Group analyses

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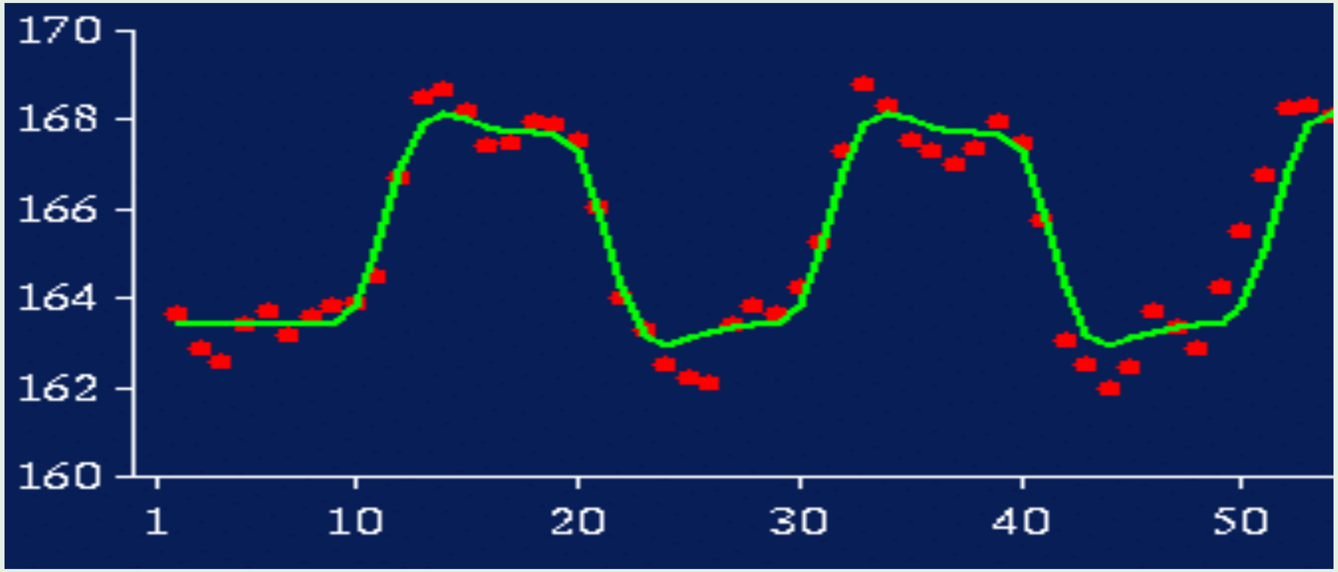
Subject 1

