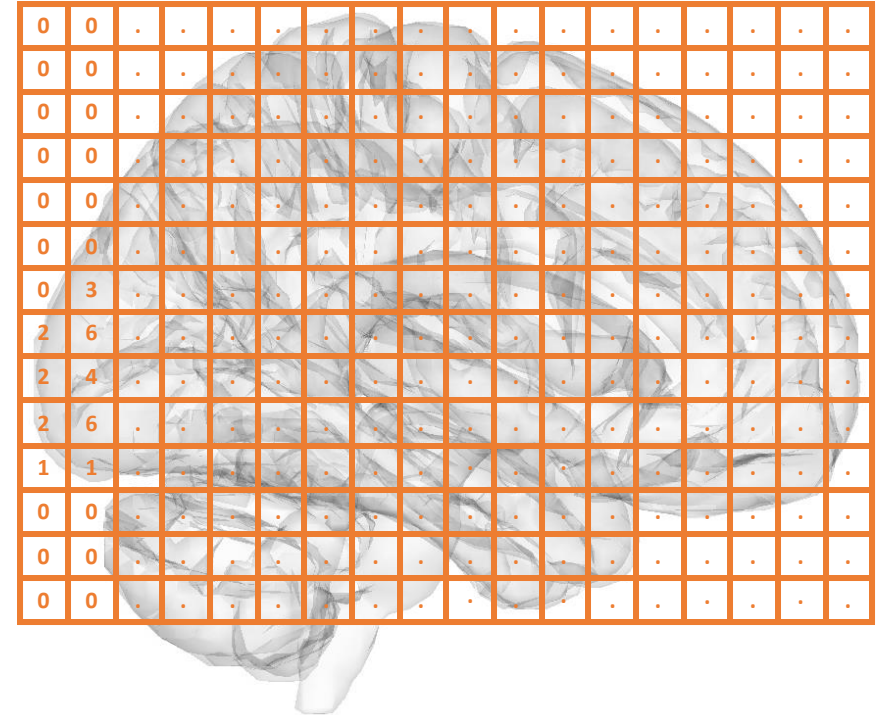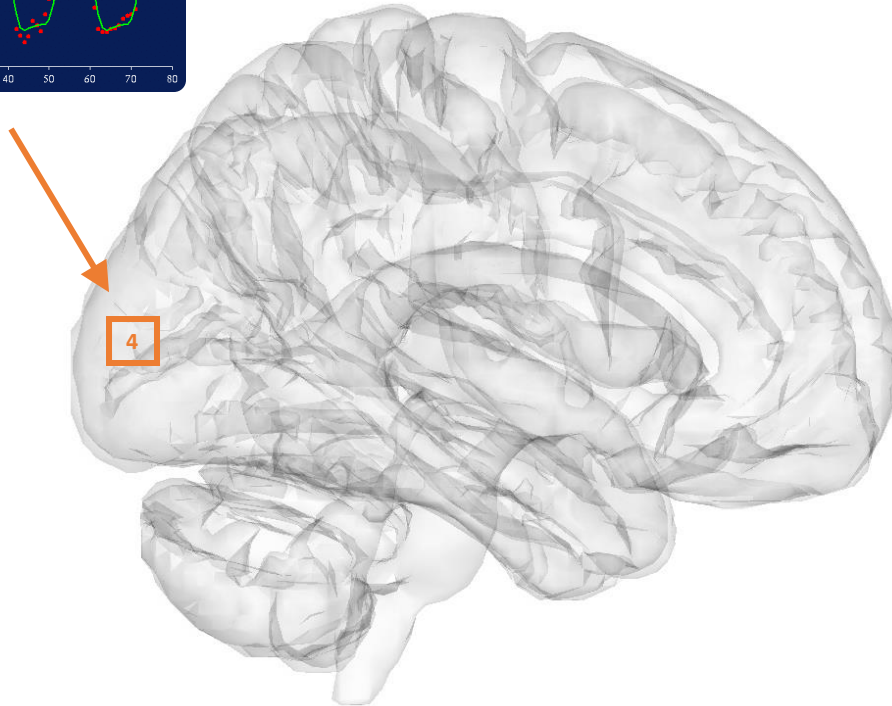- Has some random and some fixed effects.
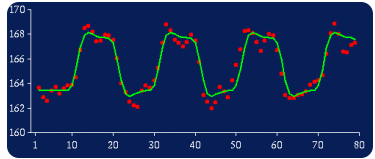
- spm_mfx

Beyond a single voxel...

