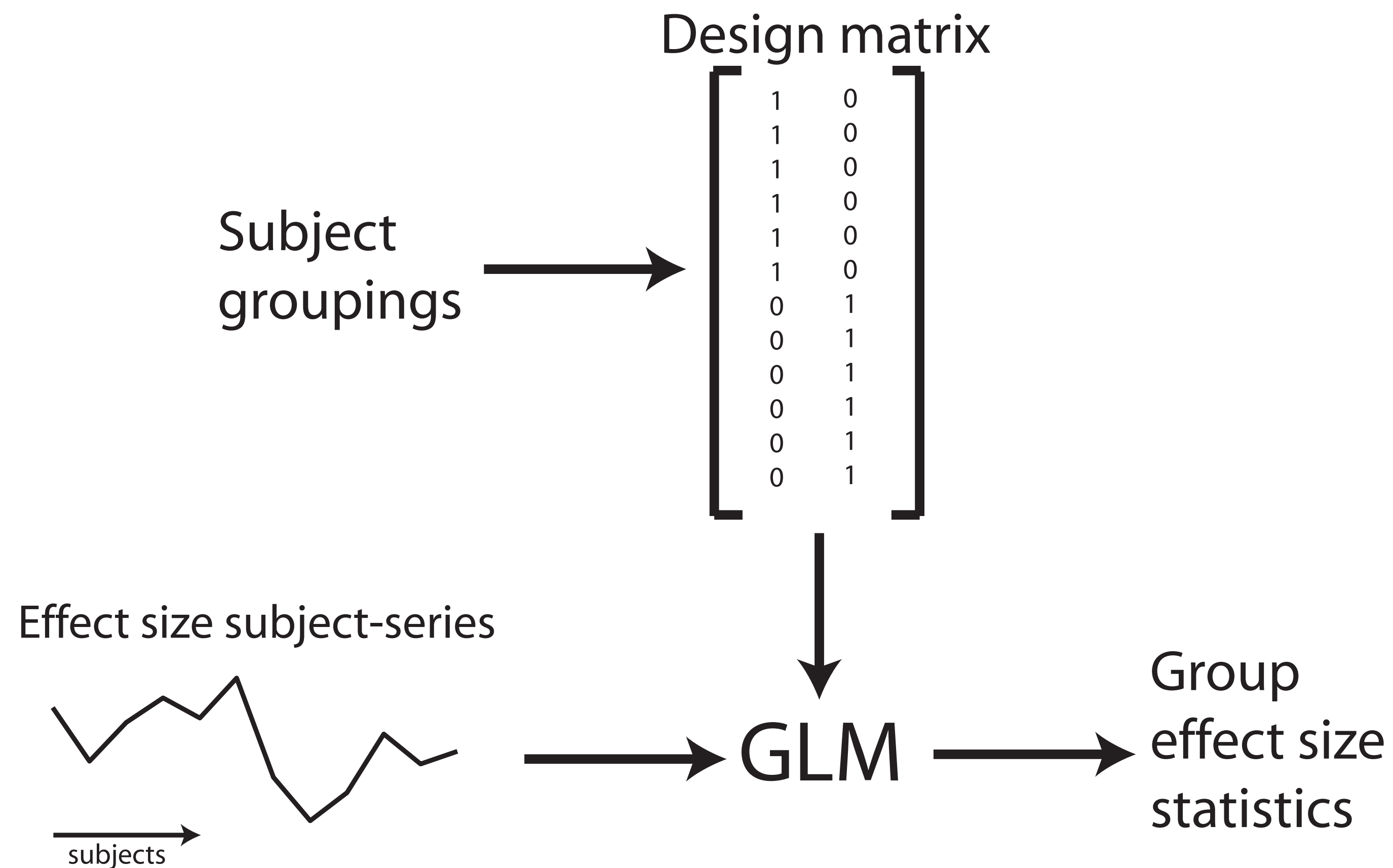
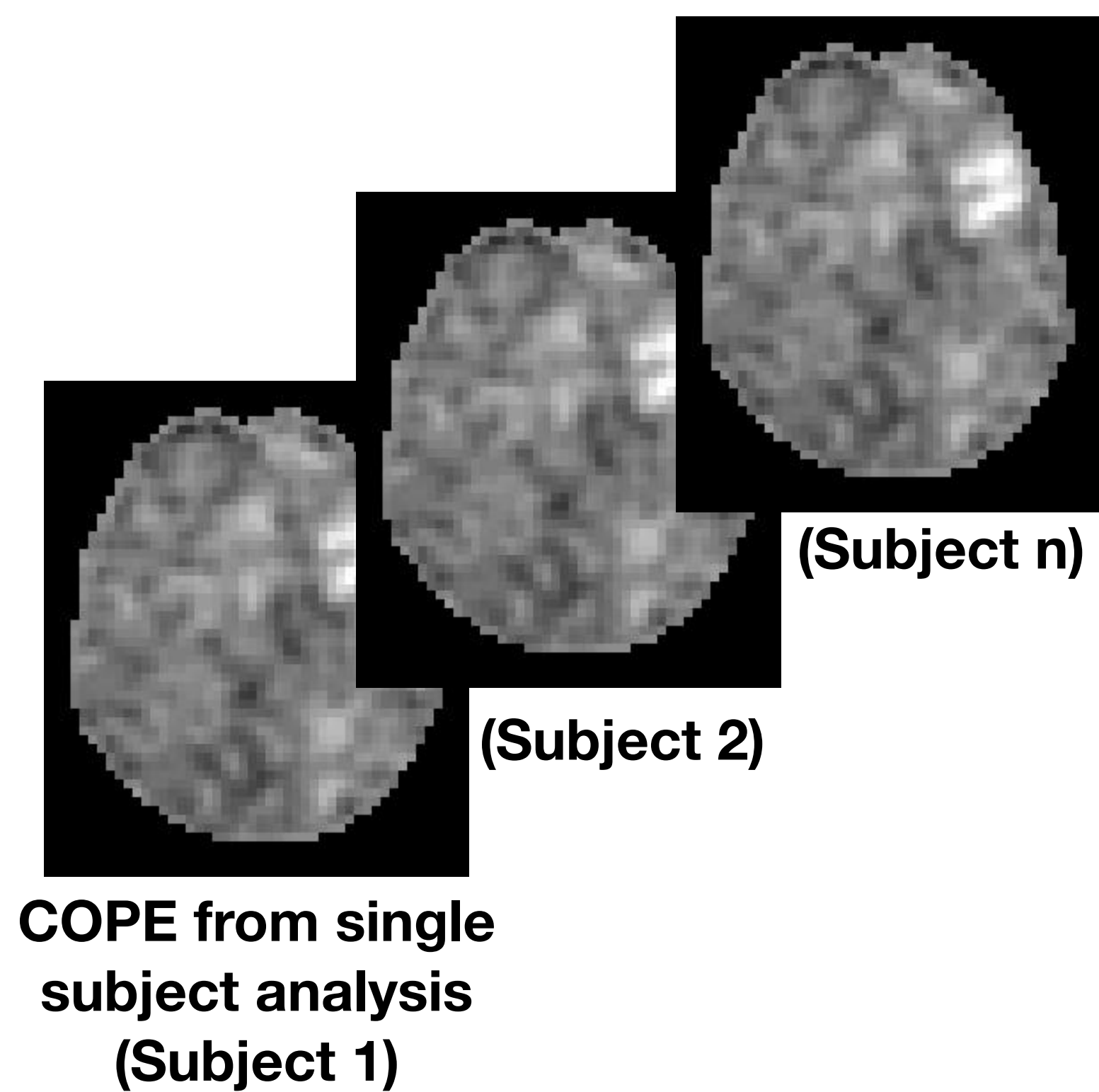


FMRI group analysis



The GLM for group analysis



OUTPUTS from single subject analysis are INPUT for group analysis

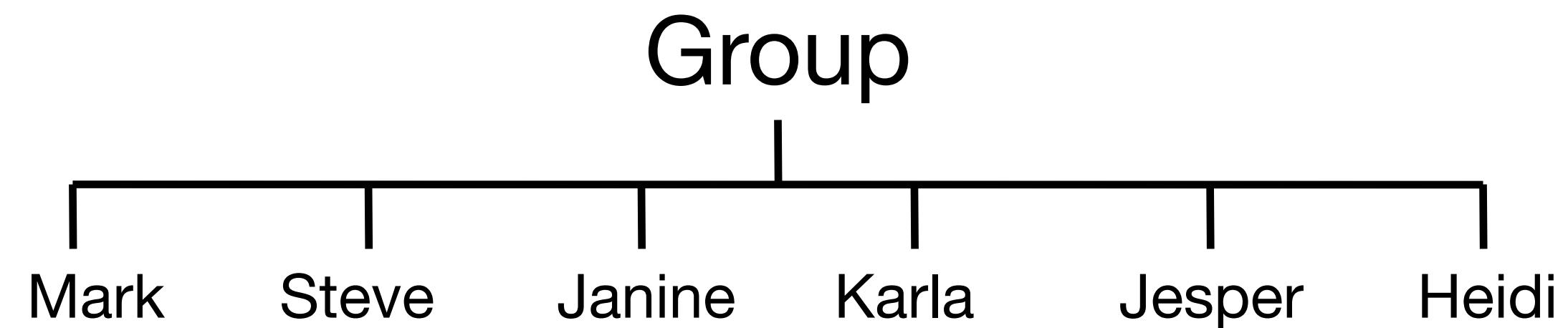
Explanatory Variables (EVs)

Parameter Estimates (PEs)

$$\begin{array}{c}
 \text{subjects} \downarrow \\
 \text{COPEs from a voxel across subjects}
 \end{array}
 \mathbf{y} =
 \begin{array}{c}
 \mathbf{X}_1 \quad \mathbf{X}_2 \\
 \begin{bmatrix}
 1 & 0 \\
 1 & 0 \\
 1 & 0 \\
 1 & 0 \\
 1 & 0 \\
 1 & 0 \\
 0 & 1 \\
 0 & 1 \\
 0 & 1 \\
 0 & 1 \\
 0 & 1 \\
 0 & 1
 \end{bmatrix}
 \end{array}
 \begin{array}{c}
 \beta_1 \\
 \beta_2
 \end{array}
 + \mathbf{e}$$

Design Matrix

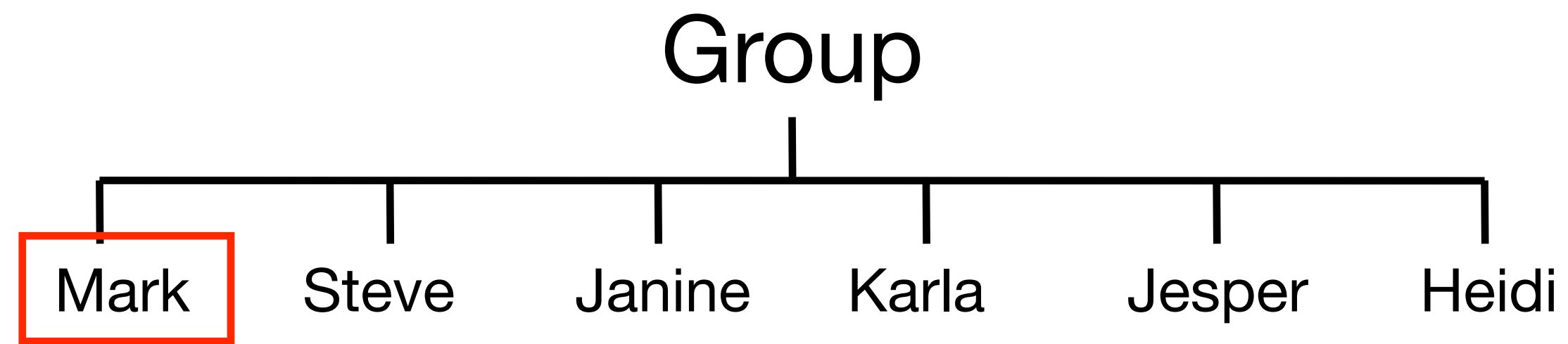
A simple example



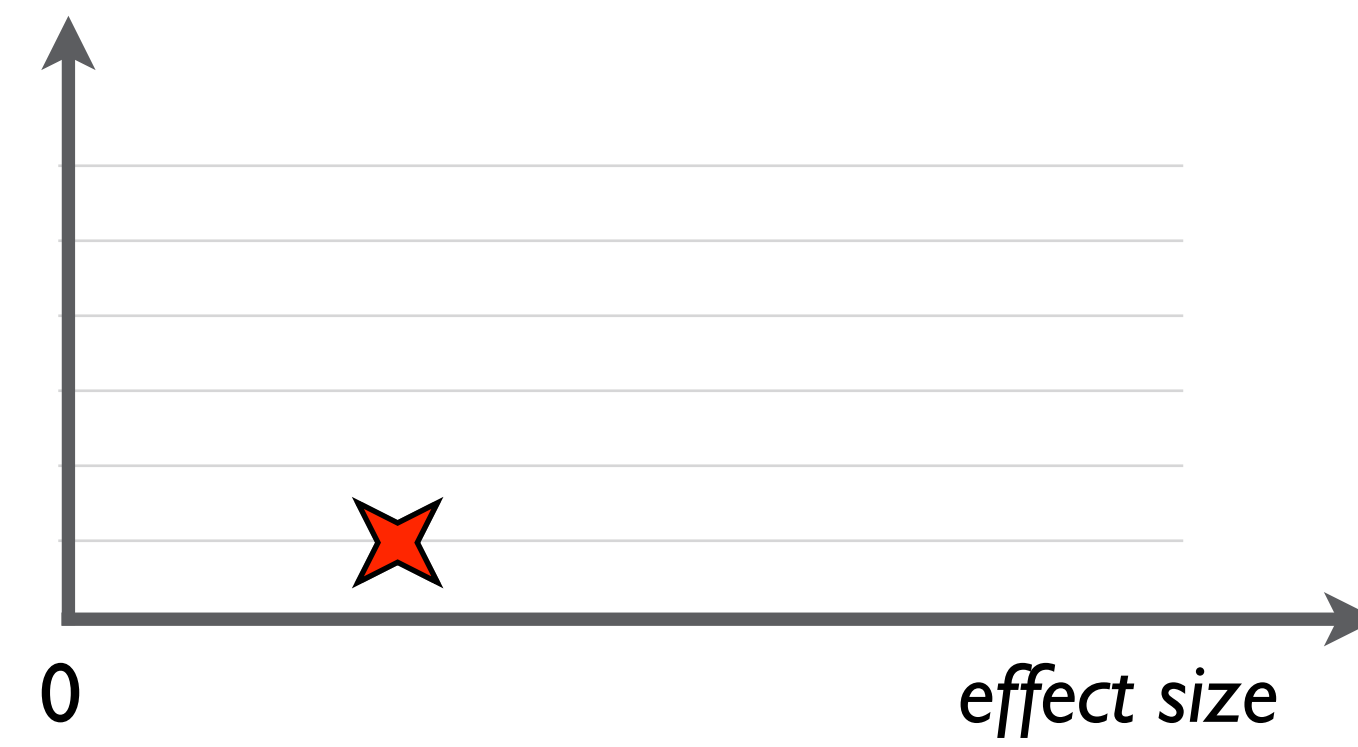
Does the group activate on average?

For a specific PE/contrast from the first level analysis,
which part of the brain were significantly activated across all subjects?

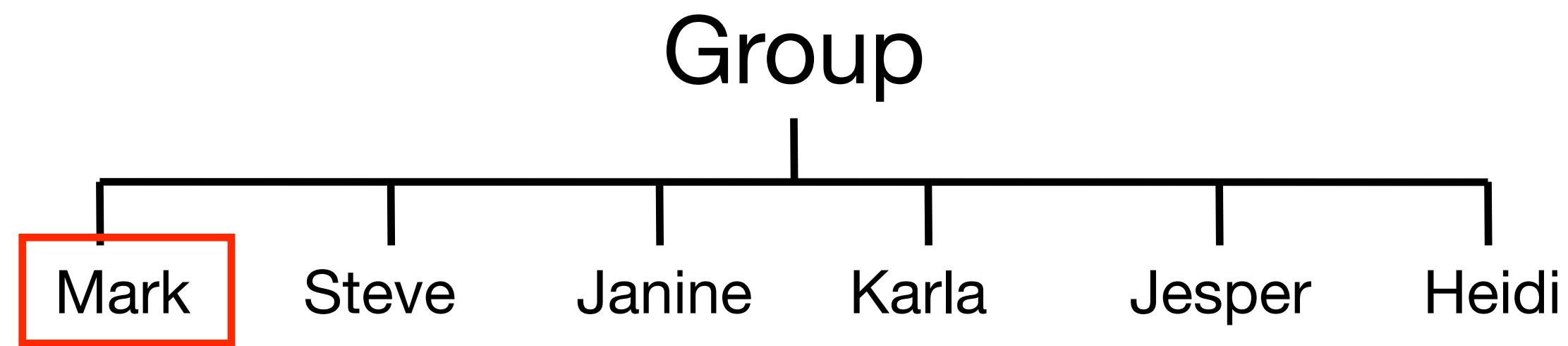
A simple example



Does the group activate on average?



