Outline of Part 2

- Preprocessing Steps
- Practical overview of Design and Analysis
- Analysis issues
- Goal: talk the talk of analysis
Before statistical analysis

- Check for artifacts
- Subjects Move so realign scans
- Slices take a bit of time, so slice time correction
- For group analysis: normalize Individual EPI to template and smooth image to account for variations
- For Individual analysis Coregister Individual EPI to T1

Specific steps will vary by site, experiment and preferences!
Smoothed and Normalized

Subject

Template

Smoothed by Full Width Half Maximum of 8mm Gaussian kernel
Normalizing is Warping

Deformation Map: provides a measure of Differences (Voxel Based Morphometry)
Talairach Coordinate System
MNI Space – templates from Montreal Neurological Institute

Avg. T1 of 305 brains

Avg. T1 of 1 S (27 scans)

Rough extents in mm,
Y: -90 post. to +60 ant.; X: -55 left to +55 right; Z: -40 down to +65 up
Normalizing on the Sphere

Surface Matching

(P. Thompson)
Analysis in a Nutshell

Equation: $\text{DATA} = \text{some relation that I deem important}$

What is the DATA?
- A large number of time series of BOLD measurements,

The relations I deem important could be many things:
- For an inference run a statistical model - hypothesis driven
- For a description look at factors - data driven or exploratory analysis
Hypothesis Driven Inferencing

- Correlation of Voxels with Task
  - Linear Correlation Map

- ANOVA model
  - \( \text{DATA} = \text{Experimental Effect} + \text{Error} \)
  - Perform T-test or F-test
Hypothesis Driven Inferencing

- General Linear Model
  - DATA = Design Matrix * Betas + Other Covariates + Error
    - Betas are parameters that represent effect sizes
    - Other covariates could be motion and session effects

- 1 voxel at a time called massive univariate
  - Beta Differences => 'contrast map'

\[ \text{Beta cond. A minus beta cond. B} = \text{Contrast A-B for T-test p-values; superimpose} \]
HRF - Hemodynamic Response Function

What is the typical response to a stimulus?

How does HRF vary?

How to deal with this?

- 1. fit an HRF curve
  - Betas are then an estimate of change in HRF
- 2. fit each time point
  - Beta are estimate of signal change in a predefined post-stimulus window
- 3. fit an HRF curve with extra regressors to handle variations
Canonical HRF shape
Typical Response Properties – BOLD sums linearly

(Boynton)
BOLD Saturates and Lags

Design matrix adjusts the square wave to account for saturation and delay by convolving with HRF
Fitting a Canonical HRF

Stimulus impulse at $t=0$ leads to HRF. Betas are an estimate of change in HRF.
HRF Variation Exists

HRF varies between subjects
HRF varies across regions
HRF is consistent within a region within a subject

(Miezin et al)
Modeling HRF Variation

Extra regressor to account for time variation

Canonical +/- Derivative changes the shape

(R. Henson)
Experimental Setups

- Block design: steady state response
- Event Related design: trial by trial transient response
  - can also try to get both (Mixed effects design)
  - Often, experimental considerations dictate block or event-related design
Box-car Design: Comparing Active to Rest States

Stimulus: +, Tap, ... 

Task:
- 30s-R
- Tap
- 30s-R
- Tap
- 30s-R

Image: [image representation of the task sequence]
Block Designs

- Cluster trials together
- Good power to detect signal difference

Guidelines:
- between 15-30s task on/task off
- >15s rest allows HRF to return to baseline
- >30s gets close to low frequency artifacts
Event Related Design:

Inter Trial Interval: 2+ seconds ‘jittered’

Stimulus

2s  +  4s  +  ...

no cigarette  cigarette

Can we capture the transient response to viewing a cigarette ad?
Event-Related

- ITI should be ‘jittered’
  - 2 or more seconds with exponential distribution (Dale, 1999)

- Note:
  - Event or blocked design need balanced time for a control condition (i.e., a rest period or null trials)
Sources of Noise
(ie Variance Components)

Many sources:
- physiological, scanner, subject differences, movement...

