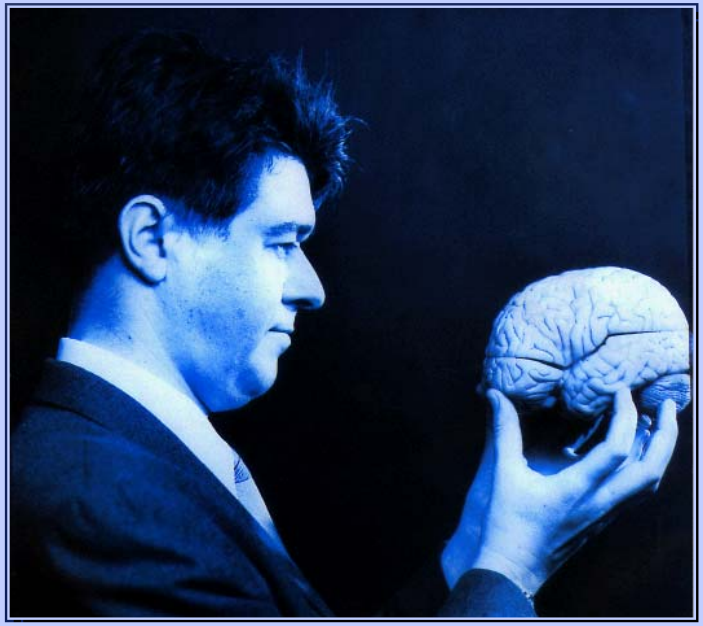
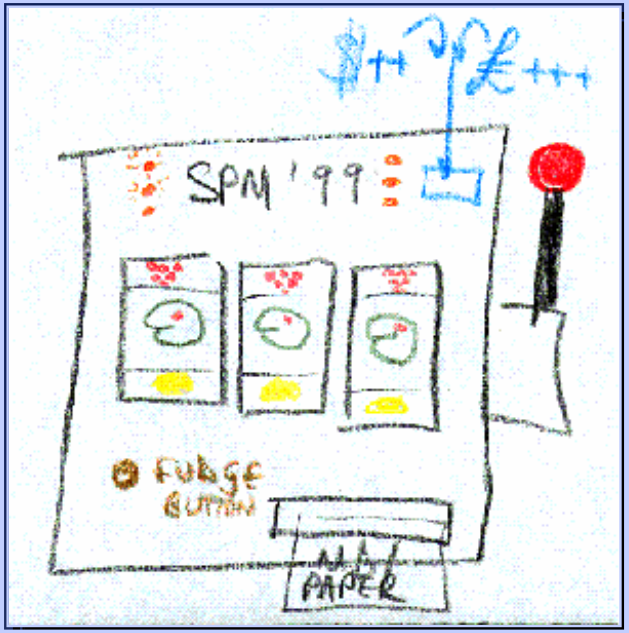
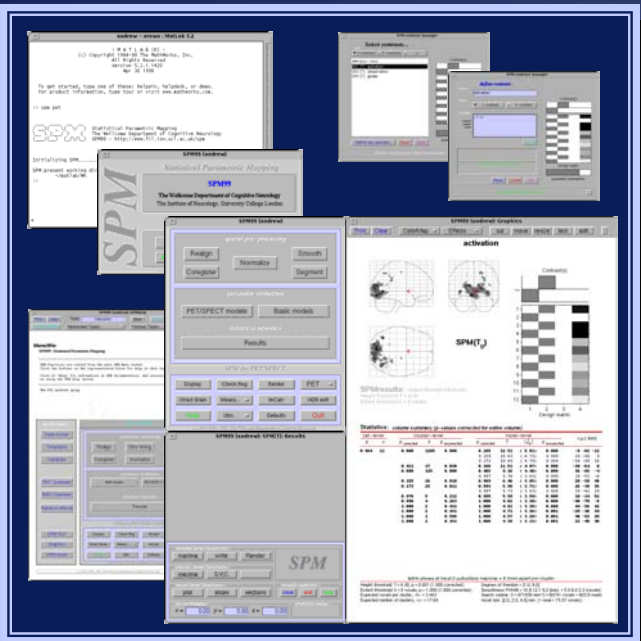
Experimental Design

Rik Henson

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

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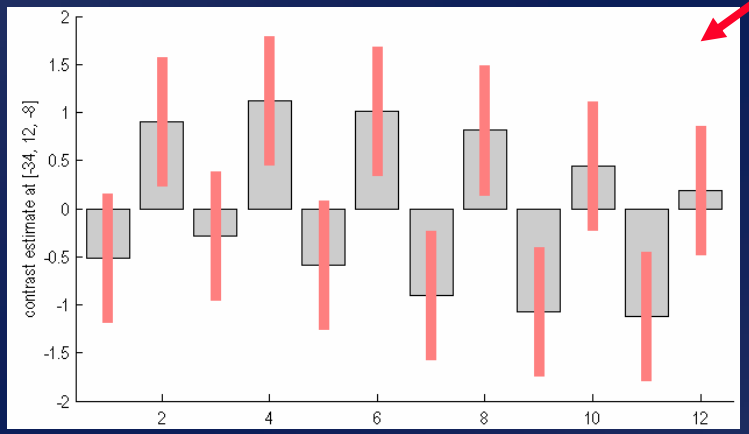
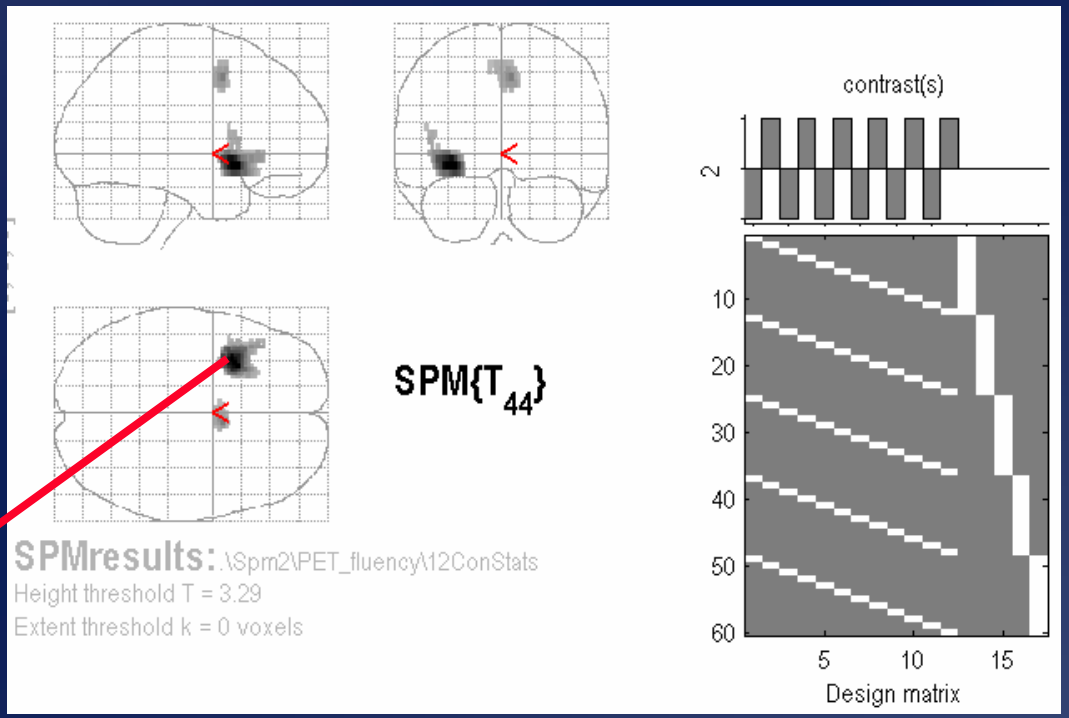
A categorical analysis

Experimental design

Word generation G
Word repetition R

R G R G R G R G R G R G





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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Cognitive Conjunctions

- One way to minimise problem of pure insertion is to isolate same process in several different ways (ie, 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

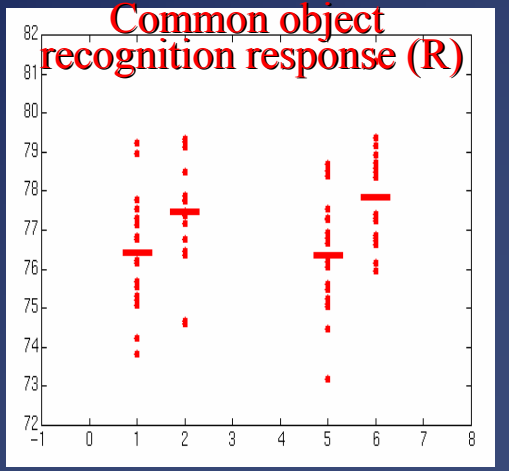
(Object - Colour viewing) [1 -1 0 0]
&
(Object - Colour naming) [0 0 1 -1]

