Experimental Design

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With thanks to:
Karl Friston, Andrew Holmes
Overview

1. A Taxonomy of Designs
2. Epoch vs Event-related
3. Mixed Epoch/Event Designs
A taxonomy of design

- **Categorical designs**
  - Subtraction: Additive factors and pure insertion
  - Conjunction: Testing multiple hypotheses

- **Parametric designs**
  - Linear: Cognitive components and dimensions
  - Nonlinear: Polynomial expansions

- **Factorial designs**
  - Categorical: Interactions and pure insertion
    - Adaptation, modulation and dual-task inference
  - Parametric: Linear and nonlinear interactions
    - Psychophysiological Interactions
A taxonomy of design

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A categorical analysis

Experimental design

Word generation G
Word repetition R

G - R = Intrinsic word generation

...under assumption of pure insertion, ie, that G and R do not differ in other ways
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One way to minimise problem of pure insertion is to isolate same process in several different ways (i.e., multiple subtractions of different conditions).

Visual Processing \( V \)
Object Recognition \( R \)
Phonological Retrieval \( P \)

Object viewing \( R,V \)
Colour viewing \( V \)
Object naming \( P,R,V \)
Colour naming \( P,V \)

\[(\text{Object - Colour viewing}) = [1 -1 0 0] \]
\&
\[(\text{Object - Colour naming}) = [0 0 1 -1] \]


(assuming \( RxP = 0 \); see later)

Price et al, 1997
Cognitive Conjunctions

Select contrasts...

- 002 {T} : A1 - A2
- 003 {T} : B1 - B2

Design matrix

Selected 2 contrasts for conjunction, press "Done" when finished.
Cognitive Conjunctions

- Original (SPM97) definition of conjunctions entailed sum of two simple effects \((A1-A2 + B1-B2)\) plus exclusive masking with interaction \((A1-A2) - (B1-B2)\)

- I.e., “effects significant and of similar size”

- (Difference between conjunctions and masking is that conjunction p-values reflect the conjoint probabilities of the contrasts)

- SPM2 definition of conjunctions uses advances in Gaussian Field Theory (e.g., \(T^2\) fields), allowing corrected p-values

- However, the logic has changed slightly, in that voxels can survive a conjunction even though they show an interaction
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A (linear) parametric contrast

Linear effect of time

SPM\{T_{44}\}
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Nonlinear parametric design matrix

E.g, F-contrast [0 1 0] on Quadratic Parameter =>

Inverted ‘U’ response to increasing word presentation rate in the DLPFC

Polynomial expansion:

\[ f(x) \sim \beta_1 x + \beta_2 x^2 + \ldots \]

...(N-1)th order for N levels
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Interactions and pure insertion

- Presence of an interaction can show a failure of pure insertion (using earlier example)...

### Task (1/2)

<table>
<thead>
<tr>
<th>Stimuli (A/B)</th>
<th>Colours</th>
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<tbody>
<tr>
<td>A1</td>
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<td>V</td>
<td>R</td>
<td>P</td>
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<tr>
<td>Naming</td>
<td>R,V</td>
<td>V</td>
<td>P,R,V,RxP</td>
</tr>
<tr>
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<td>V</td>
<td>V</td>
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(Object – Colour) x (Viewing – Naming)

\[
\begin{bmatrix}
1 & -1 & 0 & 0
\end{bmatrix}
- \begin{bmatrix}
0 & 0 & 1 & -1
\end{bmatrix} = \begin{bmatrix}
1 & -1 & 0 & 0
\end{bmatrix} \otimes \begin{bmatrix}
1 & -1
\end{bmatrix} = \begin{bmatrix}
1 & -1 & -1 & 1
\end{bmatrix}
\]

\[
\begin{bmatrix}
R,V - V
\end{bmatrix}
- \begin{bmatrix}
P,R,V,RxP - P,V
\end{bmatrix} = R - R,RxP = RxP
\]
Interactions and pure insertion

Define contrast...

Name: (A1 - A2) x (B1 - B2)
Type: t-contrast
Contrast: 1 -1 -1 1

Design matrix
Parameter estimability

Name defined, contrast defined
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(Linear) Parametric Interaction

A (Linear) Time-by-Condition Interaction (“Generation strategy”?)

Contrast: \([5 \ 3 \ 1 \ -1 \ -3 \ -5] \otimes [-1 \ 1]\)
Nonlinear Parametric Interaction

F-contrast tests for nonlinear Generation-by-Time interaction (including both linear and Quadratic components)

Factorial Design with 2 factors:
1. Gen/Rep (Categorical, 2 levels)
2. Time (Parametric, 6 levels)

Time effects modelled with both linear and quadratic components…
## A taxonomy of design

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Psycho-physiological Interaction (PPI)

Parametric, factorial design, in which one factor is **psychological** (e.g., attention)
...and other is **physiological** (*viz.* activity *extracted from a brain region of interest*)

Attentional modulation of **V1 - V5 contribution**
Psycho-physiological Interaction (PPI)

- V1 activity
- V5 activity
- V1xAttention

SPM\{Z\}

- V1 activity vs. time
- Attention vs. V1 activity
- No Attention vs. V1 activity