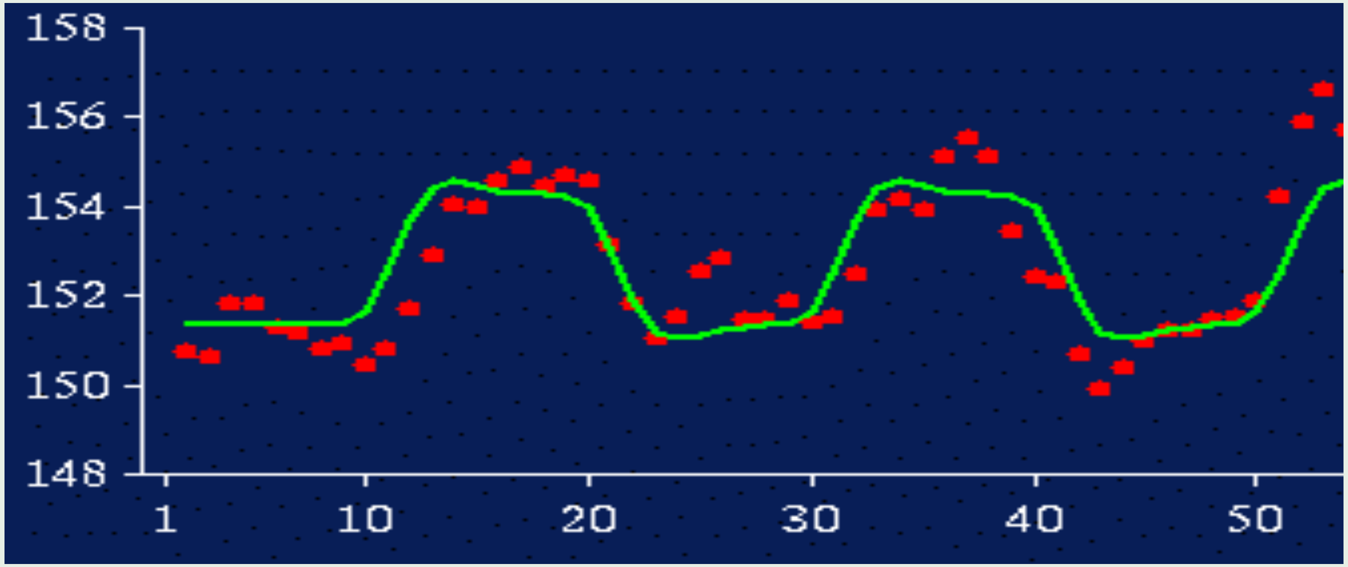
For voxel v in the brain



Effect size, c ~ 4

Subject 3

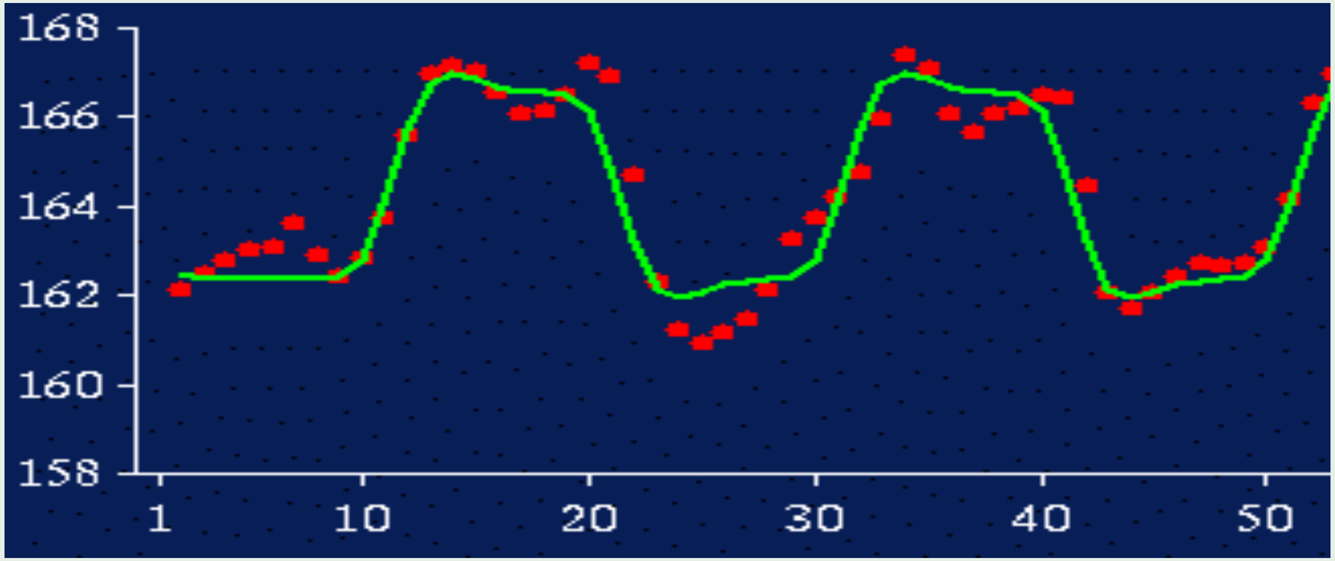
For voxel v in the brain



Effect size, c ~ 2

Subject 12

For voxel v in the brain



Effect size, c ~ 4

Whole Group

For group of N=12 subjects effect sizes are

$c = [4, 3, 2, 1, 1, 2, 3, 3, 3, 2, 4, 4]$

Group effect (mean), m=2.67
Between subject variability (stand dev), s_b =1.07
Standard Error Mean (SEM) = s_b /sqrt(N)=0.31

Is effect significant at voxel v?
t=m/SEM=8.61
$p=10^{-6}$

Random Effects Analysis

For group of N=12 subjects effect sizes are

c= [3, 4, 2, 1, 1, 2, 3, 3, 3, 2, 4, 4]

Group effect (mean), m=2.67
Between subject variability (stand dev), s_b =1.07

This is called a Random Effects Analysis (RFX) because we are comparing the group effect to the between-subject variability.