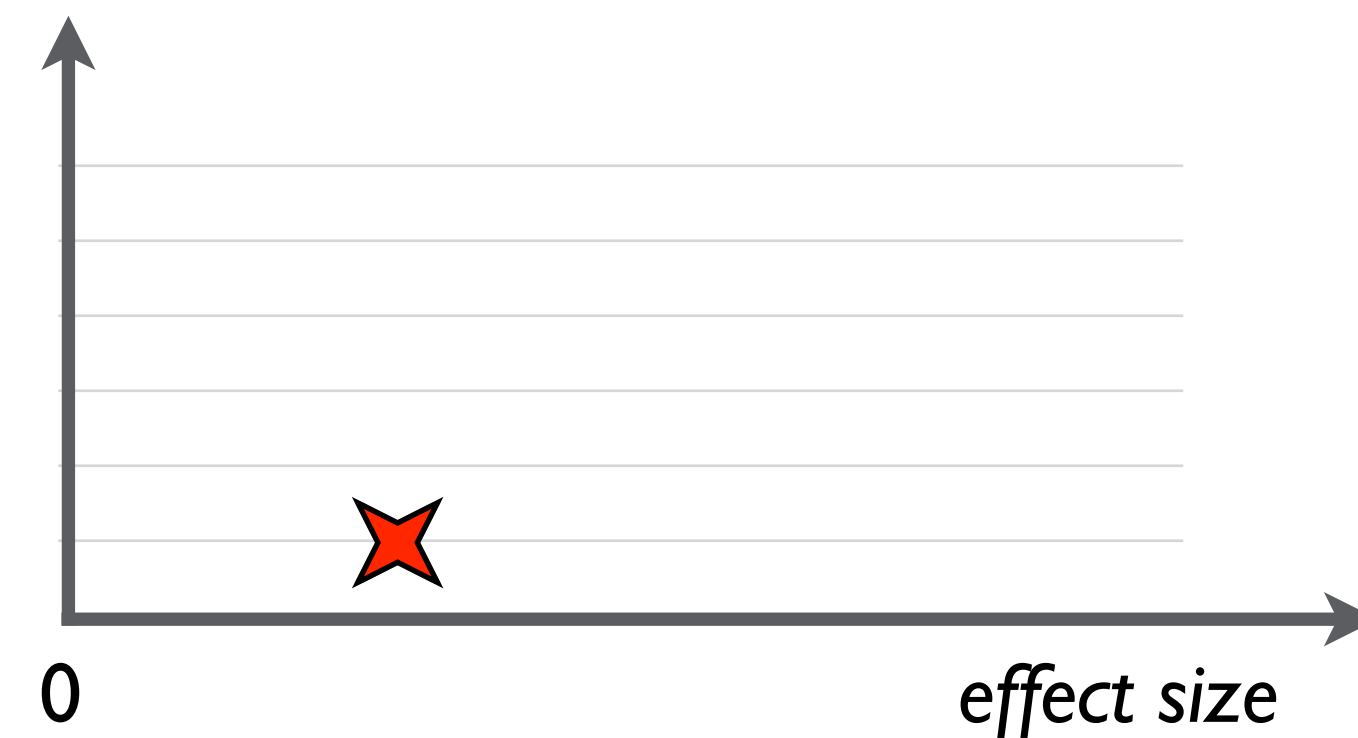
A simple example



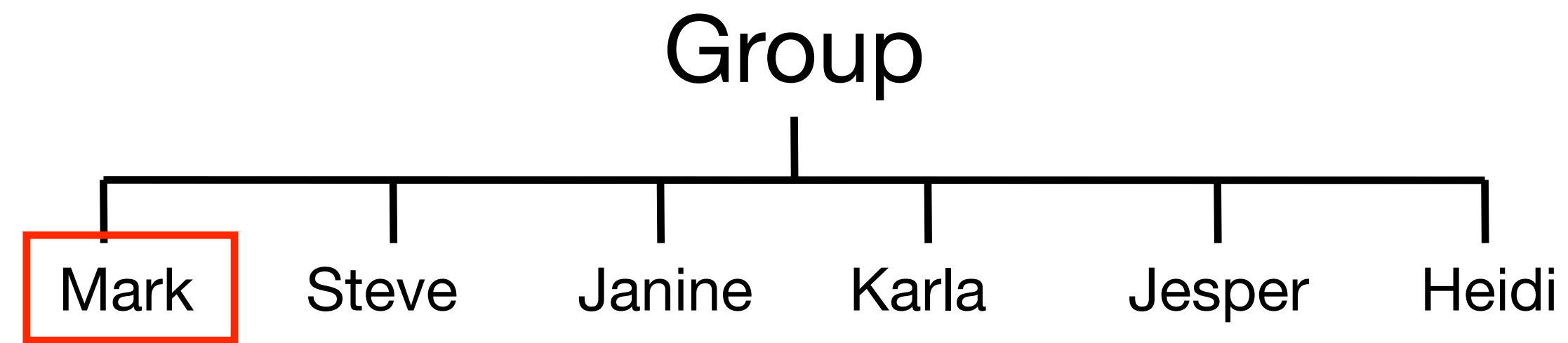
Does the group activate on average?

$$Y_k = X_k \beta_k + \epsilon_k$$

First-level GLM
on Mark's 4D FMRI
data set

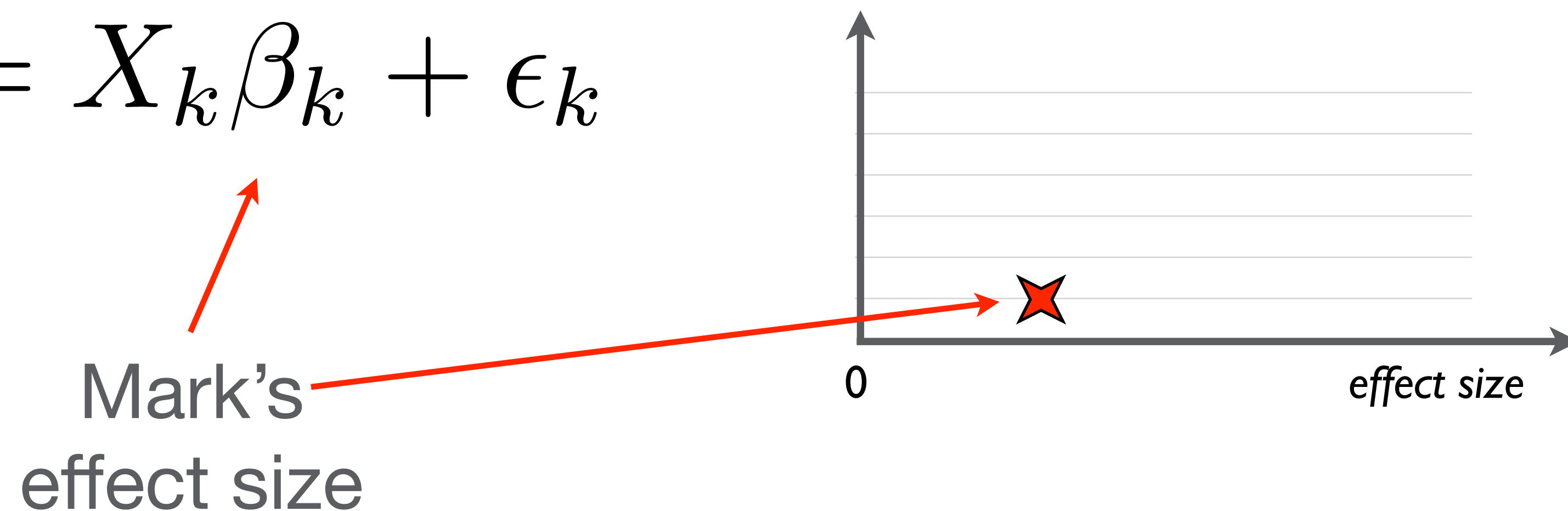


A simple example

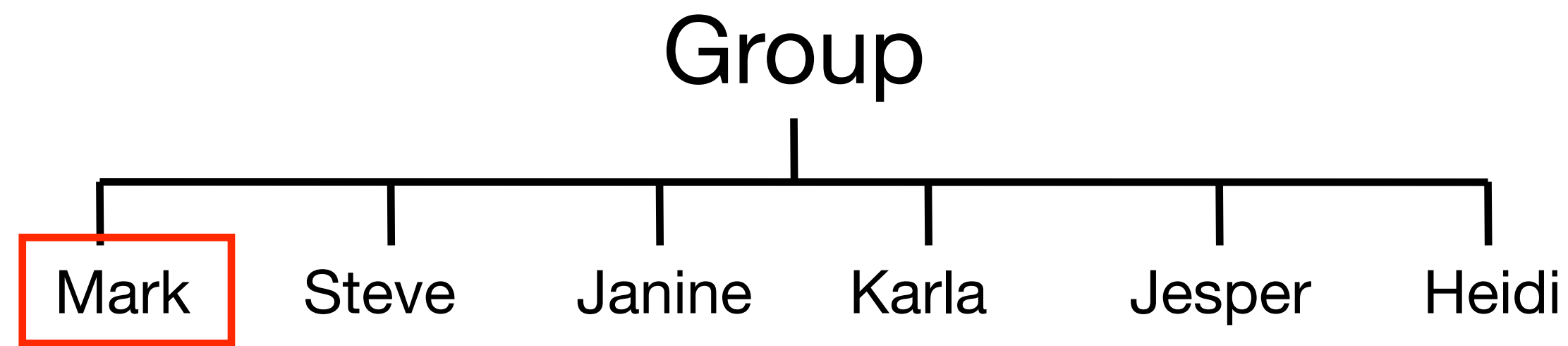


Does the group activate on average?

$$Y_k = X_k \beta_k + \epsilon_k$$

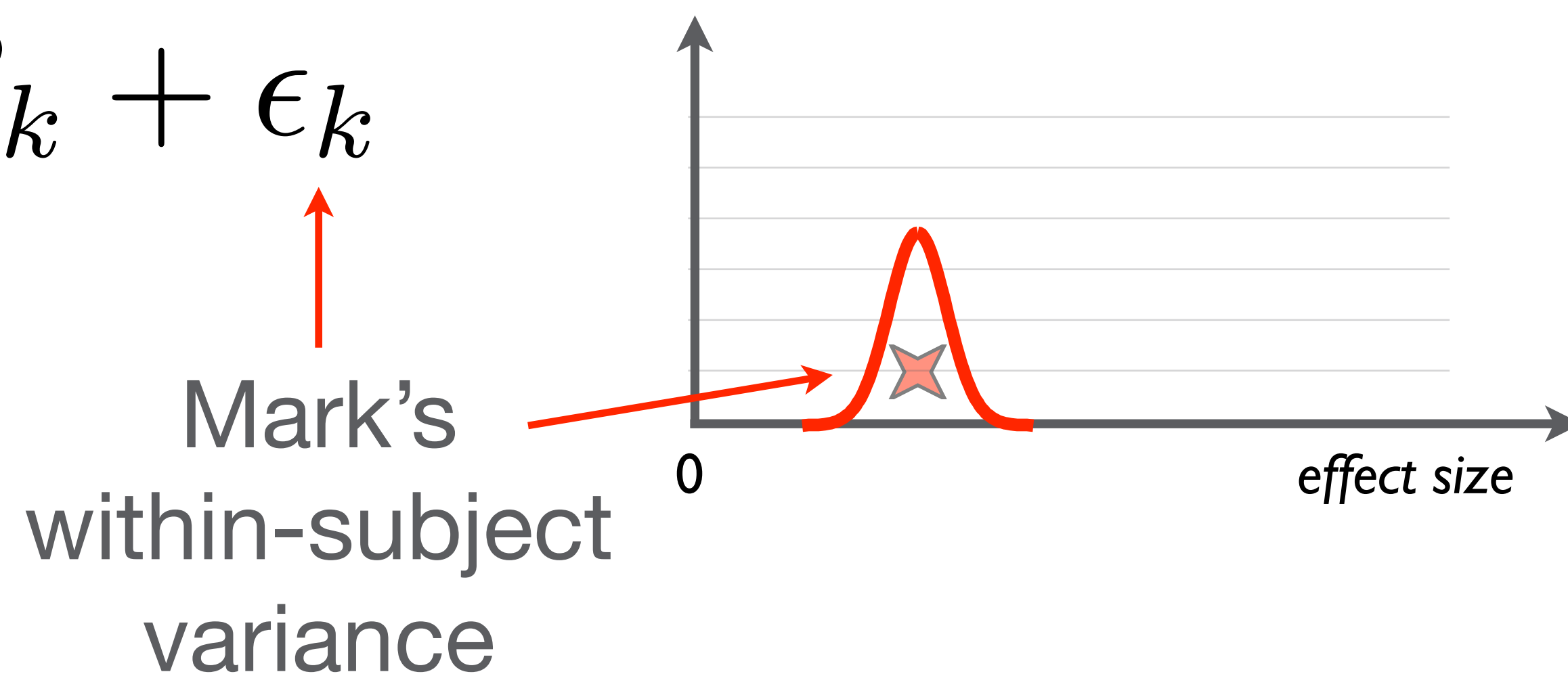


A simple example

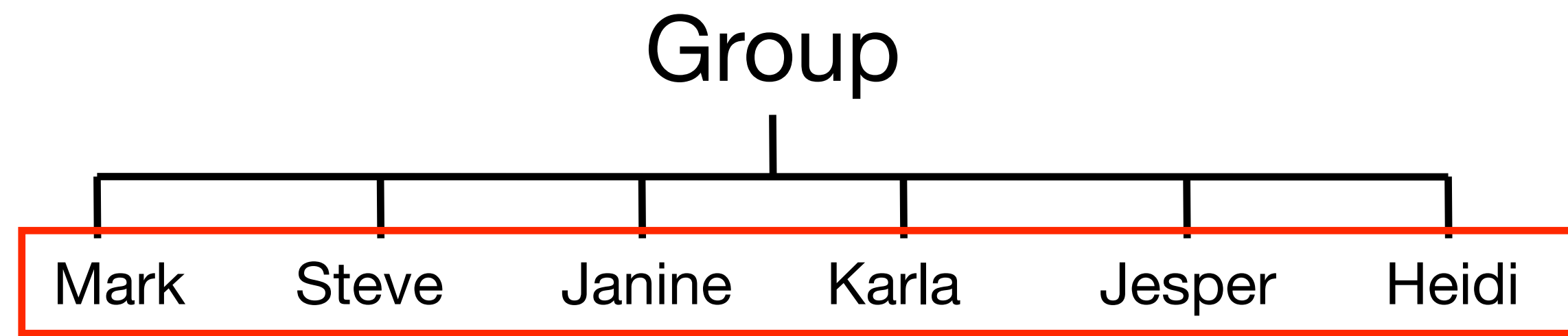


Does the group activate on average?

$$Y_k = X_k \beta_k + \epsilon_k$$



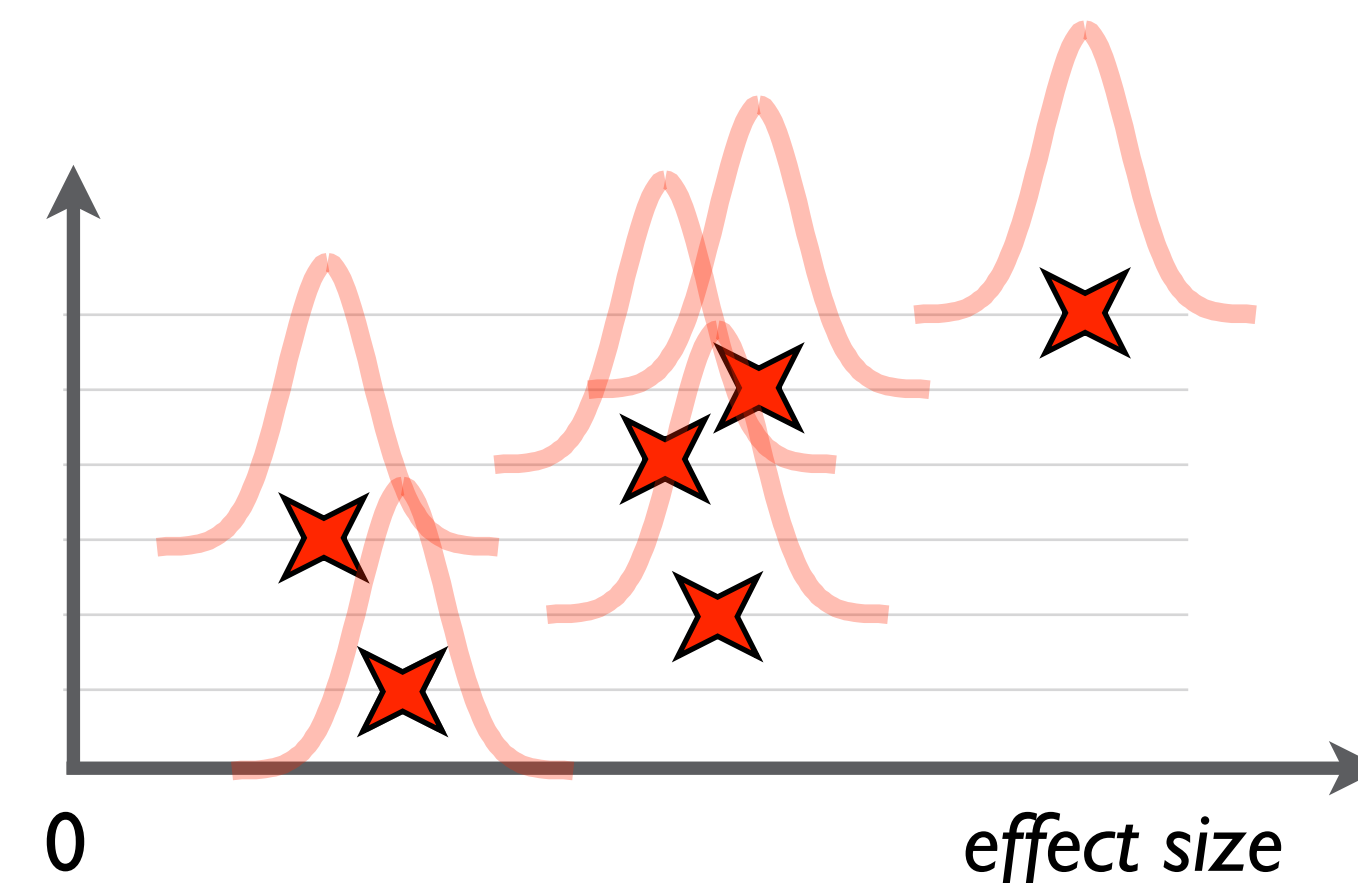
A simple example



Does the group activate on average?

