Few images are from Google

Neural Imaging and Signal Systems

(BT 640)

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Ack: This is an Aggregated Lecture from lot of resources especially SPM12.

Feedback for Tutorial (Next week)

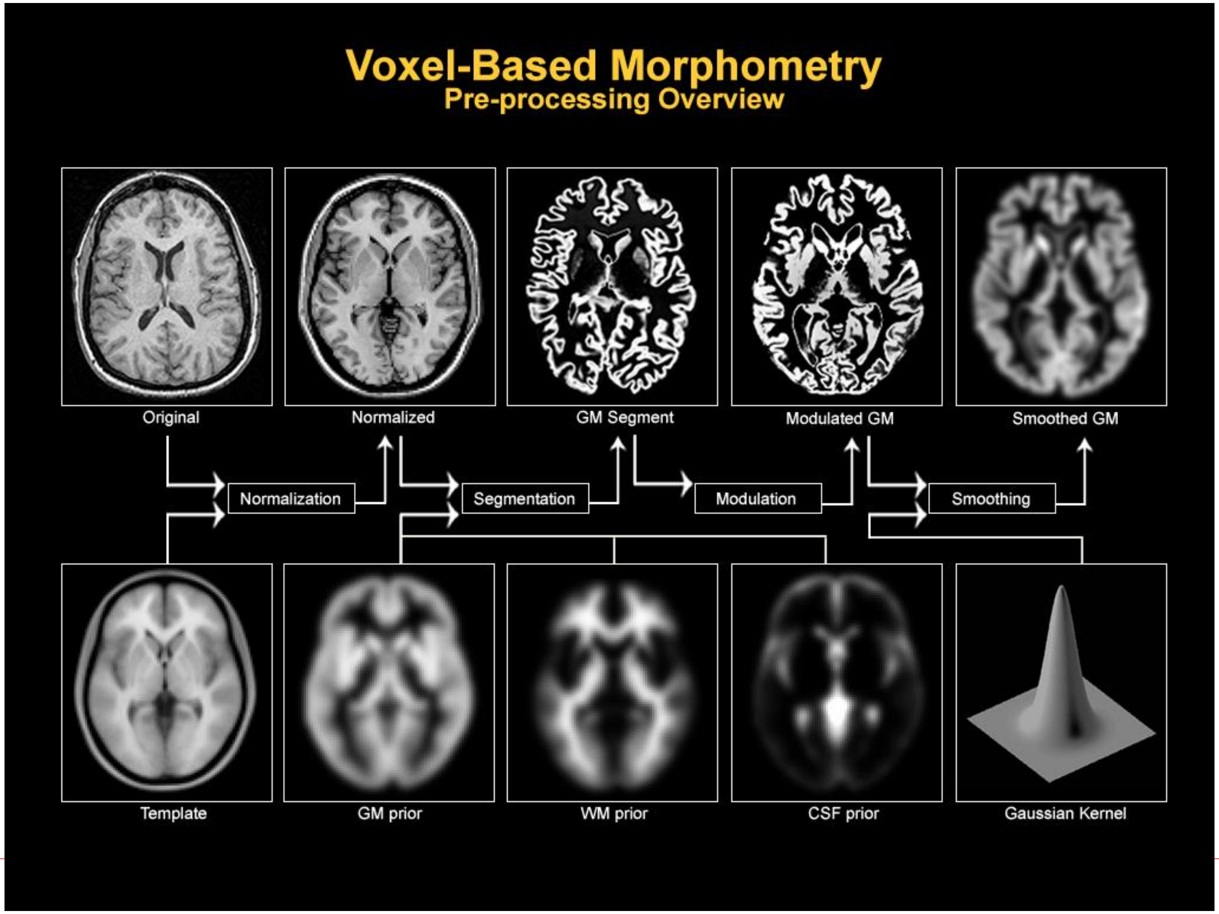
How did Tutorial 4 go?

Quick Recap

Voxel Based Morphometry Blocks

Quick Recap

Voxel Based Morphometry Blocks



Quick Recap

How will you find faulty MRI scans given 10,000 Scans

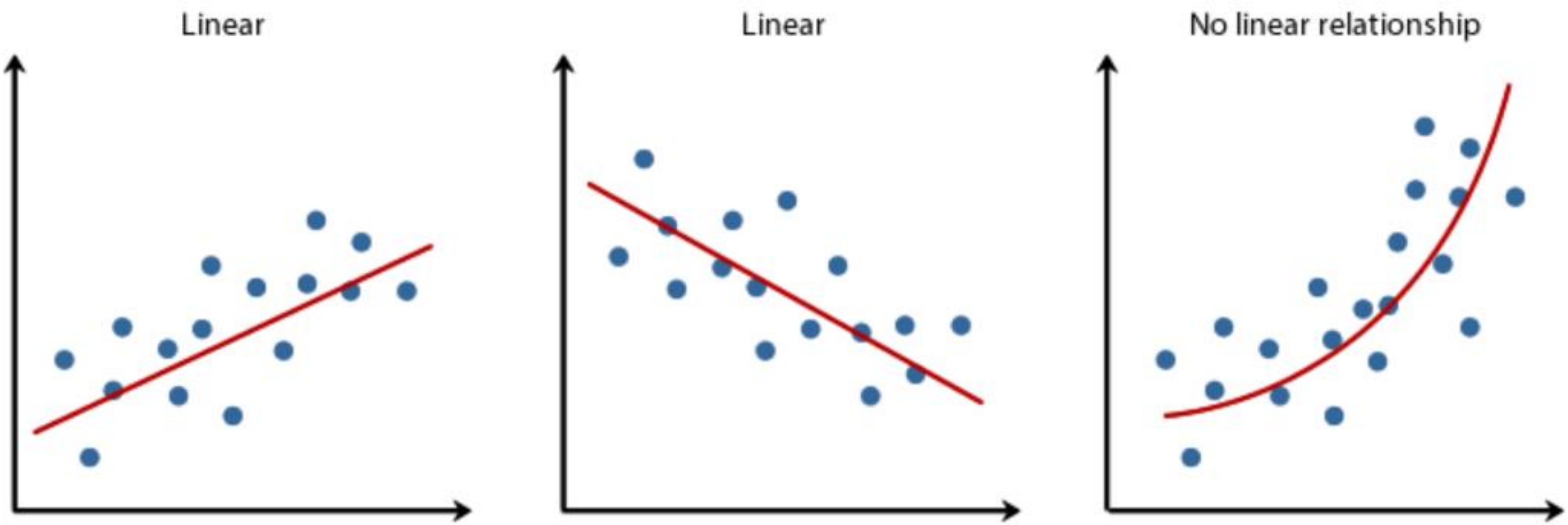
Todays Lectures

General Linear Model (GLM)

