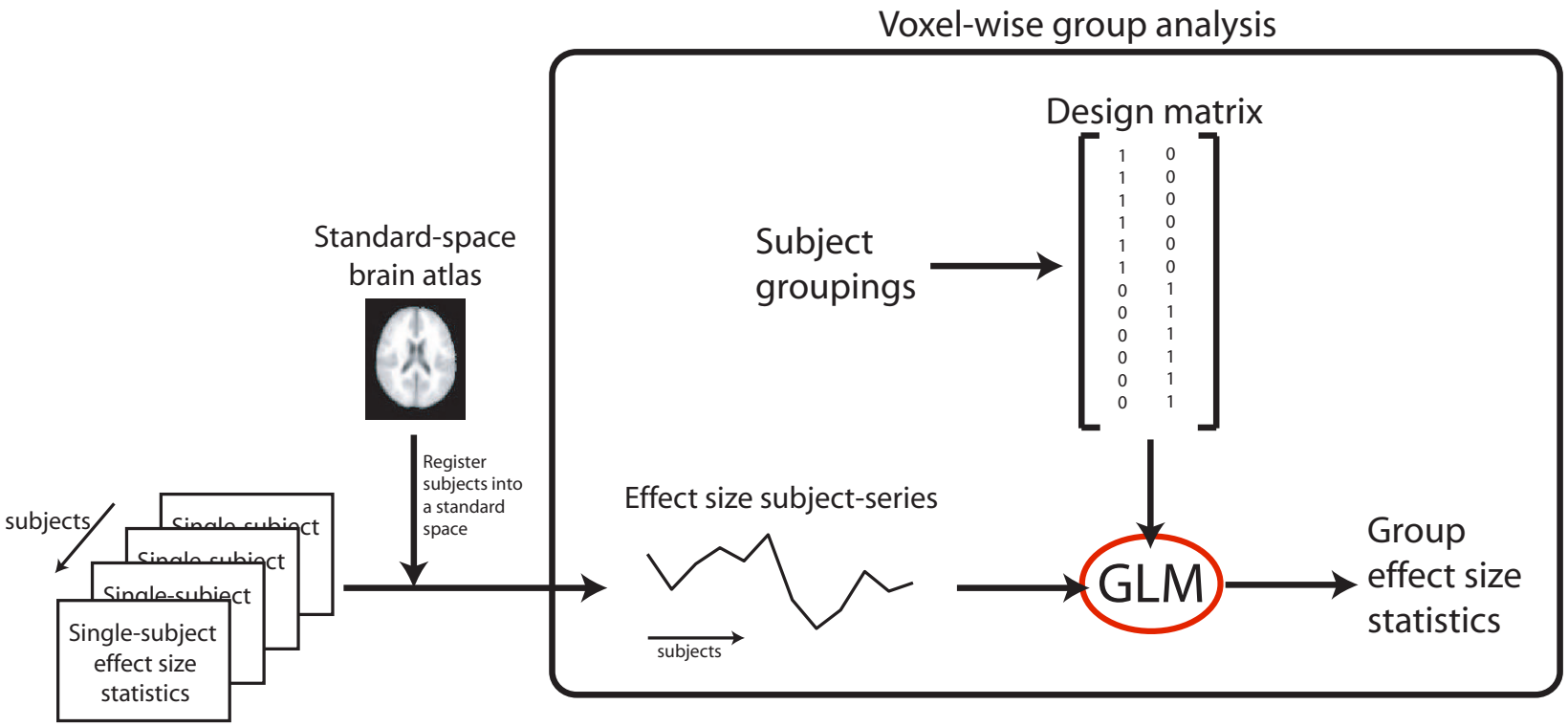
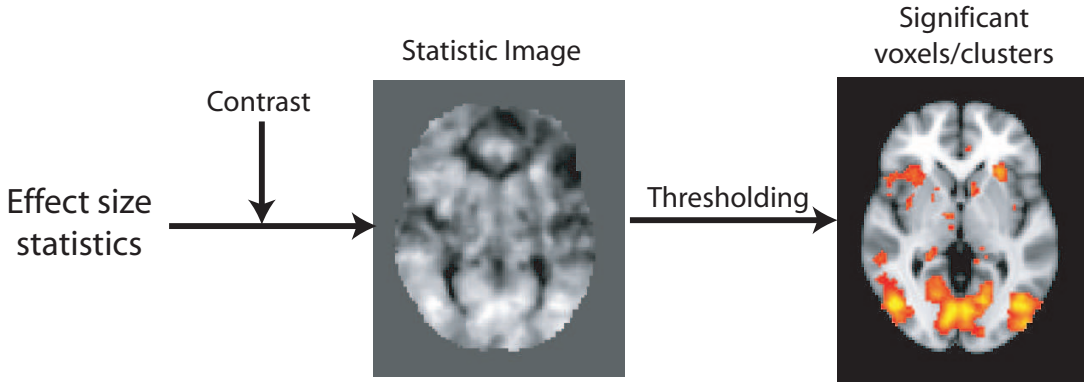
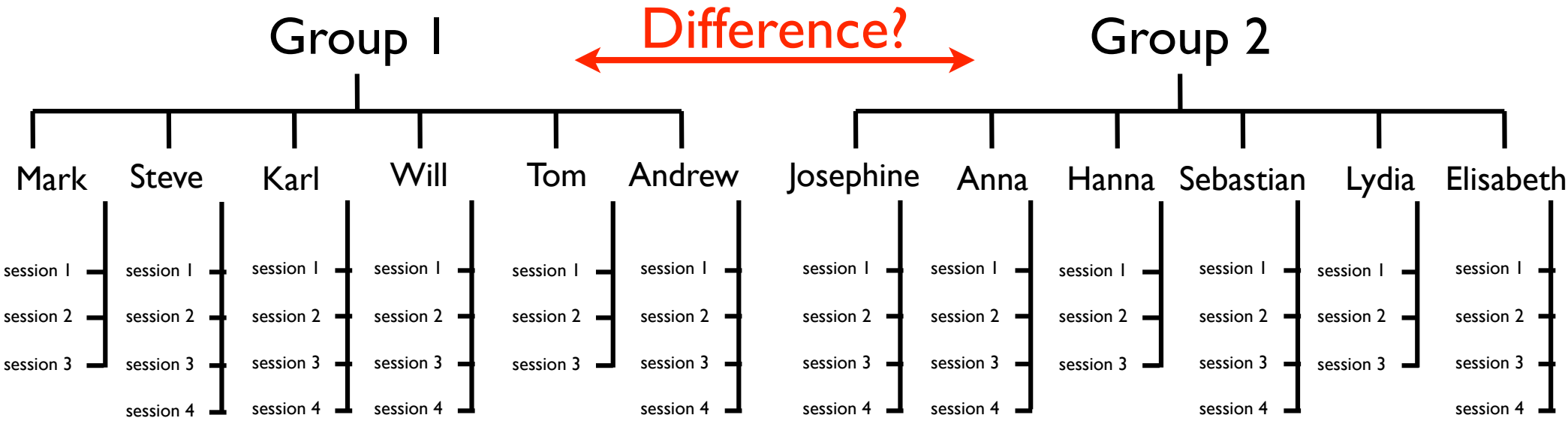
FMRI Group Analysis





