Experimental design for Cognitive fMRI

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Edinburgh SPM course 2017

Thanks to Rik Henson, Thomas Wolbers, Jody Culham, and the SPM authors for slides

Overview

- Categorical designs
- Factorial designs
- Conjunction designs

- Parametric designs
- fMRI adaptation

- Paradigm timing

Isolating a process

- Basic aim: neural correlates of a single process
- Assume that addition of the component process does not alter other task components

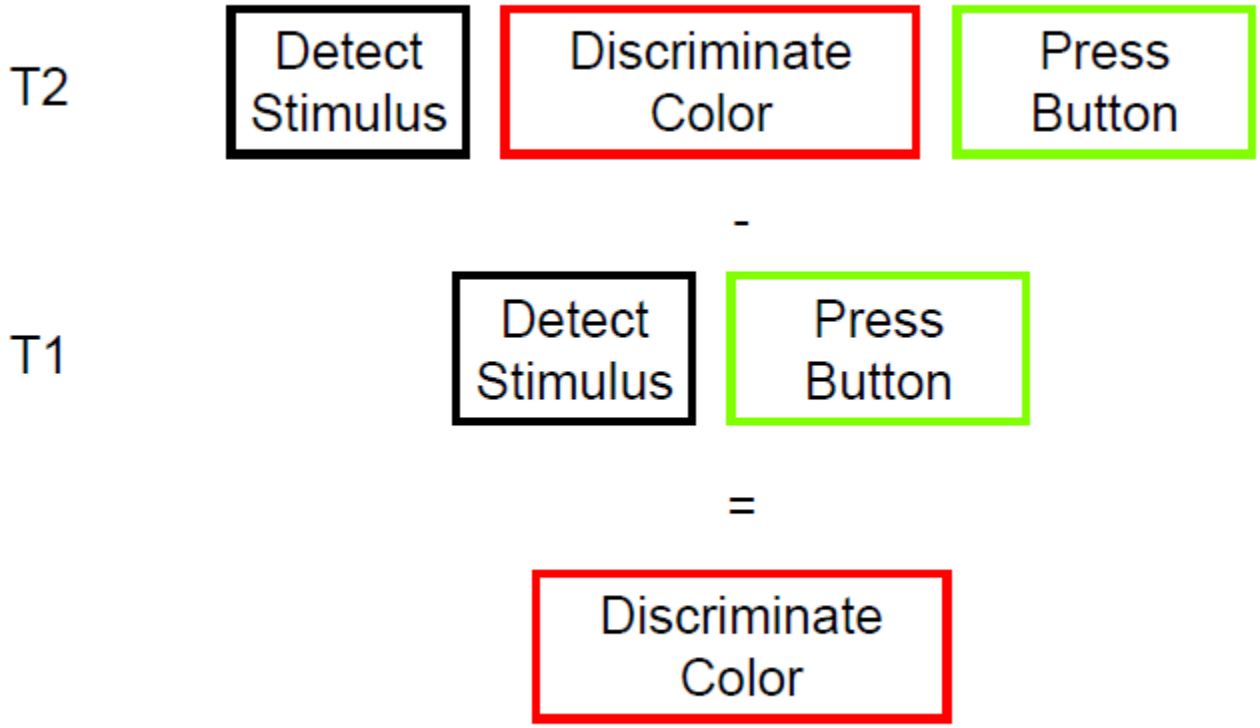
  "pure insertion"

- And: a meaningful cognitive question

Donders (1898-9)