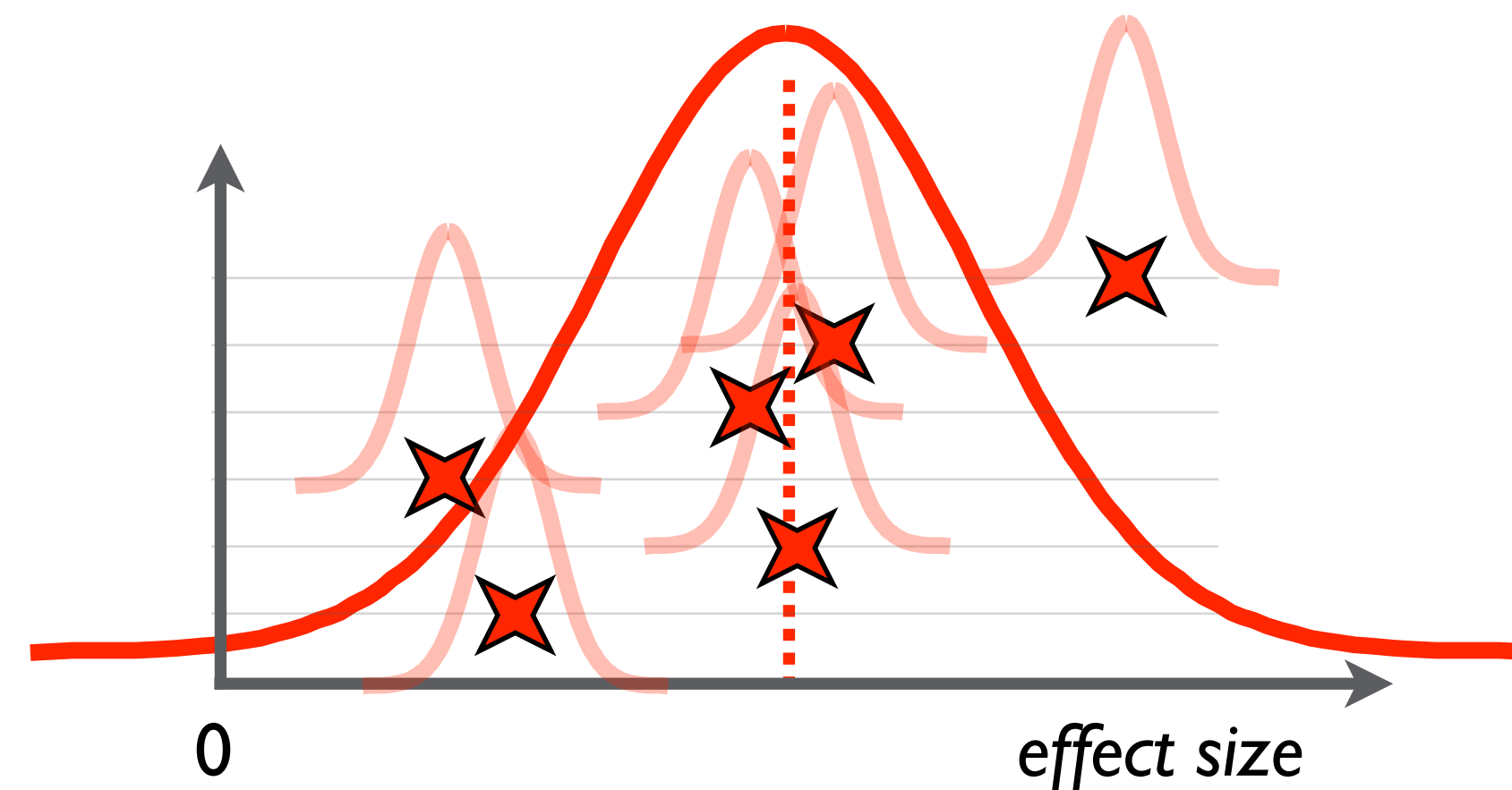
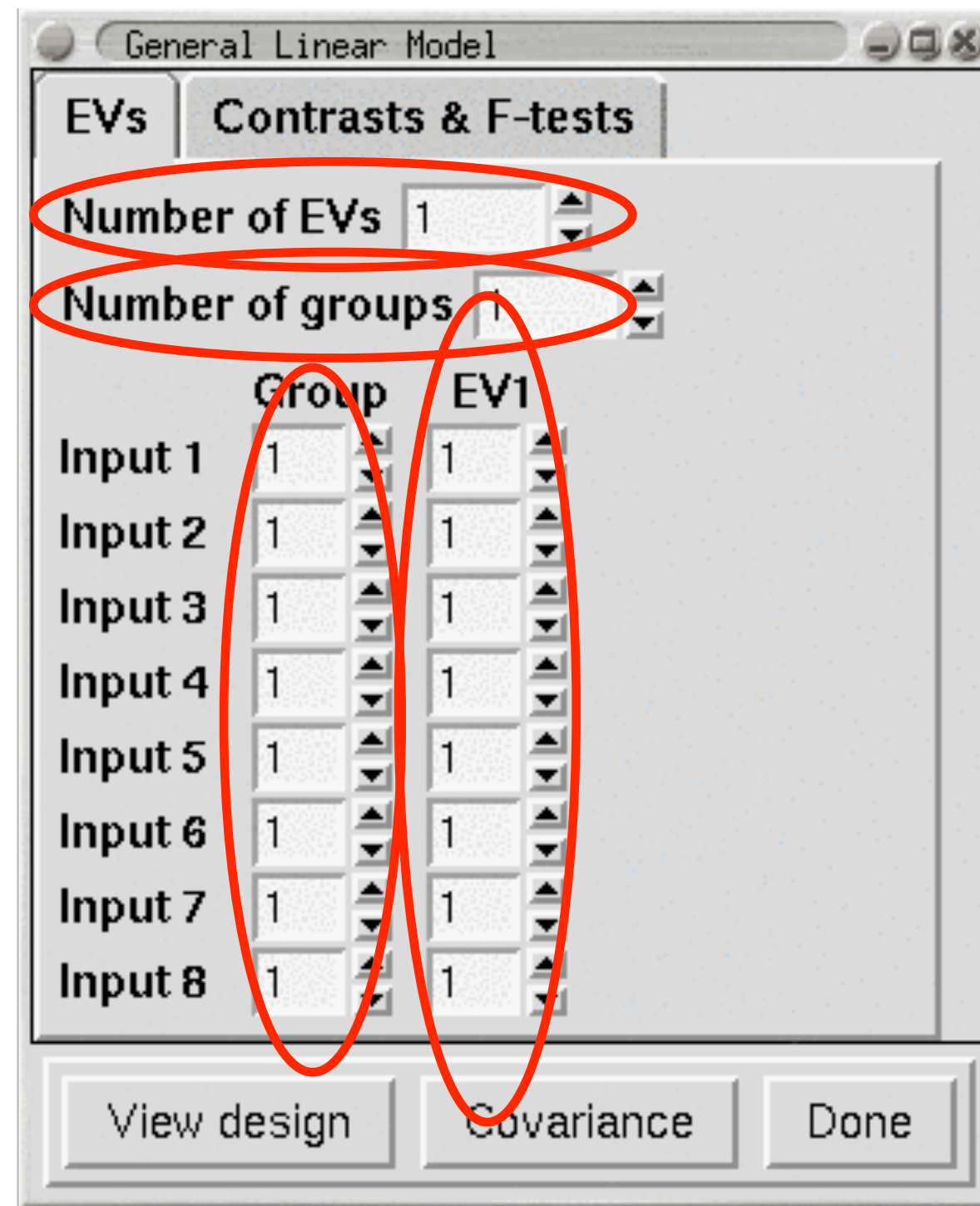
$$Y_k = X_k \beta_k + \epsilon_k$$

All first-level GLMs
on 6 FMRI data set



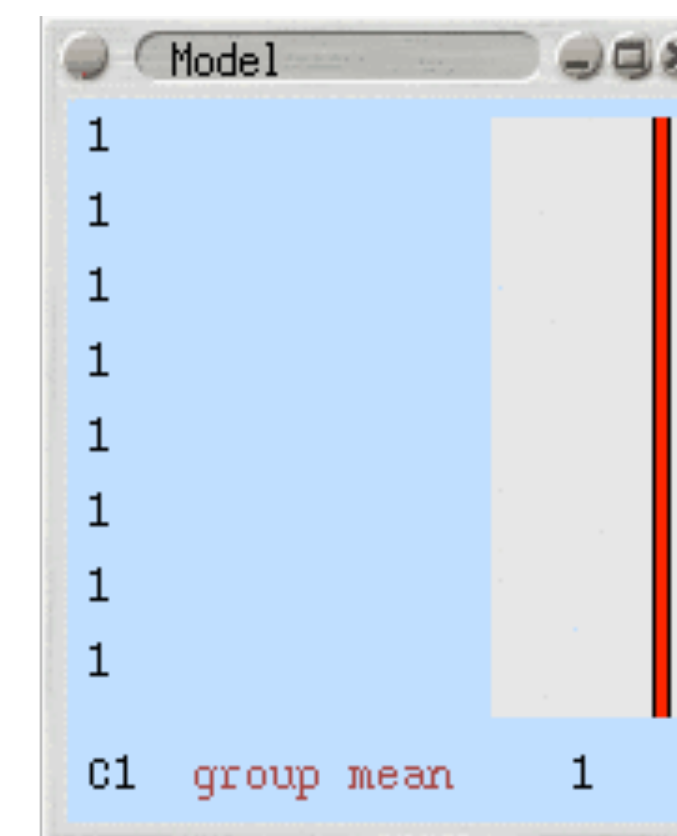
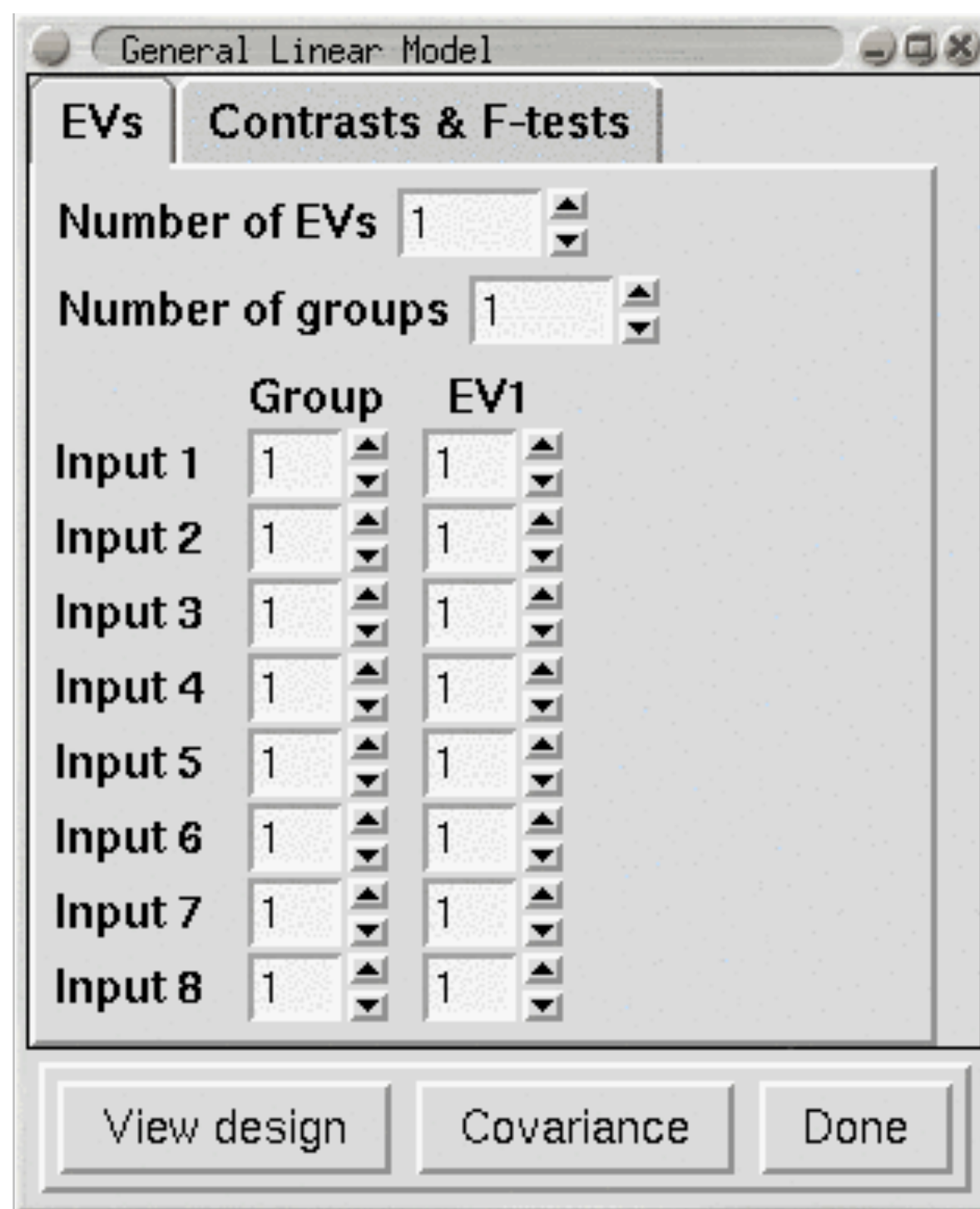
Single Group Average

Does the group activate on average?



Single Group Average

Does the group activate on average?

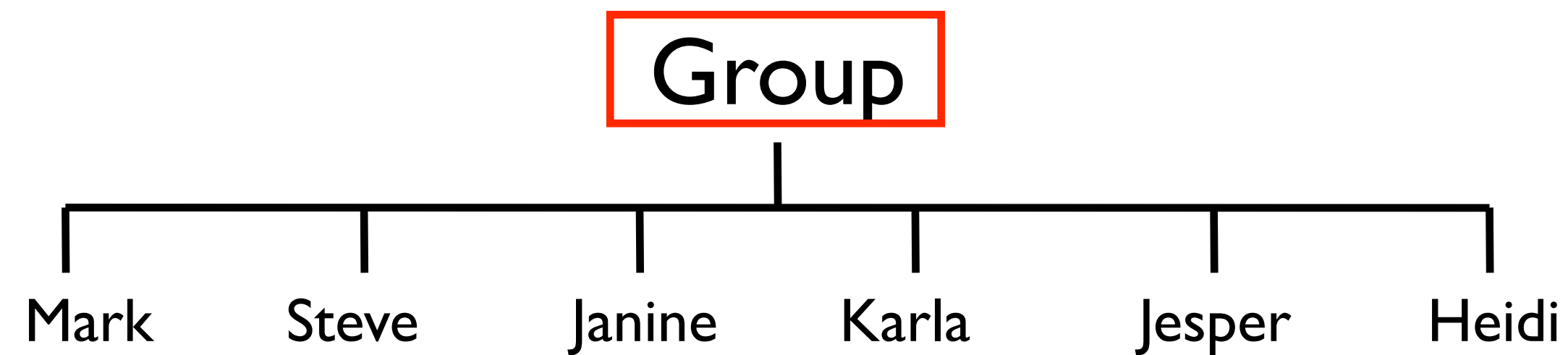




Fixed versus mixed effects

Fixed-Effects Analysis

Do these exact 6 subjects activate on average?

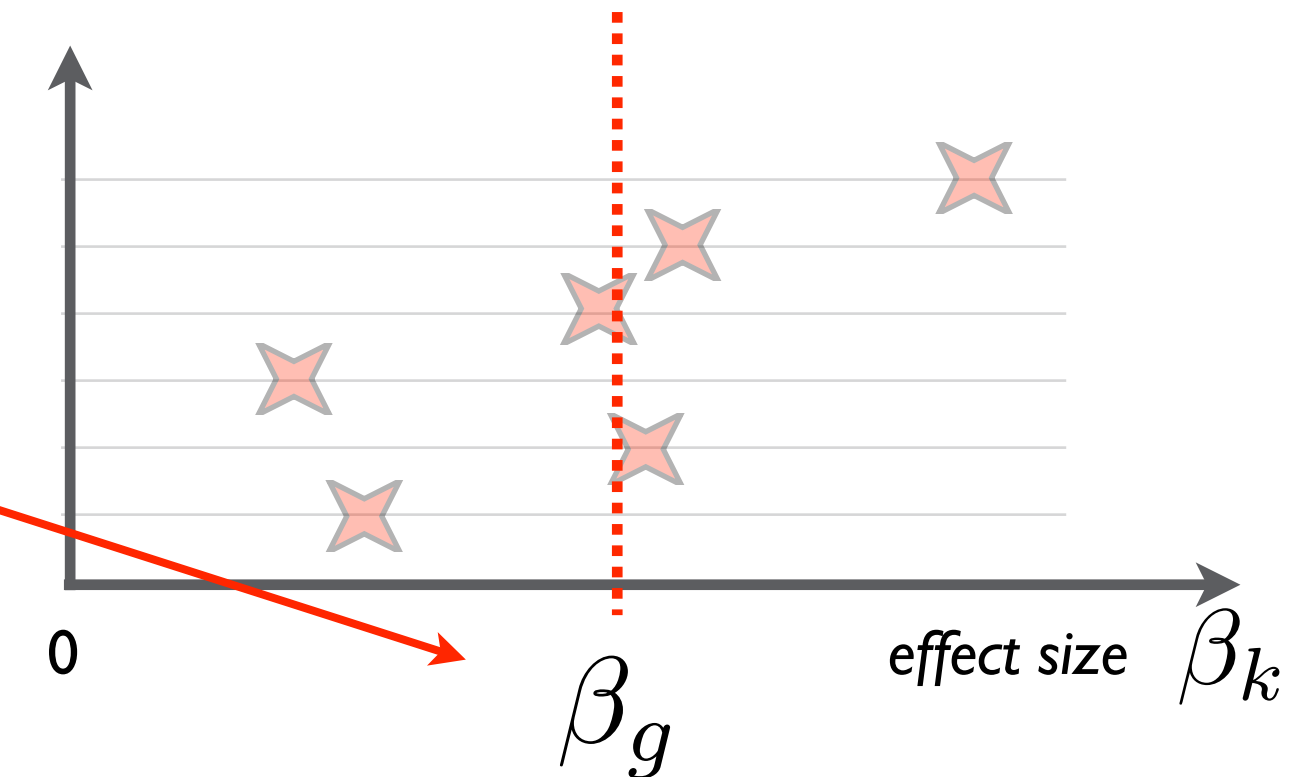


$$Y_K = X_K \beta_K + \epsilon_K$$

$$\beta_K = X_g \beta_g$$

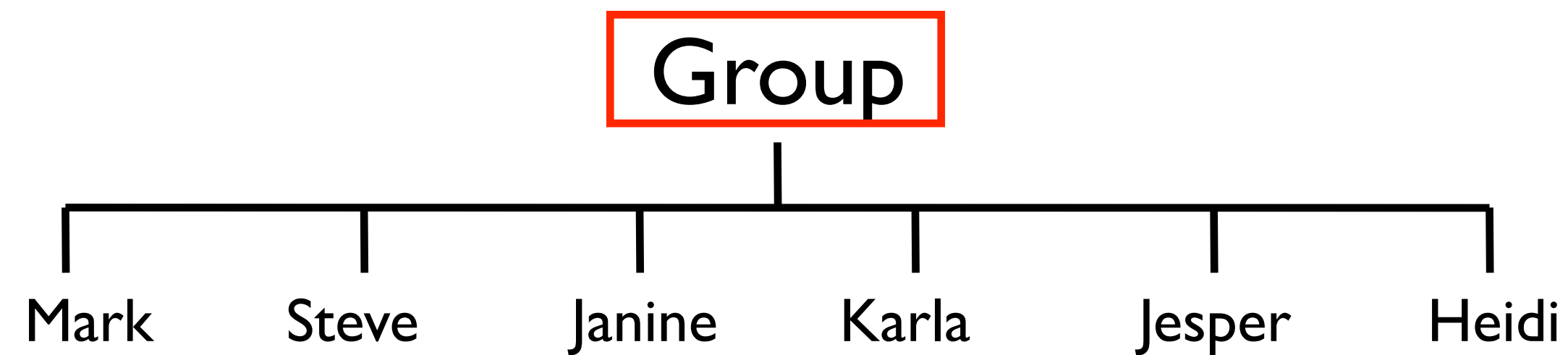
Fixed Effects Analysis:

- *Consider only these 6 subjects*
- *estimate the mean across these subject*
- *only variance is within-subject variance*



Mixed-Effects Analysis

Does the population activate on average?