GLM for Voxel Based Morphometry

Simple regression

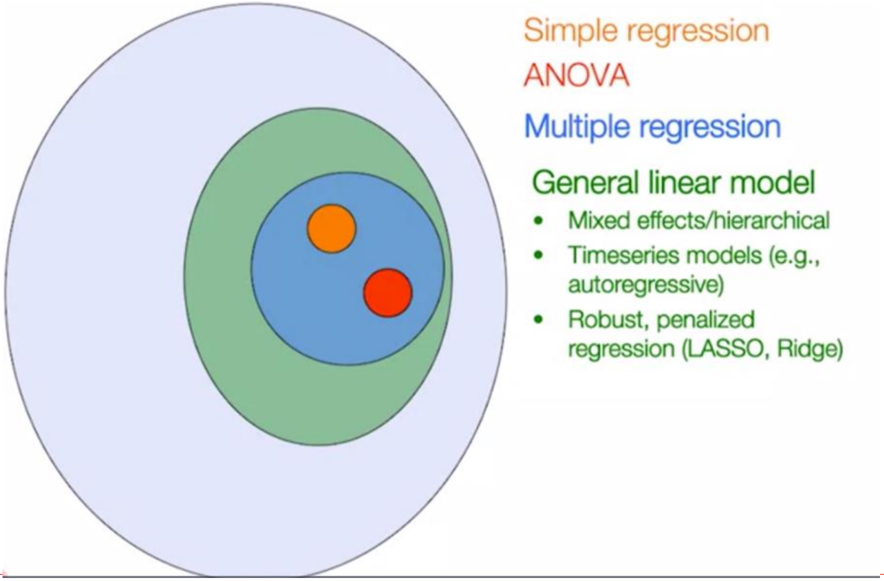
- One predictor and one outcome.



"Essentially, all models are wrong, but some are useful."
George Box, 1987.

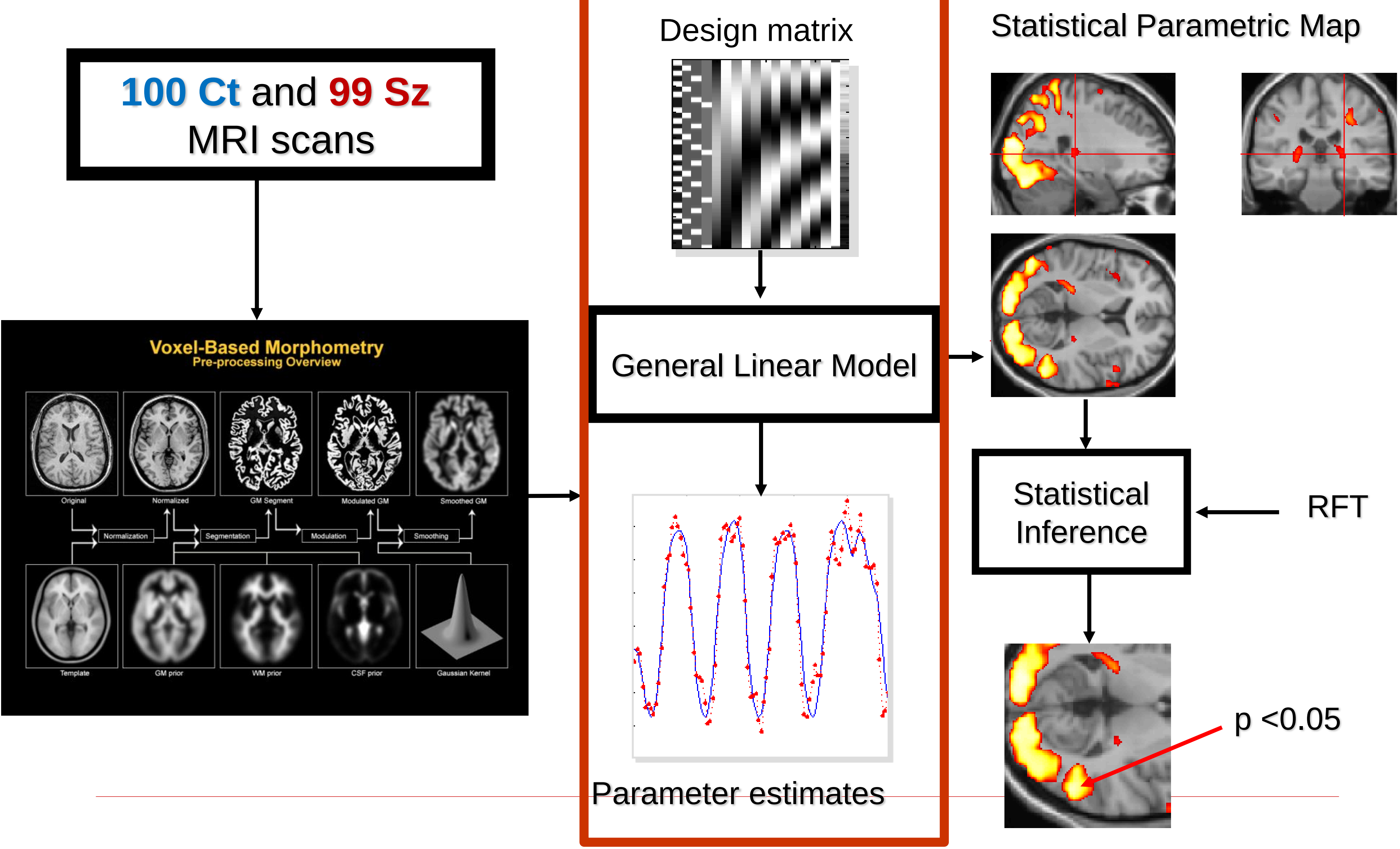
General Linear Model(GLM)

- GLM treats data as a linear combination of model functions (predictors) plus noise (error).
- The model functions are assumed to have known shapes (line or curve) but their amplitudes (slopes) are unknown and have to be estimated.