Multi-Level FMRI analysis

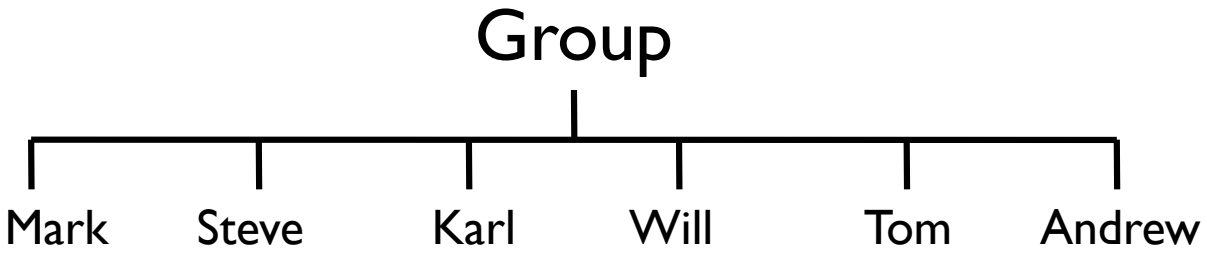
- uses GLM at both lower and higher levels
- typically need to infer across multiple subjects, sometimes multiple groups and/or multiple sessions



- questions of interest involve comparisons at the highest level

A simple example

Does the group activate on average?



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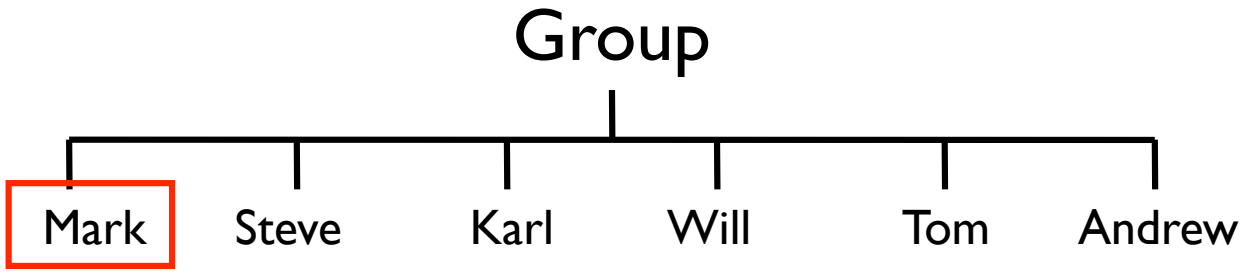

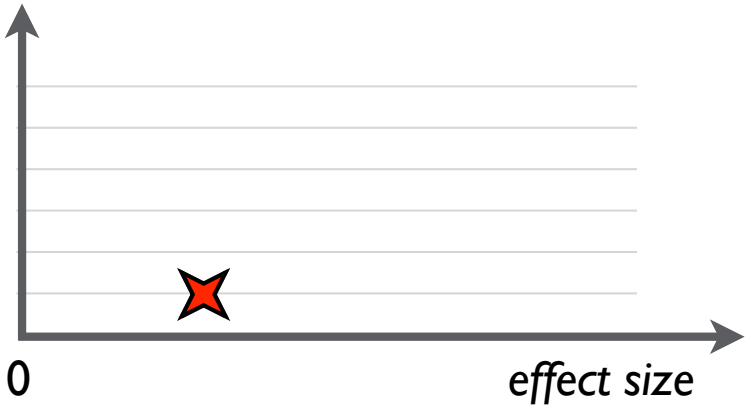

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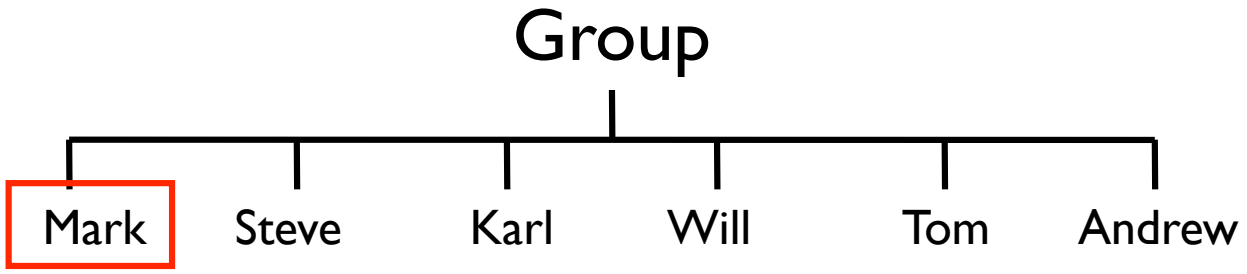
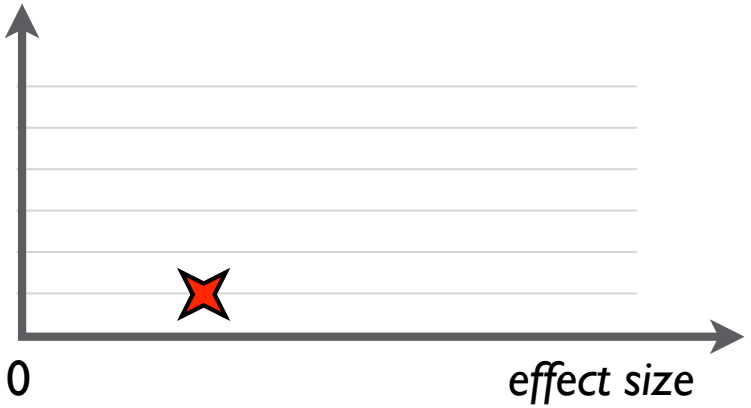


$$Y_k = X_k \beta_k + \epsilon_k$$

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



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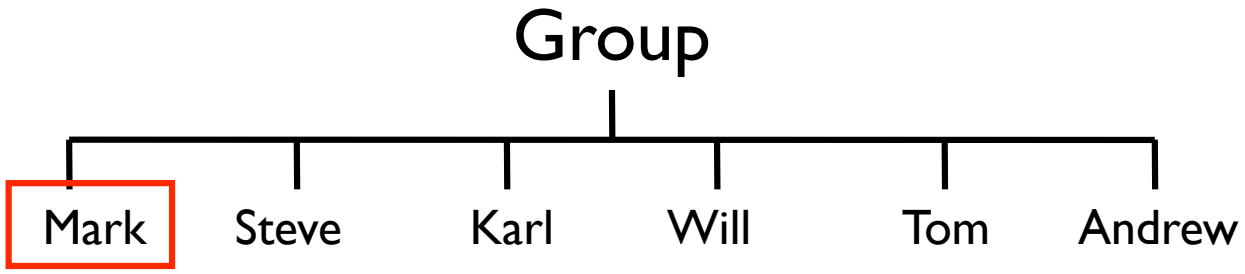