Summary Statistic Approach

For group of N=12 subjects effect sizes are

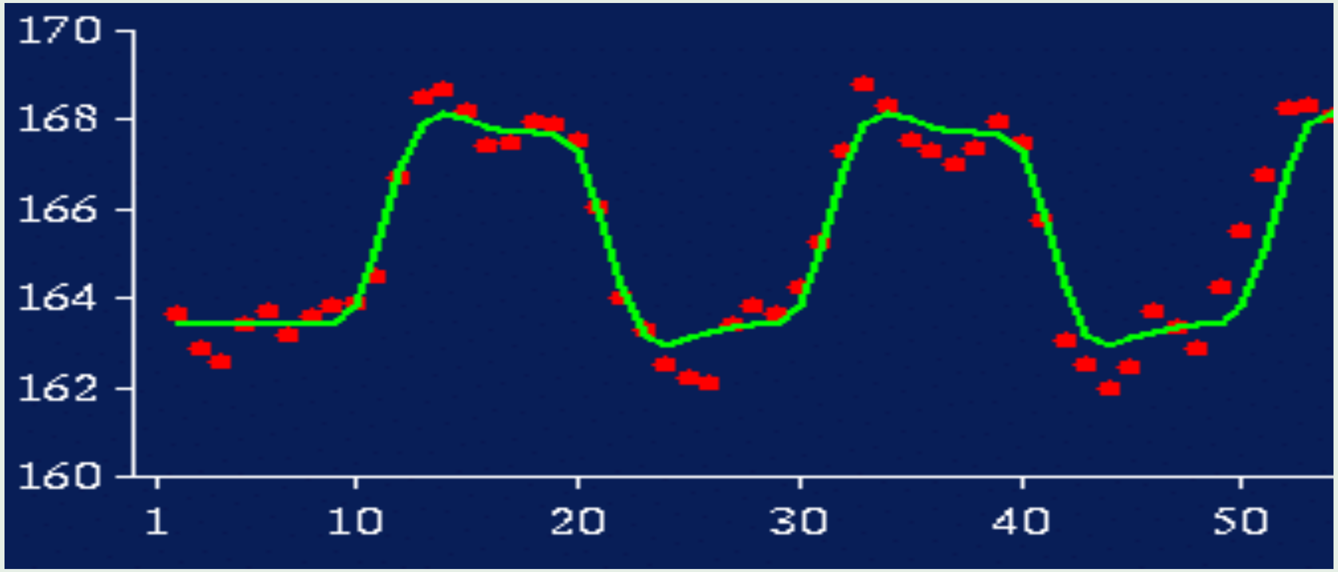
c = [3, 4, 2, 1, 1, 2, 3, 3, 3, 2, 4, 4]

Group effect (mean), m=2.67
Between subject variability (stand dev), s_b =1.07

This is also known as a summary statistic approach because we are summarising the response of each subject by a single summary statistic – their effect size.