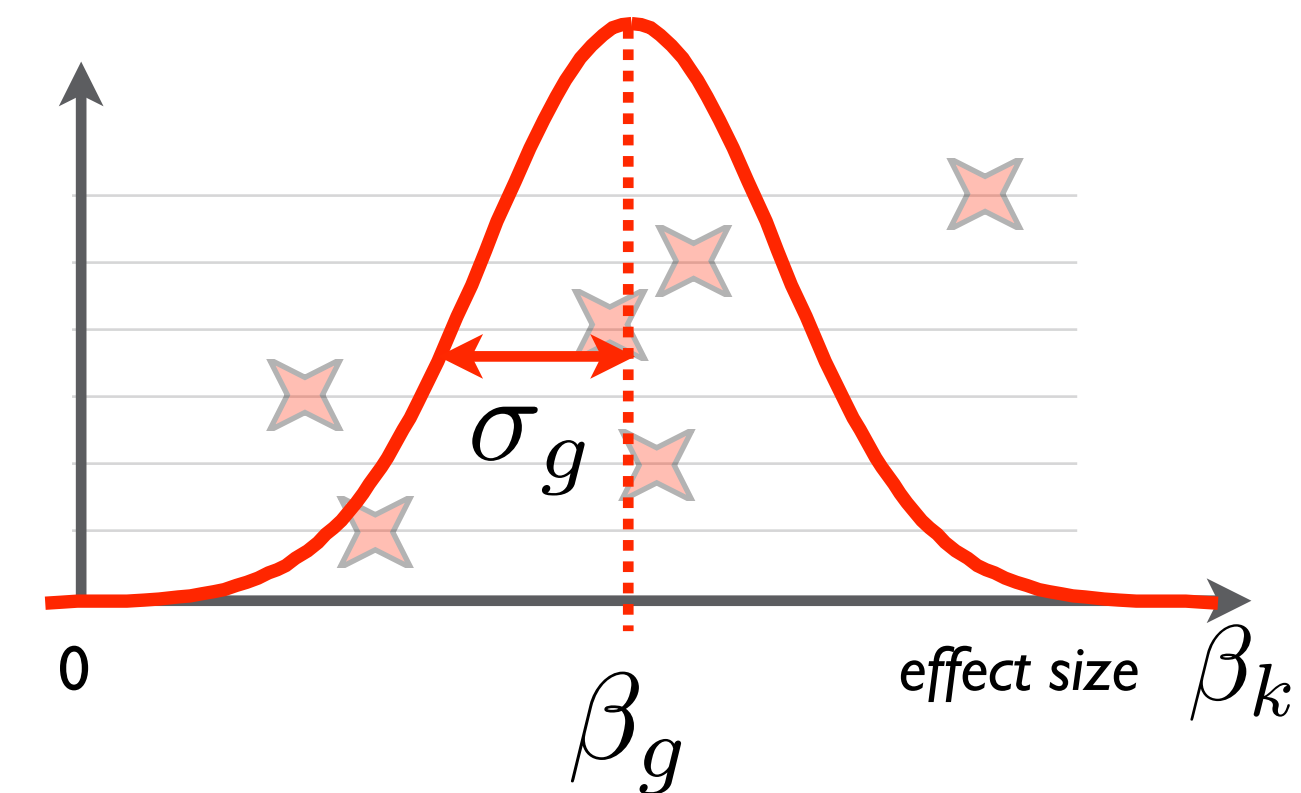


$$Y_K = X_K \beta_K + \epsilon_K$$

$$\beta_K = X_g \beta_g + \epsilon_g$$

Mixed-Effects Analysis:

- Consider the 6 subjects as samples from a wider population
- estimate the mean across the population
- between-subject variance accounts for random sampling



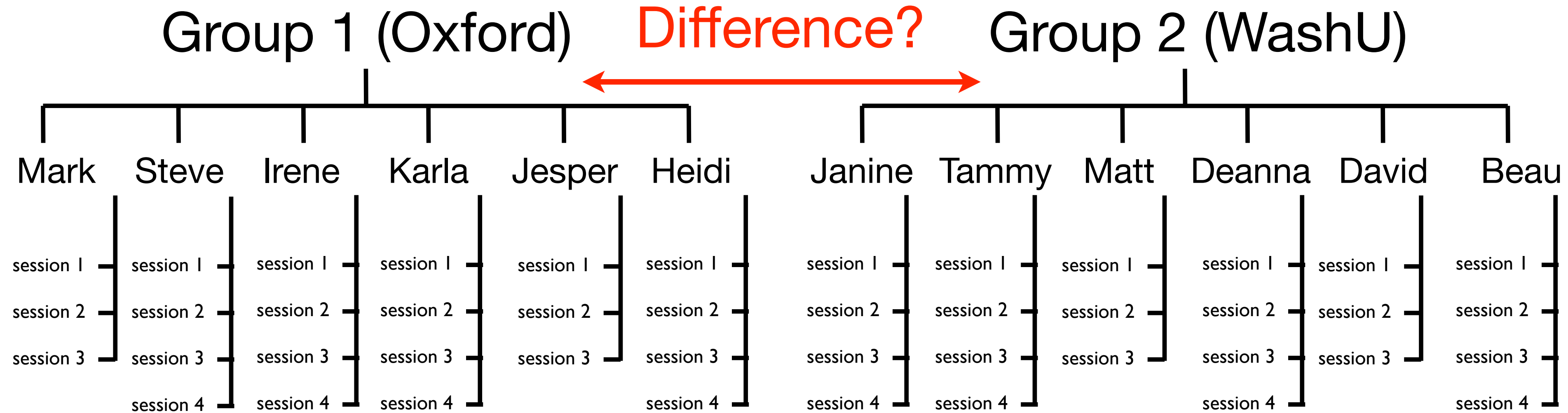
**But why are you telling
me about Fixed Effects ?**





Multiple sessions per subject

All-in-One Approach



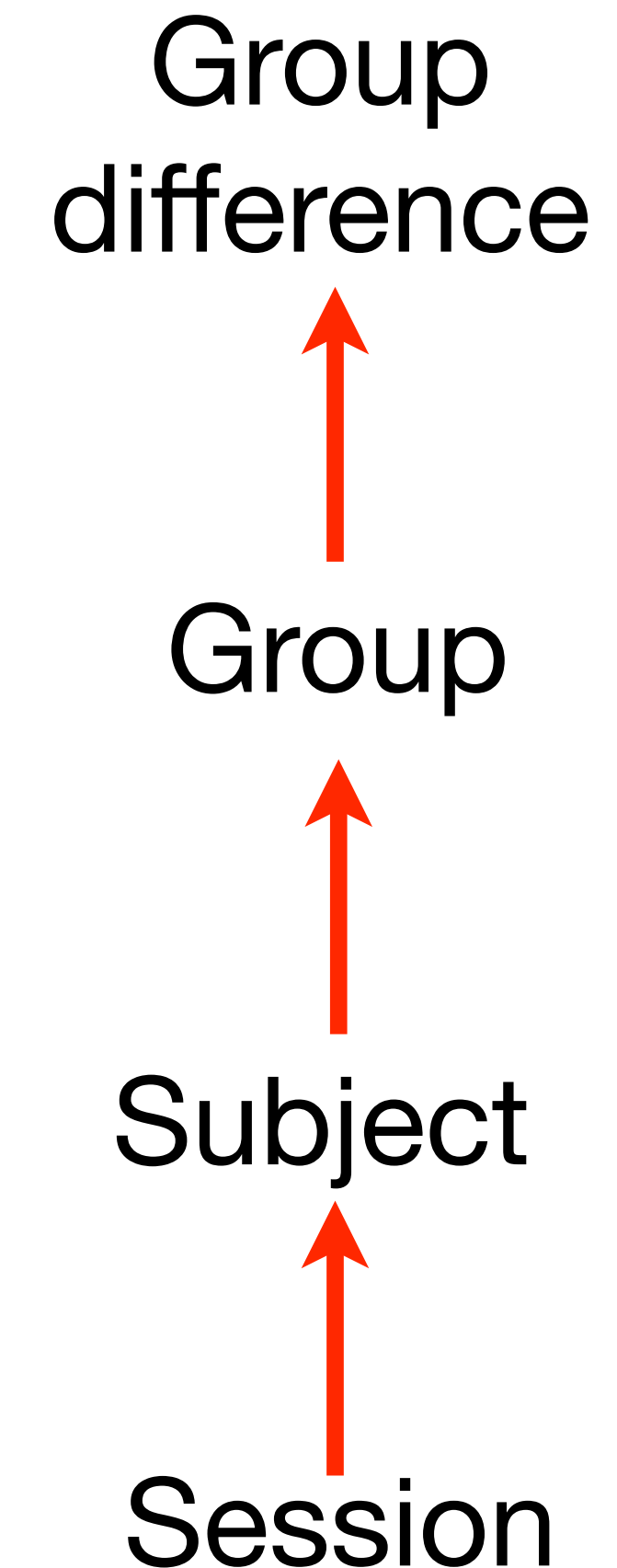
- Could use one (huge) GLM to infer group difference
 - difficult to ask sub-questions in isolation
 - computationally demanding
 - need to process again when new data is acquired



Summary Statistics Approach

In FEAT estimate levels one stage at a time

- At each level:
 - Inputs are summary stats from levels below (or FMRI data at the lowest level)
 - Outputs are summary stats or statistic maps for inference
- **Fixed Effects** at session level

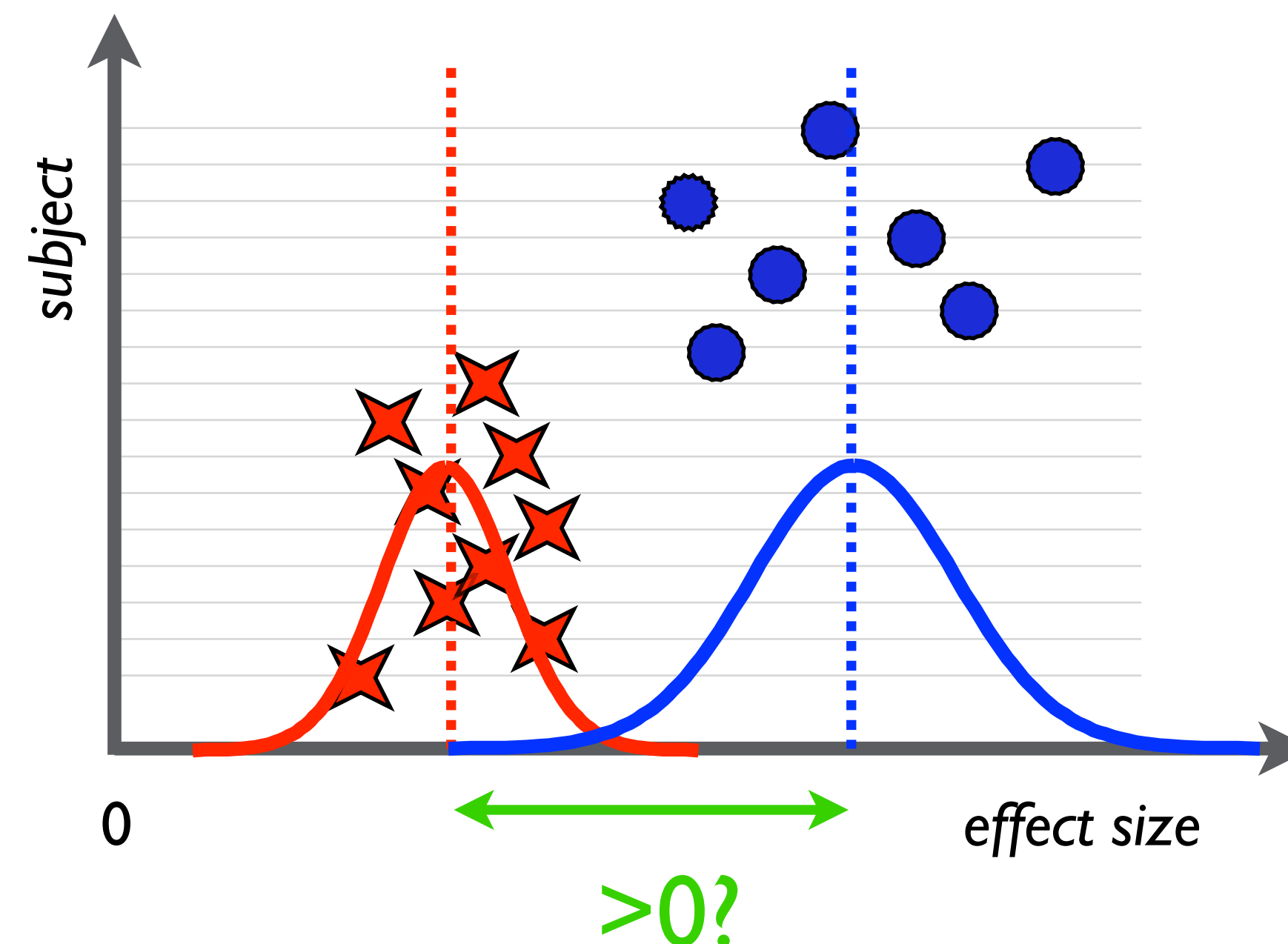


Unpaired Two-Group Difference

- We have two groups (e.g. 9 WashU, 7 Oxford) with different between-subject variance

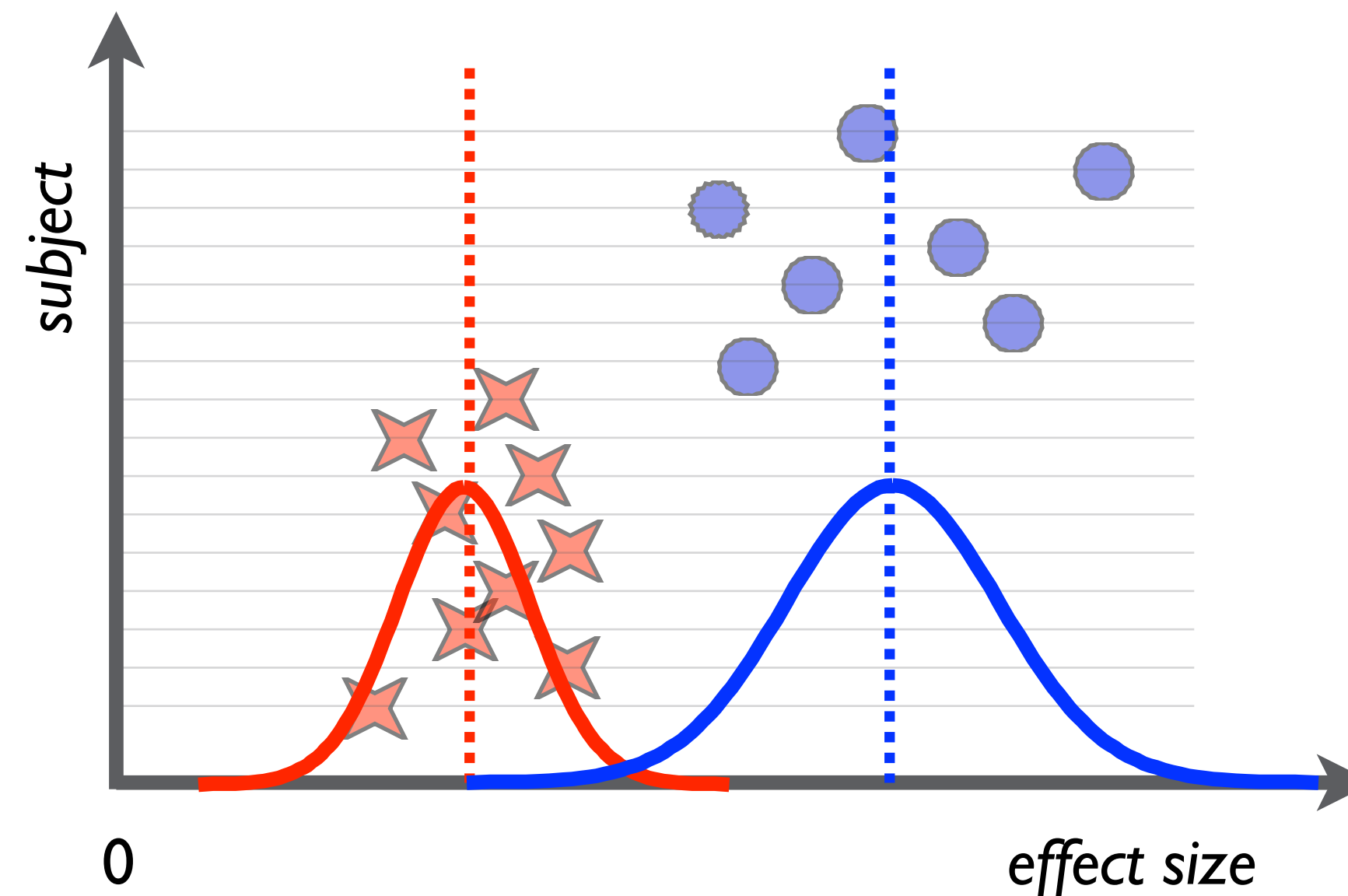
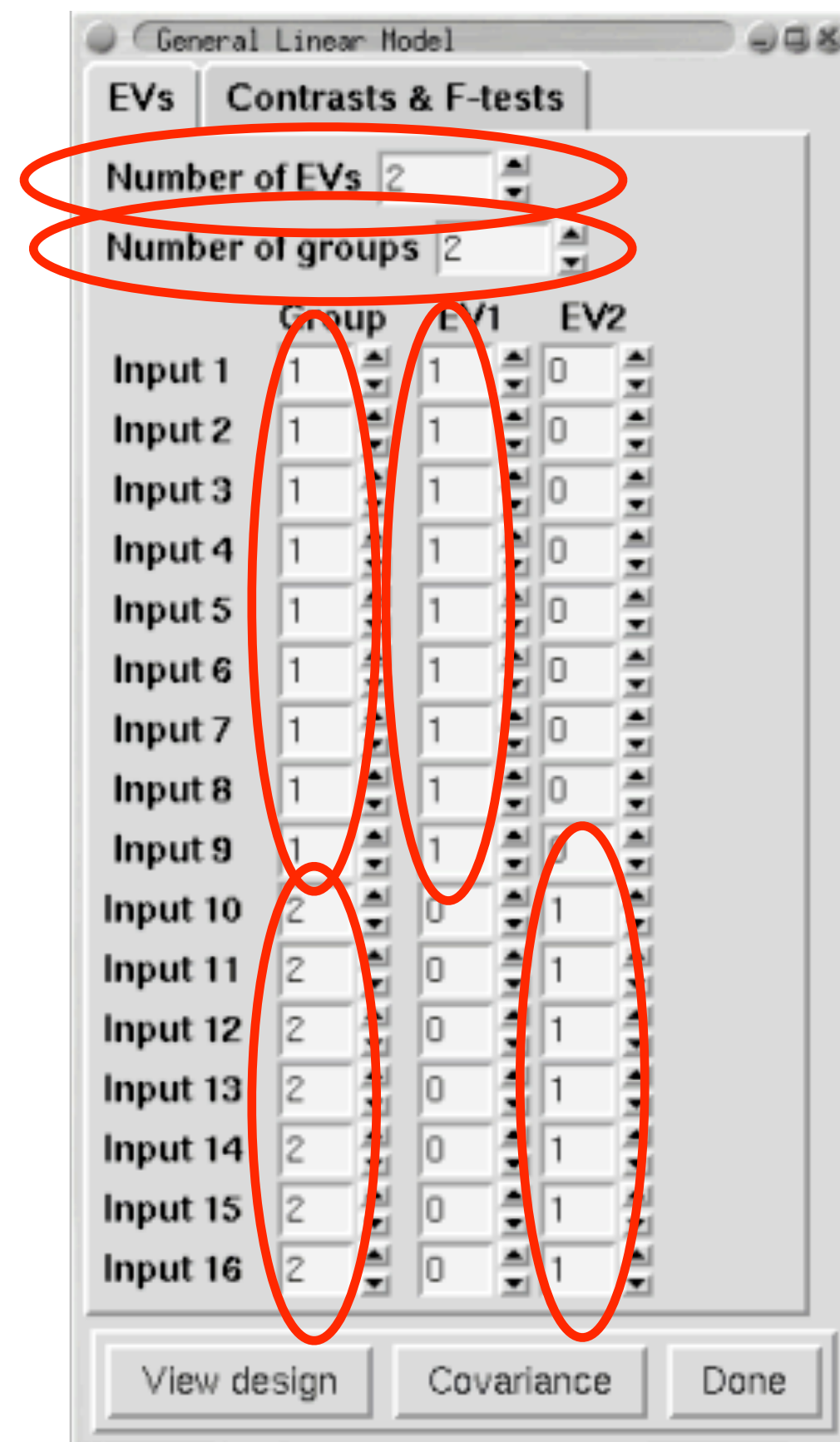
Is there a significant group difference?