[R,V - V] & [P,R,V - P,V] = R & R = R

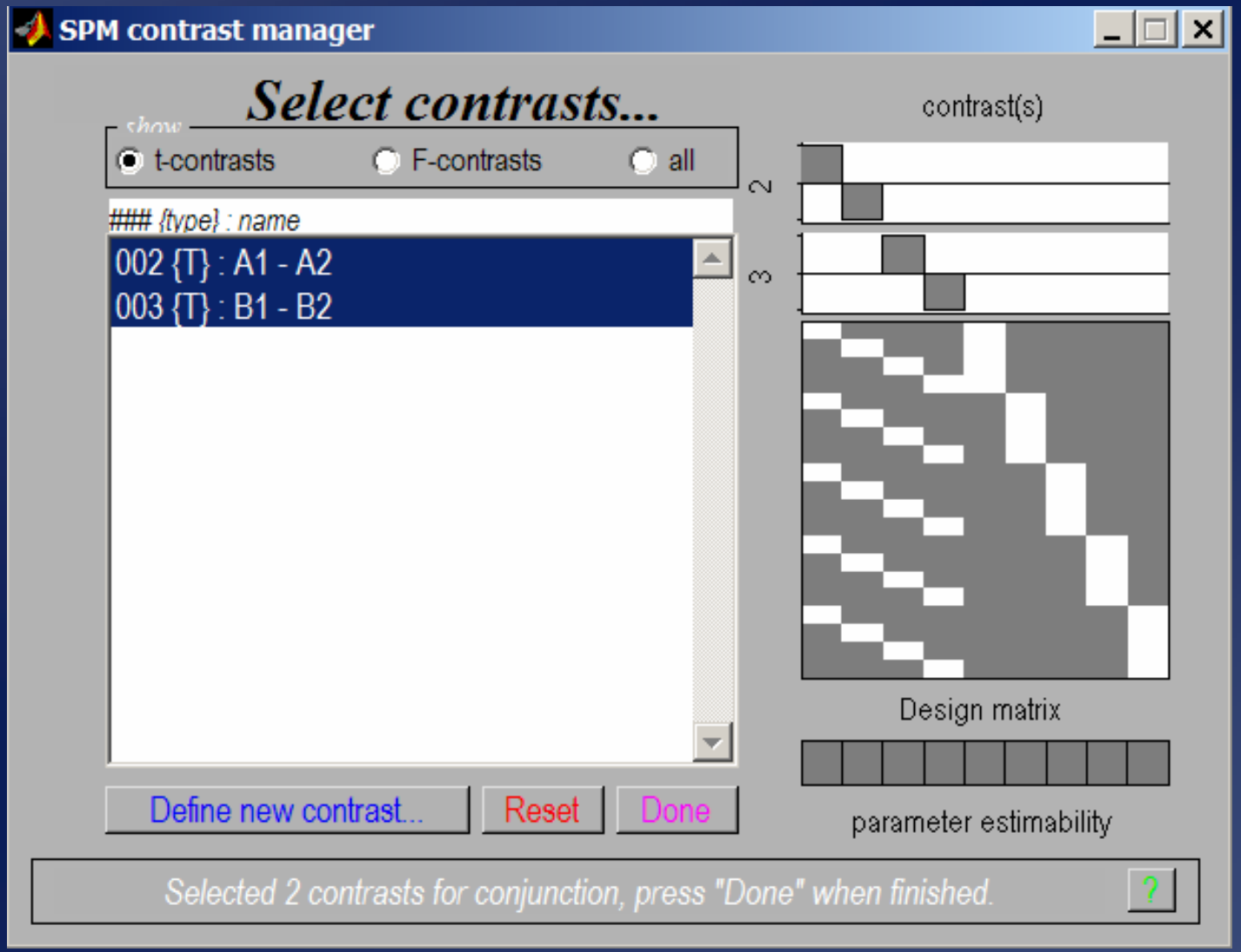
(assuming RxP = 0; see later)

Stimuli (A/B)	Task (1/2): Viewing	Task (1/2): Naming
Colours	A1	A2
Objects	B1	B2

Price et al, 1997

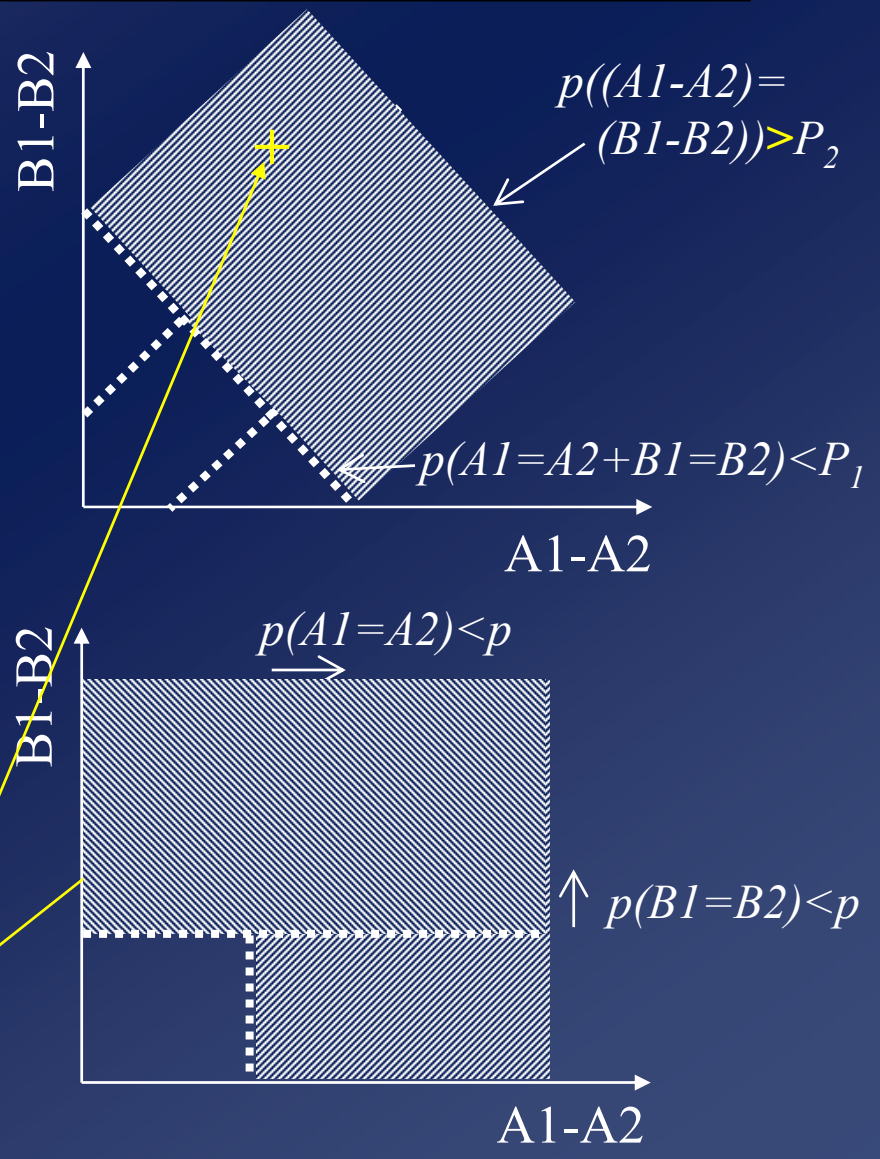


Cognitive Conjunctions



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)**
- **Ie, "effects significant and of similar size"**
- **(Difference between conjunctions and masking is that conjunction p-values reflect the conjoint probabilities of the contrasts)**
- **SPM2 defintion 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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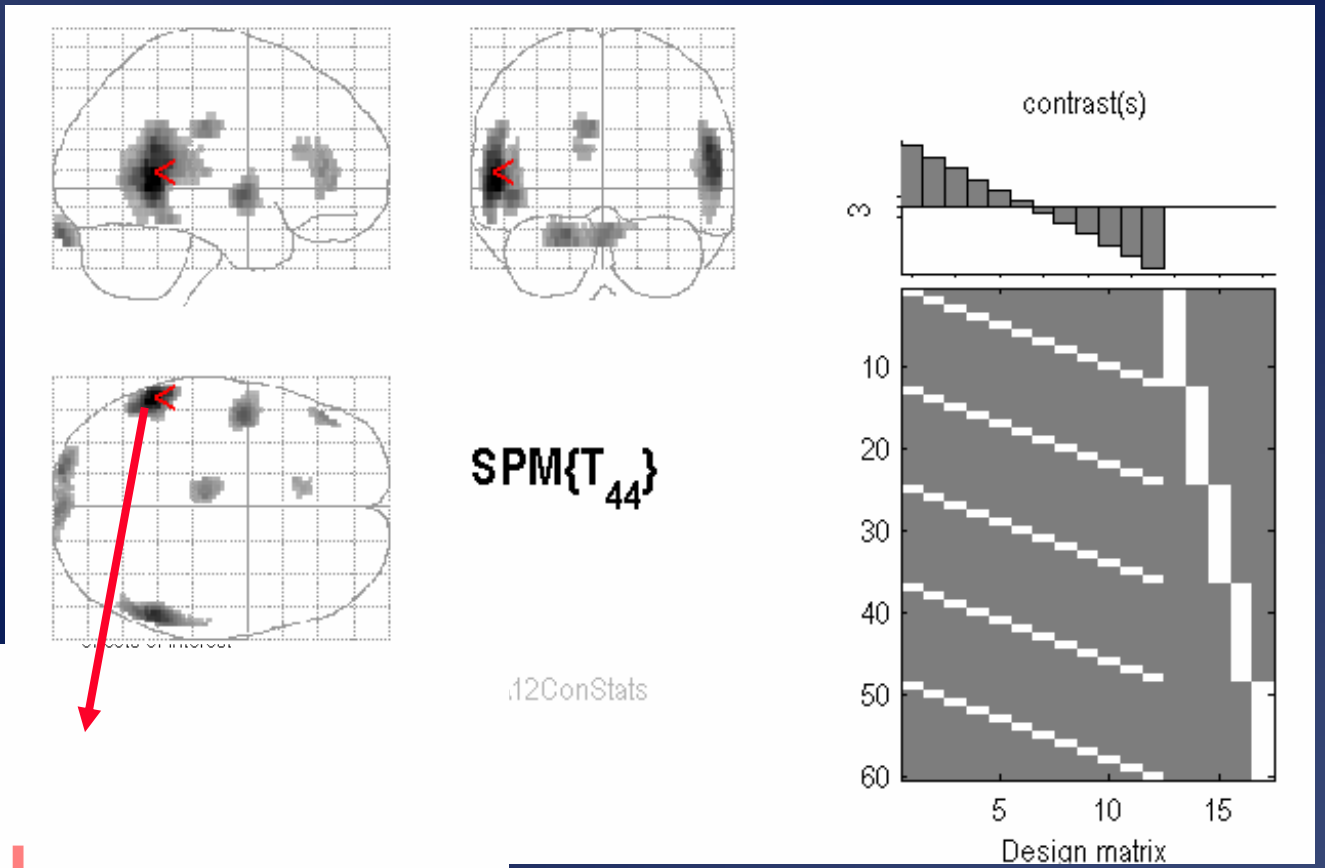
A (linear) parametric contrast

Linear effect of time



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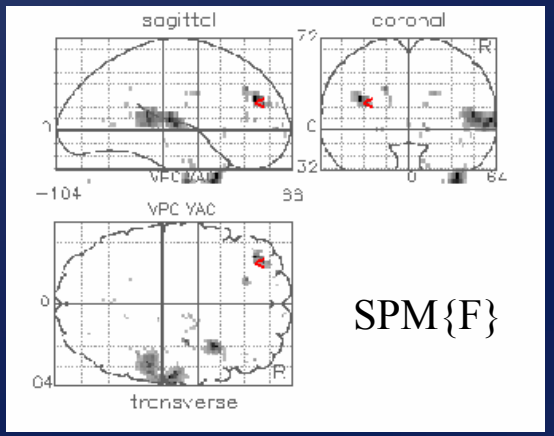
Nonlinear parametric design matrix