Subject 1

For voxel v in the brain

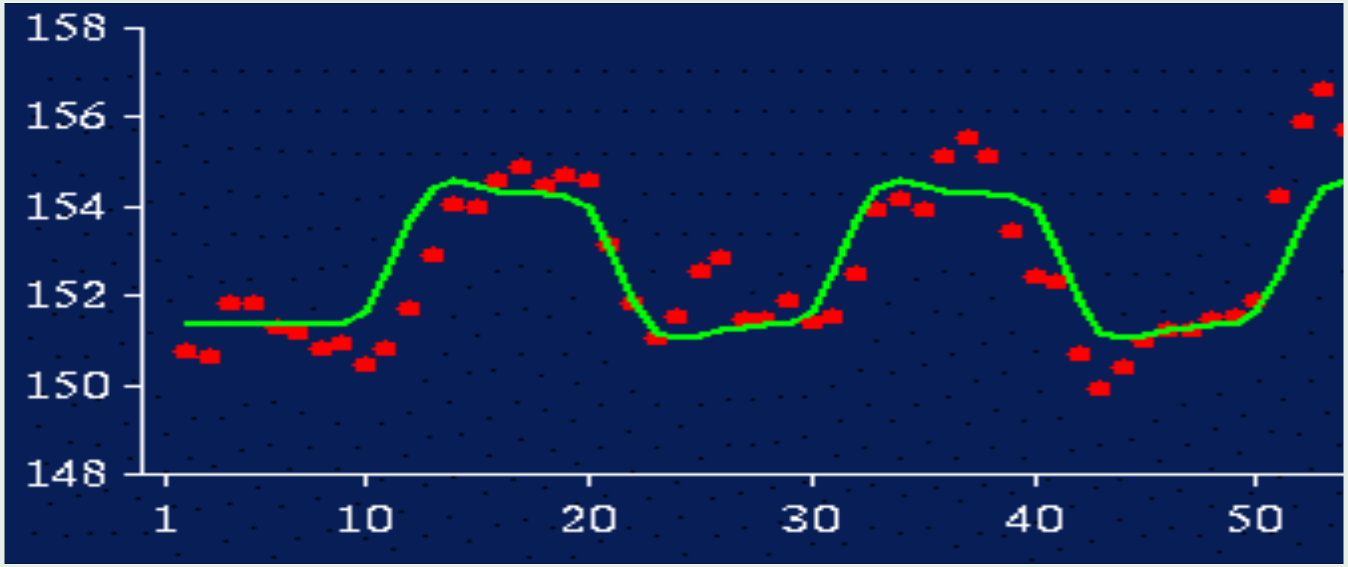


Effect size, c ~ 4

Within subject variability, s_w~0.9

Subject 3

For voxel v in the brain

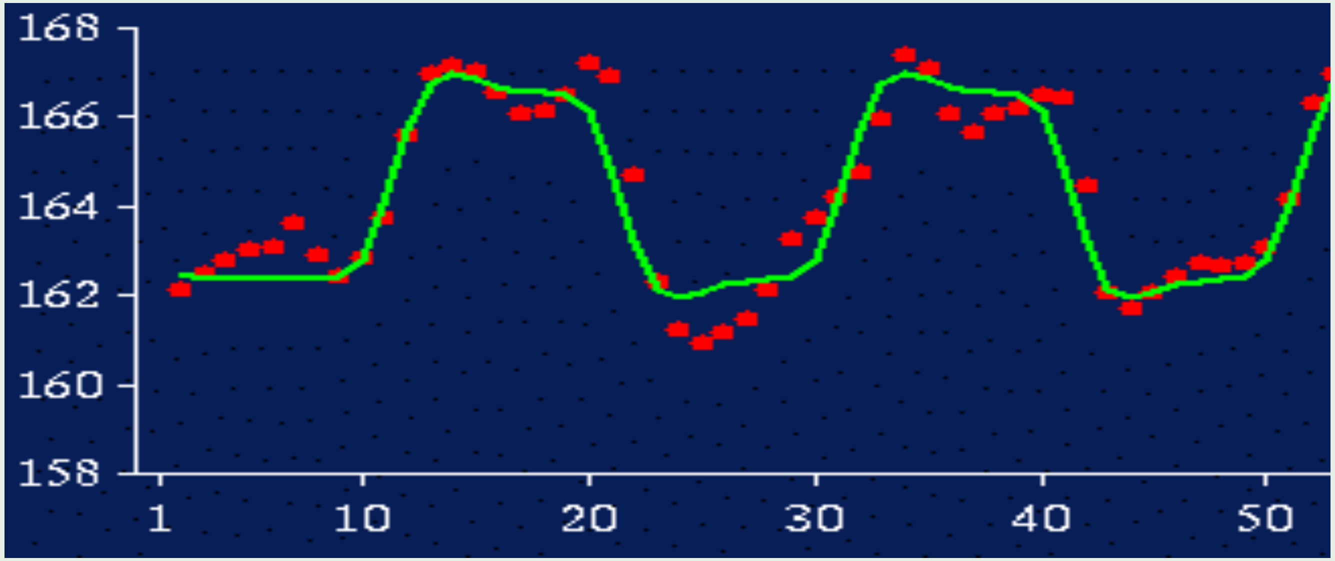


Effect size, c ~ 2

Within subject variability, s_w~1.5

Subject 12

For voxel v in the brain



Effect size, c ~ 4

Within subject variability, s_w~1.1

Fixed Effects Analysis

Time series are effectively concatenated – as though we had one subject with N=50x12=600 scans.

s_w = [0.9, 1.2, 1.5, 0.5, 0.4, 0.7, 0.8, 2.1, 1.8, 0.8, 0.7, 1.1]

Mean effect, m=2.67
Average within subject variability (stand dev), s_w =1.04

Standard Error Mean (SEM_W) = s_w /sqrt(N)=0.04
Is effect significant at voxel v?
$t=m/SEM_W=62.7$
$p=10^{-51}$

RFX versus FFX

With Fixed Effects Analysis (FFX) we compare the group effect to the within-subject variability. It is not an inference about the sample from which the subjects were drawn.