- estimate means
- estimate std-errors (FE or ME)
- test significance of difference in means



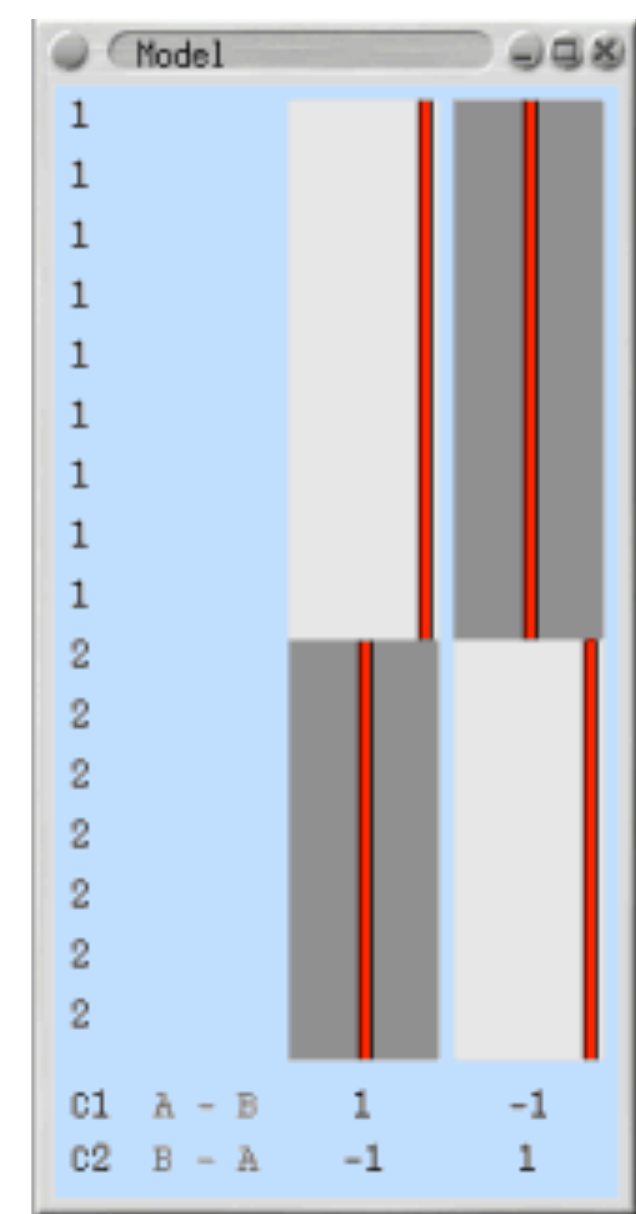
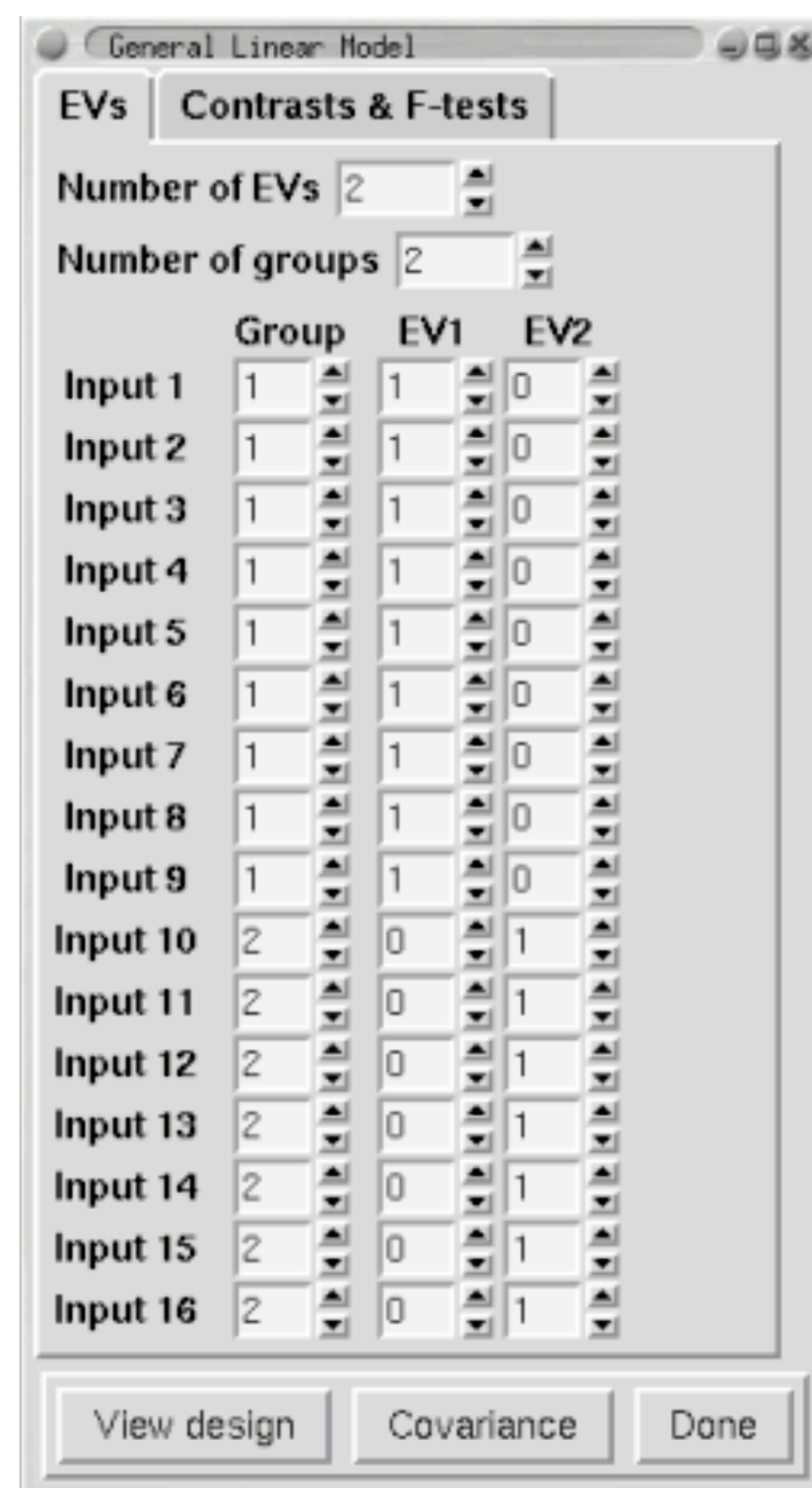
Unpaired Two-Group Difference

Is there a significant group difference?



Unpaired Two-Group Difference

Is there a significant group difference?

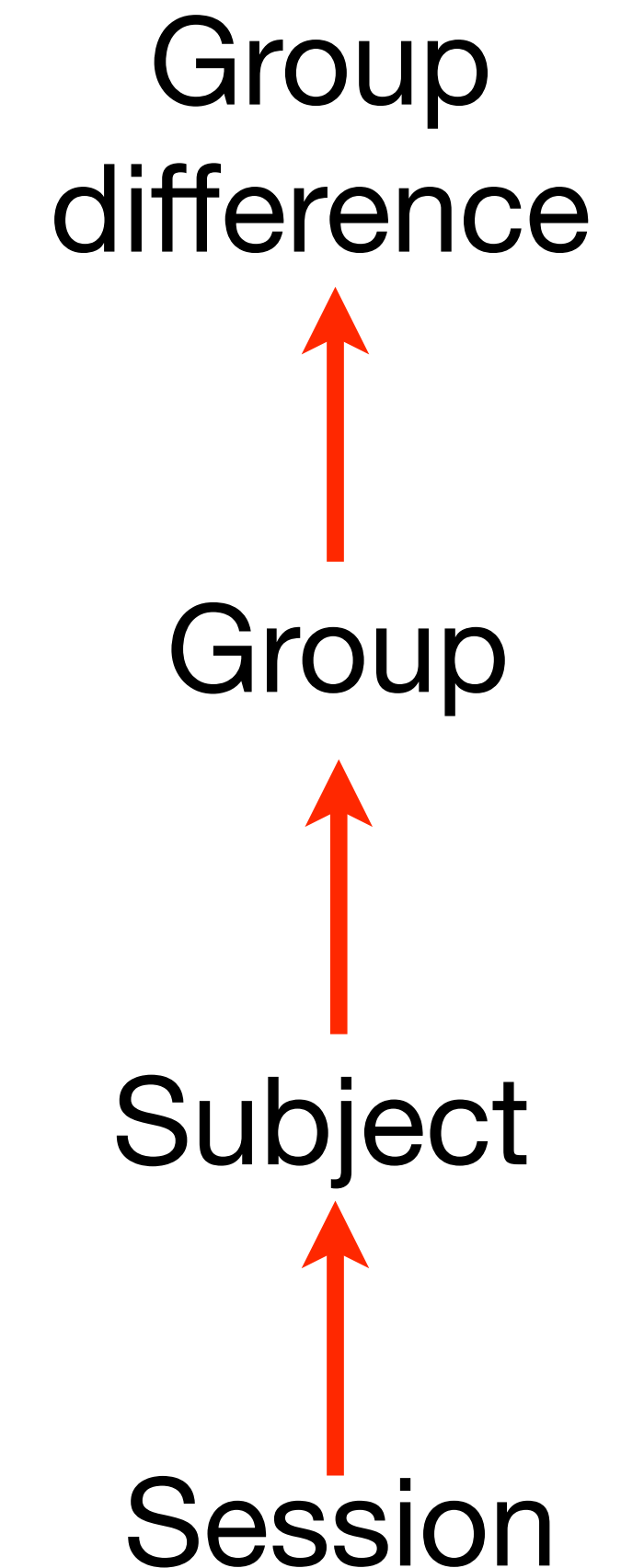




FLAME

FMRIB's Local Analysis of Mixed Effects

- Fully Bayesian framework
 - Input COPEs, VARCOPEs & DOFs from lower-level
 - estimate COPEs, VARCOPEs & DOFs at current level
 - pass these up
- Infer and threshold at top level (Z-stat)
- Equivalent to All-in-One approach





FLAME Inference

- Default is:
 - FLAME1: fast approximation for all voxels
- Optional slower, slightly more accurate approach:
 - FLAME1+2:
 - FLAME1 for all voxels, FLAME2 for voxels close to threshold
 - FLAME2: MCMC sampling technique



Choosing Inference Approach

1. Fixed Effects

Use for intermediate/top levels

2. Mixed Effects - OLS

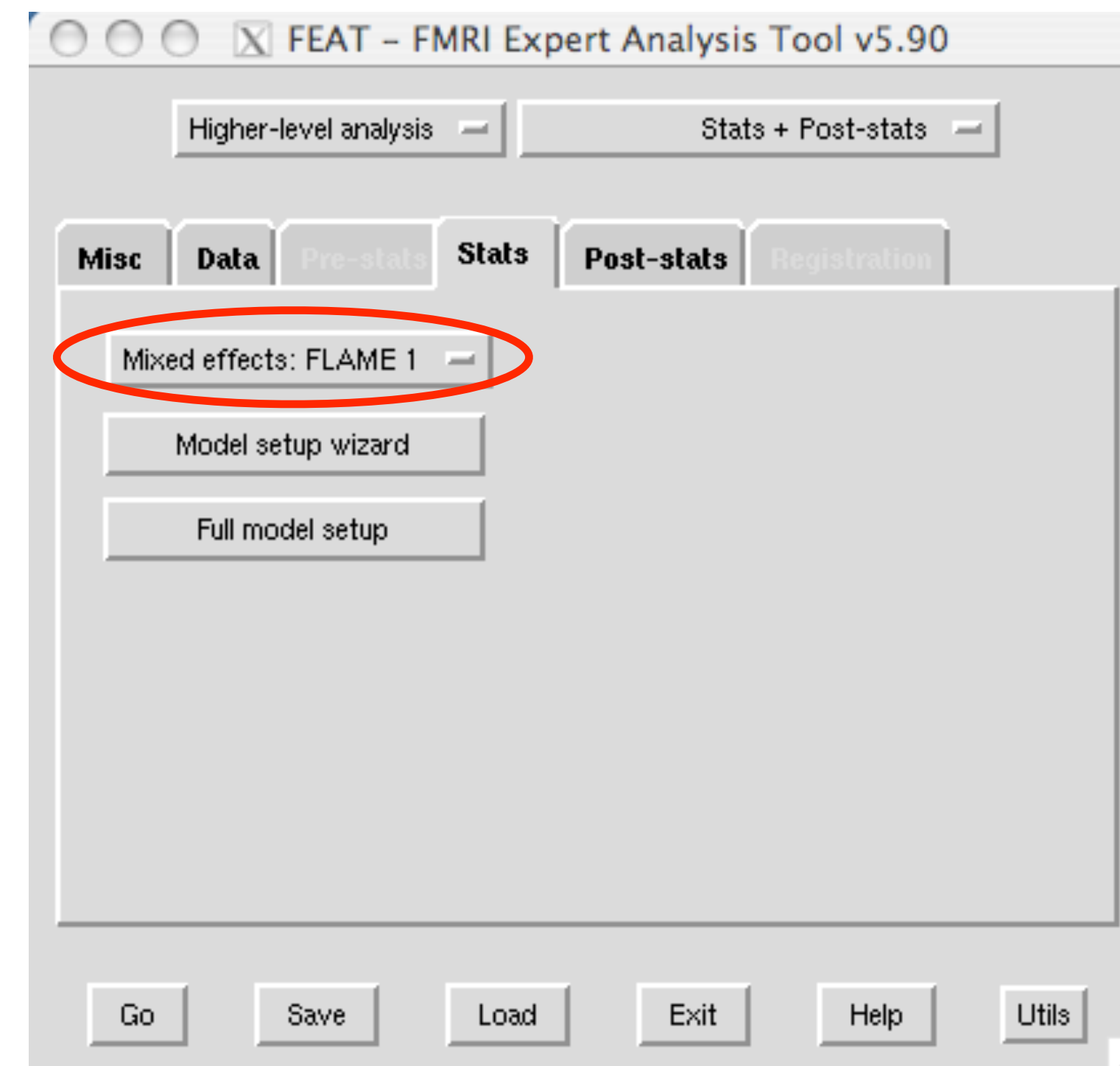
Use at top level: quick and less accurate