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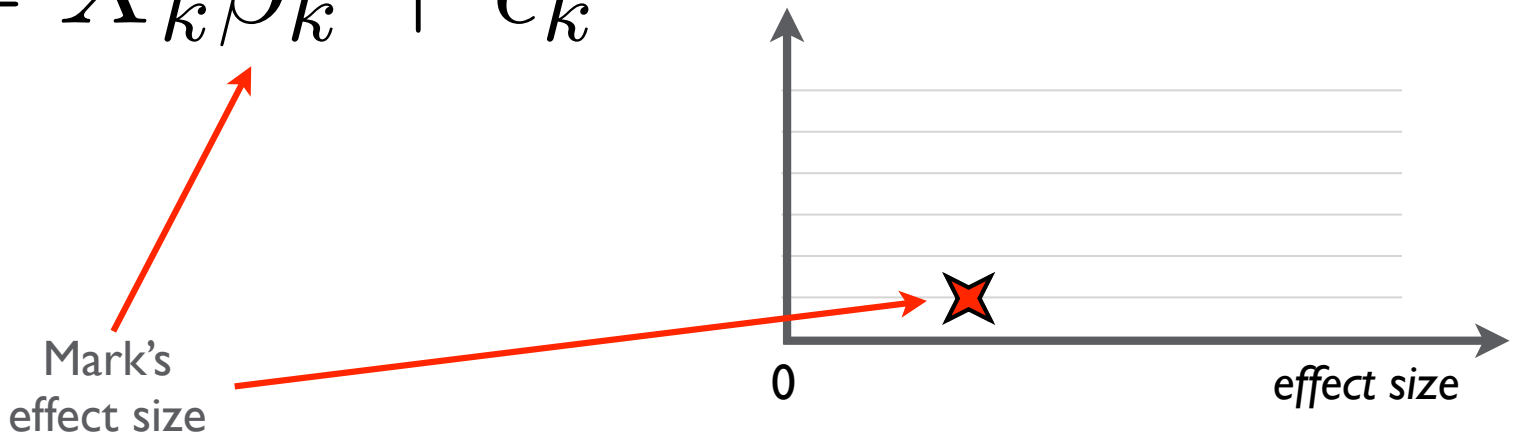

A simple example

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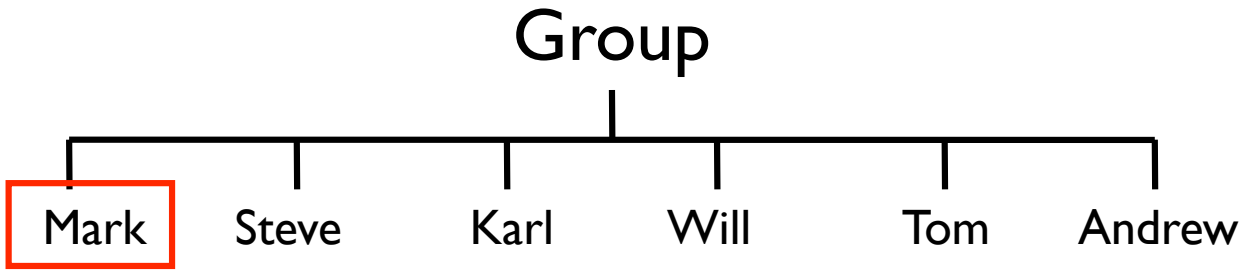

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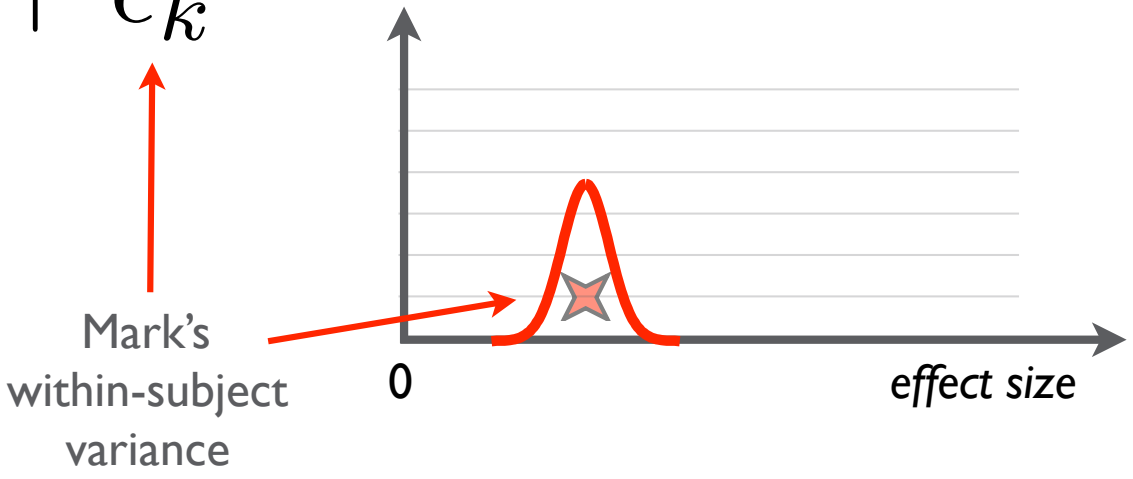

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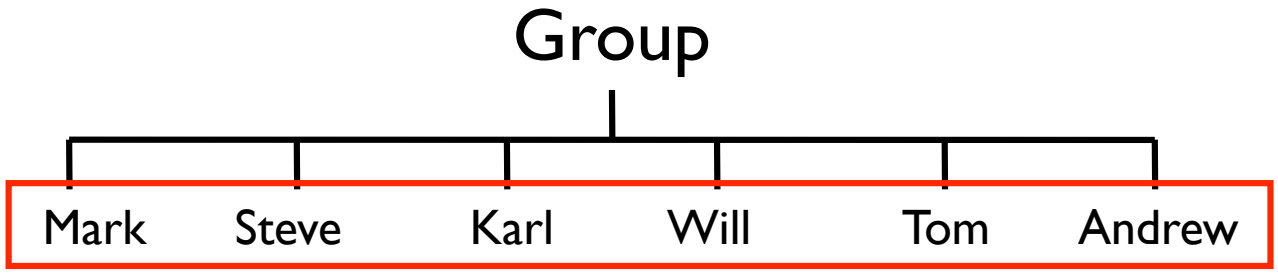
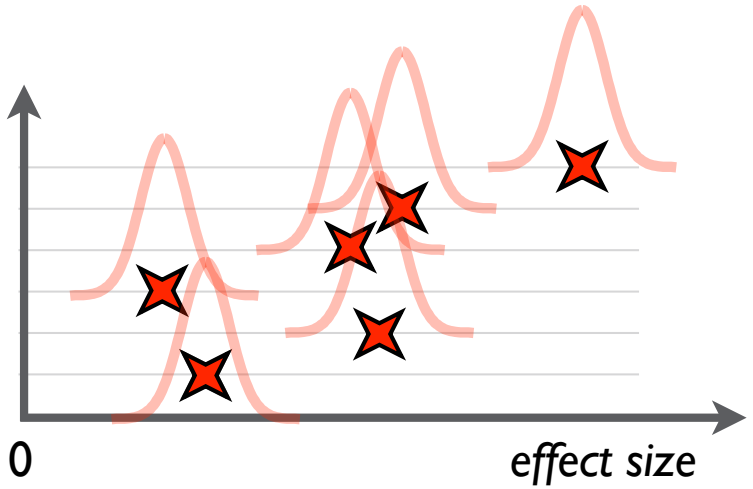