With Random Effects Analysis (RFX) we compare the group effect to the between-subject variability. It is an inference about the sample 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.

RFX versus FFX

With Fixed Effects Analysis (FFX) we compare the group effect to the within-subject variability. It is not an inference about the sample from which the subjects were drawn.

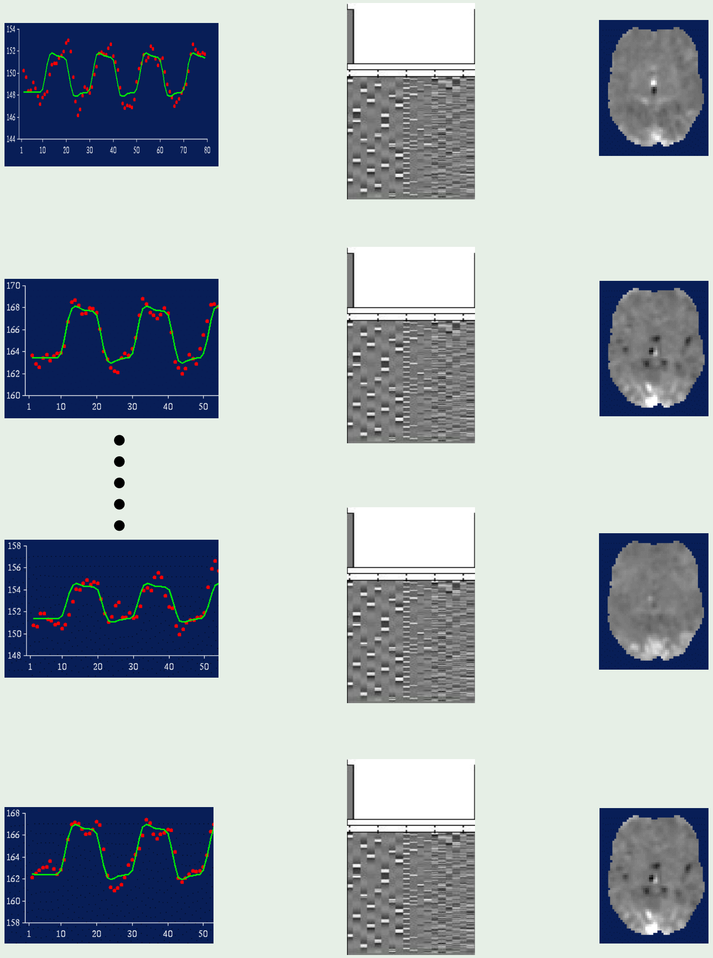
With Random Effects Analysis (RFX) we compare the group effect to the between-subject variability. It is an inference about the sample from which the subjects were drawn. If you had a new subject from that population, you could be confident they would also show the effect.

A Mixed Effects Analysis (MFX) has some random and some fixed effects.