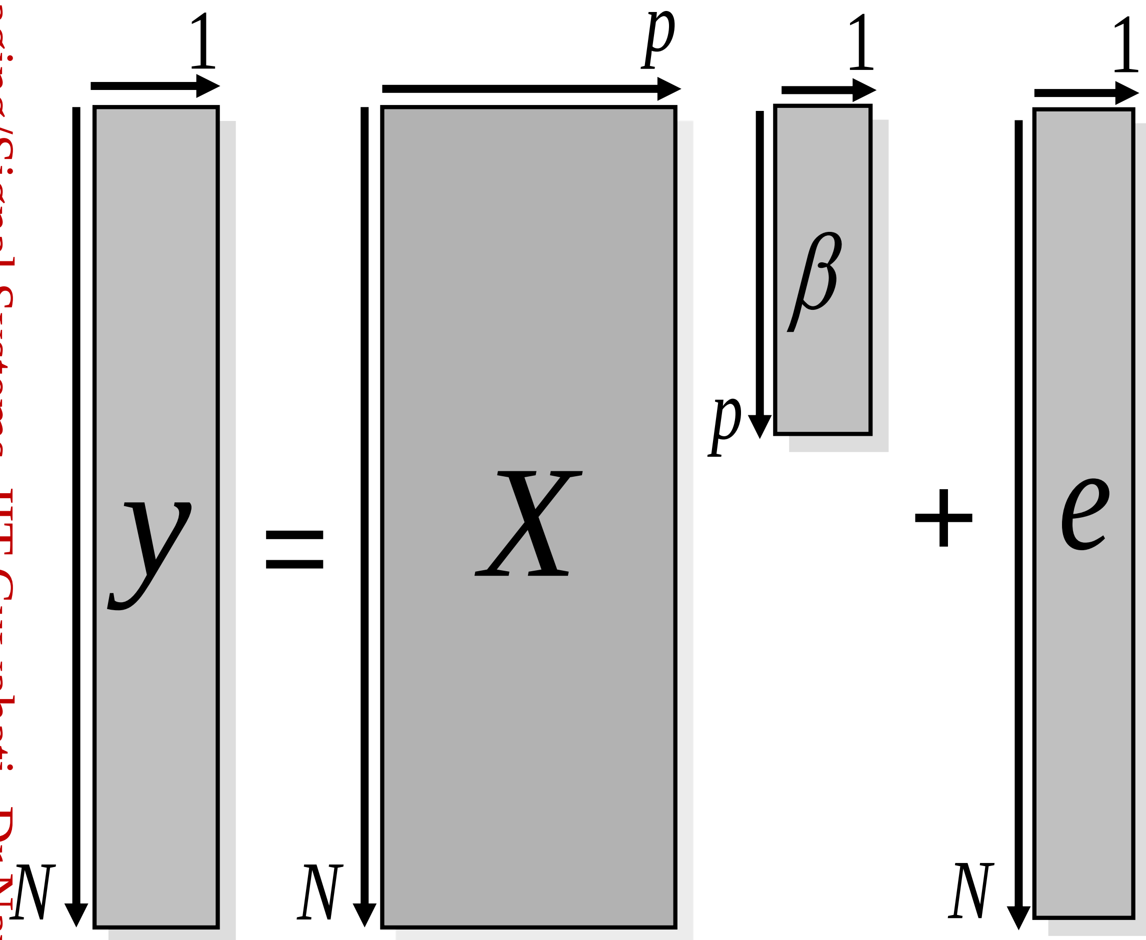


Slide from SPM 12

General Linear Model (VBM Context)



General Linear Model



$$y = X\beta + e$$

$$e \sim N(0, \sigma^2 I)$$

Model is specified by
1. Design matrix X
2. Assumptions about e

N: number of scans
p: number of regressors

The design matrix embodies all available knowledge about experimentally controlled factors and potential confounds.

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GLM: a flexible framework for parametric analyses

- one sample *t*-test
- two sample *t*-test
- paired *t*-test
- Analysis of Variance (ANOVA)
- Analysis of Covariance (ANCoVA)
- correlation
- linear regression
- multiple regression

ALL CLASSICAL TESTS possible based on DESIGN MATRIX

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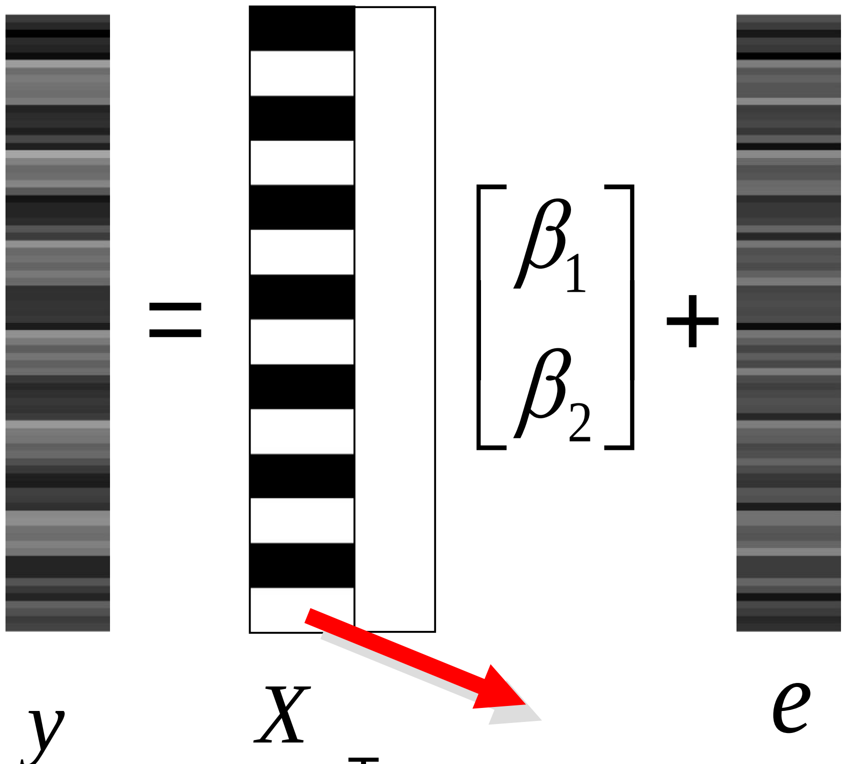
Parameter estimation