Voxel *v*
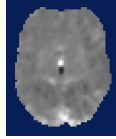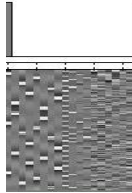
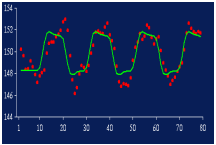# Beyond a single voxel...

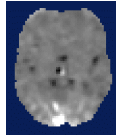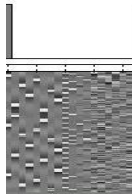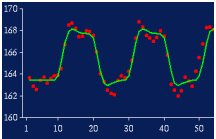Voxel *v*

Random Effects: Summary Statistic

First level

Data (per voxel)	Design Matrix	Contrast Image

S1

S2

•
•
•

S11
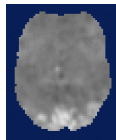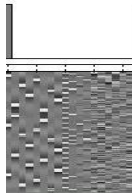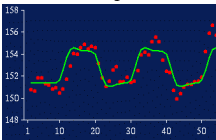
S12
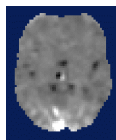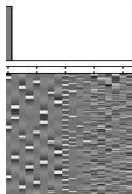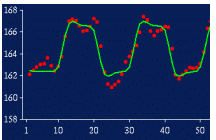
Random Effects: Summary Statistic
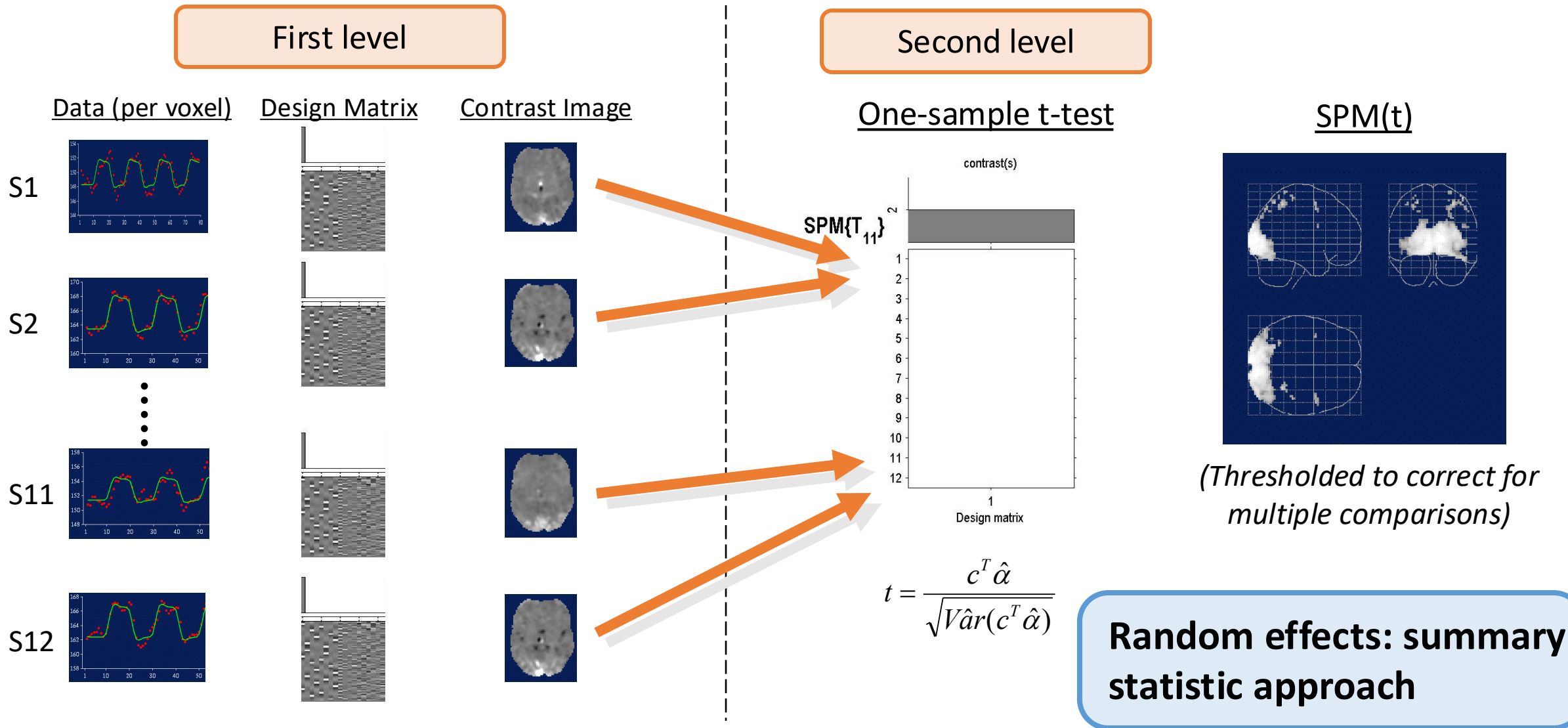
Hierarchical model