RFX: Summary Statistic

First level

Data | Design Matrix | Contrast Images

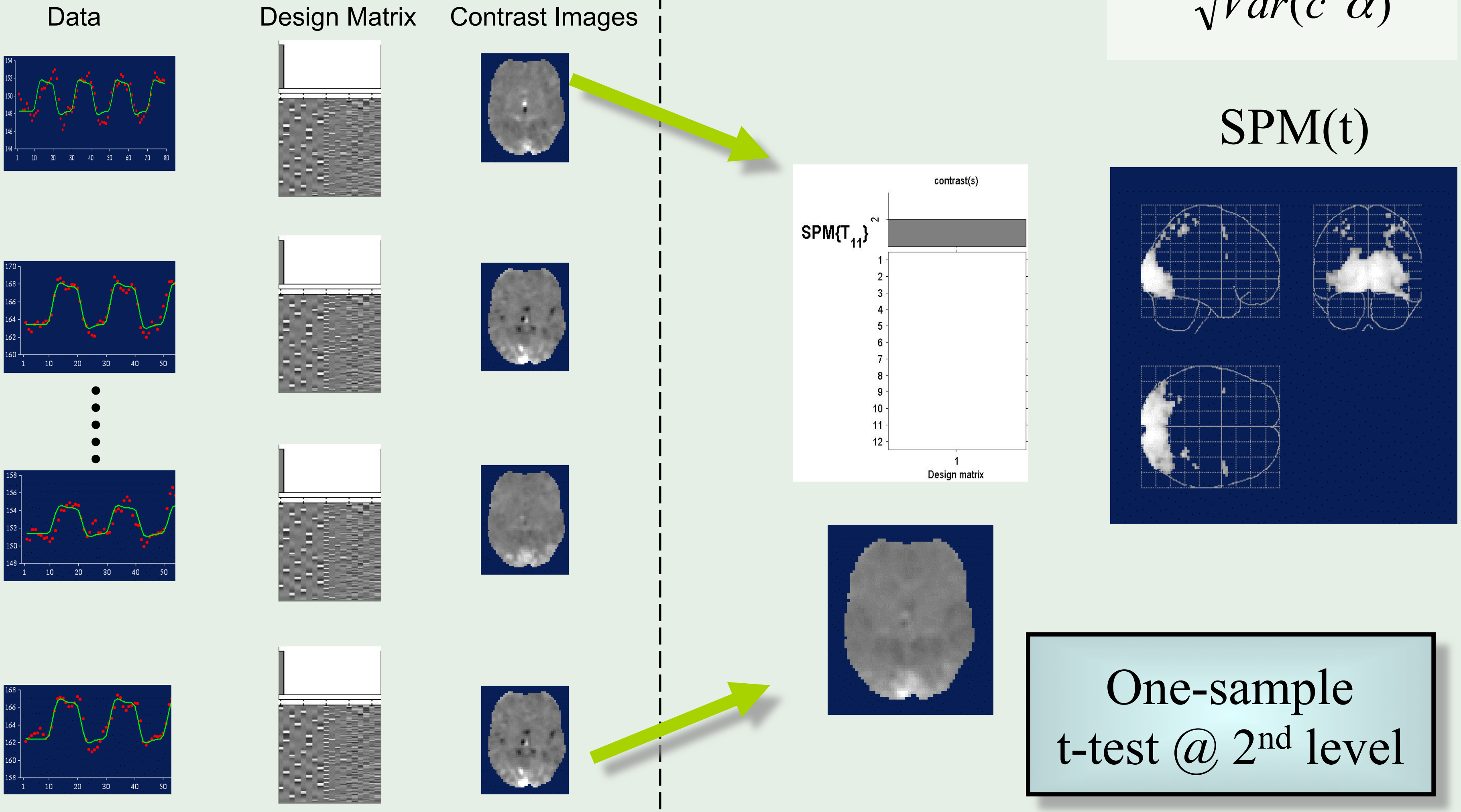


RFX: Summary Statistic

First level

Second level

$$t = \frac{c^T \hat{\alpha}}{\sqrt{V\hat{a}r(c^T \hat{\alpha})}}$$



RFX: Hierarchical model

Hierarchical model

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

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

$$\vdots$$

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

Multiple variance components at each level

$$C_{\varepsilon}^{(i)} = \sum_{k} \lambda_{k}^{(i)} Q_{k}^{(i)}$$

error covariance components Q and hyperparameters λ

At each level, distribution of parameters is given by level above.