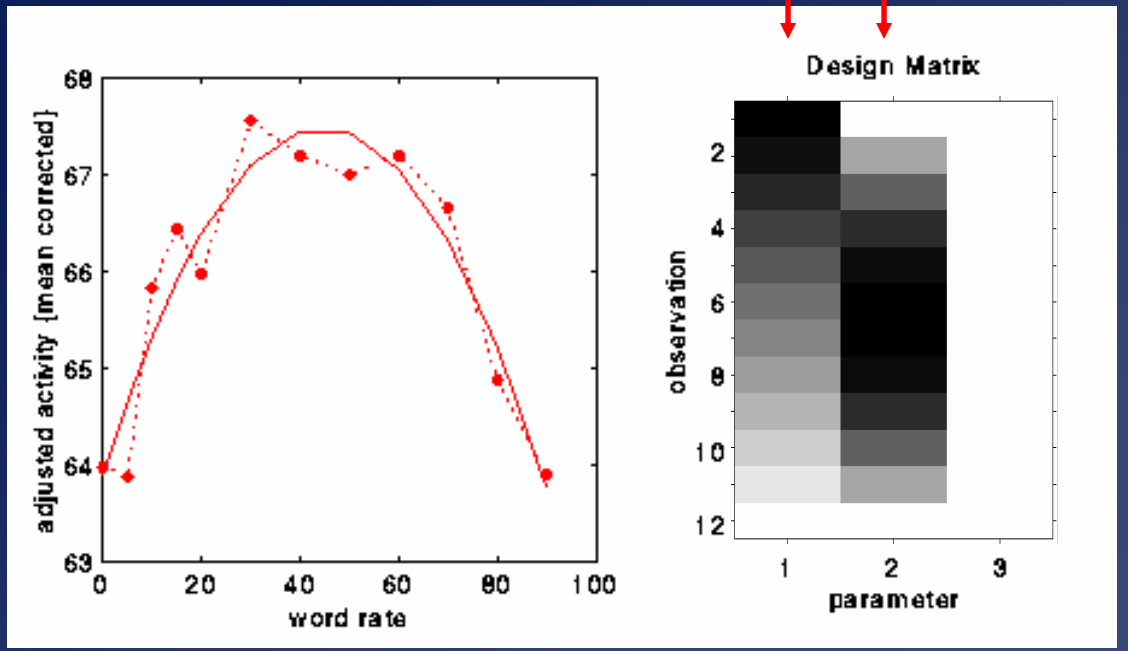
E.g, F-contrast [0 1 0] on Quadratic Parameter =>

Inverted 'U' response to increasing word presentation rate in the DLPFC



Linear

Quadratic



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)…**

Visual Processing	V
Object Recognition	R
Phonological Retrieval	P
Object viewing	R,V
Colour viewing	V
Object naming	P,R,V,RxP
Colour naming	P,V

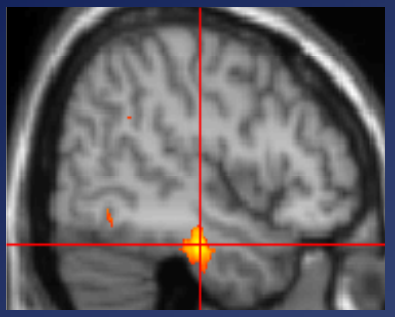
Task (1/2)

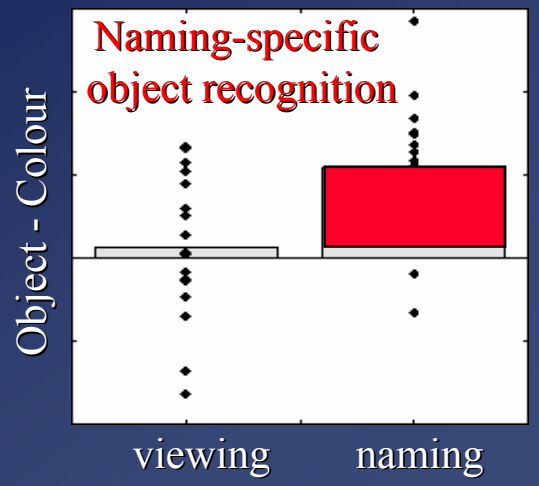
Stimuli (A/B)	Viewing	Naming
Objects	A1	A2
Colours	B1	B2

(Object – Colour) x (Viewing – Naming)

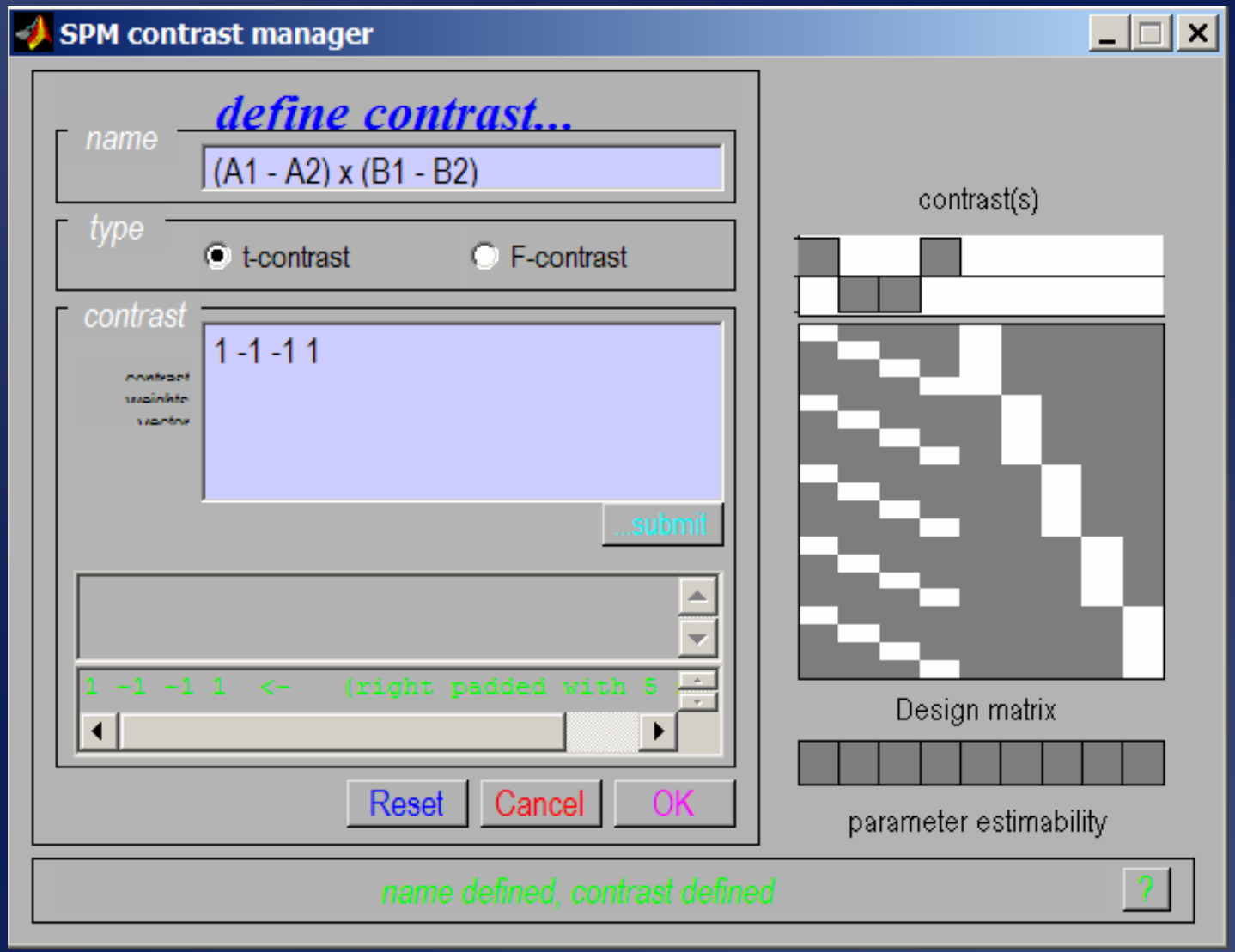
[1 -1 0 0] - [0 0 1 -1] = [1 -1] ⊗ [1 -1] = [1 -1 -1 1]

[R,V - V] - [P,R,V,RxP - P,V] = R – R,RxP = RxP





Interactions and pure insertion



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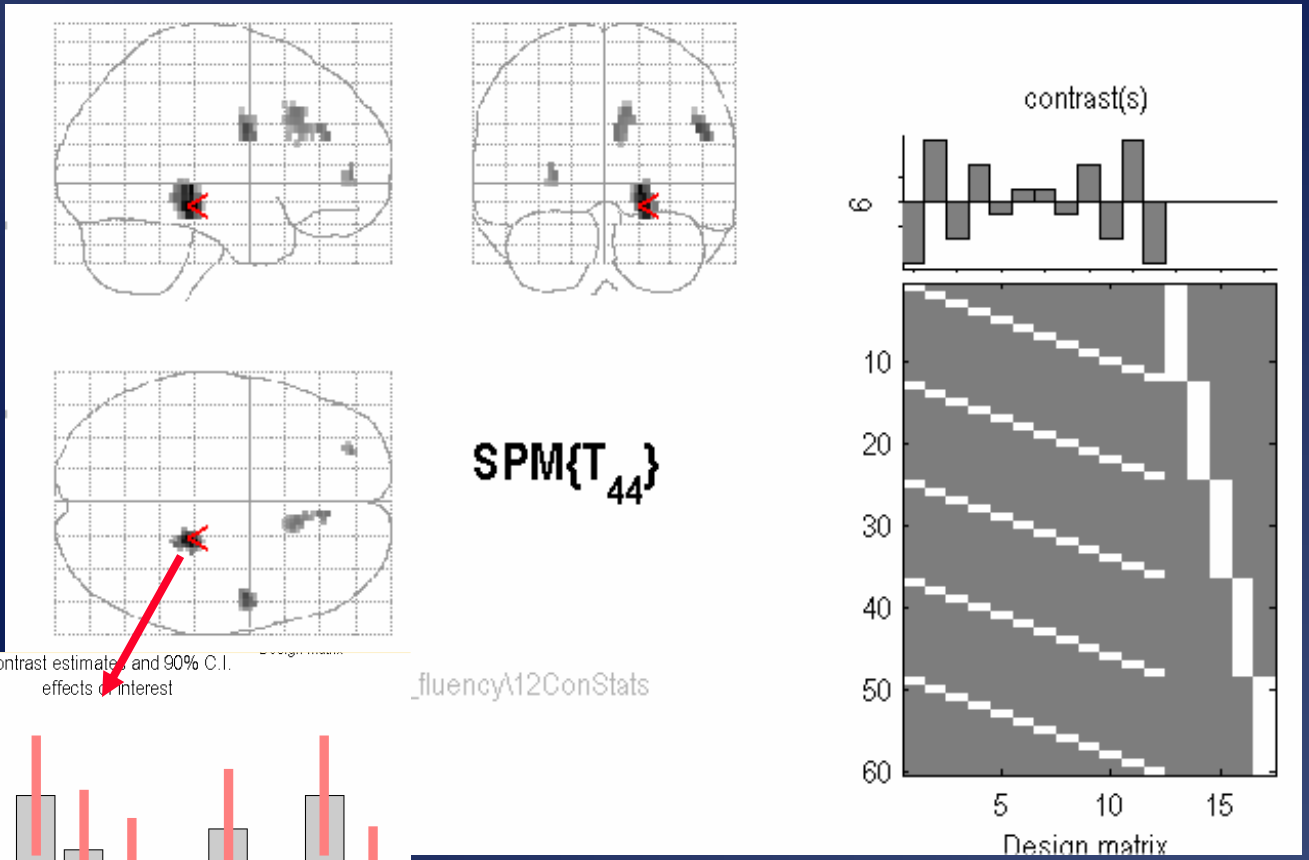
(Linear) Parametric Interaction