3. Mixed Effects - FLAME 1

Use at top level: less quick but more accurate

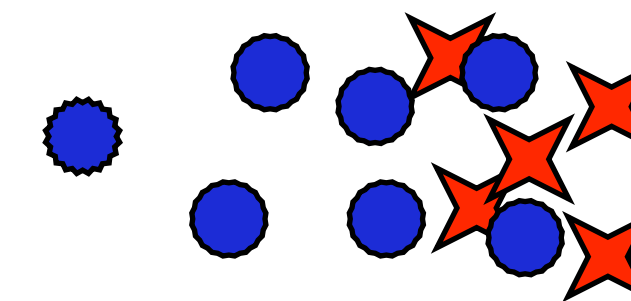
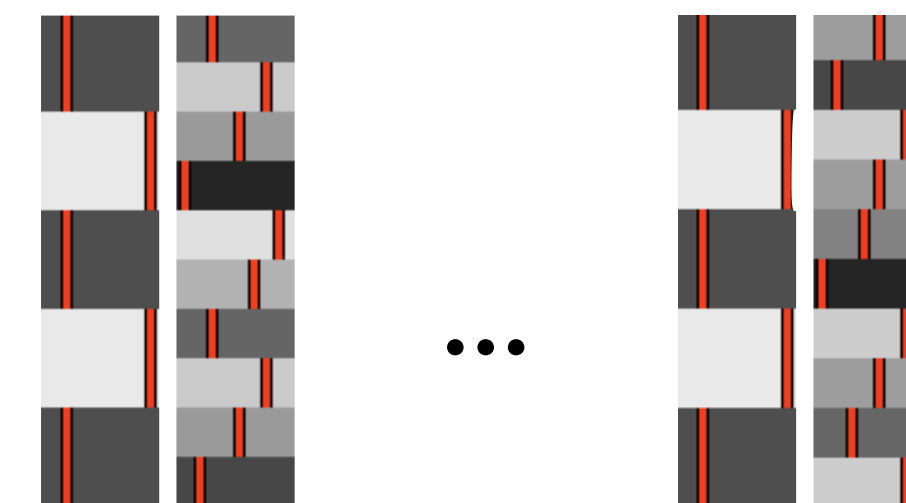
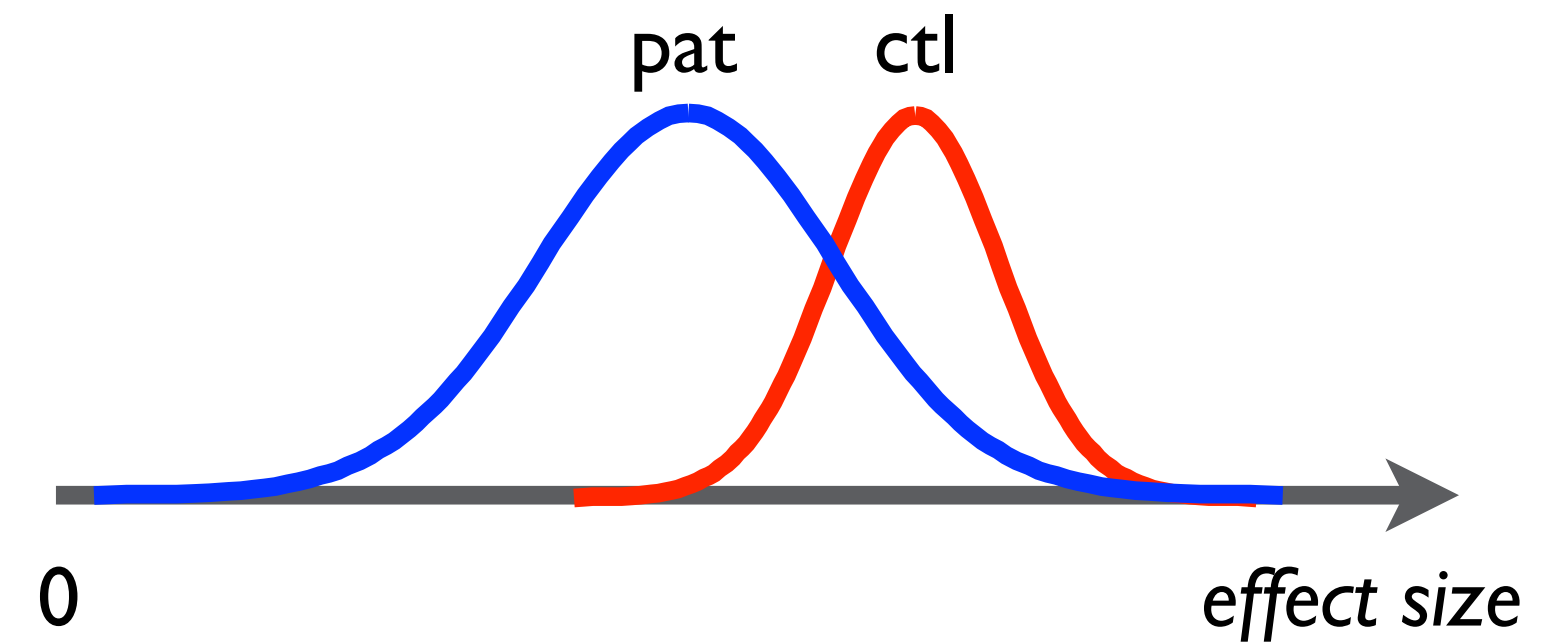
4. Mixed Effects - FLAME 1+2

Use at top level: slow but even more accurate



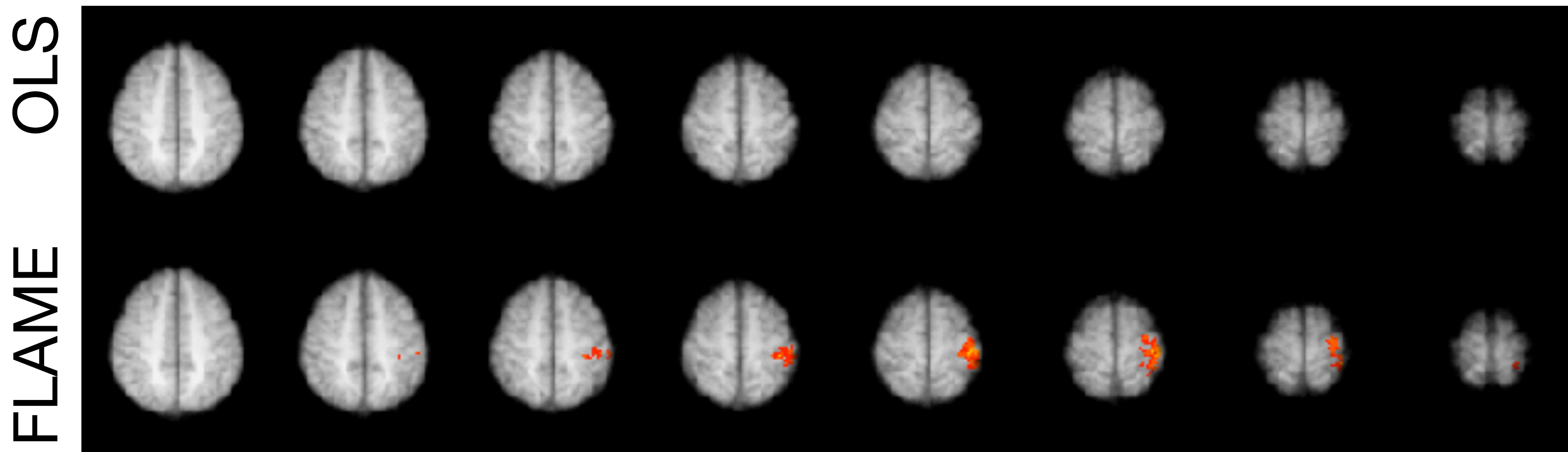
FLAME vs. OLS

- allow different within-level variances (e.g. patients vs. controls)
- allow non-balanced designs (e.g. containing behavioral scores)
- allow un-equal group sizes



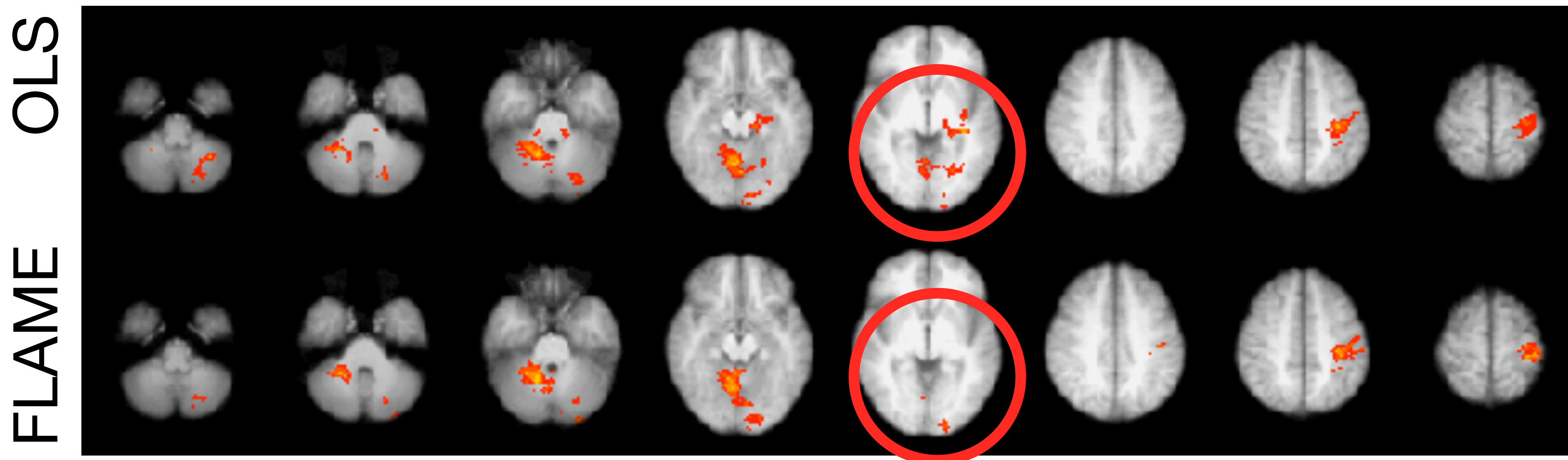
FLAME vs. OLS

- Two ways in which FLAME can give different Z-stats compared to OLS:
 - *higher Z* due to increased efficiency from using lower-level variance heterogeneity

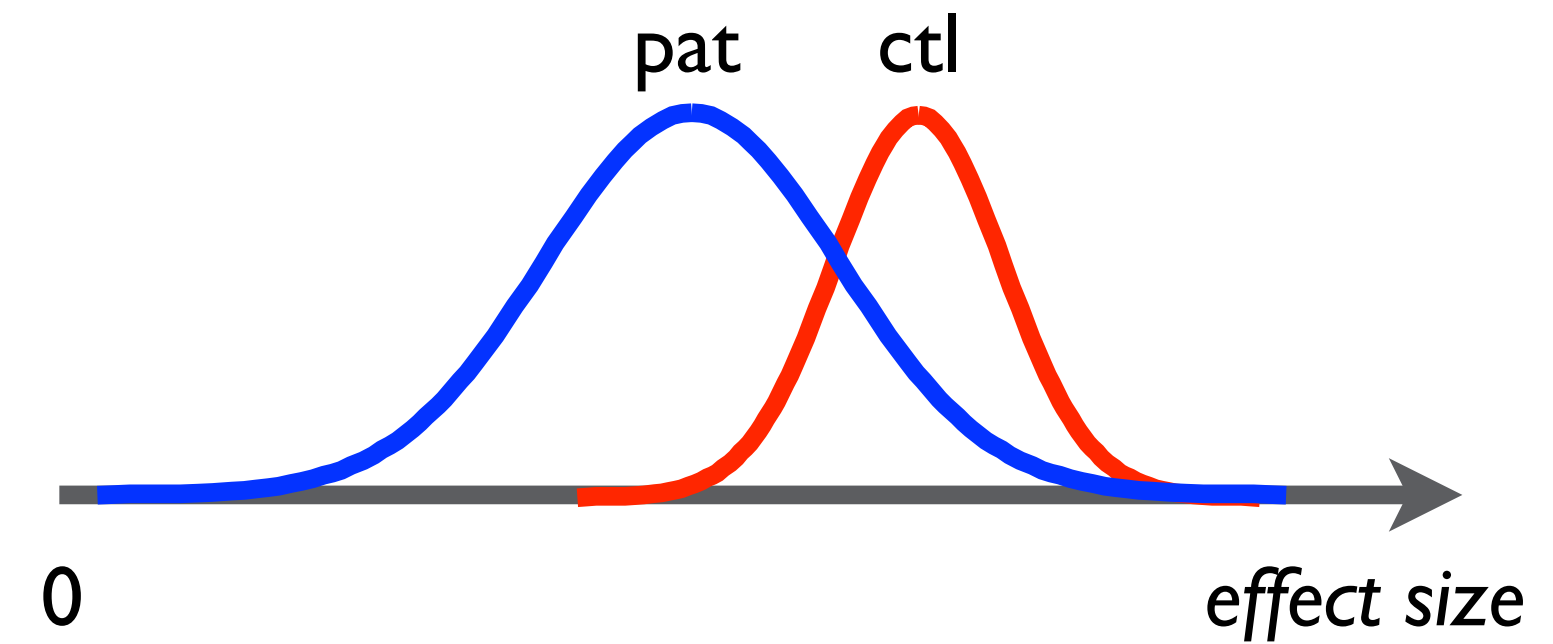


FLAME vs. OLS

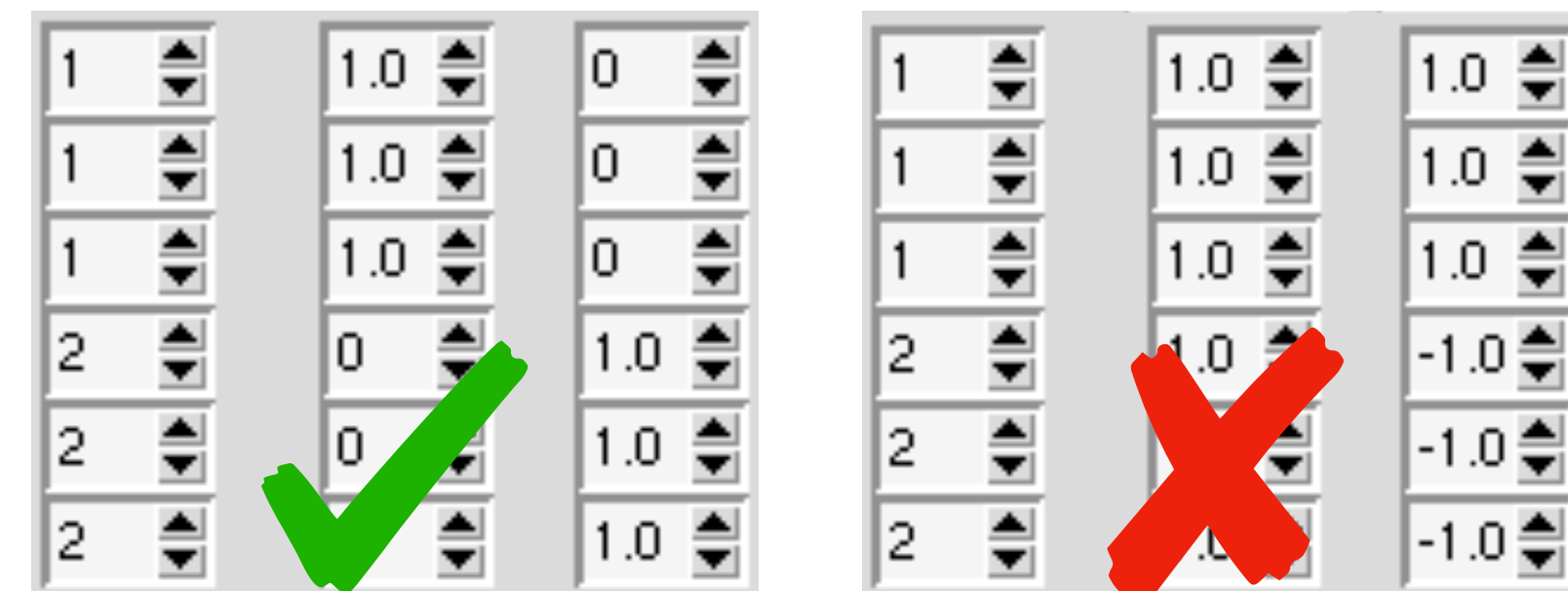
- Two ways in which FLAME can give different Z-stats compared to OLS:
 - *Lower Z* due to higher-level variance being constrained to be positive (i.e. solve the implied negative variance problem)



Multiple Group Variances



- can deal with multiple group variances
- separate variance will be estimated for each variance group (be aware of #observations for each estimate, though!)
- EVs can only have non-zero values for a single group