Physiological and Scanner effects can be
- low frequency
  - (use a highpass filter to exclude)
- high frequency
  - noise at time t is correlated to time t-1
  - model this as serial correlation (autoregressive modeling)

You can deal with noise if it can be modeled!
Scanner signal dropout happens
Motion Artifact

Task block

Movement, as estimated by realignment

Edge effect
Intersubject Variation

- Treat subjects as random effect
- For efficiency take a 2 stage approach.
  - 1. get summary statistic for each subject separately (i.e. contrast maps)
  - 2. carry forward that information to a 2\textsuperscript{nd} level analysis (i.e. group analysis)
Finding Regions of Activation

Two ways to evaluate regions

– Whole Brain
  • Or limit the volume by a mask

– Region of Interest (ROI)
  • Functionally defined
  • Anatomically defined
Analysis on the Surface

(Spiridon, et al 2006)
Finding Regions of Activation

Multiple Comparison Problem:

- Q: How many False Pos. am I willing to accept? Type I error

- If we have 1000 voxels and use $p < .05$ (T-stat threshold), then 50 are false
Can we have it both ways?

Sensitivity vs. Specificity

– sensitivity is the ability to detect true activation

– specificity is the ability to only detect true activation
True vs. False Activations

(Nandy et al. 2001)
Protect Type I error:

- Bonferroni - too conservative!
  - voxel tests not independent

- False Discovery Rate
  - number of False Pos. ~ .05

- Random Field Theory
  - treat voxels as volume of bumps
Protect Type I error:

- Random Field Theory
  - a display threshold of $p<.001$ often works
  - get a table of cluster $p$-values

Note:
- GRF maybe better at low activation large clusters
- FDR maybe better at smaller, peaked clusters
Cluster in a Random Field

A display threshold defines clusters

(M. Brett)
Beware Display Thresholds!

1 Subject, 1 task, 33 scans, but variability is not as bad as it looks

(McGonigle)
Protect Type II error:

- Type II error: false Negatives
  - Q: How many False Negatives can my experiment (funding) take?

- Statistical Power
  - Why do you need 12-24 subjects for power?
How Many Subjects?

Take home point: better to have more subjects than more scans

(Desmond, et al, 2001)
Data driven Analysis

Data = a function of some important factors

– Often, this is a multivariate problem (PCA, ICA, Part. Least Squares)

– Correlation factor is functional connectivity
  - Either across all voxels or wrt to 1 voxel
Resting state networks with ICA (Independent Component Analysis)

Subjects are resting, no stimuli, no design matrix, no GLM

ICA is model free, so it applies

(Deluca et al)
Model Driven Effective Connectivity

Dynamic Causal Model
- A model of how inputs modulate connectivity between regions.
- Bayesian analysis of effects
- Ultimately, causal directions only come from prior hypothesis!
Other GLM options

- Parametric analysis of activation trends
- Estimate delay of the hemodynamic function
- Bayesian Analysis
  - Produce Posterior probability map for Betas
On the Variation of SW packages

But recall, peak differences hide overall cluster similarities.
... this special issue it illustrates the significant methods-driven variability that potentially exists in the literature. Variable results from different methods reported here should provide a cautionary note and motivate the Human Brain Mapping community to explore more thoroughly the methodologies they use for analyzing fMRI data. (Poline, HBM, 2006 eprint)
Why fMRI is fun!

Functional MRI is difficult because one must have a good working knowledge of (from Savoy):

- the physics and engineering underlying the device
- the temporal and spatial properties of the physiology and hemodynamic responses
- functional and structural anatomy
- the myriad of data analytic steps to get a statistically meaningful map of an activation pattern
- the way all of the above interact with each other and with psychology in the design of experiments
- and perhaps most importantly, a feel for the way all these things interact when trying to interpret the results of experiments
References


Books has sections on Cognitive Neuroscience and Statistical Methods, methods are both introductory and technical, some of which focus on SPM package, chapters build upon each other, but not a textbook

from the FSL group, Jezzard, Matthews, Smith (2001) Functional MRI: Introduction to methods (chs 9,14, 16)

physics and Physiology, and Overview chapters of Statistical Analysis, some technical, chapters self-contained

Gentle introduction, textbook. Functional magnetic resonance imaging / Scott A. Huettel, Allen W. Song, Gregory McCarthy


R. Henson and W. Penny ANOVAs and SPM, (1) Institute of Cognitive Neuroscience, (2) Wellcome Department of Imaging Neuroscience, University College London. November 20, 2003