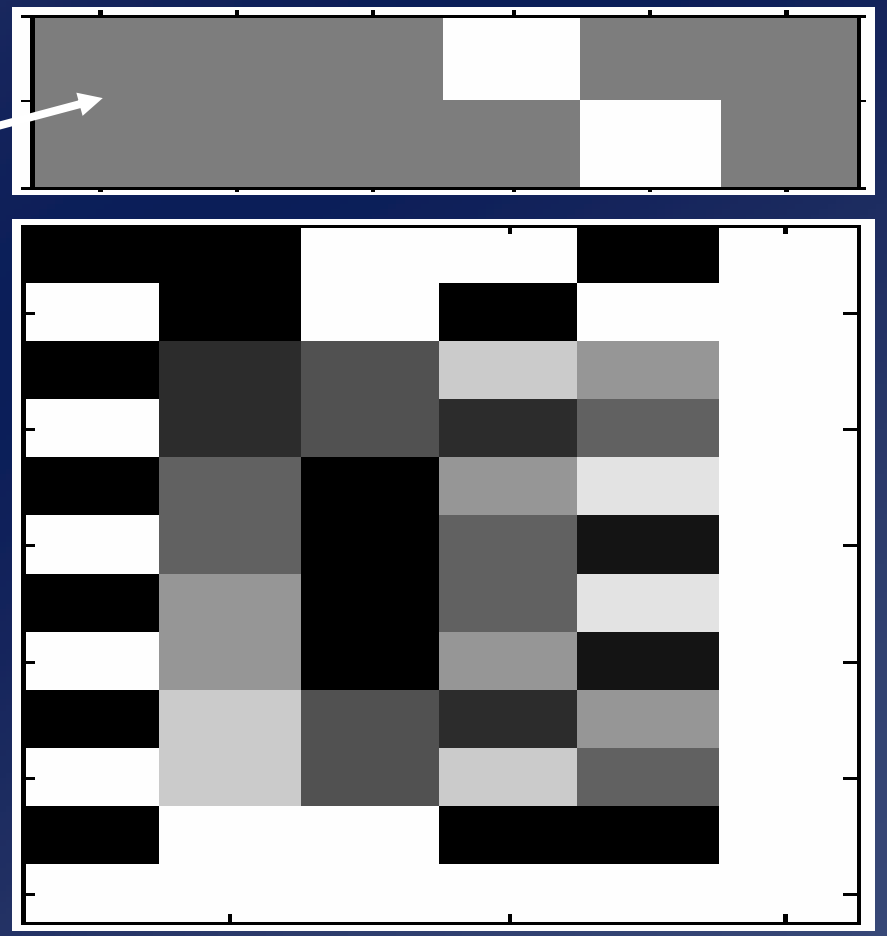
A (Linear)
Time-by-Condition
Interaction
("Generation strategy"?)



Contrast: [5 3 1 -1 -3 -5] ⊗ [-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…

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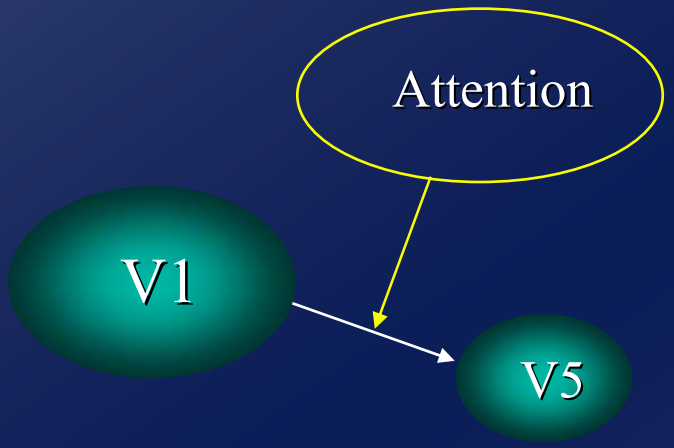
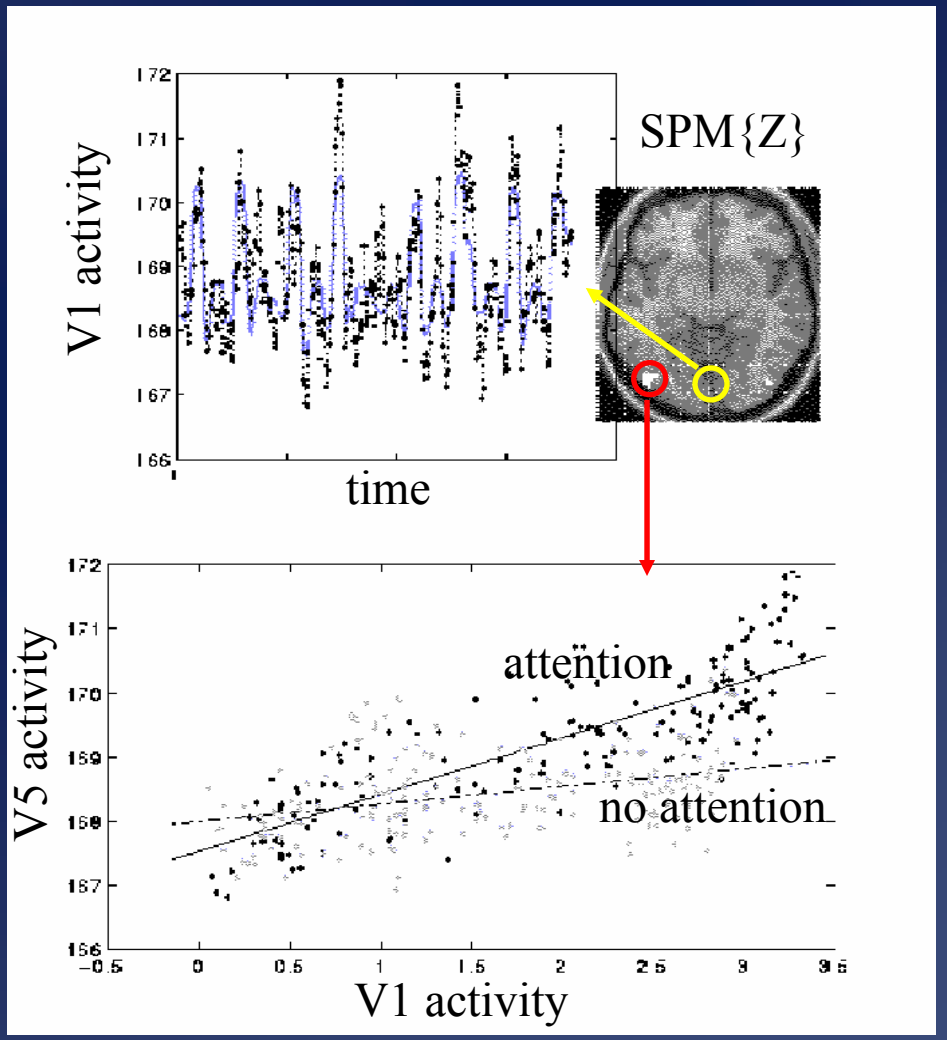
Psycho-physiological Interaction (PPI)

Parametric, factorial design, in which one factor is psychological (eg attention)

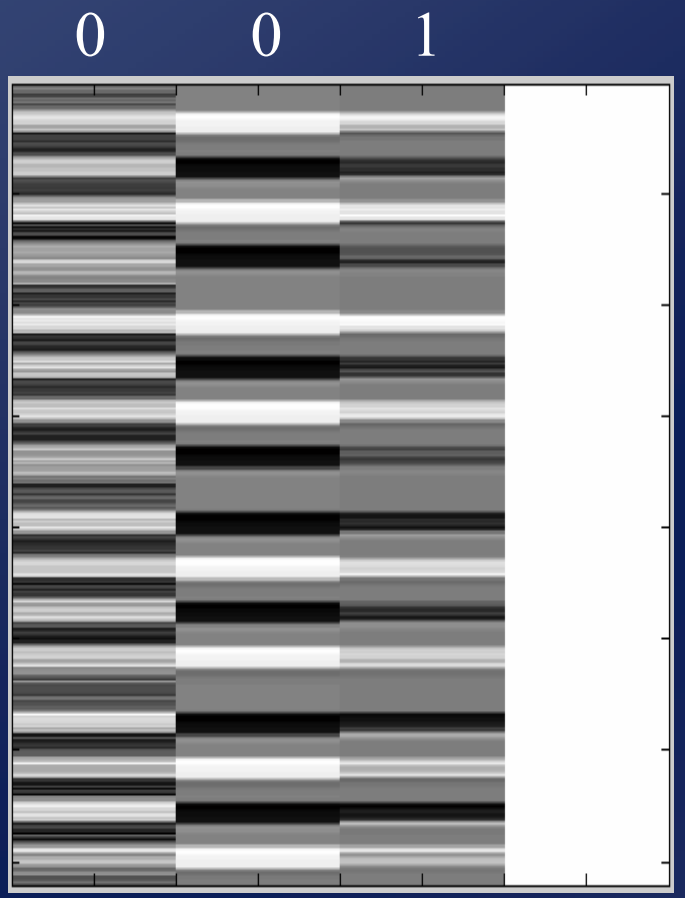
...and other is physiological *(viz. activity extracted from a brain region of interest)*