$$y = X\beta + e$$

Two regressors: x_1 x_2

$$\begin{bmatrix} \beta_1 \\ \beta_2 \end{bmatrix}$$

Objective: estimate parameters to minimize $\sum_{t=1}^{N} e_t^2$

Ordinary least squares estimation (OLS) (assuming i.i.d. error):

$$\hat{\beta} = (X^T X)^{-1} X^T y$$

$$\hat{\beta} \sim N(\beta, \sigma^2 (X^T X)^{-1})$$

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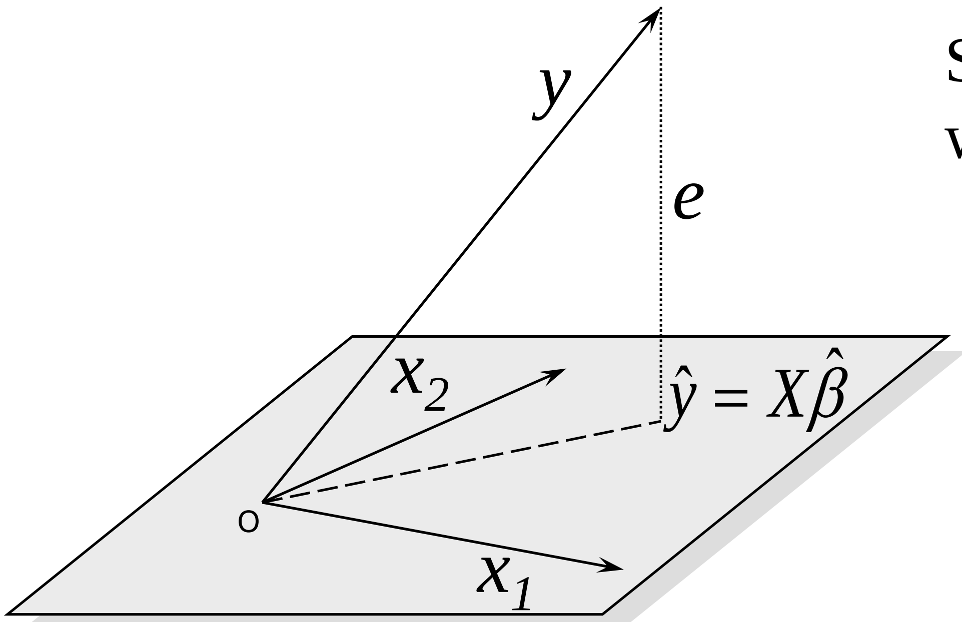
GLM- Geometric Perspective

Consider x_1 and x_2 as two regressors



Smallest errors (shortest error) when e is orthogonal to X

$$X^T e = 0$$

$$X^T (y - X\hat{\beta}) = 0$$

$$X^T y = X^T X\hat{\beta}$$

$$\hat{\beta} = (X^T X)^{-1} X^T y$$

Design space defined by *X*

Objective:
estimate parameters
to minimize

$$\sum_{t=1}^{N} e_t^2$$

Ordinary Least Squares (OLS)

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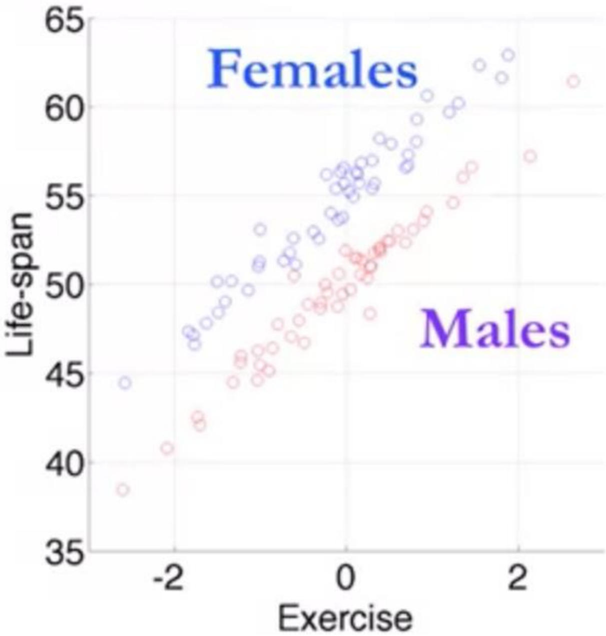
General Linear Model (Exercise affect life span)

- Non Neural Imaging Example
  - Does exercise predict life-span?
  - Made-up (not real data)
  - Control for other variables that might be important, i.e., gender (M/F)



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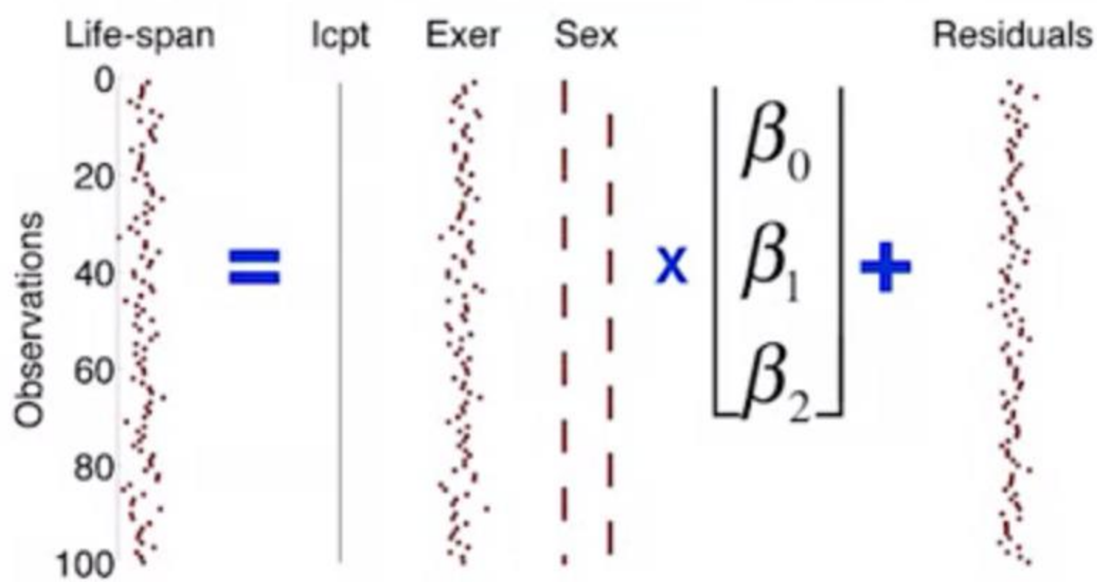
General Linear Model