$$Y_K = X_K \beta_K + \epsilon_K$$

All first-level GLMs
on 6 FMRI data set



A simple example

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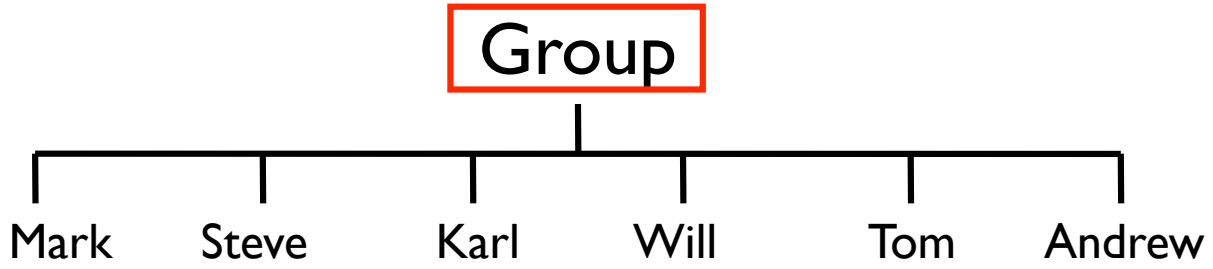
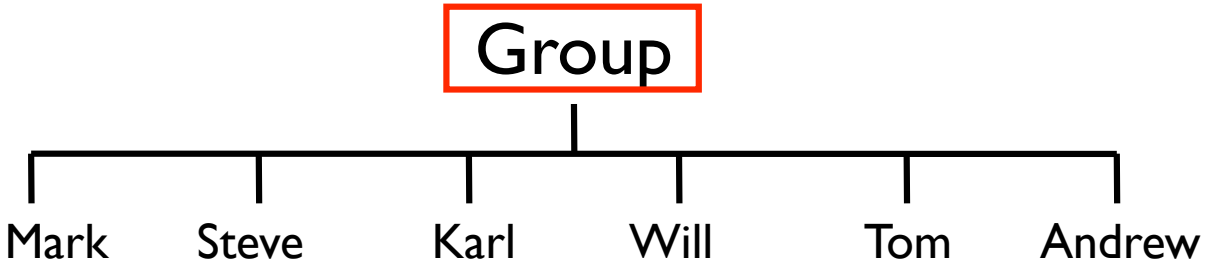


What group mean are we after? Is it:

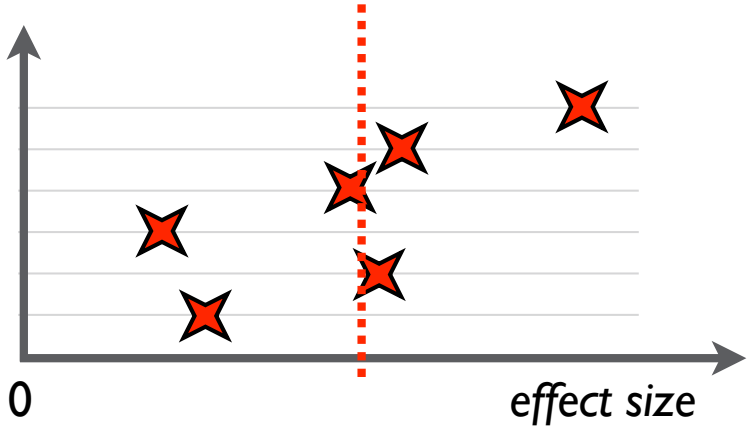
1. The group mean for those exact 6 subjects?
   Fixed-Effects (FE) Analysis
2. The group mean for the population from which these 6 subjects were drawn?
   Mixed-Effects (ME) analysis

Fixed-Effects Analysis

Do these exact 6 subjects activate on average?



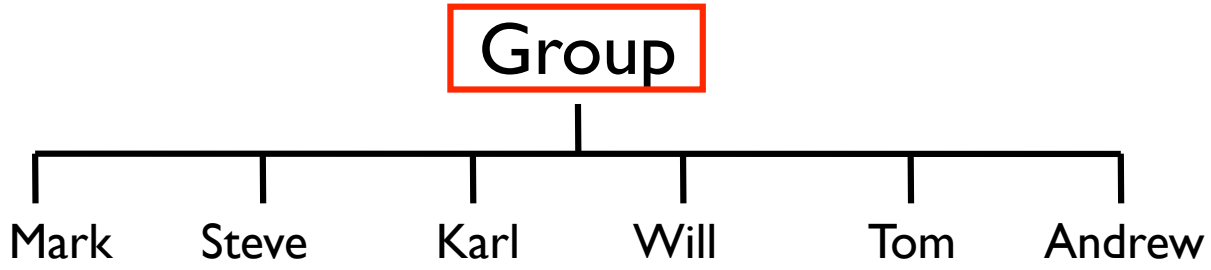
estimate group effect size as
straight-forward mean
across lower-level estimates



$$\beta_g = \frac{1}{6}\sum_{k=1}^{6}\beta_k$$

Fixed-Effects Analysis

Do these exact 6 subjects activate on average?