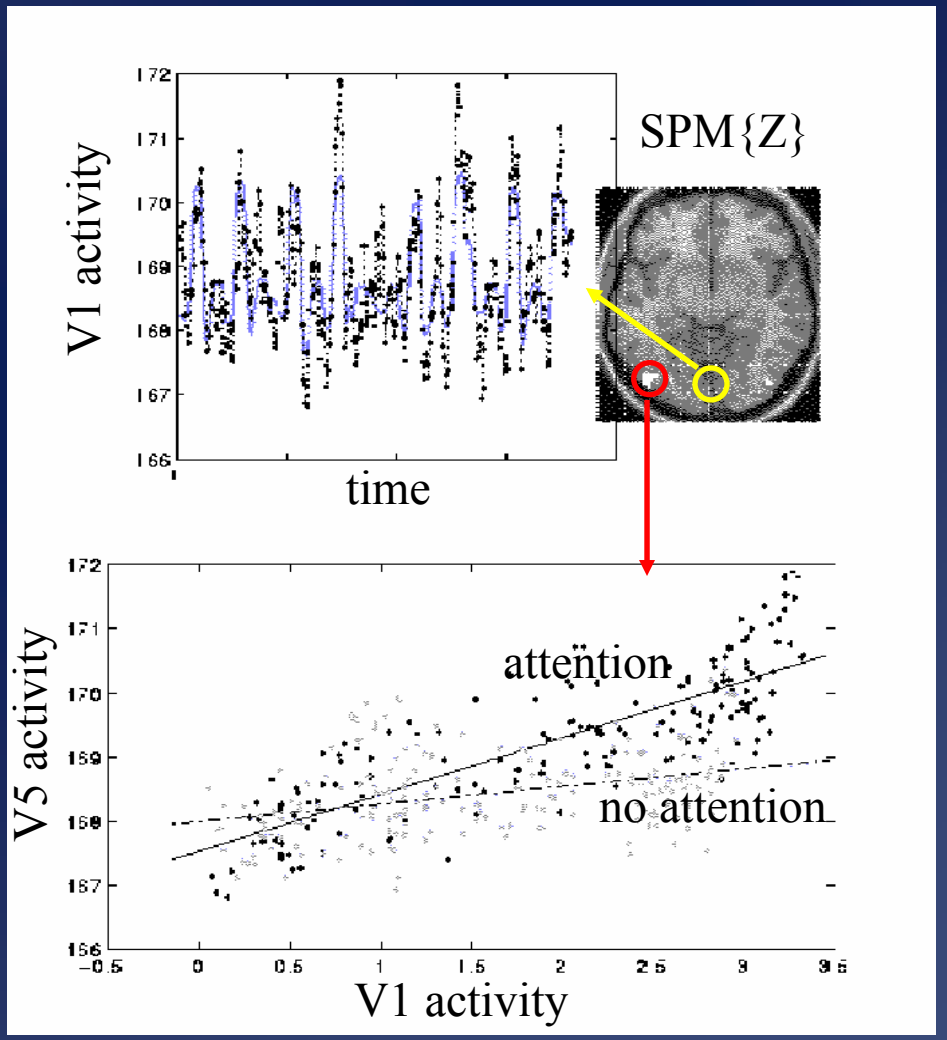


Attentional modulation of V1 - V5 contribution



Psycho-physiological Interaction (PPI)





Psycho-physiological Interaction (PPI)

- PPIs tested by a GLM with form:

$$\mathbf{y} = (\mathbf{V1}\times\mathbf{A}).\beta_1 + \mathbf{V1}.\beta_2 + \mathbf{A}.\beta_3 + \varepsilon \qquad \mathbf{c} = [1\ 0\ 0]$$

- However, the interaction term of interest, **V1×A**, is the product of V1 activity and Attention block AFTER convolution with HRF
- We are really interested in interaction at neural level, but:

$$(\mathrm{HRF} \otimes \mathrm{V1}) \times (\mathrm{HRF} \otimes \mathrm{A}) \quad \neq \quad \mathrm{HRF} \otimes (\mathrm{V1} \times \mathbf{A})$$

(unless A low frequency, eg, 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

2. Epoch vs Event-related

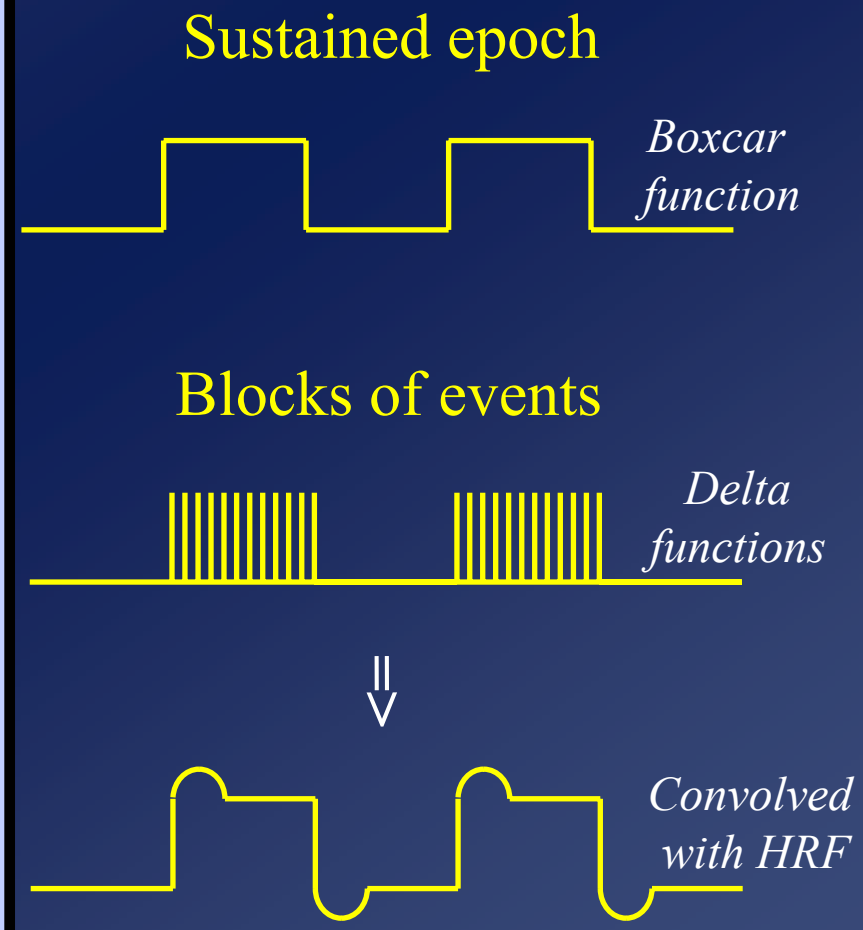
3. Mixed Epoch/Event Designs

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 (eg, in choice of basis functions)
- In SPM2, all conditions are specified in terms of their 1) onsets and 2) durations…

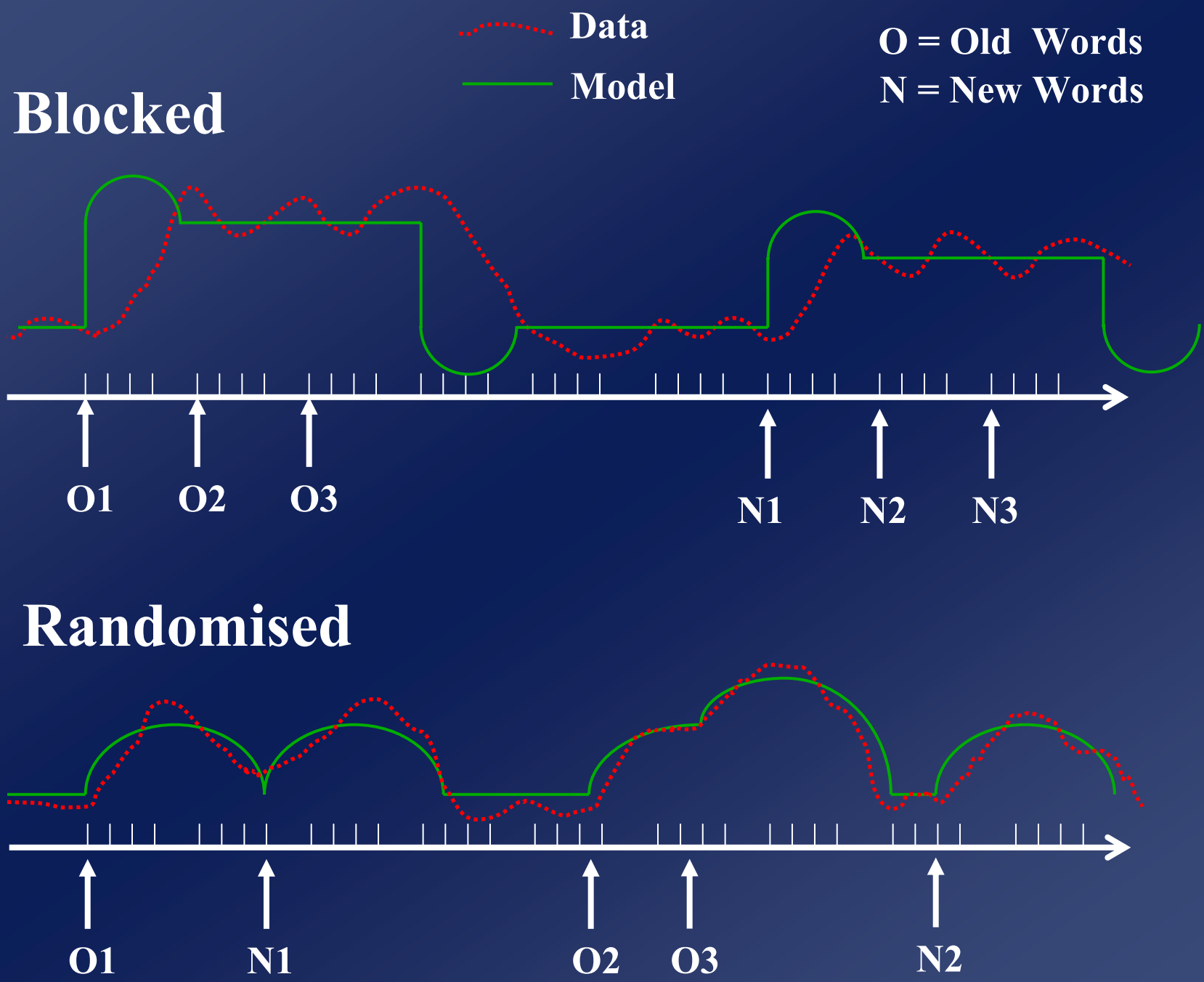
  … events simply have zero duration

- 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



Advantages of Event-related fMRI

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


Data
Model
O = Old Words
N = New Words
Blocked
O1
O2
O3
N1
N2
N3
Randomised
O1
N1
O2
O3
N2