Level 1: $$y = X^{(1)}\theta^{(1)} + \varepsilon^{(1)}$$

Level 2: $$\theta^{(1)} = X^{(2)}\theta^{(2)} + \varepsilon^{(2)}$$

$$\vdots$$

Level n: $$\theta^{(n-1)} = X^{(n)}\theta^{(n)} + \varepsilon^{(n)}$$

At each level, the distribution of parameters is dependent on the level above

Multiple variance components at each level

$$C_\varepsilon^{(i)} = \sum_k \lambda_k^{(i)} Q_k^{(i)}$$

What we don't know: distribution of parameters and variance parameters

Friston (2008) Hierarchical models in the brain. PLOS Comp. Bio.

Hierarchical Model

$$y = X^{(1)}\theta^{(1)} + \varepsilon^{(1)}$$

$$\theta^{(1)} = X^{(2)}\theta^{(2)} + \varepsilon^{(2)}$$

(1) Within subject variance, $s_w(i)$
(2) Between subject variance, s_b

First level

Second level

$$y = \begin{bmatrix} X_1^{(1)} & & \\ & X_2^{(1)} & \\ & & X_3^{(1)} \end{bmatrix} \theta^{(1)} + \varepsilon^{(1)}$$

$$\theta^{(1)} = X^{(2)}\,\theta^{(2)} + \varepsilon^{(2)}$$

spm_reml
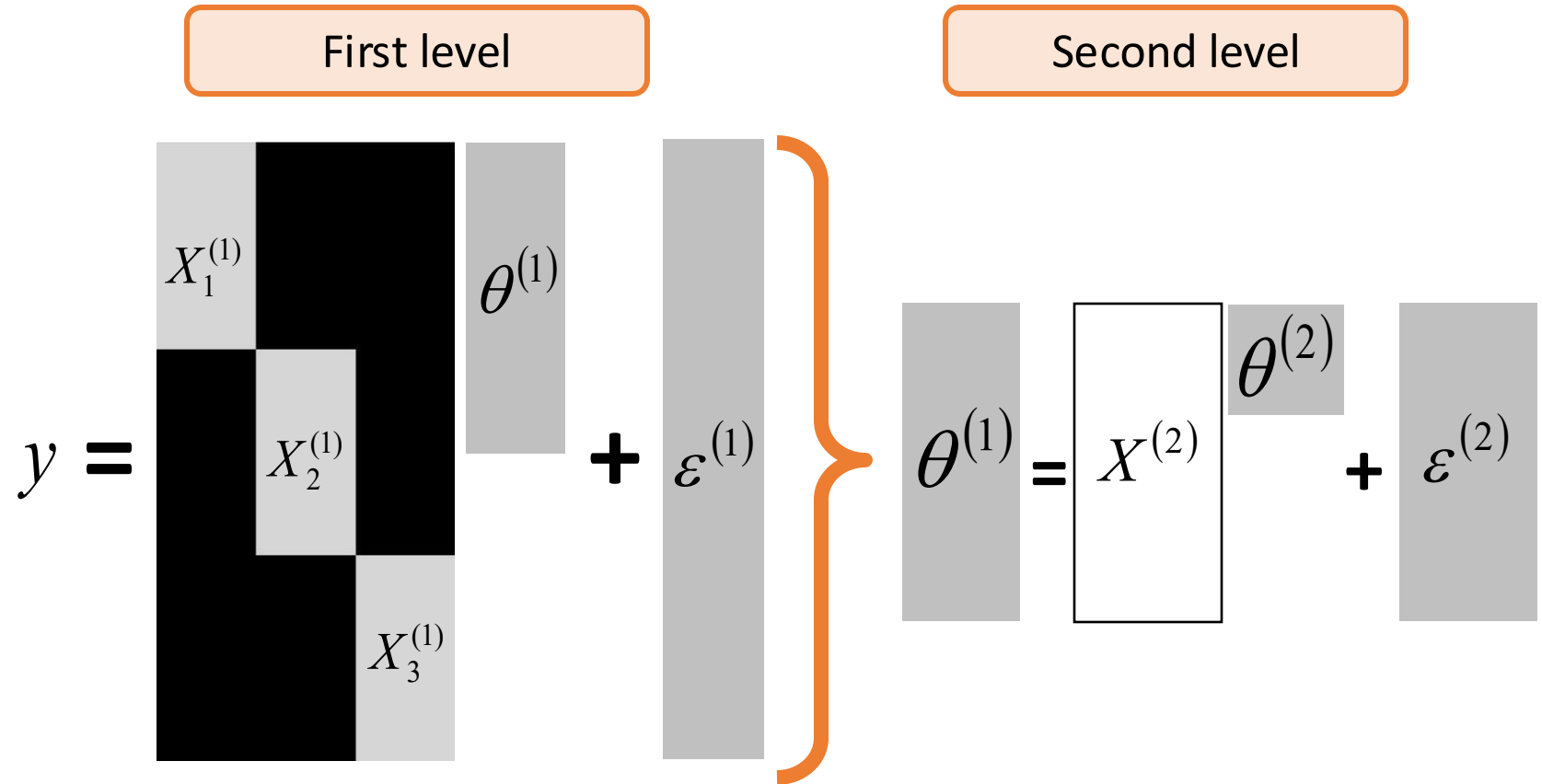
Example Results: Auditory Experiment

Summary statistic

Separates first and second level estimates
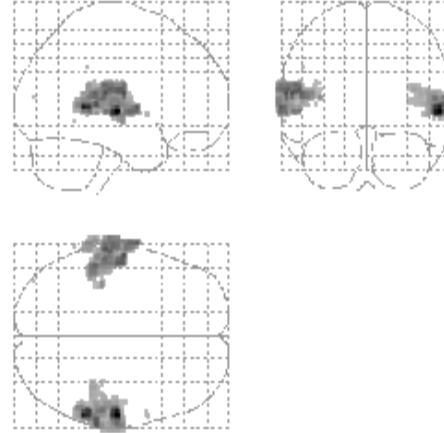
Hierarchical model

Computationally intensive!
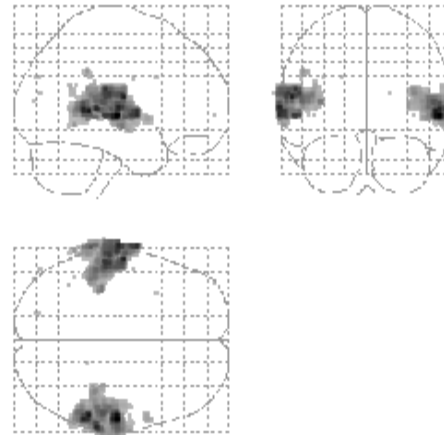
Friston et al. (2004) Mixed effects and fMRI studies, Neuroimage

Summary Statistic vs. Hierarchical Model

- The summary stats approach is exact if, for each session/subject:
  - Within-subject variances are the same
  - First-level design (e.g. number of trials) are the same

- The summary stats approach is robust against typical violations (SPM book 2006; Mumford and Nichols, 2009, Neuroimage).