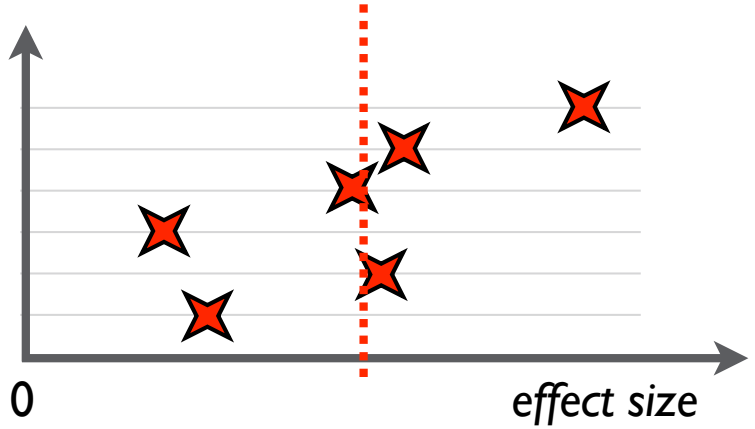


$$Y_K = X_K \beta_K + \epsilon_K$$

$$\beta_K = X_g \beta_g$$

$$X_g = \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \end{bmatrix}$$

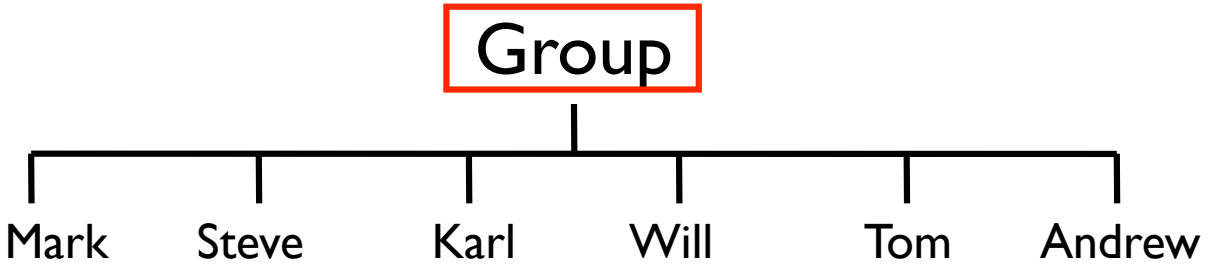
Group mean



$$\beta_g = \frac{1}{6} \sum_{k=1}^{6} \beta_k$$

Fixed-Effects Analysis

Do these exact 6 subjects activate on average?



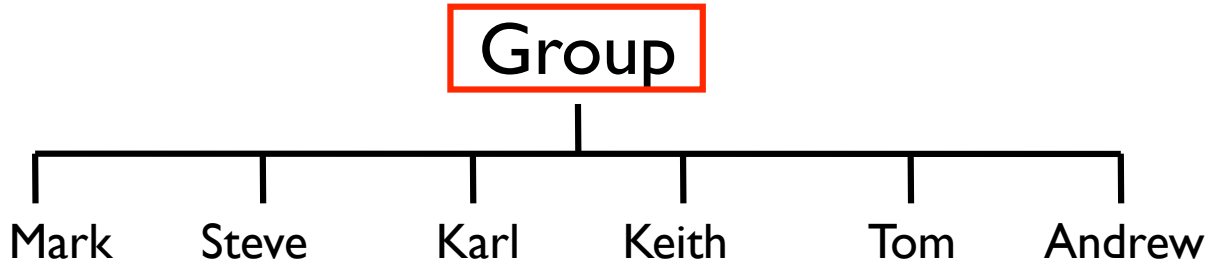
$$Y_K = X_K \beta_K + \epsilon_K$$
$$\beta_K = X_g \beta_g$$

Fixed Effects Analysis:

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

A simple example

Does the group activate on average?

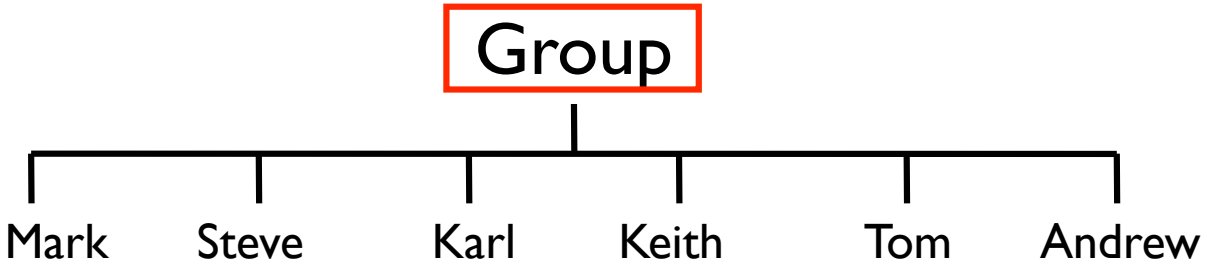


What group mean are we after? Is it:

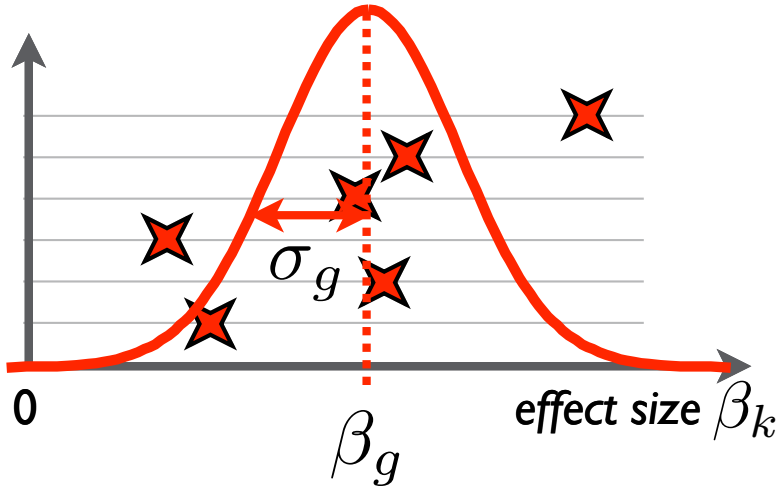
1. The group mean for those exact 6 subjects?
   Fixed-Effects (FE) Analysis
2. The group mean for the population from which these 6 subjects were drawn?
   Mixed-Effects (ME) analysis

Mixed-Effects Analysis

Does the population activate on average?



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

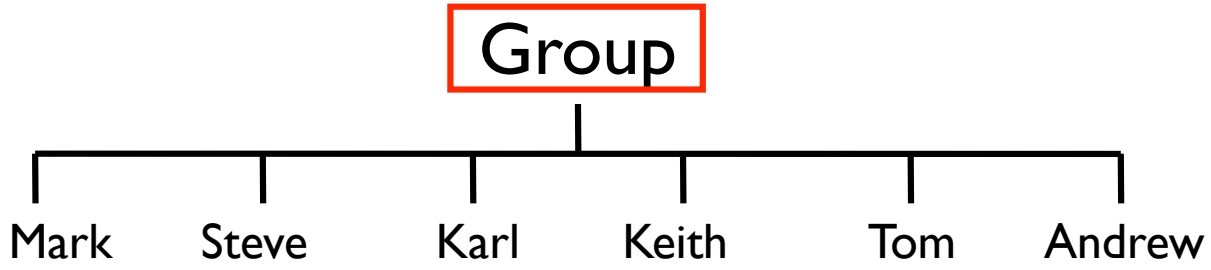


Consider the distribution over the population from which our 6 subjects were sampled:

σ_g^2 is the between-subject variance

Mixed-Effects Analysis

Does the population activate on average?