Advantages of Event-related fMRI

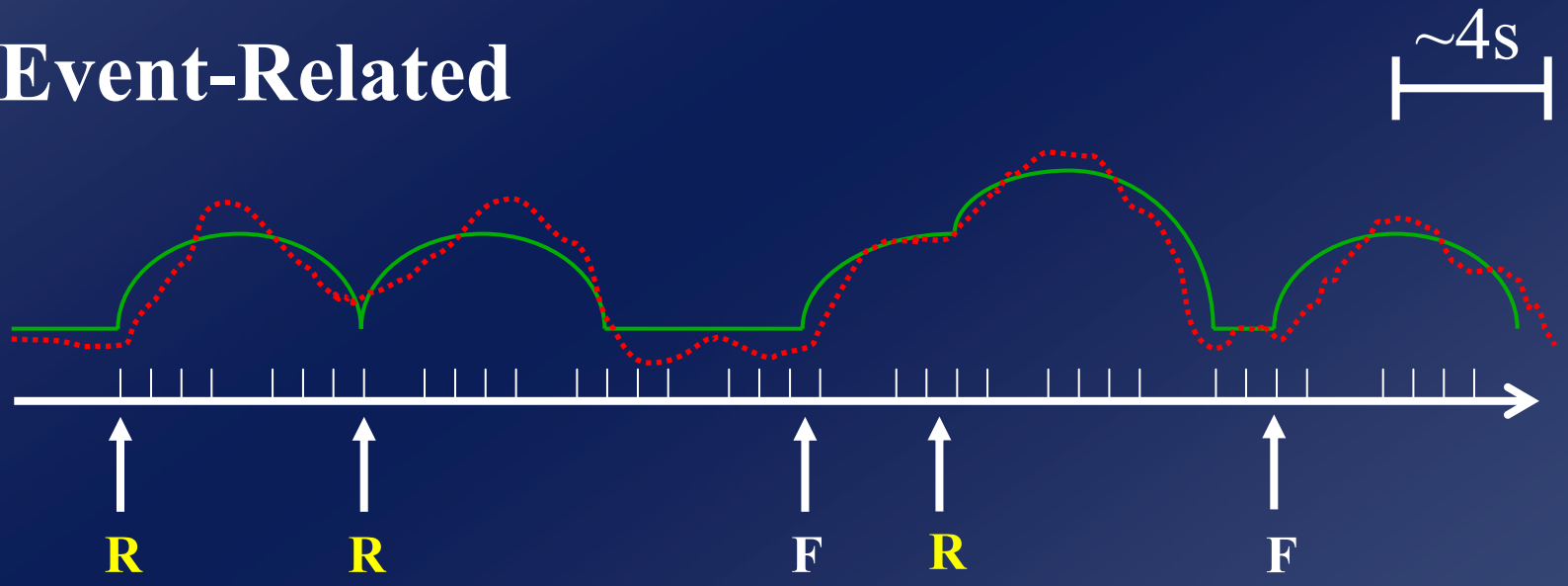
1. Randomised (intermixed) trial order
   c.f. confounds of blocked designs (Johnson et al 1997)

2. Post hoc / subjective classification of trials
   e.g, according to subsequent memory (Wagner et al 1998)

R = Words Later Remembered

F = Words Later Forgotten

Event-Related



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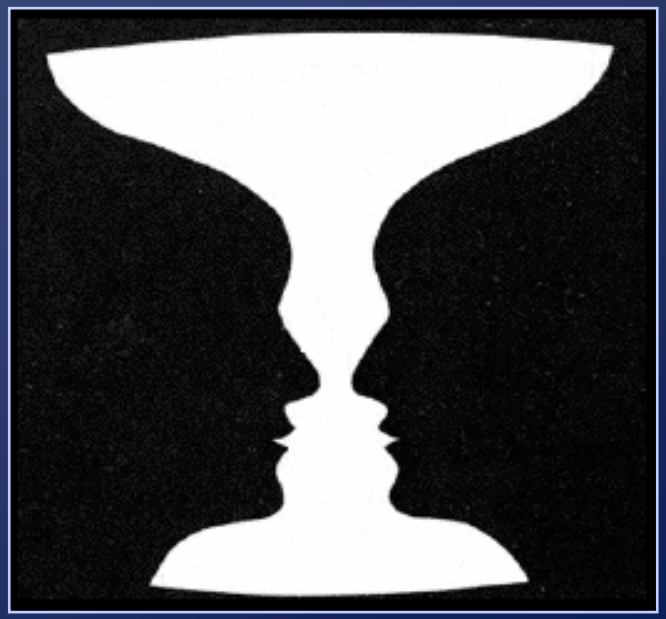
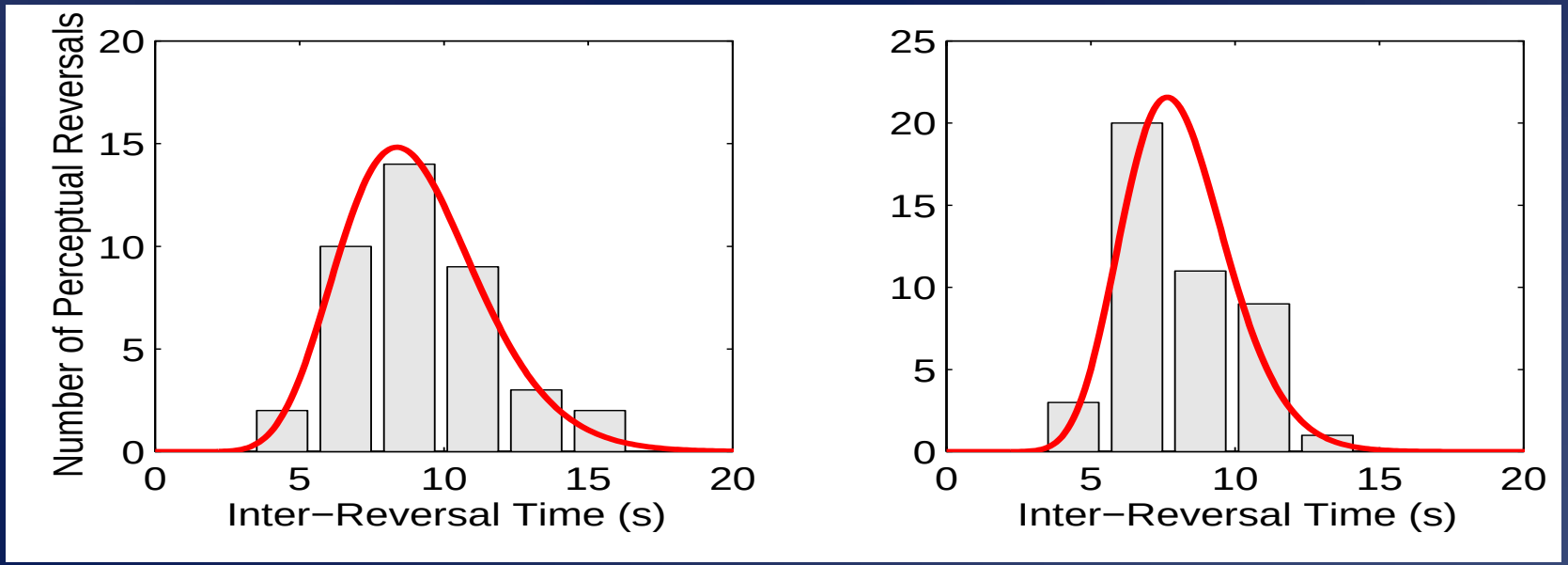
3. Some events can only be indicated by subject (in time)
   e.g, spontaneous perceptual changes (Kleinschmidt et al 1998)




Number of Perceptual Reversals
0
5
10
15
20
Inter−Reversal Time (s)
0
5
10
15
20
25
Inter−Reversal Time (s)