- Non Neural Imaging Example

$$\mathbf{Y} = \mathbf{X}\beta + \varepsilon$$

$$\begin{bmatrix} Y_1 \\ Y_2 \\ \vdots \\ Y_n \end{bmatrix} = \begin{bmatrix} 1 & X_{11} & \cdots & X_{1p} \\ 1 & X_{21} & \cdots & X_{2p} \\ \vdots & \vdots & & \vdots \\ 1 & X_{np} & \cdots & X_{np} \end{bmatrix} \times \begin{bmatrix} \beta_0 \\ \beta_1 \\ \vdots \\ \beta_p \end{bmatrix} + \begin{bmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \vdots \\ \varepsilon_n \end{bmatrix}$$

Outcome Data **Design matrix** **Model parameters** **Residuals**



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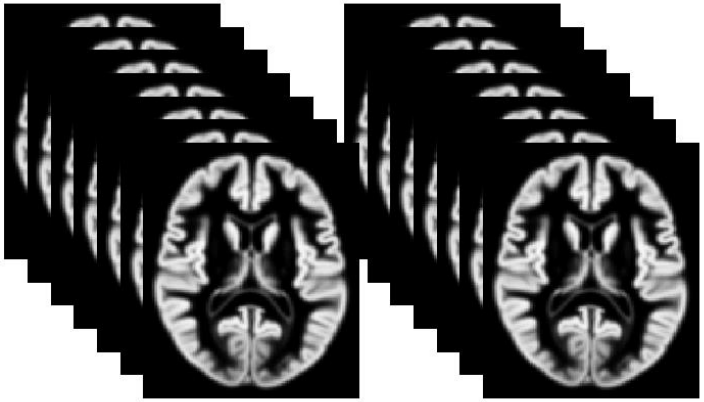
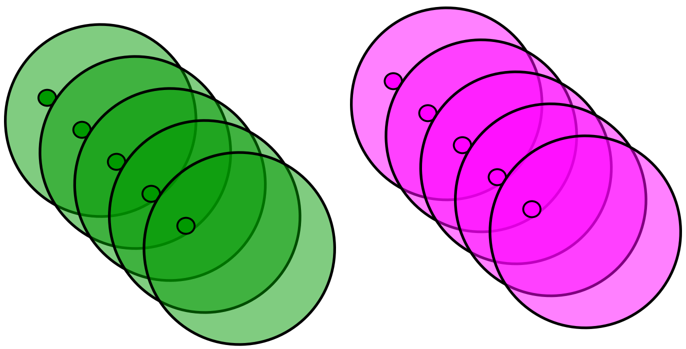
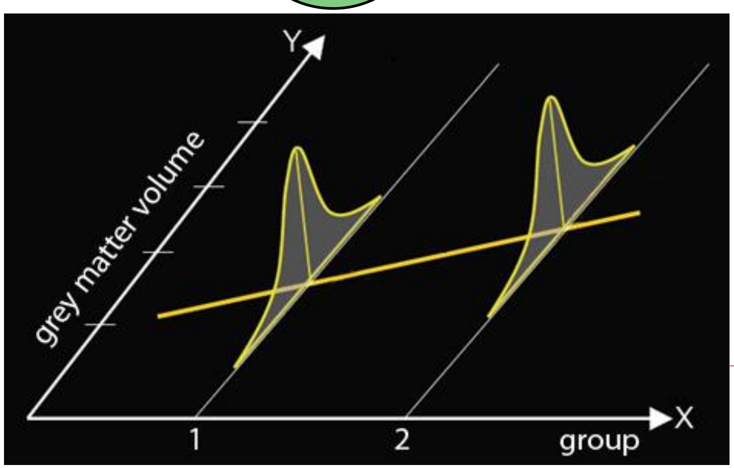
Using GLM for VBM (sMRI Images)







Compare the GM/ WM differences between 2 groups

Control

grey matter

$$\begin{pmatrix} Y_1 \\ Y_1 \\ Y_1 \\ Y_1 \\ Y_1 \\ Y_2 \\ Y_2 \\ Y_2 \\ Y_2 \\ Y_2 \end{pmatrix} = \begin{pmatrix} 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \end{pmatrix} \begin{pmatrix} \beta_1 \\ \beta_2 \end{pmatrix} + \varepsilon$$

β_1 ← mean group 1

β_2 ← mean group 2

Ho: There is no difference between these groups

β: Other covariates, not just the mean

Slide from SPM 12

GLM for VBM

$$\mathbf{Y} = \mathbf{X}\boldsymbol{\beta} + \boldsymbol{\varepsilon}$$

Slide from SPM 12

- **Intensity** for each voxel (V) is a function that models the different things that account for differences between scans:
- $V = \beta_1(AD) + \beta_2(control) + \beta_3(covariates) + \beta_4(global\ volume) + \mu + \varepsilon$

- $V = \beta_1(AD) + \beta_2(control) + \beta 3(age) + \beta 4(gender) + \beta 5(global\ volume) + \mu + \varepsilon$

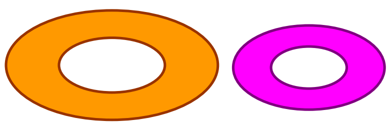
- which covariate (β) best explains the values in GM/ WM

- In practice, the contrast of interest is usually t-test between β_1 and $\beta_{2,}$ ***

*** Eg, "is there significantly more GM (higher v) in the controls than in the AD scans and does this explains the value in v much better than any other covariate?"