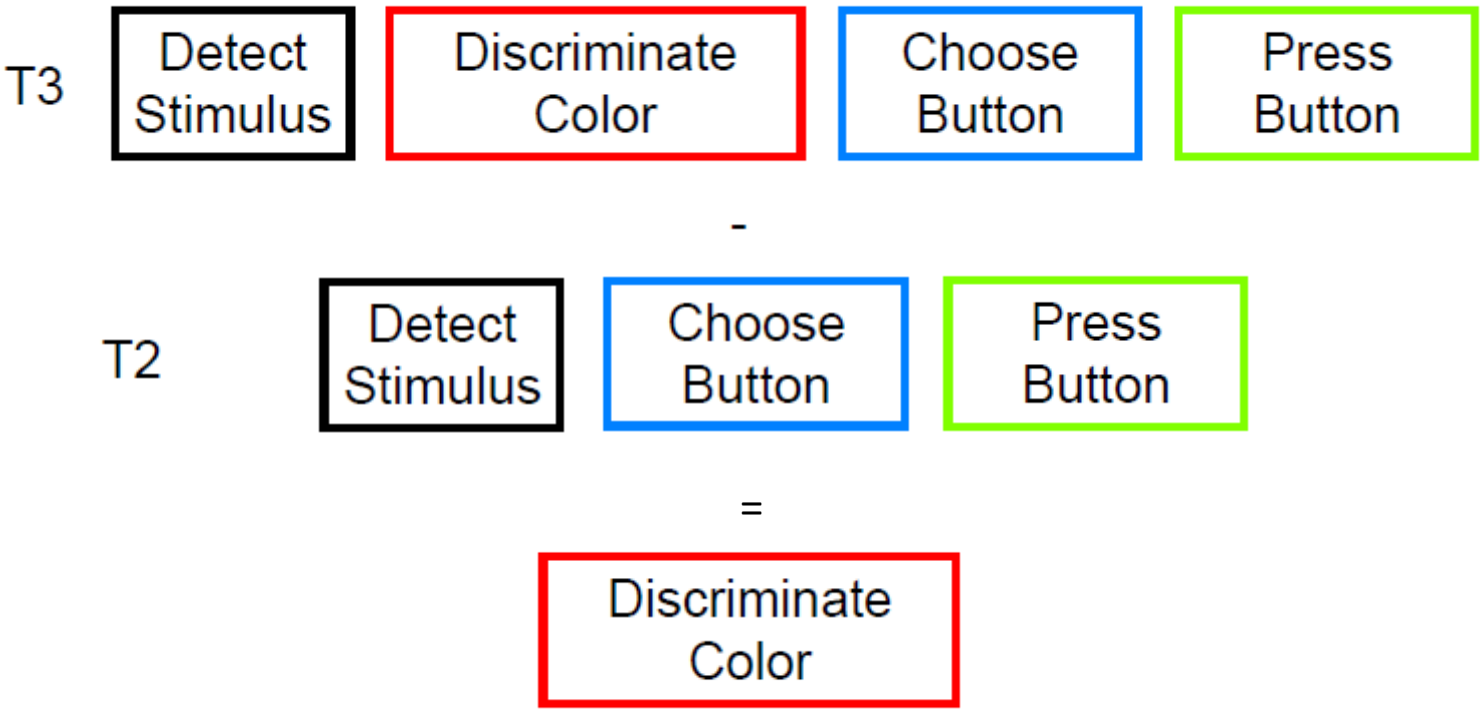
Cognitive subtraction

Use a simple reaction time task to isolate a process



Cognitive subtraction

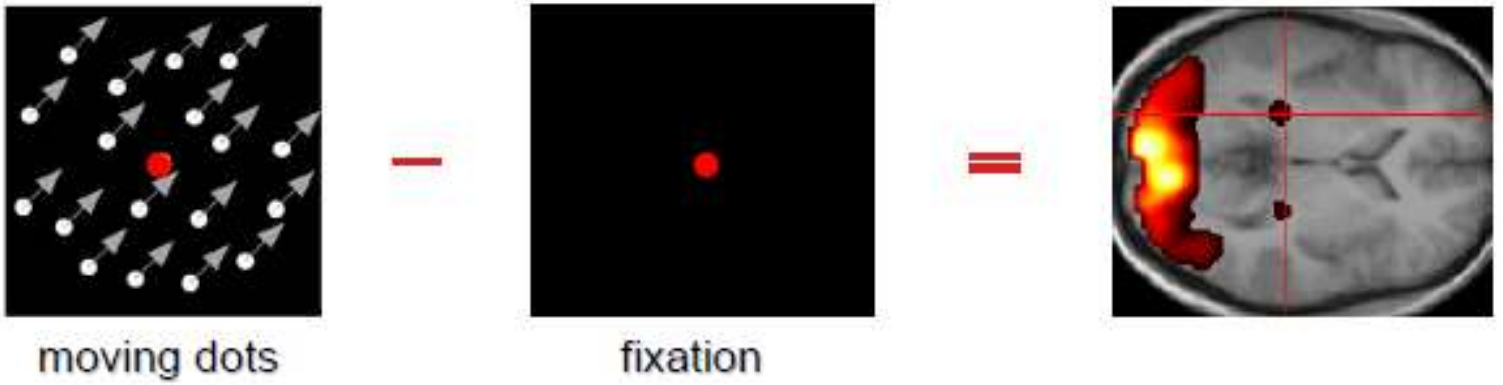
Use a choice reaction time task – get the same results