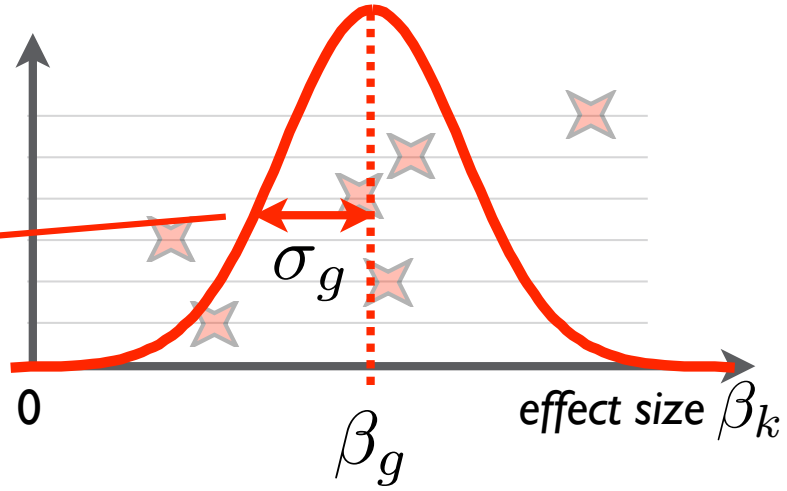
$$Y_K = X_K \beta_K + \epsilon_K$$

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

$$X_g = \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \end{bmatrix}$$

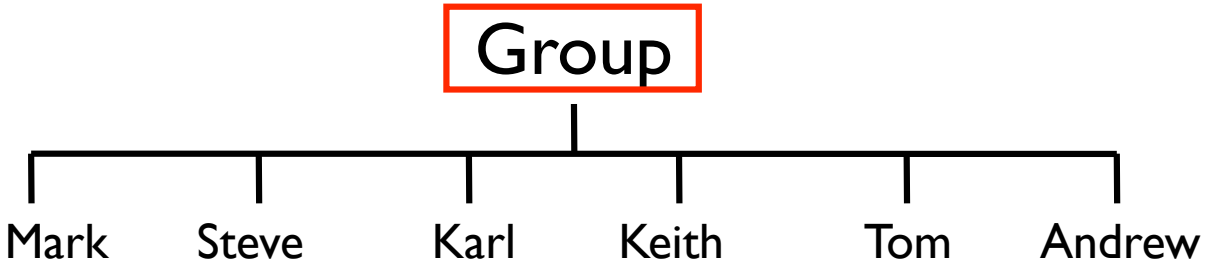
Population mean

between-subject variation



Mixed-Effects Analysis

Does the population activate on average?

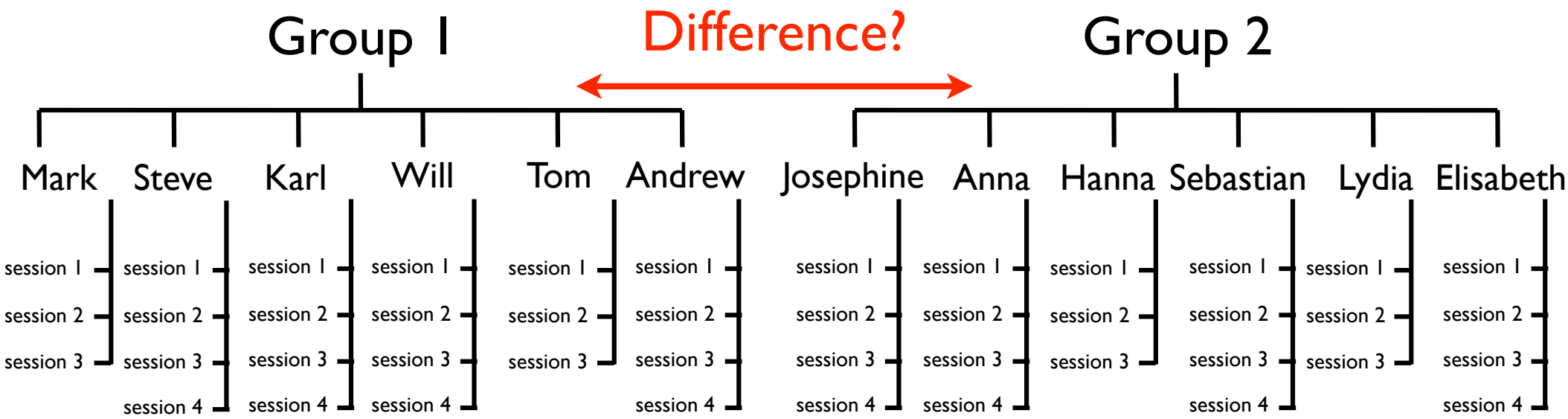


$$Y_K = X_K \beta_K + \epsilon_K$$
$$\beta_K = X_g \beta_g + \epsilon_g$$

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*

All-in-One Approach

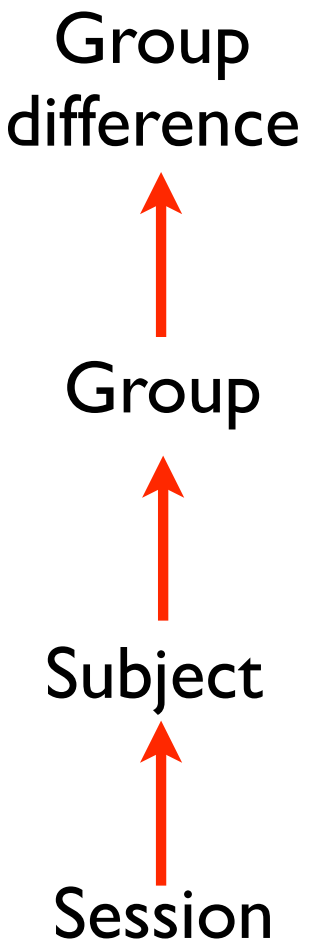


- Could use one (huge) GLM to infer group difference
  - difficult to ask sub-questions in isolation
  - computationally demanding
  - need to process again when new data is acquired