In your VBM Model: TIV as covariate

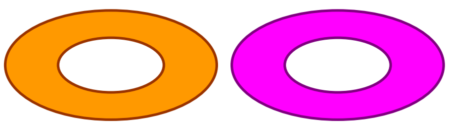
- Global or local differences
  - *Uniformly* bigger brains may have *uniformly* more GM/WM
  - considering the effects of overall size (total intracranial volume) may make a difference at a local level



Brain A Brain B

Differences without accounting for TIV

(TIV = global measure)



Brain A Brain B

Differences after TIV has been “covaried out” (differences caused by bigger size are uniformly distributed with hardly any impact at local level)

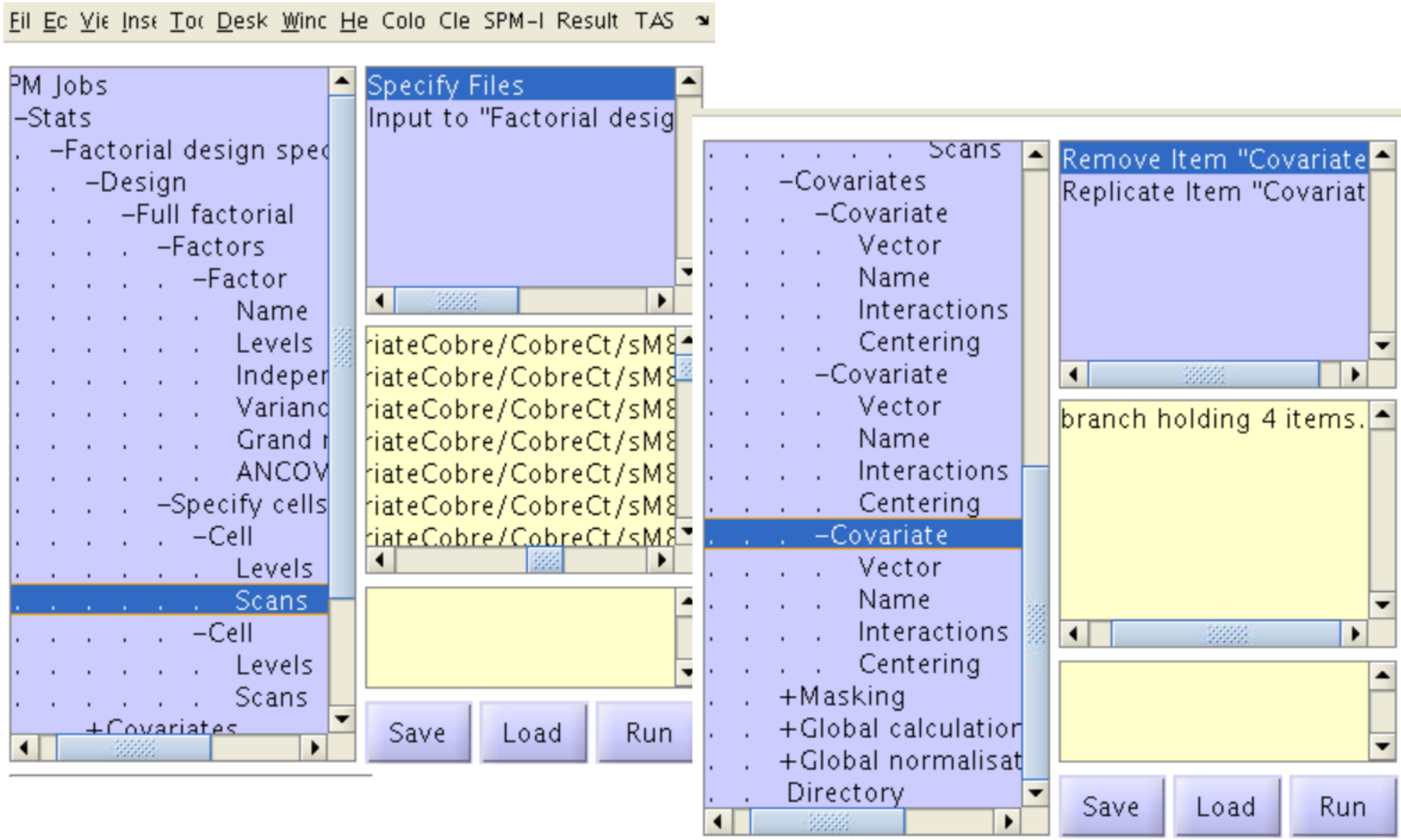
In your VBM Model: Scanner Site as covariate

- Include site of the scan as co-variate

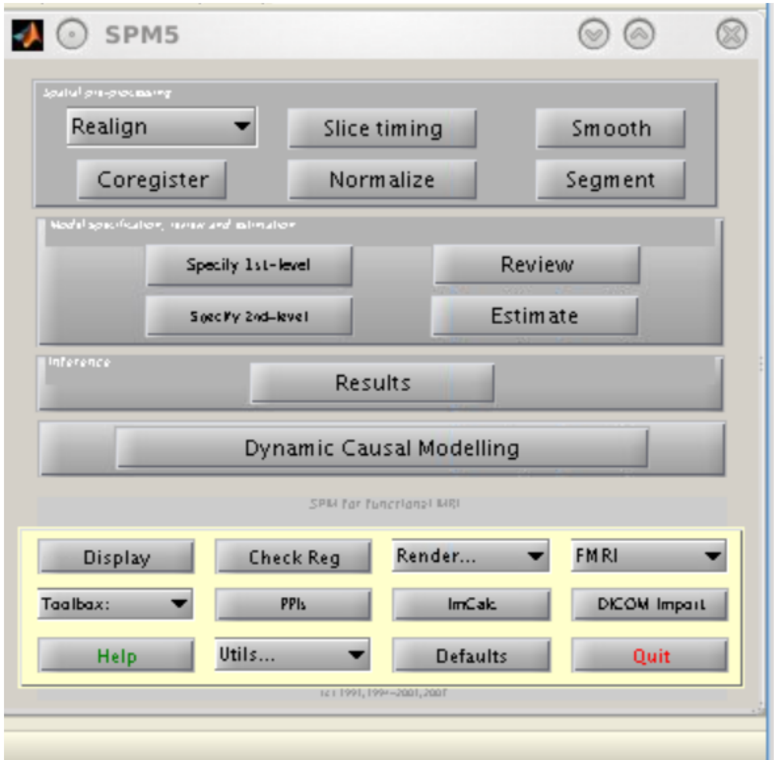
  (if Different scanners)