V1Att, Att, V1xAtt
Psycho-physiological Interaction (PPI)

• PPIs tested by a GLM with form:

\[ y = (V1 \times A) \beta_1 + V1 \beta_2 + A \beta_3 + \varepsilon \quad c = [1 \ 0 \ 0] \]

• However, the interaction term of interest, \( V1 \times A \), is the product of V1 activity and Attention block AFTER convolution with HRF

• We are really interested in interaction at neural level, but:

\[ (HRF \otimes V1) \times (HRF \otimes A) \neq HRF \otimes (V1 \times A) \]

(unless A low frequency, e.g., blocked; so problem for event-related PPIs)

• SPM2 can effect a deconvolution of physiological regressors (V1), before calculating interaction term and reconvolving with the HRF

• Deconvolution is ill-constrained, so regularised using smoothness priors (using ReML)
Overview

1. A Taxonomy of Designs

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3. Mixed Epoch/Event Designs
Epoch vs Events

- **Epochs** are periods of sustained stimulation (e.g., box-car functions)
- **Events** are impulses (delta-functions)
- In SPM99, epochs and events are distinct (e.g., in choice of basis functions)
- In SPM2, all conditions are specified in terms of their 1) onsets and 2) durations…
  … events simply have zero duration
- Near-identical regressors can be created by: 1) sustained epochs, 2) rapid series of events (SOAs<~3s)
- i.e., *designs* can be blocked or intermixed
  … *models* can be epoch or event-related

Sustained epoch

Blocks of events

Boxcar function

Delta functions

Convolved with HRF
Advantages of Event-related fMRI

1. Randomised (intermixed) trial order
   c.f. confounds of blocked designs (Johnson et al 1997)
Randomised O1 N1 O3
O2
O = Old Words
N = New Words
Blocked

Data
Model

Randomised
O1 N1 O2 O3
N1 N2 N3

O1
N1
O2
O3
N2
Advantages of Event-related fMRI

1. Randomised (intermixed) trial order
c.f. confounds of blocked designs (Johnson et al 1997)

2. Post hoc / subjective classification of trials
e.g, according to subsequent memory (Wagner et al 1998)
$R = \text{Words Later Remembered}$

$F = \text{Words Later Forgotten}$

**Event-Related**

- R = Words Later Remembered
- F = Words Later Forgotten

![Event-Related Data and Model Graph](image-url)
Advantages of Event-related fMRI

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3. Some events can only be indicated by subject (in time)
   e.g, spontaneous perceptual changes (Kleinschmidt et al 1998)
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4. Some trials cannot be blocked  
   e.g, “oddball” designs (Clark et al., 2000)
"Oddball"
Advantages of Event-related fMRI

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e.g, “oddball” designs (Clark et al., 2000)

5. More accurate models even for blocked designs?
e.g, “state-item” interactions (Chawla et al, 1999)
Blocked Design

“Epoch” model

“Event” model

Data

Model

N1 N2 N3

O1 O2 O3

N1 N2 N3

O1 O2 O3
Epoch vs Events

• Though blocks of trials can be modelled as either epochs (boxcars) or runs of events… … interpretation of parameters differs…

• Consider an experiment presenting words at different rates in different blocks:
  • An “epoch” model will estimate parameter that increases with rate, because the parameter reflects response per block
  • An “event” model may estimate parameter that decreases with rate, because the parameter reflects response per word
Disadvantages of Intermixed Designs

1. Less efficient for detecting effects than are blocked designs
   *(see later…)*

2. Some psychological processes may be better blocked
   *(e.g., task-switching, attentional instructions)*
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Recent interest in simultaneously measuring effects that are:

- transient ("item- or event-related")
- sustained ("state- or epoch-related")

What is the best design to estimate both…?
A bit more formally… “Efficiency”

- Sensitivity, or “efficiency”, \( e \) (see later):
  \[
e(c,X) = \{ c^T (X^TX)^{-1} c \}^{-1}
  \]

  - \( X^TX \) represents covariance of regressors in design matrix
  - High covariance increases elements of \((X^TX)^{-1}\)

  \[ \Rightarrow \text{So, when correlation between regressors is high, sensitivity to each regressor alone is low} \]
Item effect only…

Blocks = 40s, Fixed SOA = 4s

Efficiency = 565
(Item Effect)

Design Matrix (X)

OK...
Item and State effects

Blocks = 40s, Fixed SOA = 4s

Efficiency = 16 (Item Effect)

Correlation = .97

Design Matrix (X)

Not good...
Efficiency = 54
(Item Effect)

Better!

Correlation = .78
Design Matrix (X)

Blocks = 40 s, Randomised SOA_{min} = 2 s
Mixed Designs (Chawla et al 1999)

- Visual stimulus = dots periodically changing in colour or motion
- Epochs of attention to: 1) motion, or 2) colour
- Events are target stimuli differing in motion or colour

- Randomised, long SOAs between events (targets) to decorrelate epoch and event-related covariates

- Attention modulates BOTH:
  - 1) baseline activity (state-effect, additive)
  - 2) evoked response (item-effect, multiplicative)
V5 Motion change under attention to motion (red) or color (blue)

V4 Color change under attention to motion (red) or color (blue)

Mixed Designs (Chawla et al 1999)