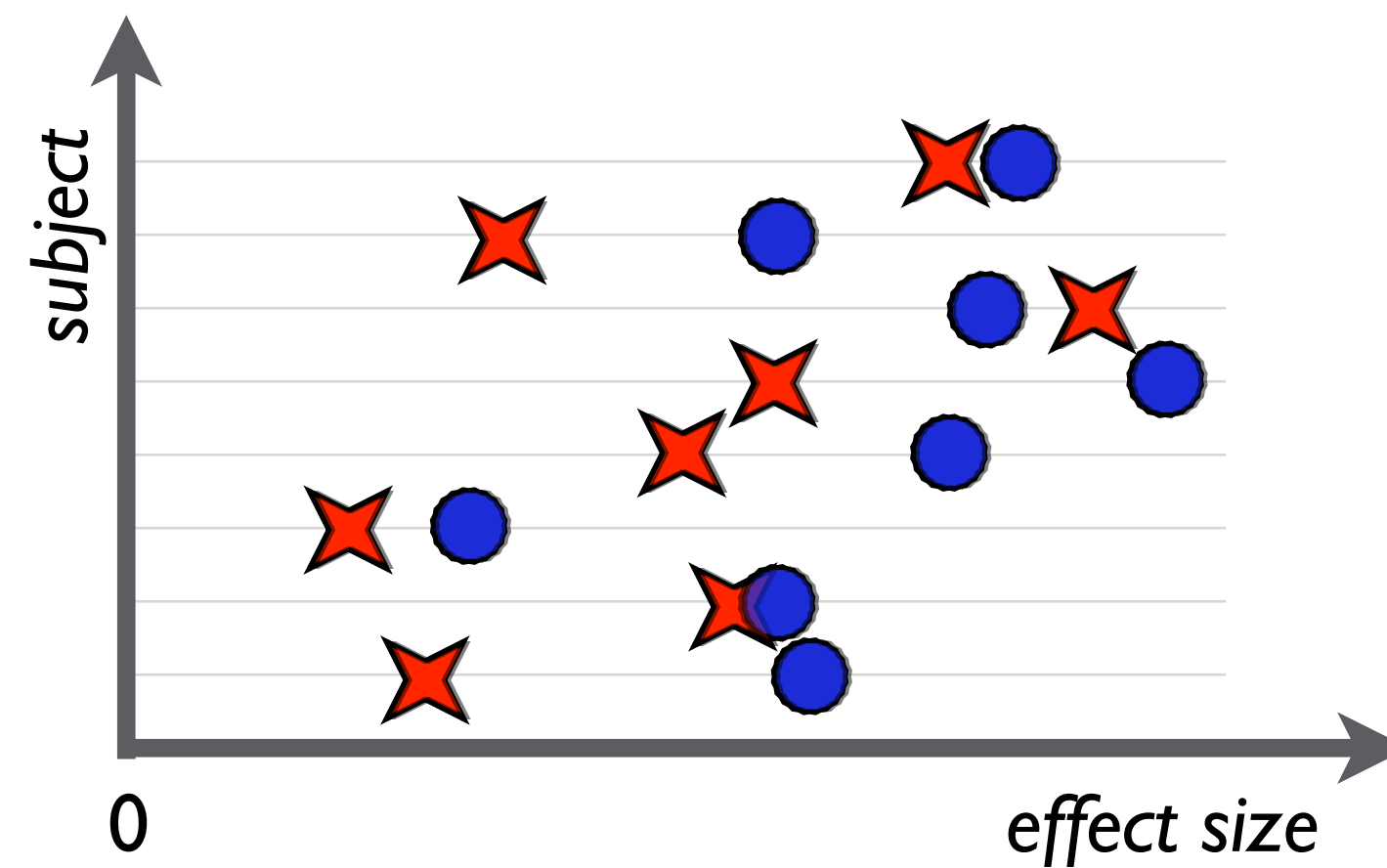


Paired T-test

Paired T-Test

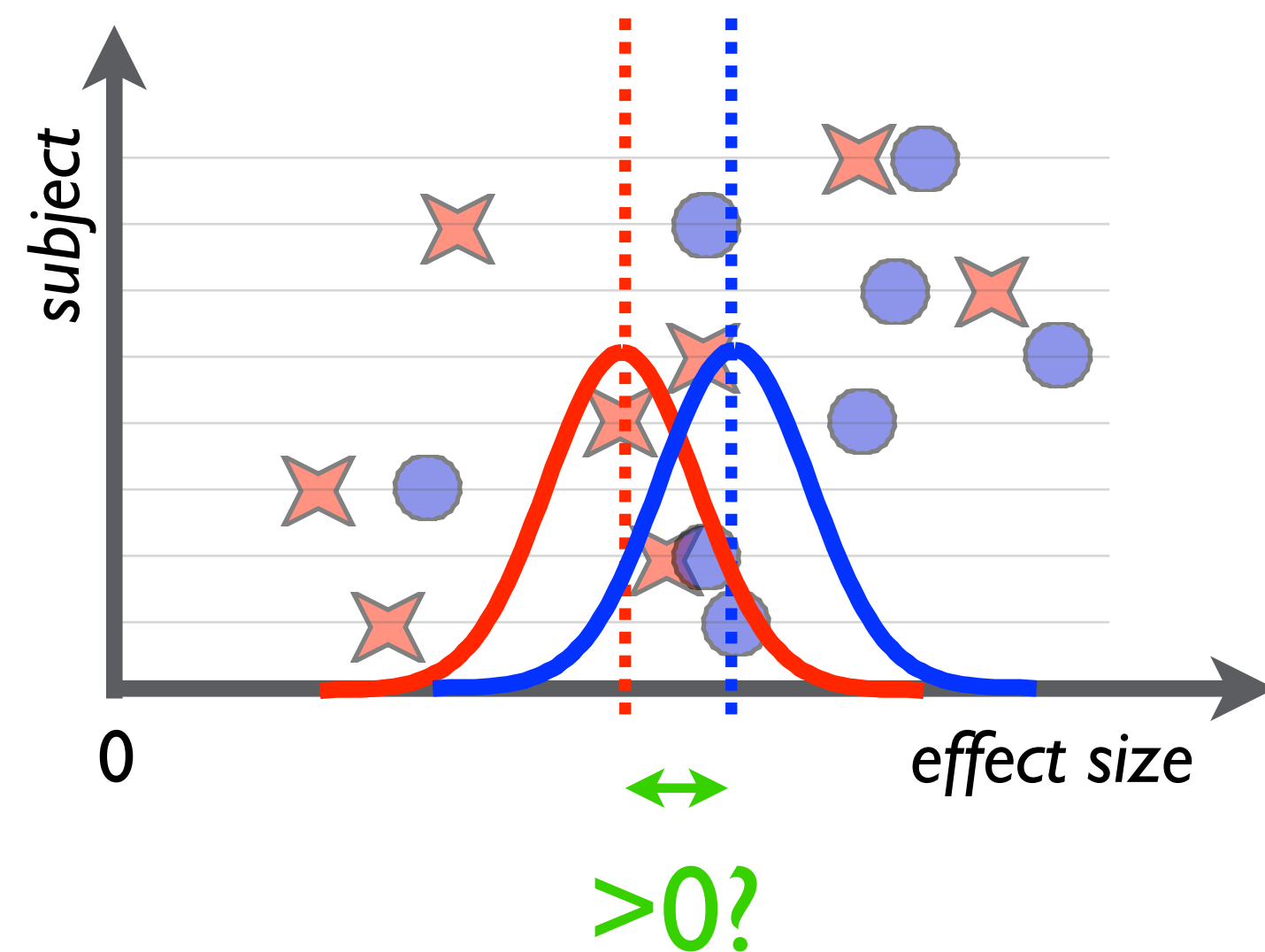
- 8 subjects scanned under 2 conditions (A,B)

Is there a significant difference between conditions?



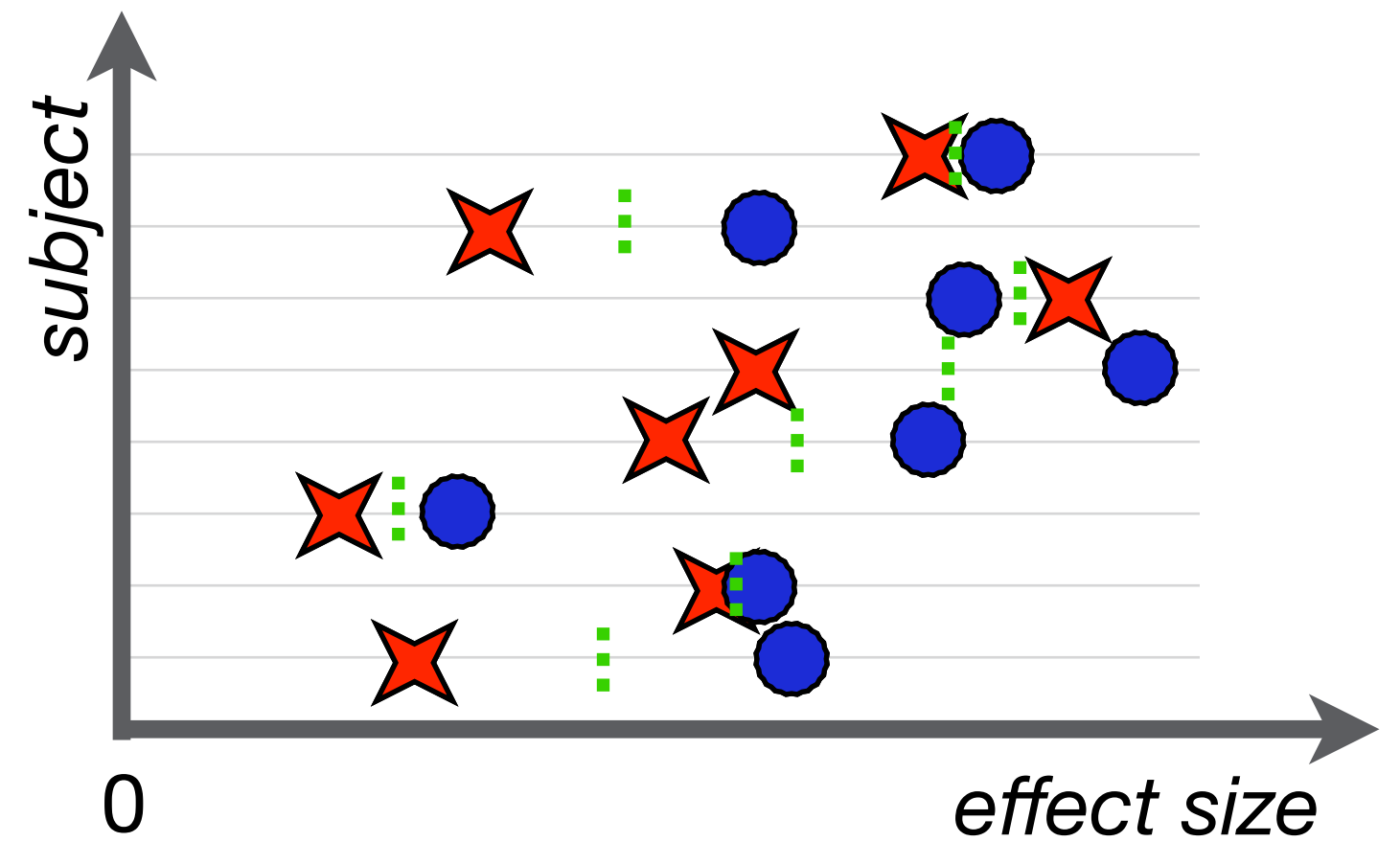
Paired T-Test

First, let's try an unpaired T-test

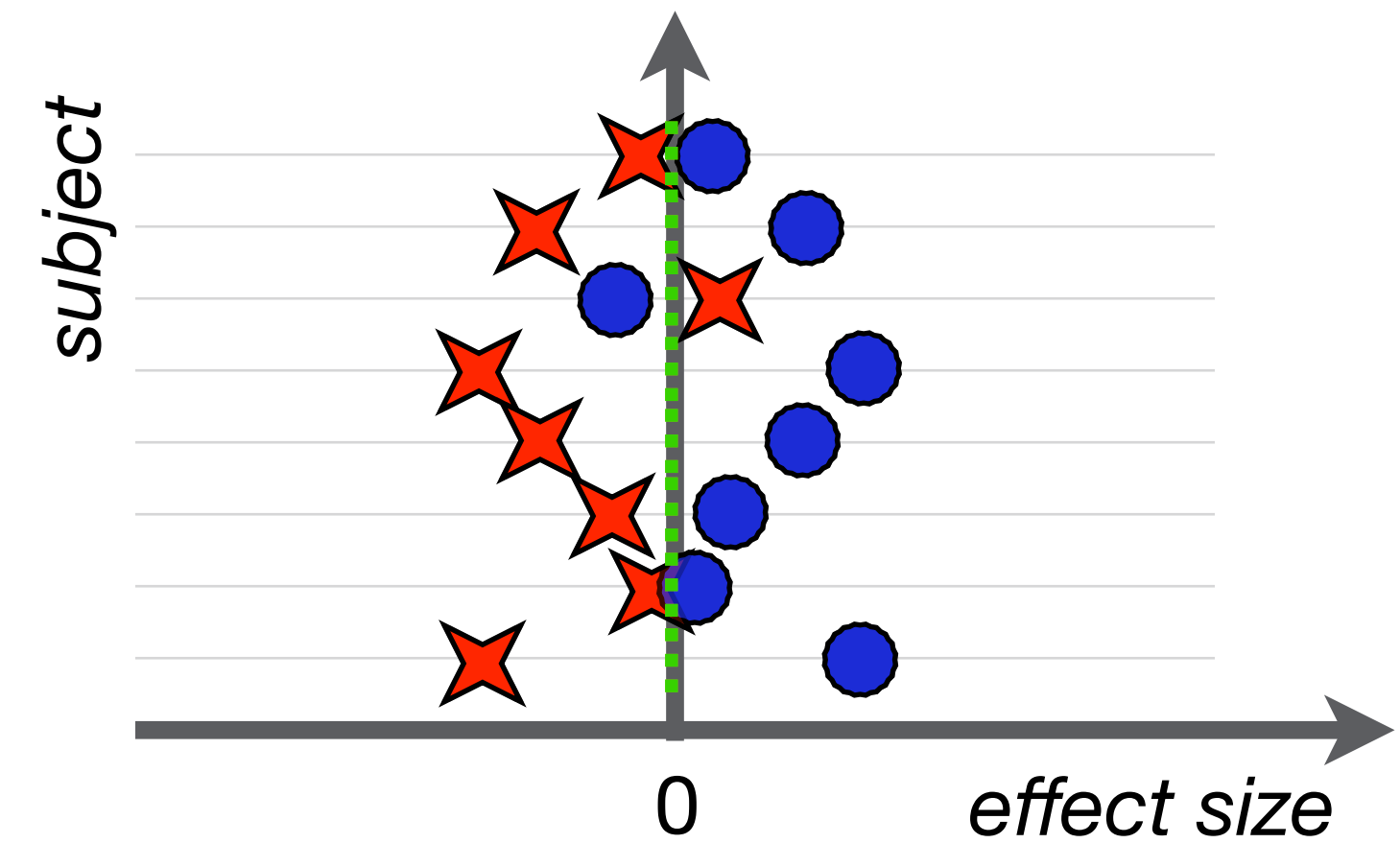


Paired T-Test

data



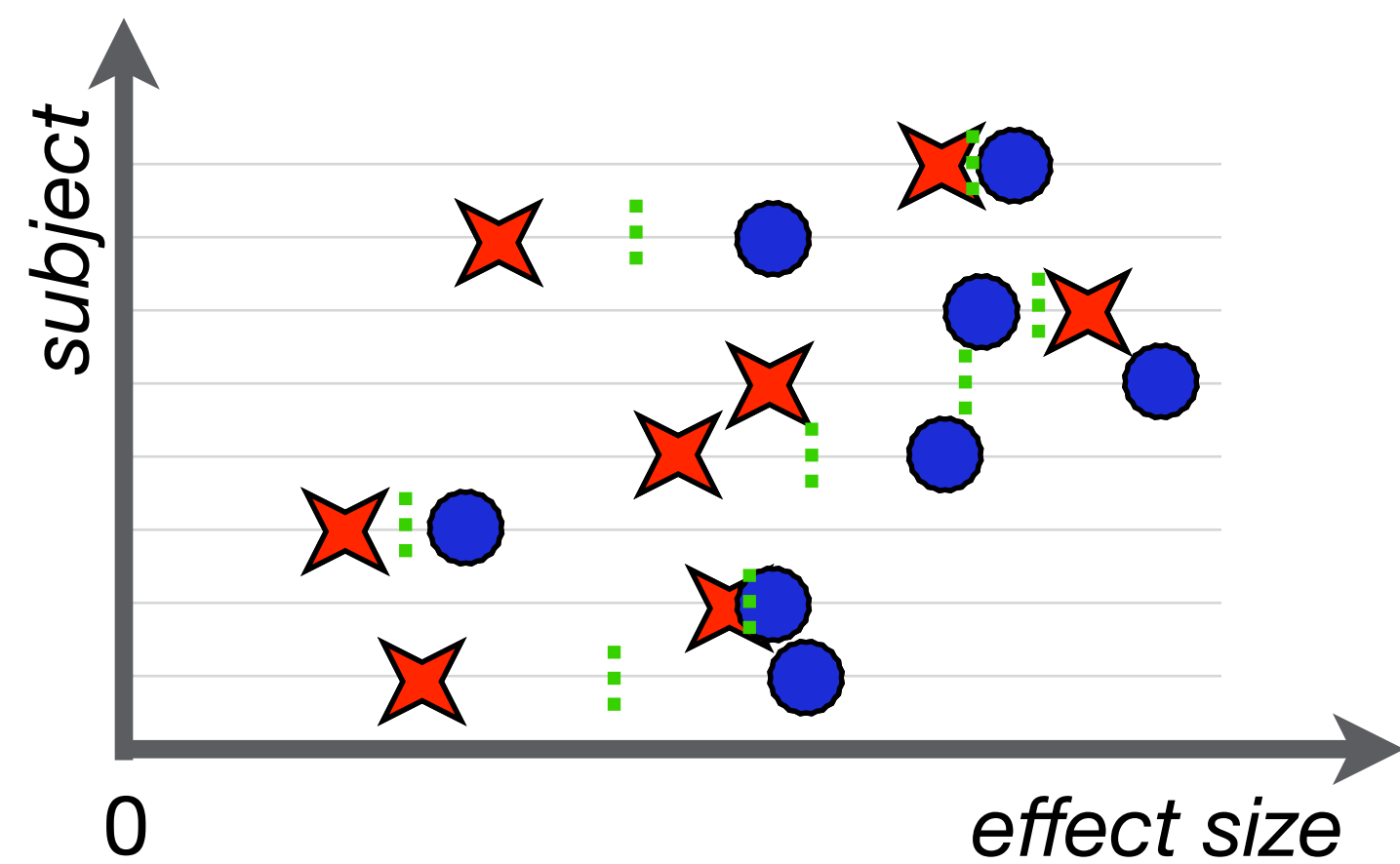
de-meaned data



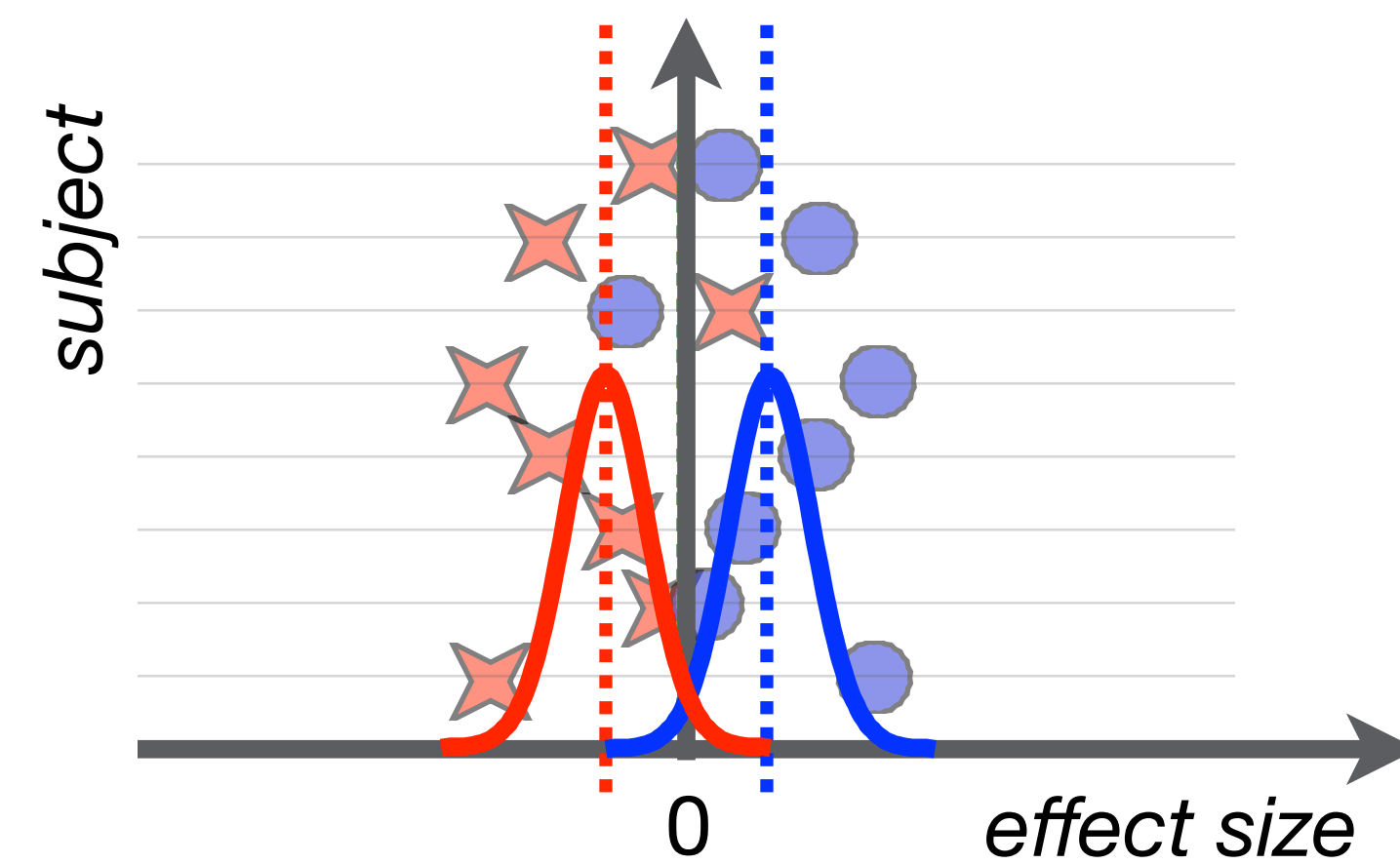
subject mean
accounts for large prop.
of the overall variance