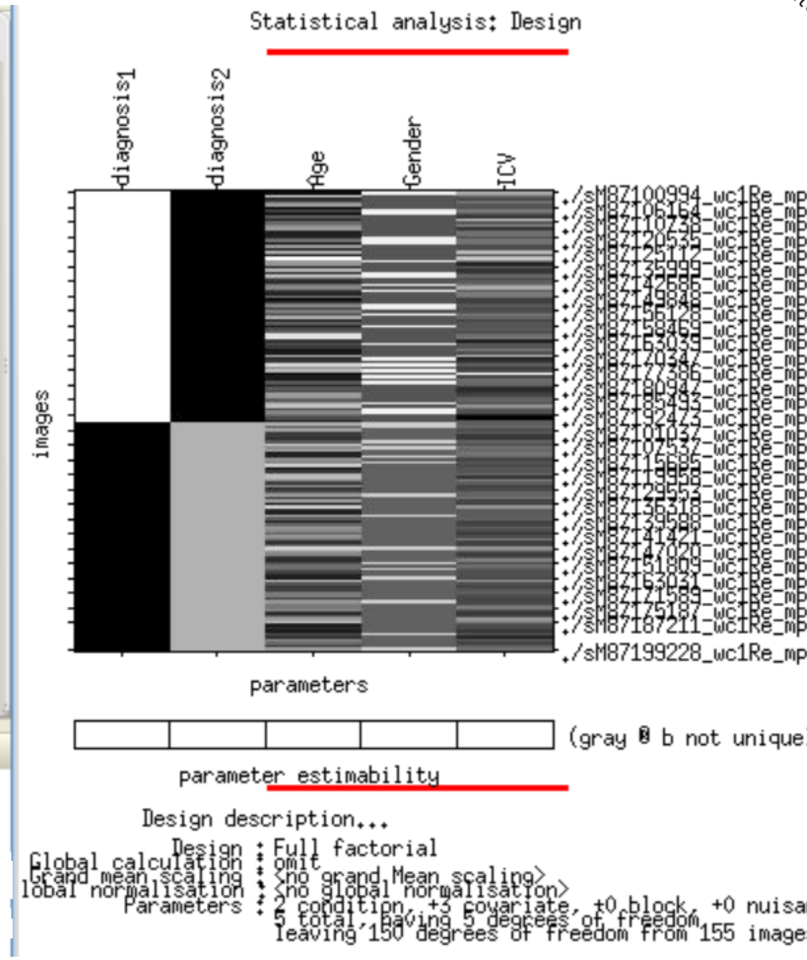
VBM Model in SPM 12 Toolbox

VBM Model Setup

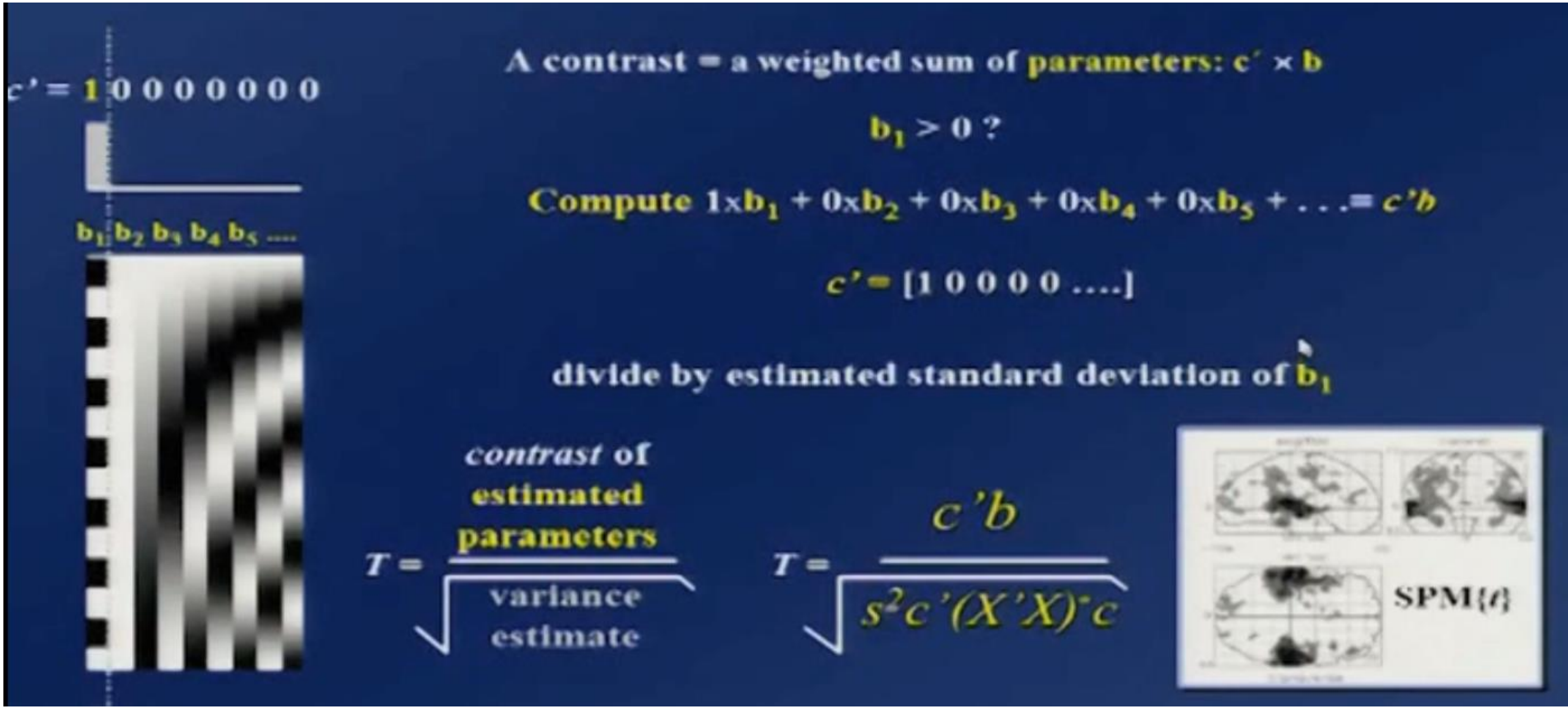


VBM Model Setup





Contrasts for T-test

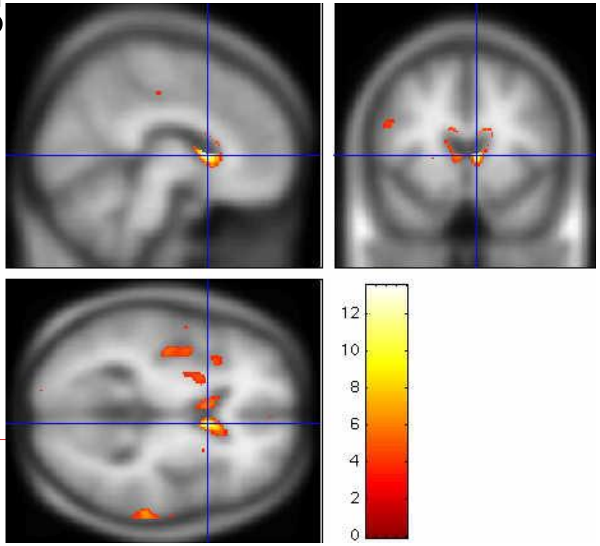


Multiple Comparison Problem

- Introducing false positives when you deal with more than one statistical comparison
  - detecting a difference/ an effect when in fact it does not exist.
- Bonferroni-Correction (controls false positives at individual voxel level):
  - divide desired p value by number of comparisons
  - $.05/1000000 = p < 0.00000005$ at every single voxel

VBM Output in SPM12 on T_1 Template

- Voxelwise (mass-univariate: independent statistical tests for every single voxel)
- Employs GLM, providing the residuals are normally distributed, GLM: $Y = X\beta + \varepsilon$
- Outcome: statistical parametric maps, showing areas of significant difference/ correlations
  - Look like blobs
  - Uses same software as fMRI.



