Functional MRI Mapping Cognition

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Outline

• Why fMRI?
• fMRI - How it works
• Research Design
• Paradigm Development
  → The Binding Task
• Data Acquisition
• Data Preprocessing
• Statistical Parametric Mapping
• Summary

Why fMRI?

• Functional vs. Structural (static)
  • Structural: Snapshot of the brain
  • Functional: Regional changes in cerebral blood flow

fMRI – How it works

Earth's Magnetic Field
3T Magnet

0.5 Gauss
30,000 Gauss

Spin Physics

Hydrogen protons in random motion
Magnetic field (B0)
Protons wobble
RF pulse knocks some protons out of alignment
Protons snap back into alignment emitting RF
**fMRI – How it works**

- RF emitted differs by tissue type → MRI contrast
- Blood O₂ level is a good contrast agent
- De-ox vs. Oxy Hemoglobin

**The BOLD Response**

*Blood Oxygenation Level Dependent*
- Hemodynamic response
- Functional sensitivity
- Secondary signal

**Hemodynamic Response Function (HRF)**

Source: Nature Reviews | Neuroscience

**Research Design**

- Bright Idea
  e.g. investigate language processing in schizophrenic individuals
- Preliminary Hypothesis
  Schizophrenics process language differently from normal individuals
- Refined hypothesis
  Cortical disconnection in fronto-thalamic circuits correlates with abnormal language processing in schizophrenia

**Paradigm Development**

- Most difficult part of the research
- Often uses prior knowledge about brain activation in response to certain tasks
- Two types:  
  1. Novel task
  2. Known task
     (adapted for fMRI environment)

**Epoch (Blocked) Design**

- Rest
- Active

Source: Edward Auerbach – U. Wisconsin

1/29/04
**Epoch (Blocked) Design**

**Advantages:**
- Lots of events → Increased SNR
- Easy to design and implement
- Easy to Analyse (ON minus OFF)

**Limitations:**
- Sometimes too simple
- Unable to infer processing sequence
- Assumes single activity type at a constant level during activation

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**Single Event Design**

**Advantages:**
- Obtain crucial timing information
- Isolate single events (compare different types of stimuli or responses)

**Limitations:**
- Low SNR (smaller number of events)
- Longer scan time
- More difficult to design and implement

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**Out of Scanner Testing**
- Reaction time
- How challenging?
- Instructions

**In-Scanner Testing**
- # events, blocks or stimuli
- Total scan time
- Tweak acquisition parameters
**Paradigm Development**

Example: Feature binding

Desert  Humps

CAMEL

**The Binding Task**

Questions:
- Do SZ use the same areas of the brain as NC to bind stimuli?
- Do SZ activate brain areas to the same extent as NC?
- Do SZ differ from NC in performance on a binding task?
- Do performance differences correlate with rCBF?

etc…

**The Binding Task**

Stimulus

0 s 8 s
time course

Desert + Humps

Slice + Sharp

Add events and subtract baseline activation

What do we know?
- Successful binding in normal individuals activates the thalamus and anterior cingulate
- Schizophrenics do not perform well on this task

Source: Kraut et al., J Cog Neurosci 2002

- Correct bind
e.g. sharp + slice → knife
- Incorrect bind
e.g. bullet + cheese → clown
- Correct non-bind
e.g. camel + dollar → N/A
- Incorrect non-bind
e.g. desert + humps → N/A
The Binding Task

Research Plan

• Use the binding task to model semantic processing in schizophrenia
• Compare schizophrenics with normal controls on performance-related activation during binding

fMRI Data Acquisition

- fMRI data were acquired on a Philips 1.5 Tesla scanner using a TR of 1000 ms
- Binding task was synchronized with scanner timing in intervals of TR
- Time series were acquired in raw format.
- Raw matrix was transformed to images.
- 4D images were saved and exported from scanner to lab.

fMRI 4D volume (time series)

Each picture is a complete 3D volume of the brain
3D volumes are acquired at intervals of TR (1000ms)
3D volumes are combined to create the 4D volume of the time series

fMRI Data Preprocessing

Motion Correction
Correct for subject’s head motion in scanner

Normalization
Fit subject’s data to standard EPI template

Why?
To compare scans from different subjects, they have to be in the same space for voxel-wise analysis
**fMRI Data Preprocessing**

**Smoothing**
- Smoothing with a Gaussian kernel at least twice the size of the voxel.

**Why?**
- Hemodynamic response is smooth
- Increase SNR
- Reduce bias due to anatomic differences
- Conform data to Gaussian field model

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**Statistical Parametric Mapping**

**General Linear Model (GLM)**
- Test the null hypothesis that all estimates are zero using the $F$ statistics to give $SPM(F)$.
- Test for whether a particular linear combination (contrast) of the estimates is zero using $SPM(T)$.

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**Gaussian Field Theory**
- SPM calculates statistics voxel-wise.
- Multiple Comparison Problem

Solution: Gaussian Field Correction
- Neighboring voxels are not independent (remember spatial smoothing).

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**To Correct or Not to Correct**

**Anatomically Constrained Hypothesis**
- A priori hypothesis with specific ROI in mind
- No correction or small volume correction

**Anatomically Open Hypothesis**
- No a priori hypothesis. Look for activation anywhere.
- Must use corrected statistics.
**Statistical Parametric Mapping**

**Group-level Analysis**

**Fixed Effects Modeling**
- All subjects and sessions treated as a single session
- Can only make inferences regarding the sample.
- Sample size ~ 6

**Limitation:**
Effect could be driven by a few subjects

**Group-level Analysis**

**Random Effects Modeling**
- E.g.: One sample t-test testing whether the effect size is greater than zero.
- One observation per subject per condition
- Allows population-level inferences
- Allows higher-level statistical modeling and group comparisons
- Sample size ~ 12

**The Binding Task - Results**

N = 12 SZ
1 sample t-test
p < 0.01 uncorrected

Results:
Activation in the left thalamus during binding.
No other activation observed.

**What can we infer?**
- Individuals with schizophrenia process language differently from normal individuals;
- Individuals with schizophrenia have abnormal or no recruitment of the anterior cingulate during binding;
- Thalamic activation during binding is intact in individuals with schizophrenia;
- Implications for understanding the neural mechanisms behind abnormal language processing in schizophrenia.

**SUMMARY**

- Technology
- Experimental Design
- Epoch and Single Event Paradigms
- Case Study: The Binding Task
- fMRI Data Preprocessing and Analysis
- Group Analysis
- Results from Binding
- Inferences