Advantages of Event-related fMRI

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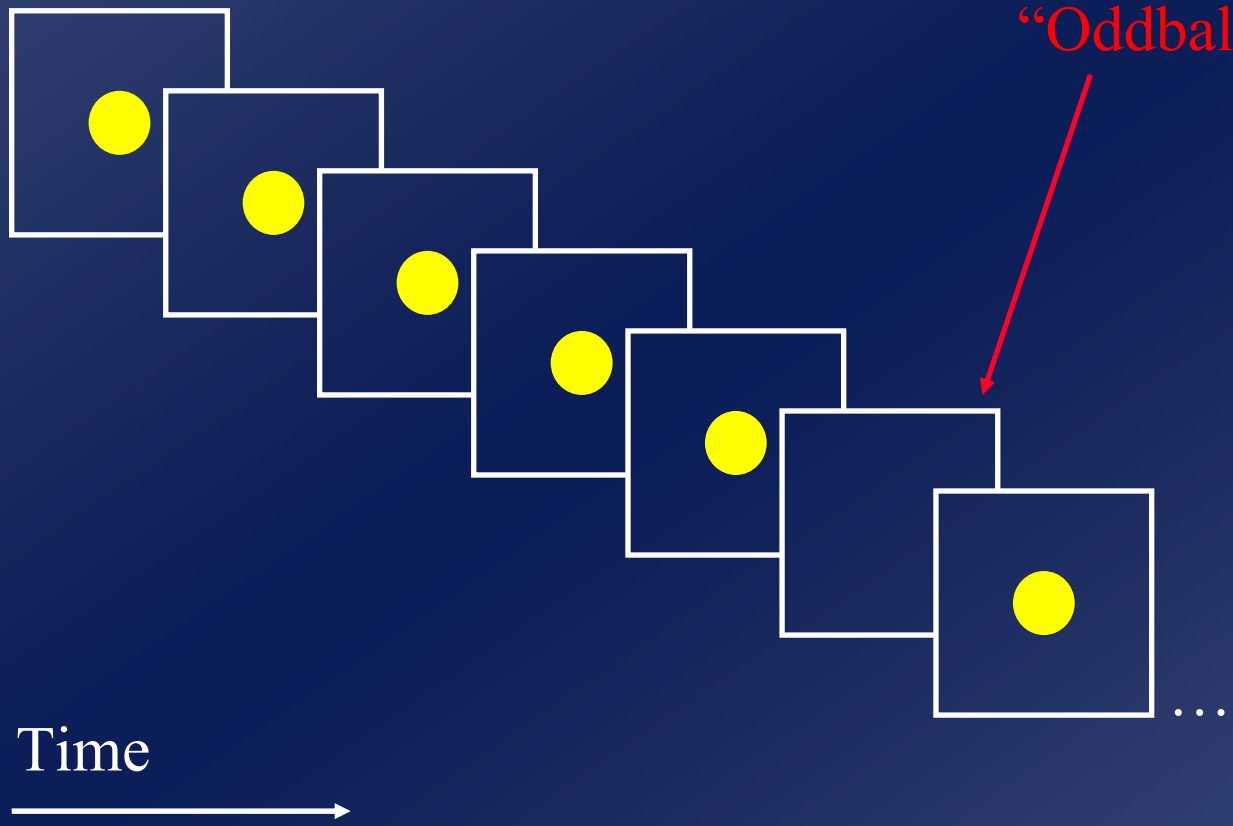
   c.f. confounds of blocked designs (Johnson et al 1997)

2. Post hoc / subjective classification of trials
   e.g, according to subsequent memory (Wagner et al 1998)

3. Some events can only be indicated by subject (in time)
   e.g, spontaneous perceptual changes (Kleinschmidt et al 1998)

4. Some trials cannot be blocked
   e.g, "oddball" designs (Clark et al., 2000)


"Oddball"
...
Time

Advantages of Event-related fMRI

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

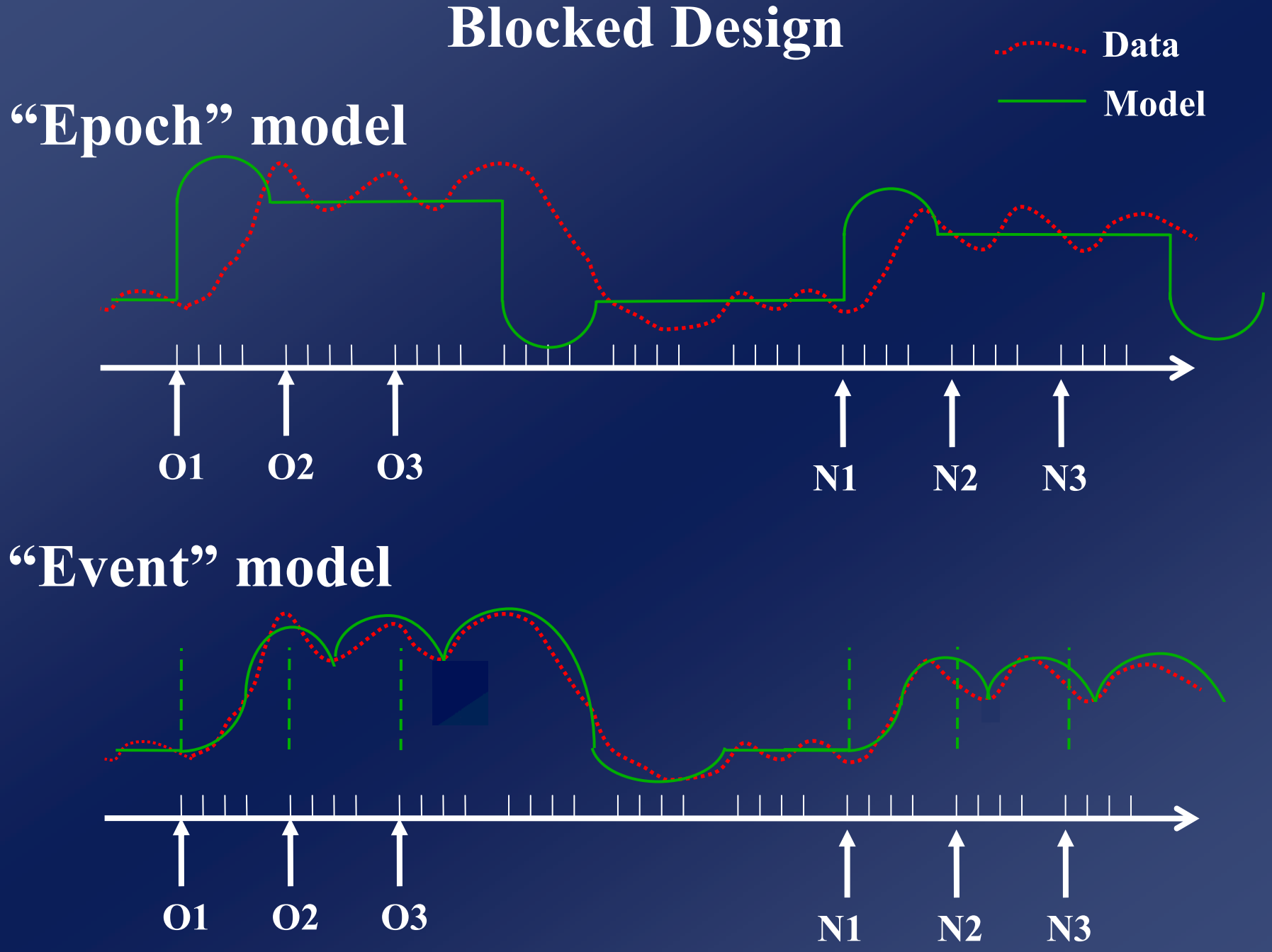
2. Post hoc / subjective classification of trials
   e.g, according to subsequent memory (Wagner et al 1998)

3. Some events can only be indicated by subject (in time)
   e.g, spontaneous perceptual changes (Kleinschmidt et al 1998)

4. Some trials cannot be blocked
   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

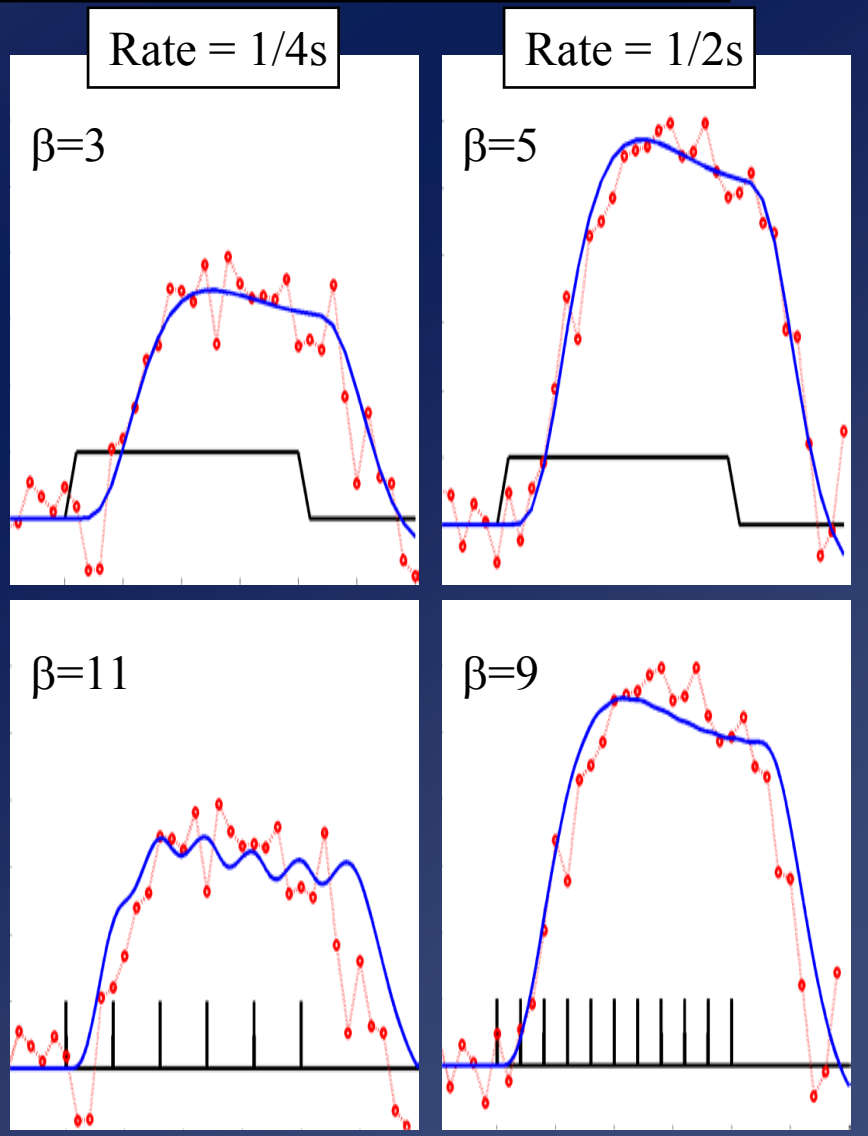


Epoch vs Events

- 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
   (eg task-switching, attentional instructions)

Overview

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Mixed Designs

- 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):**

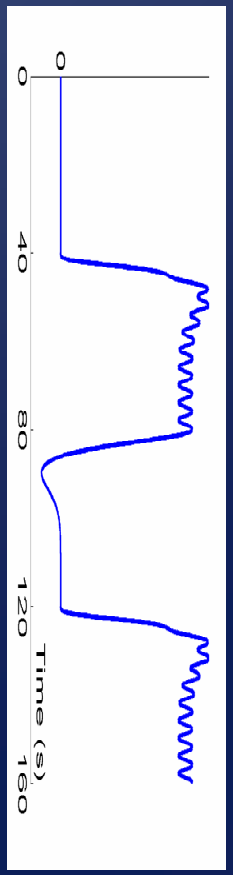
$$e(c,X) = \{ c^T (X^T X)^{-1} c \}^{-1}$$