Summary Statistics Approach

In FEAT estimate levels one stage at a time

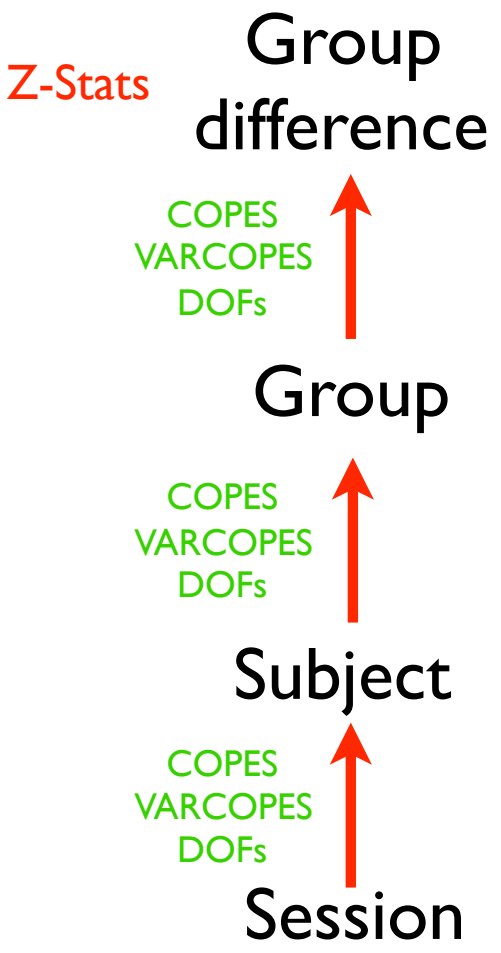
- At each level:
  - Inputs are summary stats from levels below (or FMRI data at the lowest level)
  - Outputs are summary stats or statistic maps for inference
- Need to ensure formal equivalence between different approaches!



FLAME

FMRIB's Local Analysis of Mixed Effects

- Fully Bayesian framework
  - use non-central t-distributions: Input COPES, VARCOPES & DOFs from lower-level
  - estimate COPES, VARCOPES & DOFs at current level
  - pass these up
- Infer at top level
- Equivalent to All-in-One approach



FLAME Inference

- Default is:
  - FLAME1: fast approximation for all voxels (using marginal variance MAP estimates)
- 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

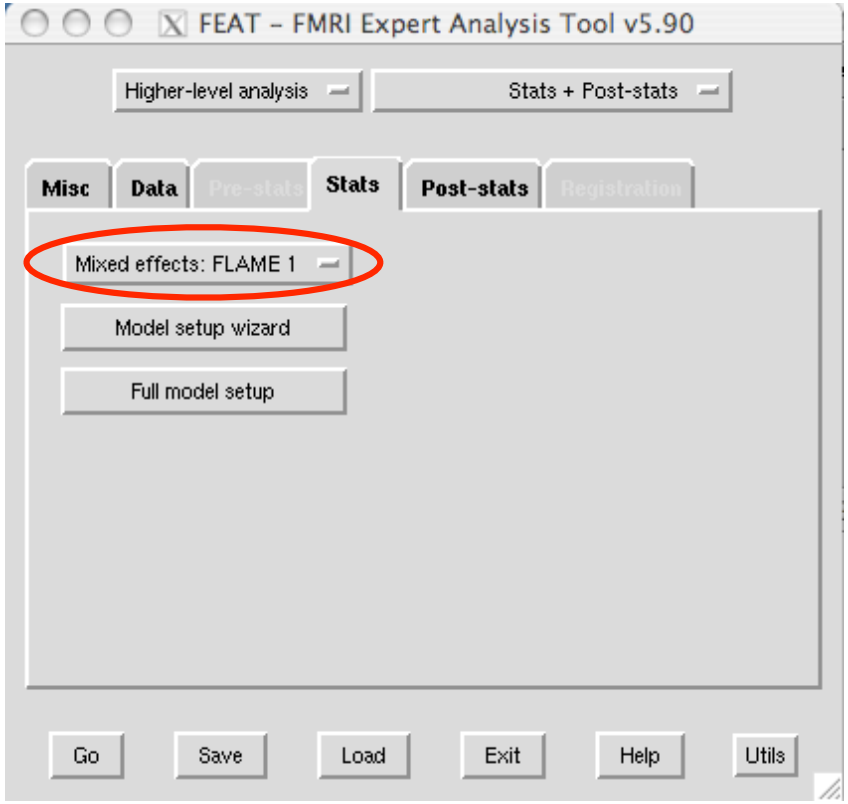
   Use at top level: quick and less accurate

3. Mixed Effects - FLAME 1

   Use at top level: less quick but more accurate

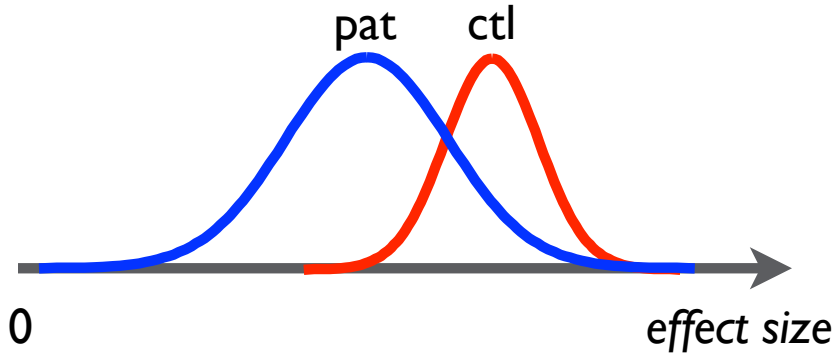
4. Mixed Effects - FLAME 1+2

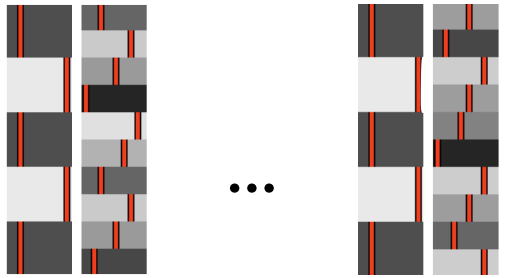
   Use at top level: slow but even more accurate

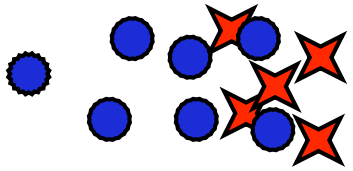


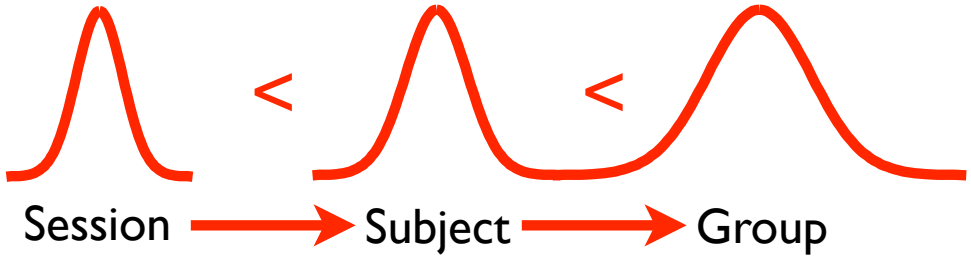
FLAME vs. OLS

- allow different within-level variances (e.g. patients vs. controls)
- allow non-balanced designs (e.g. containing behavioural scores)
- allow un-equal group sizes
- solve the 'negative variance' problem