- We might use a hierarchical model in epilepsy research where number of seizures is not under experimental control and is highly variable over subjects.

Beyond the one sample t-test…
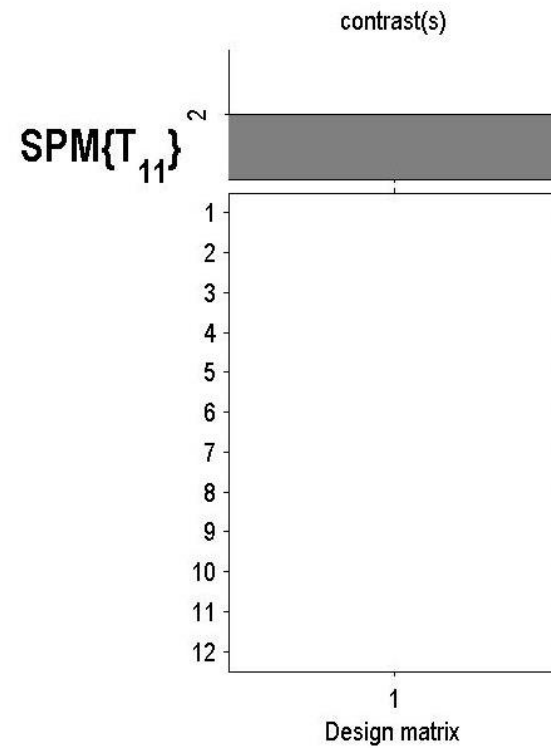
Multiple Conditions (within subjects)

Condition 1	Condition 2	Condition 3
Subject 1	Subject 1	Subject 1
Subject 2	Subject 2	Subject 2
…	…	…
Subject 12	Subject 12	Subject 12

Second level: One-way within-subjects ANOVA

Multiple Conditions (between subjects)

Condition 1	Condition 2	Condition 3
Subject 1	Subject 13	Subject 25
Subject 2	Subject 14	Subject 26
…	…	…
Subject 12	Subject 24	Subject 36

e.g., effects of a drug

Second level: One-way between-subjects ANOVA
(or if only two conditions, a two-sample t-test)

Testing for interactions

- **Within-within interactions:** Can be done at the first level (i.e., specify contrasts according to the interaction to be tested)

- **Between-between interactions:** Test at the second level

- **Within-between interactions:** Specify within-subjects factor(s) at the first level, then the between-subjects factor(s) at the second level

This afternoon

Semantic matching fMRI task ▱

What is second-level/group-level analysis?

Second-level fMRI analysis (also known as group-level analysis) is a critical step in neuroimaging research that aggregates data from multiple participants to draw broader conclusions about brain function. Unlike first-level analysis, which focuses on each participant's brain activity in isolation, group-level analysis examines patterns of brain activity that are consistent across a group of participants. By pooling data from multiple individuals, researchers can identify common neural responses associated with specific tasks, conditions, or populations.

In this section, we will go through different second-level models:

- **One-sample t-test**: what is the average brain response across all participants?

- **Two-sample t-test**: are there differences between two groups of participants?

- **Factorial**: do multiple factors and their interaction(s) explain differences between participants?

Summary

- **Group inference usually proceeds with random effects analysis, not fixed effects analysis. Group effects are compared to between rather than within subject variability**

- **Hierarchical models provide a gold-standard for random effects group analysis, but are computationally intensive**

- **Summary statistics are a robust method for random effects group analysis when conditions are met**

- **If you want to contrast two conditions within subjects, you can use a one-sample t-test at the second level. If more conditions, you can use a one-way ANOVA. If different groups, you can use a between-subjects ANOVA or two-sample t-test**