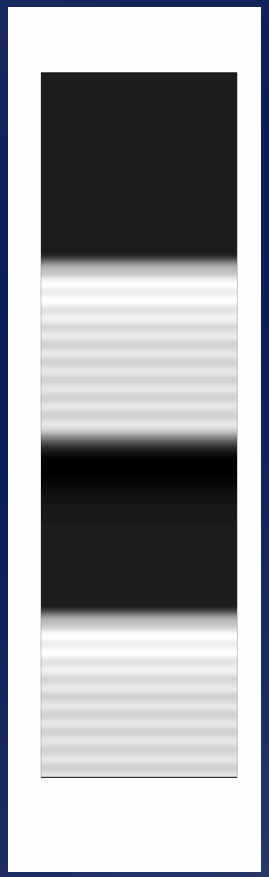
- **$X^T X$ represents covariance of regressors in design matrix**
- **High covariance increases elements of $(X^T X)^{-1}$**

=> So, when correlation between regressors is high, sensitivity to each regressor alone is low

Item effect only…

Blocks = 40s, Fixed SOA = 4s





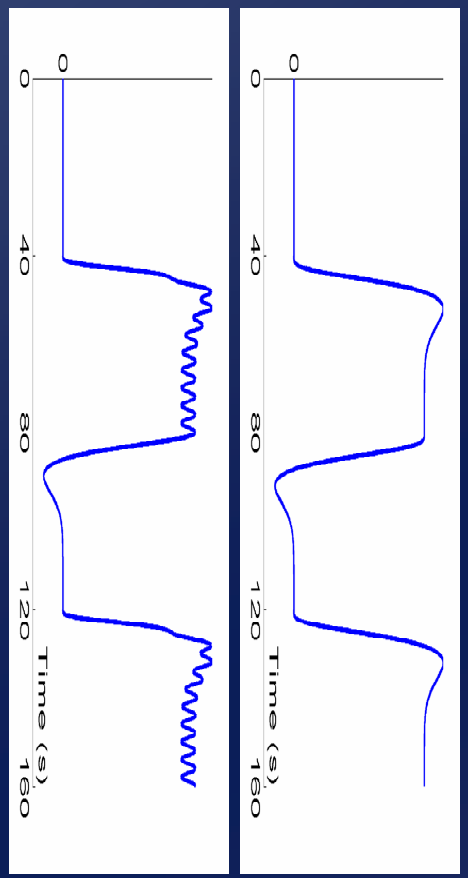
Design Matrix (X)

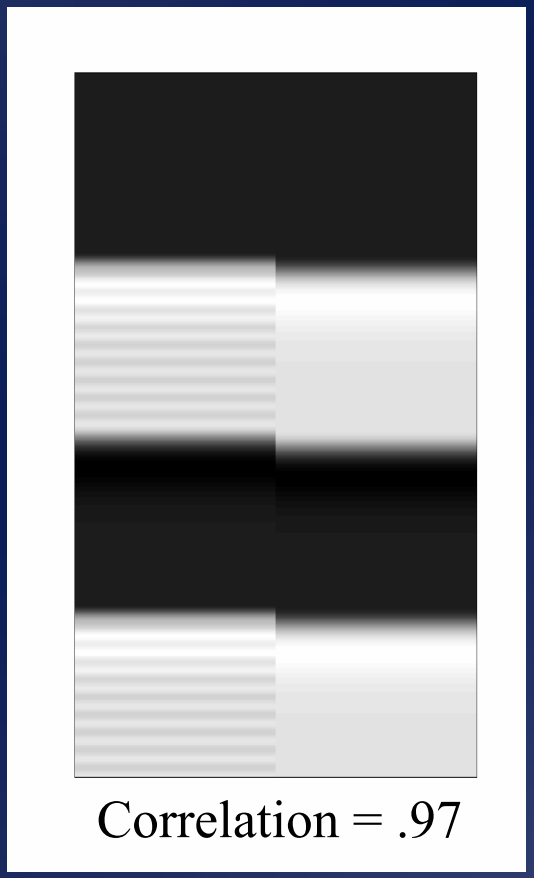
Efficiency = 565
(Item Effect)

OK…

Item and State effects

Blocks = 40s, Fixed SOA = 4s





Correlation = .97

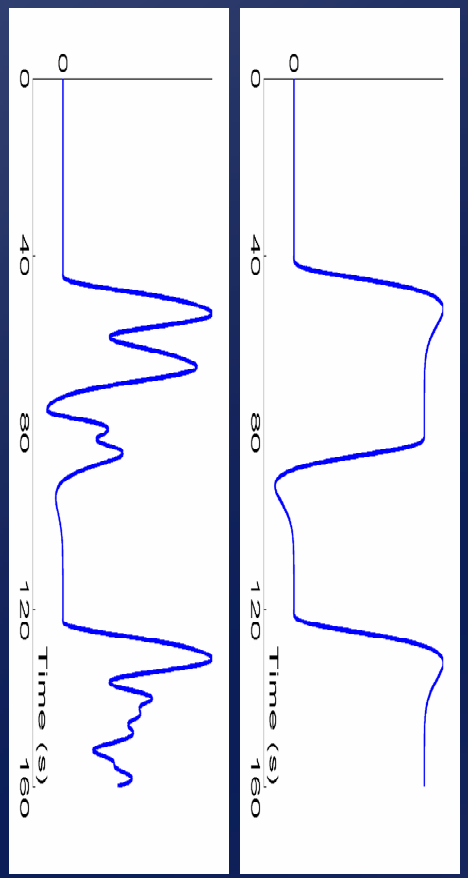
Design Matrix (X)

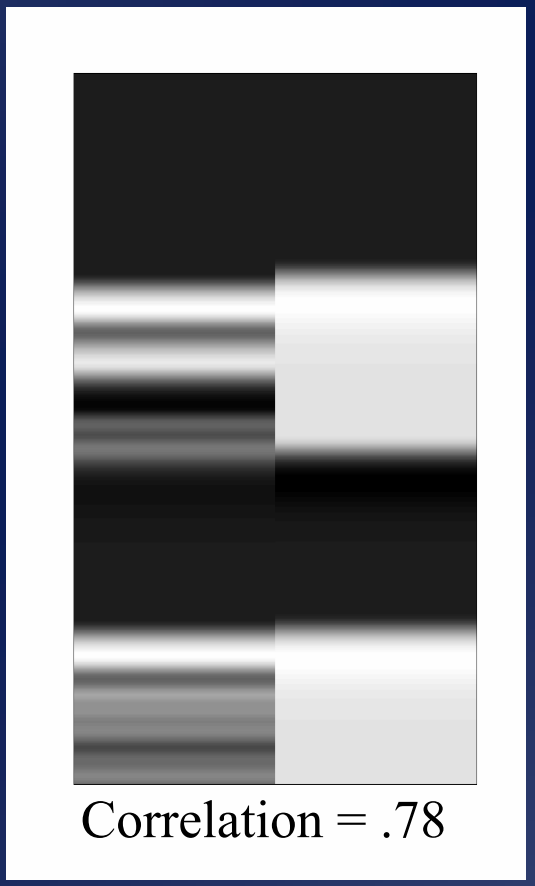
Efficiency = 16
(Item Effect)

Not good…

Item and State effects

Blocks = 40s, Randomised SOA_{min} = 2s





Correlation = .78

Design Matrix (X)

Efficiency = 54
(Item Effect)

Better!

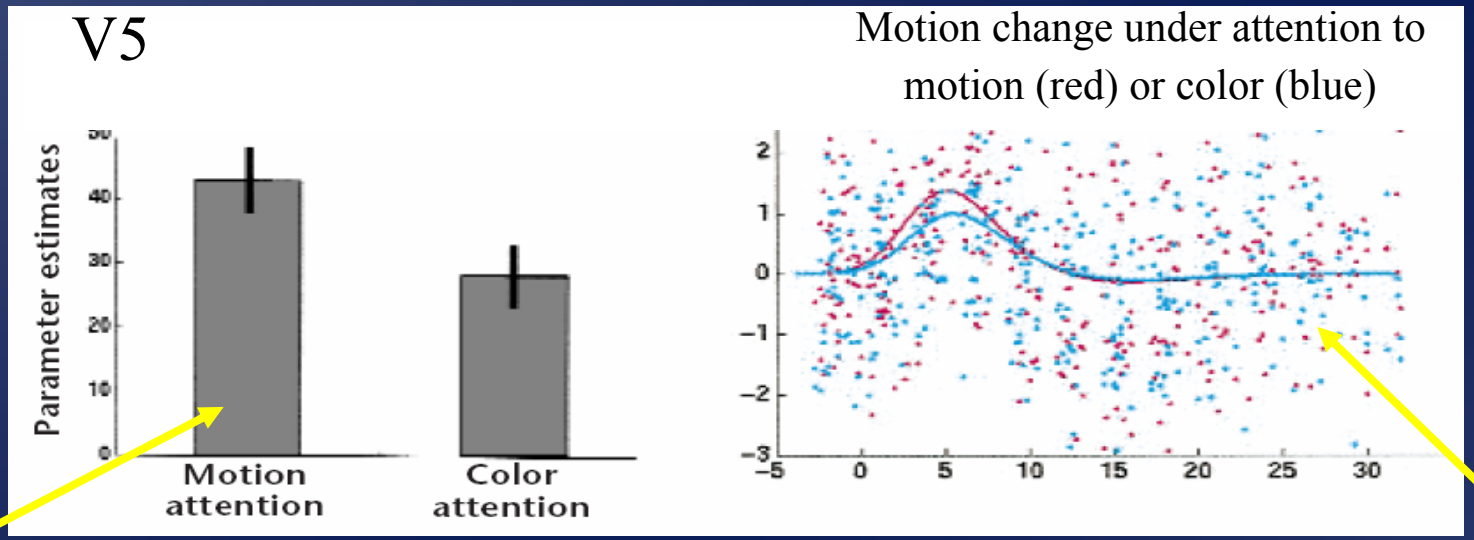
Mixed Designs (Chawla et al 1999)

- 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)

Mixed Designs (Chawla et al 1999)



State Effect (Baseline)

Item Effect (Evoked)