Paired T-Test

data



de-meaned data



subject mean
accounts for large prop.
of the overall variance

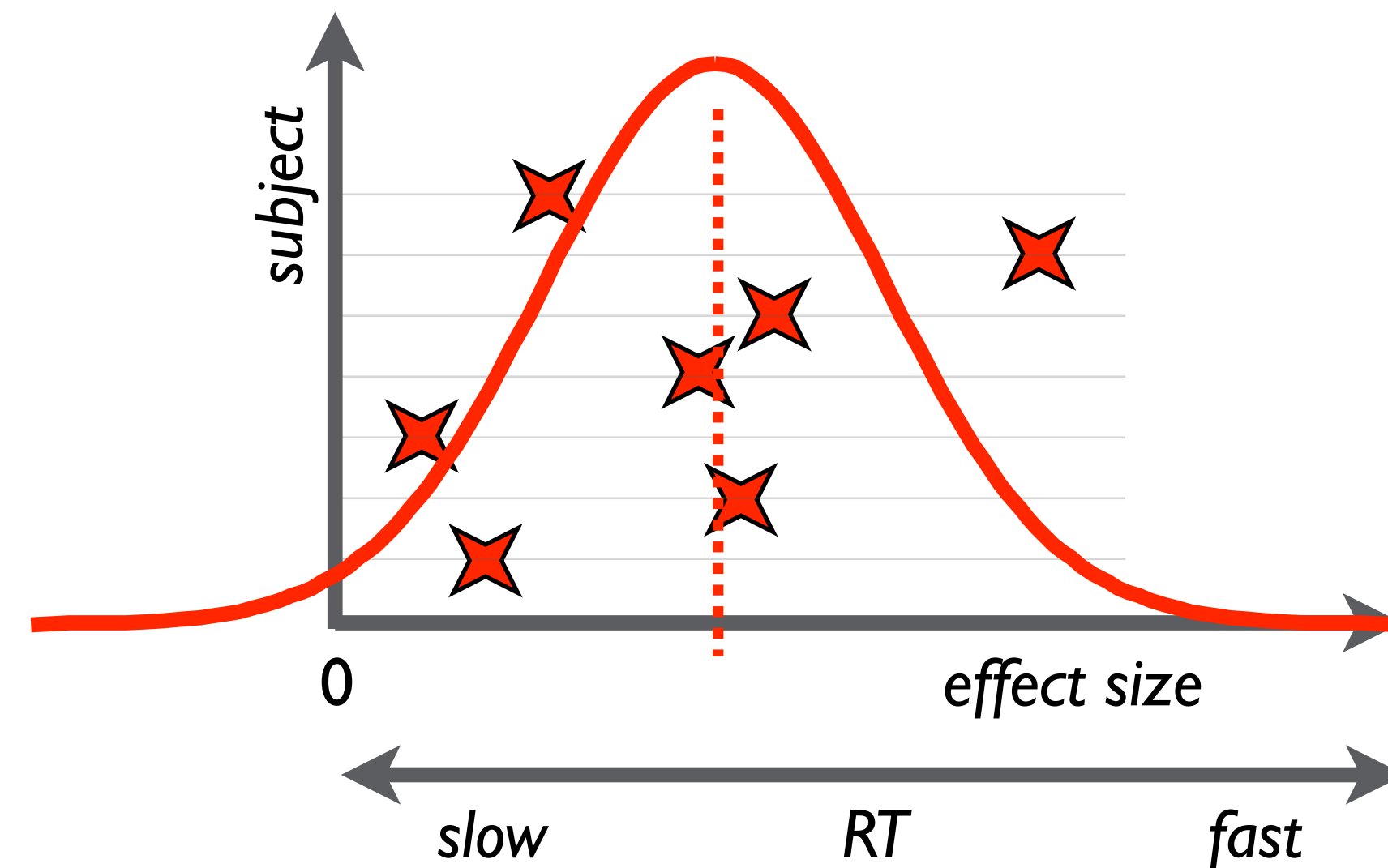
>0?



Group average with covariate

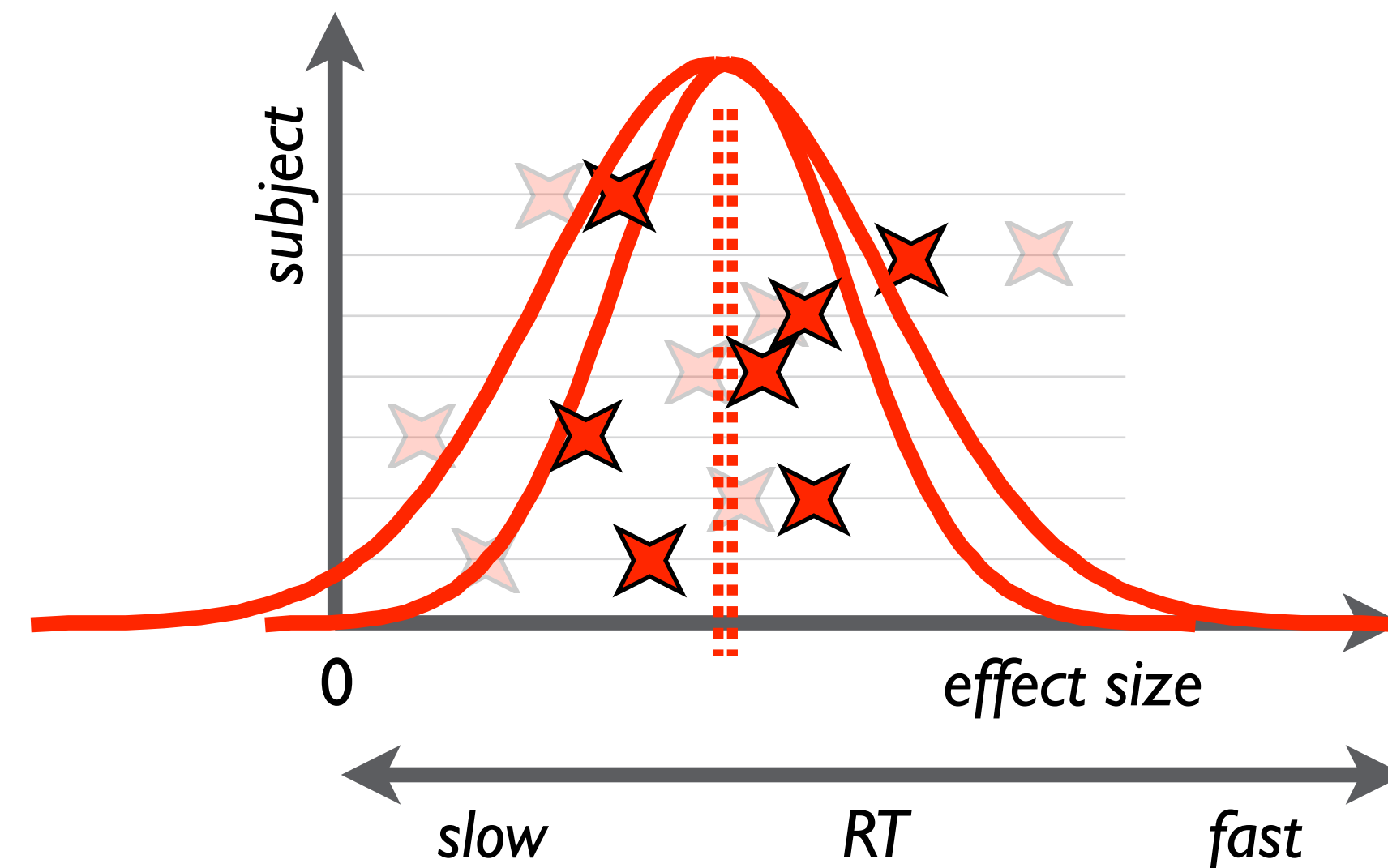
Group average with covariate

- Additional measurements (e.g. age; disability score; behavioral measures like reaction times)
- use covariates to 'explain' variation



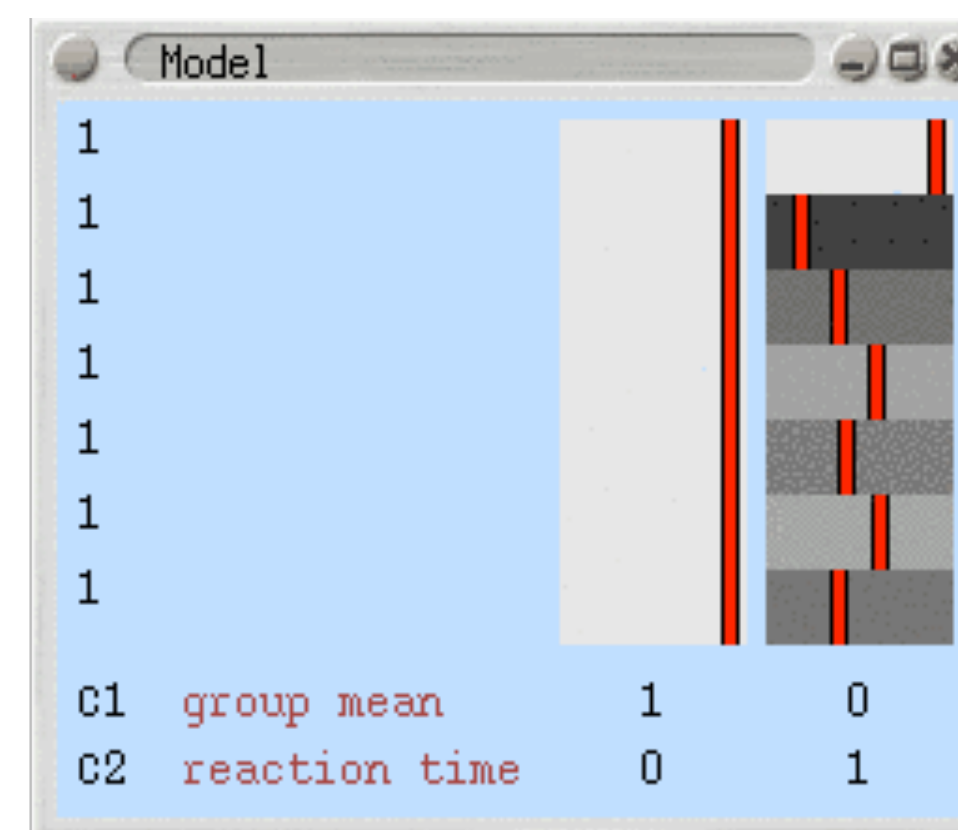
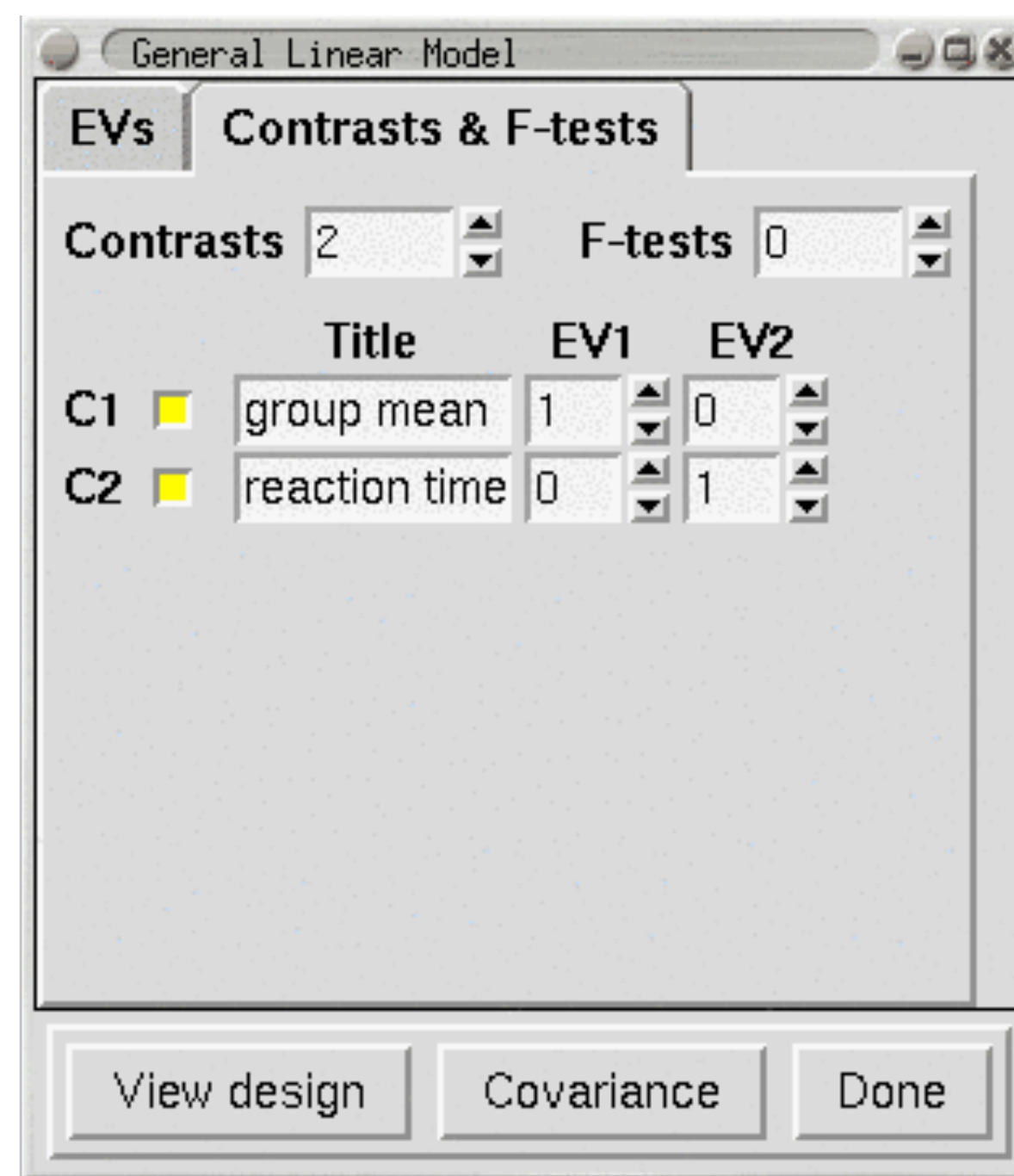
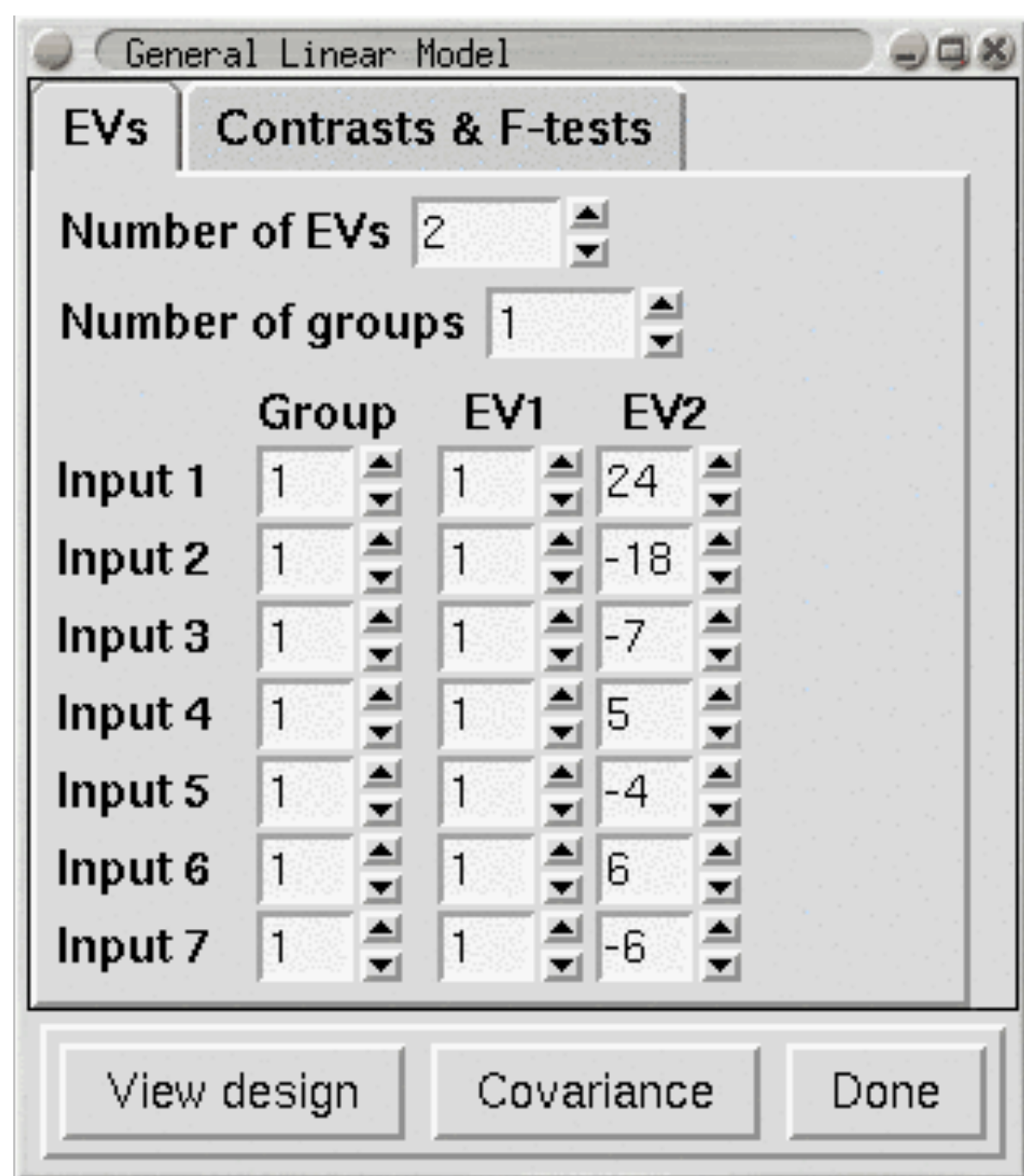
Group average with covariate

- Additional measurements (e.g. age; disability score; behavioral measures like reaction times)
- use covariates to 'explain' variation



Group average with covariate

Need to demean covariates



Break Time!