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

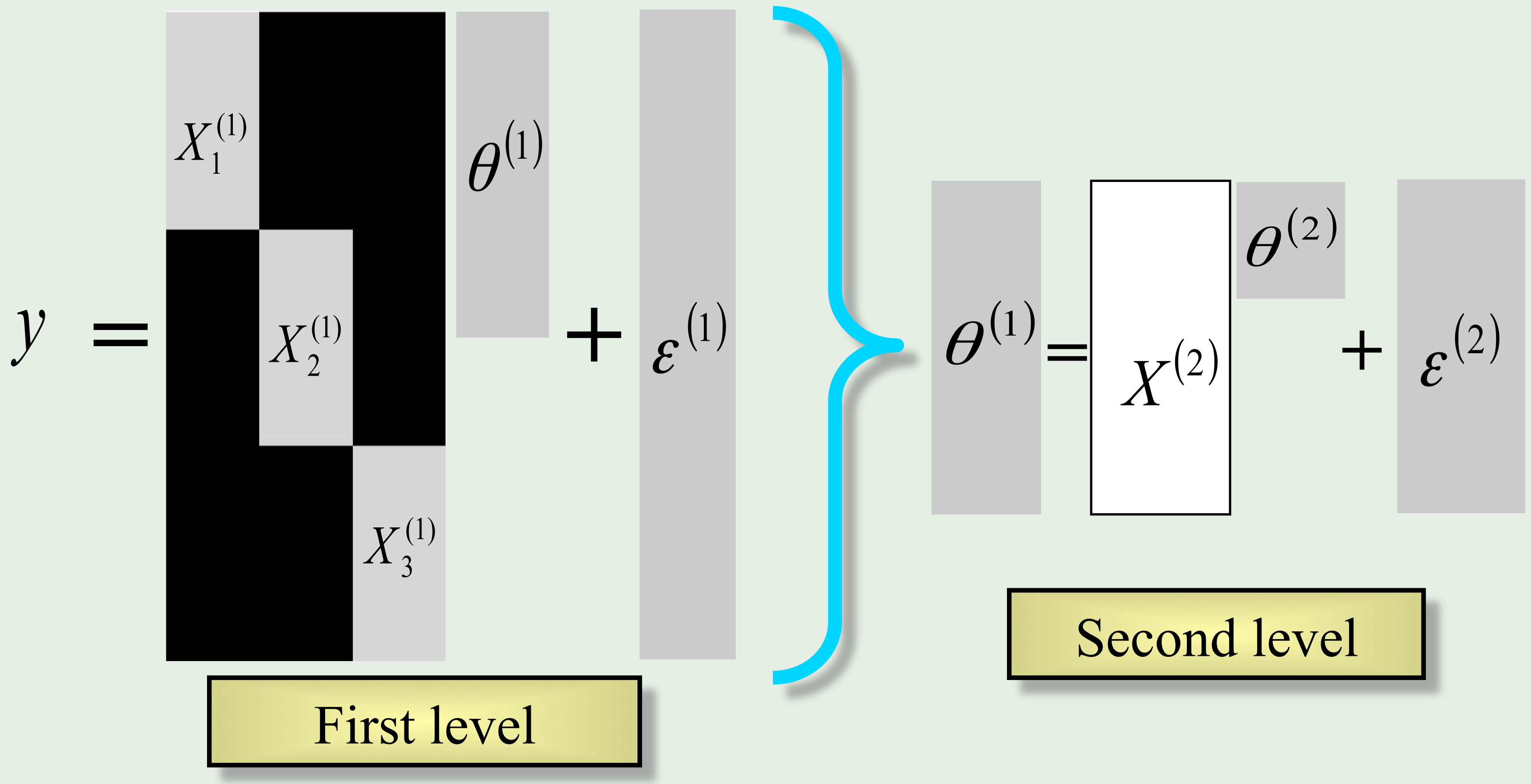
RFX: Hierarchical Model

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

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

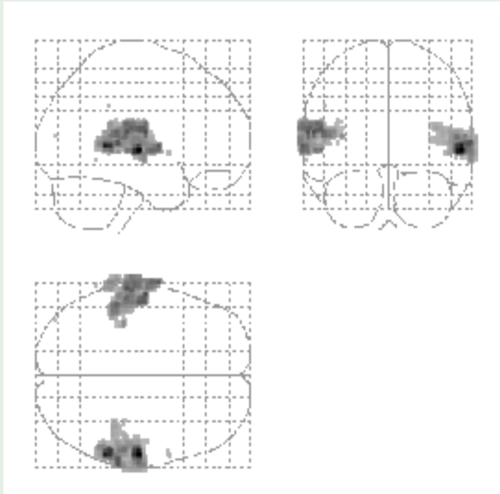
(1) Within subject variance, $s_w(i)$

(2) Between subject variance, s_b

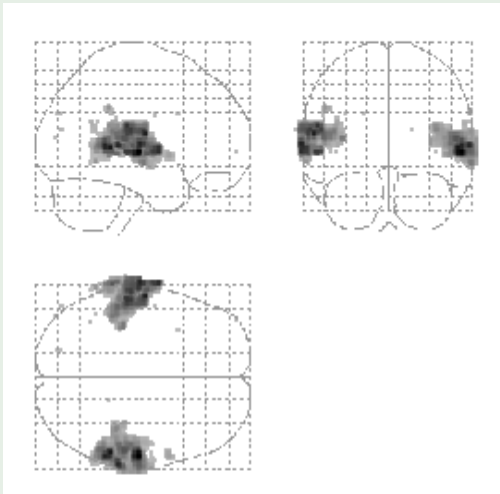


RFX:Auditory Data

Summary statistics



Hierarchical Model



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

RFX: SS versus Hierarchical

The summary stats approach is exact if for each session/subject:

Within-subject variances the same

First-level design (eg number of trials) the same

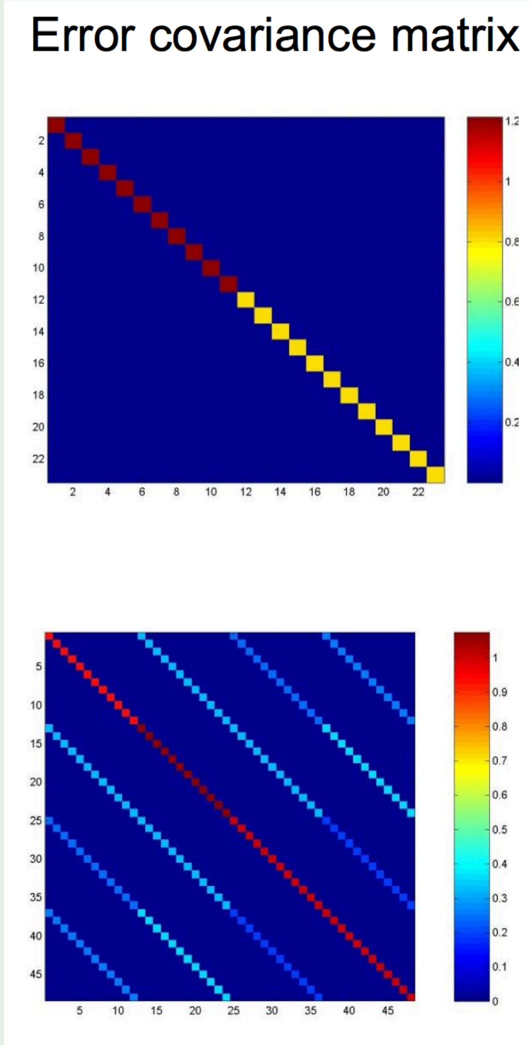
Other cases: Summary stats approach is robust against typical violations (SPM book 2006 , Mumford and Nichols, NI, 2009).

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

2^{nd} level: non-sphericity

Errors are independent but not identical (e.g. different groups: controls, patients)

Errors are not independent and not identical (e.g. repeated measures for each subject)



Multiple Conditions

Condition 1	Condition 2	Condition3
Sub1	Sub13	Sub25
Sub2	Sub14	Sub26
...	...	...
Sub12	Sub24	Sub36

ANOVA at second level (eg drug). If you have two conditions this is a two-sample t-test.

Multiple Conditions

Condition 1	Condition 2	Condition3
Sub1	Sub1	Sub1
Sub2	Sub2	Sub2
...	...	...
Sub12	Sub12	Sub12

ANOVA within subjects at second level.

This is an ANOVA but with average subject effects removed. If you have two conditions this is a paired t-test.

2 by 2 factorial design within subject

	Easy	Difficult
Words		
Non words		

First level: 4 contrasts per subject

- Overall effect (1, 1, 1, 1)
- Main effect of factor 1 (1, 1, -1, -1)
- Main effect of factor 2 (1, -1, 1, -1)
- Interaction (1, -1, -1, 1)

Second level: 4 designs => 4 one sample t-tests

Summary

Group Inference usually proceeds with RFX analysis, not FFX. Group effects are compared to between rather than within subject variability.

Hierarchical models provide a gold-standard for RFX analysis but are computationally intensive (spm_mfx).

Summary statistics are a robust method for RFX group analysis (SPM book, Mumford and Nichols, NI, 2009)

Can also use 'ANOVA' or 'ANOVA within subject' at second level for inference about multiple experimental conditions..

Conclusion

Summary statistics are robust approximation to mixed-effects analysis.

Recommendation:

To minimize number of variance components to be estimated at 2^{nd} level, compute relevant contrasts at 1^{st} level and use simple test at 2^{nd} level.