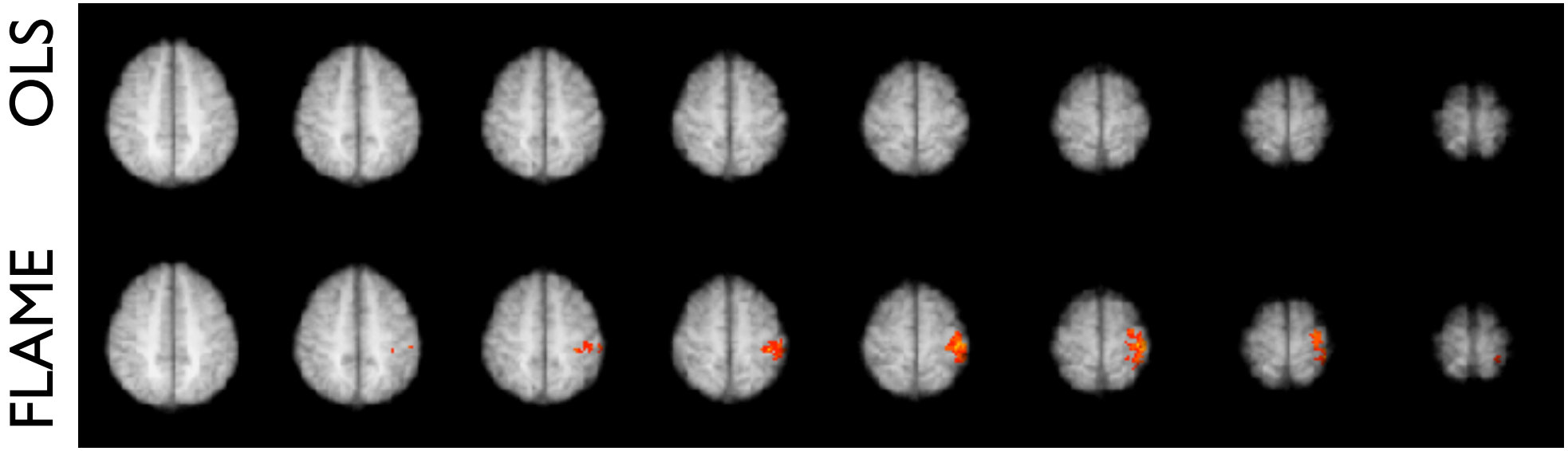






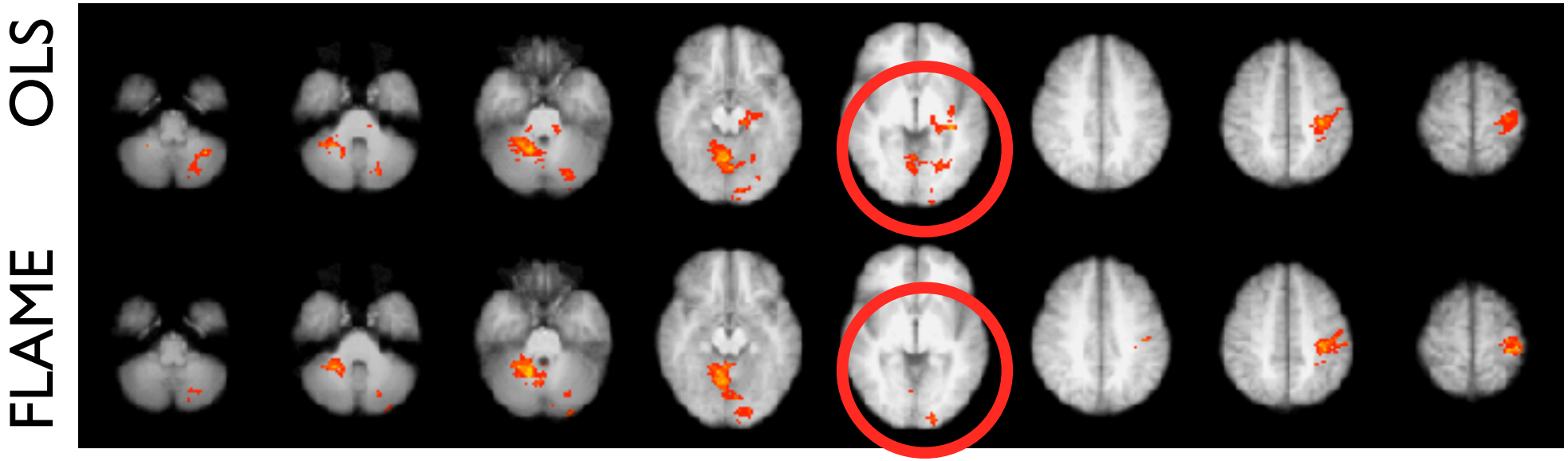
FLAME vs. OLS

- 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



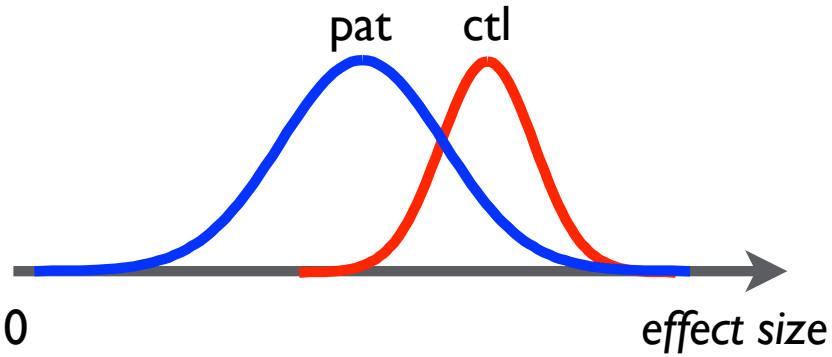
FLAME vs. OLS

- 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!)
- design matrices need to be 'separable', i.e. EVs only have non-zero values for a single group

1	1.0	0
1	1.0	0
1	1.0	0
2	0	1.0
2	0	1.0
2	0	1.0

valid

1	1.0	1.0
1	1.0	1.0
1	1.0	1.0
2	1.0	-1.0
2	1.0	-1.0
2	1.0	-1.0

invalid

FMRI Group Analysis

Summary:

- Fixed Effects analyses give results for specific sample
- Mixed Effects analyses give results for the population
- Summary statistics separates whole analysis into different levels, passing up COPE, VARCOPE & DOF
- We use the GLM at every level

- FLAME (FSL) can cope with unbalanced designs, unequal group sizes, and solves 'negative variance'
- Multiple variances can be modelled but only when justified and subject to some constraints