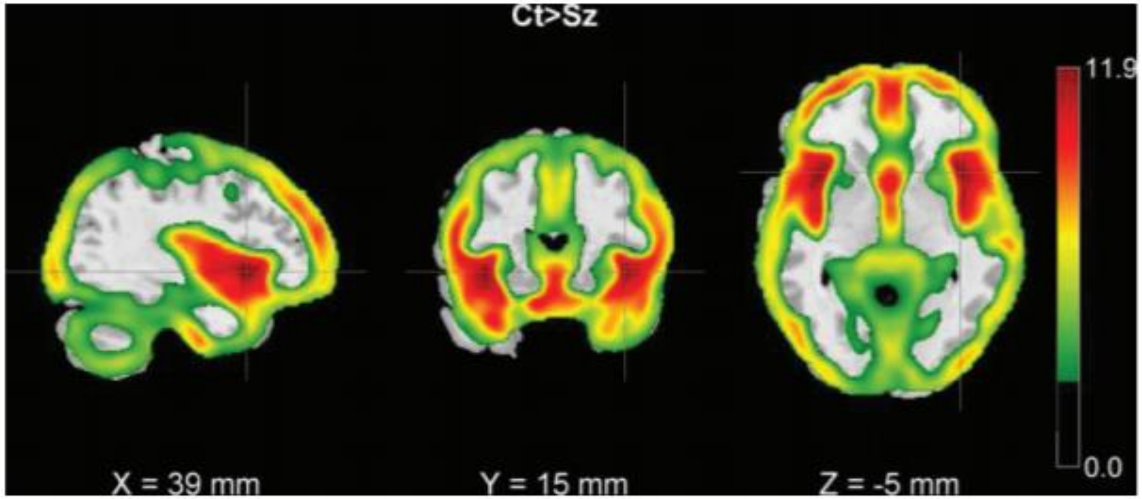
VBM Pros

- Fully automated: quick and not susceptible to human error and inconsistencies
- Unbiased and objective
- Not based on regions of interests; more exploratory
- Picks up on differences/ changes at a local scale
- In vivo, not invasive
- **Has highlighted structural differences and changes between groups of people as well as over time**
  - AD, schizophrenia, taxi drivers, quicker learners etc

VBM Cons

- Data collection constraints (exactly the same way)
- Statistical challenges:
  - Multiple comparisons, false positives and negatives
- Results may be flawed by preprocessing steps (poor registration, smoothing) or by motion artefacts (Huntingtons vs controls)- differences not directly caused by brain itself
  - Esp obvious in edge effects

Schizophrenia Bulletin vol. 41 no. 5 pp. 1133–1142, 2015
doi:10.1093/schbul/sbu177
Advance Access publication December 28, 2014



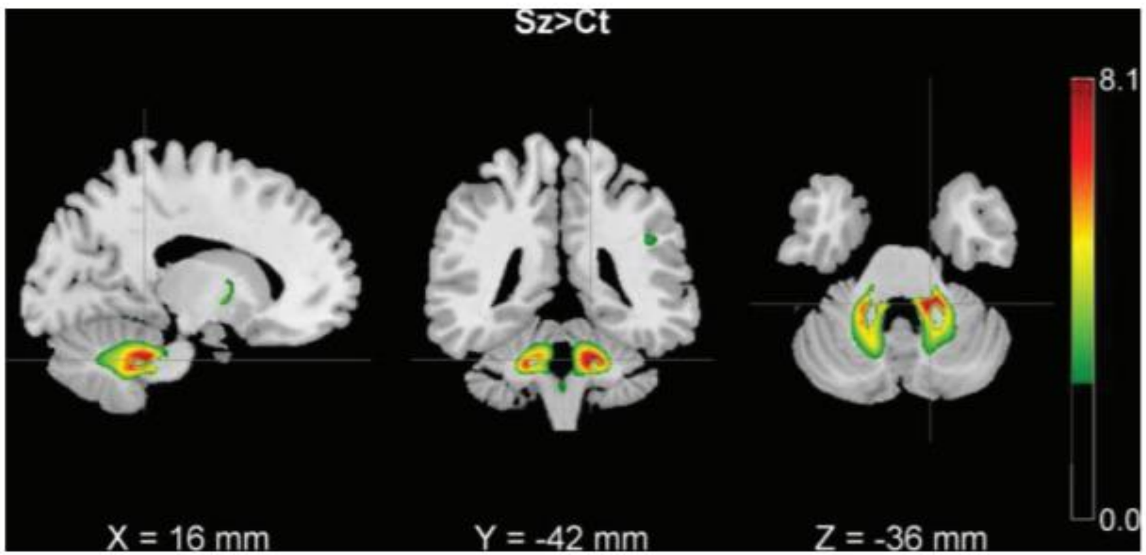


Fig. 2. Results of the VBM analysis; voxels above |*Z*| > 2.5 are shown. (a) Significant clusters where Ct > Sz. (b) Significant clusters where Sz > Ct. Ct, control; Sz, schizophrenia; VBM, voxel-based morphometry.

Thanks for Coming !

General Linear Model(Multiple regression)

- Multiple predictor and one outcome.

Variables: DV, Pred1, Pred2, Pred*k*

$$y_i = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \ldots + \beta_k x_{ik} + \varepsilon_i$$

Parameters: intercept, Slope 1, Slope 2, Slope k, Error

Matrix notation

$$y = X\beta + \varepsilon$$

- solve for beta vector
- minimize sum of squared residuals

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