Experimental Design for fMRI

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Aim: to manipulate the subject’s mental state/behavior/experience in some way to produce a neurovascular response

- Define process to examine
- Define task to manipulate process
- Measure activation during task with fMRI
- Compare fMRI signal between tasks
Types of Experimental Designs

1. **Categorical** – comparing the effect of one task on the dependent variable to the effect of another task (or rest)

2. **Factorial** - combining two or more factors within a task and looking at the effect of one factor on the response to other factor(s)

3. **Parametric** – varying ‘doses’ of task
Categorical design

Comparing activation in response to one task to another task/rest

Control/comparison condition of most importance
Categorical design

Comparing activation in response to one task to another task

Control/comparison condition of most importance
Categorical design

Comparing activation in response to one task to another task

Control/comparison condition of most importance

Try to isolate the effect of interest as much as possible!
Factorial design

Combining two or more factors within a task and looking at the effect of one factor upon the other(s)

Distraction

<table>
<thead>
<tr>
<th></th>
<th>LOW</th>
<th>HIGH</th>
</tr>
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<tbody>
<tr>
<td>LOW</td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>HIGH</td>
<td>C</td>
<td>D</td>
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</tbody>
</table>

Pain
Factorial Design

Distraction

<table>
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<th></th>
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</table>

Pain

2*2?

13*17?

1*3?

14*19?
• Main effect of pain: A+B+C+D

• Simple contrasts, e.g.: High Pain > Low Pain (C+D)-(A+B)

• Influence of one factor on the other, e.g: Which voxels show most activation with high distraction in high pain condition? (D-B)-(C-A)
Parametric Design

Exploring systematic changes in the brain responses according to various ‘doses’ of task (difficulty levels, increasing sensory input, drug doses, etc)

Hypothesis: as task dose changes, BOLD response changes

- Linear

- Nonlinear

Contrast: -3 -1 1 3
Independent of design ...

- Subject instructions
- Check for task performance
- Record additional explanatory variables / confounding factors (reaction times, accuracy, subjective ratings, autonomic measures, etc)
FMRI Experiment

- Define process to examine
- Define task to manipulate process
- Measure activation during task with fMRI
- Compare fMRI signal between tasks

47*9=?
$47 \times 9 = ?$
Signal is very noisy
No absolute signal in BOLD fMRI: BOLD is not quantitative
<table>
<thead>
<tr>
<th>Multiplication</th>
<th>Result</th>
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<tbody>
<tr>
<td>$47 \times 9$</td>
<td>?</td>
</tr>
<tr>
<td>$46 \times 8$</td>
<td>?</td>
</tr>
<tr>
<td>$45 \times 7$</td>
<td>?</td>
</tr>
<tr>
<td>$51 \times 9$</td>
<td>?</td>
</tr>
<tr>
<td>$53 \times 7$</td>
<td>?</td>
</tr>
<tr>
<td>$47 \times 8$</td>
<td>?</td>
</tr>
</tbody>
</table>

$= \beta_1$
Block designs

- Either one stimulus is presented throughout the block or several stimuli of the same type are presented at fixed intervals.

```
rest A rest A rest A rest A rest A rest A
```
**Block designs**

- Optimal block length: ~ 15 to 20 sec (blocks should be equal)
- Total cycle time: << 100 sec
- Statistically the most efficient design
But...

47*7=?
47*9=?
43*9=?

15 sec 15 sec 15 sec 15 sec 15 sec
But...

- Little control over what subject is doing (e.g. time on task)
- Stimulus predictability → anticipation
- Habituation within blocks and between blocks
- Subject might get bored
- Parallel comparison (A B A B) is problematic
- A rest A in Scan 1 versus B rest B in Scan 2 is problematic
- A rest B rest A rest B is problematic

47*7=？  47*9=？  43*9=？
Event-related Designs

- Image BOLD signal in response to very brief stimuli
Events, ISI=32 s
Events, ISI=32 s

BOLD response

Allows estimation of Hemodynamic Response Function (HRF)
Fixed ISI = 16s

Stimulus ("Neural") $\otimes$ HRF $=$ Predicted Data

Not particularly efficient…
Fixed ISI = 4s

Stimulus ("Neural")

HRF

Predicted Data

Very Inefficient…
Randomised ISI_{min} = 4s

Stimulus ("Neural") \times HRF = Predicted Data

Much more efficient
Flexibility of event-related designs

Ploner et al., PNAS 2010;107(1):355-60
Flexibility of event-related designs

Ploner et al., PNAS 2010;107(1):355-60
Pain?
No pain?
Pain?
No pain?
Pain?
No pain?
Pain?
No pain?
Pain?
No pain?
Pain?
No pain?
Pain?
No pain?
Pain?
No pain?
Pain?
No pain?
Pain?
No pain?
Ploner et al., PNAS 2010;107(1):355-60
No Pain > Pain
• Why does it work to have BOLD responses close together in time?
Why does it work to have BOLD responses close together in time?

- Two key properties of a linear system:
  - Scaling
  - Superposition
"Time-invariant response"

What is the minimum ISI for a valid linear approximation?

Event Related Designs

- Trials (events) are presented briefly in (pseudo-) random order
- ISI should be randomized ("jitter")
- ISI should be short but not shorter than 2 to 5 sec
Event-related Designs

- Flexibility in design
- Not every experiment can be turned into block design
- Randomised trial order
- Post-hoc classification of trials (correct responses, reaction times, etc)
- Some events can only be indicated by participant

But
- Assumptions about shape of HRF
- Lower statistical power
Mixed designs

- Allows investigation of phasic and tonic effects
- Perhaps different processes of interest
- Exploit advantages of block and event-related designs
Good Practices of fMRI Experimental Design

• Choose stimulus and timing to create maximal change in (cognitive) process of interest
• Get task-related measure of subject behavior in the scanner (task verification, additional regressors)
• Scan as many subjects as possible; scan as long as you can, considering psychological effects (fatigue, habituation)
• Use block design if you care about detecting differences, and event-related designs if you want to link activity to particular events
• Limit the number of conditions; pairwise comparisons far apart in time decrease power and overlap with low-frequency noise
• In event-related designs, randomize (or pseudo-randomize) the ordering of events
• Randomize (‘jitter’) intervals between events that need to be distinguished (decorrelate their predicted signals after HRF convolution)