Categorical designs

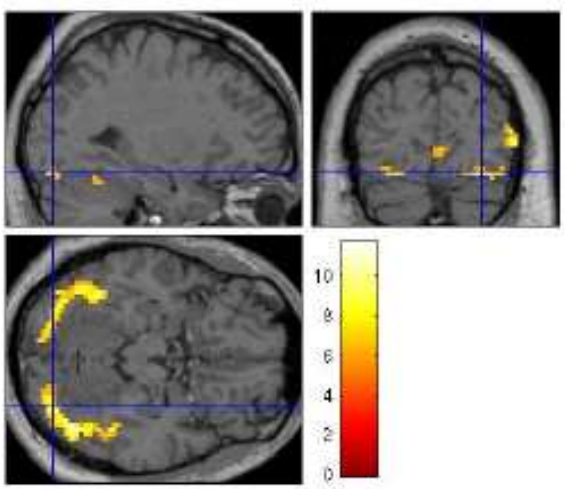
Simple subtraction

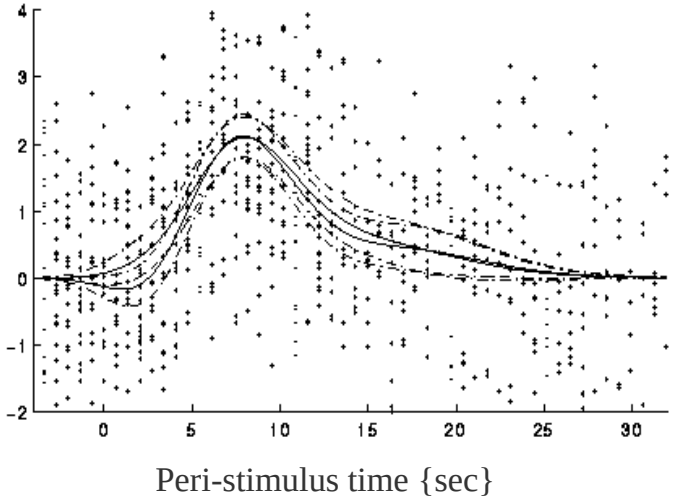
- Detect regions specialised for a function by testing for activation difference
- May also ask: do 2 tasks differ in processing?



Evoked responses

Faces vs. baseline ‘rest’





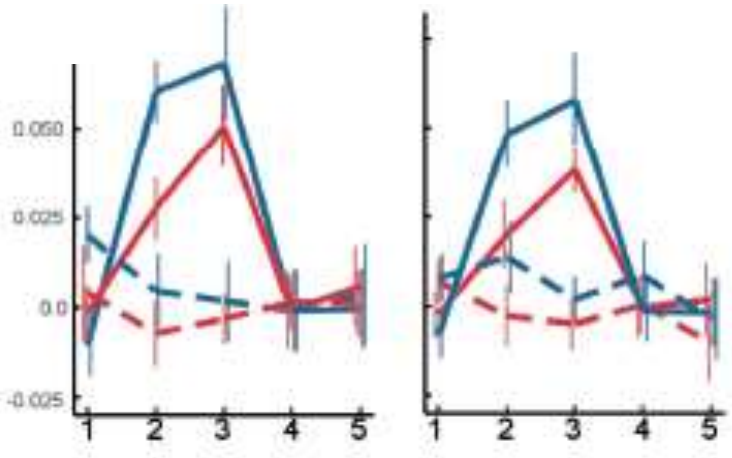
‘Null’ events or long SOAs essential for estimation of response shape

‘Implicit baseline’ in SPM = everything not specified in the model

Any baseline ok for estimation of haemodynamic response shape

But cognitive interpretation usually not possible – not a control condition

Control condition



Novel vs. Odd/Even
Familiar vs. Odd/Even

Novel vs. Rest
Familiar vs. Rest

Early “Failure to activate” the hippocampus during episodic memory tasks

Were studies of amnesia wrong?

…only if we use fixation/ rest as the baseline

→ Choice of a baseline depends on your question!

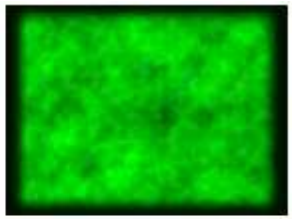
Stark & Squire (2001) PNAS

Categorical designs

Serial subtraction

- Is the inferiotemporal cortex sensitive to both object recognition and phonological retrieval of object names?

A say „yes“ when you see an abstract image
(*vis. analysis, verbal output*)



⇒ yes

B say „yes“ when you see a concrete object
(*vis. analysis, object recognition, verbal output*)

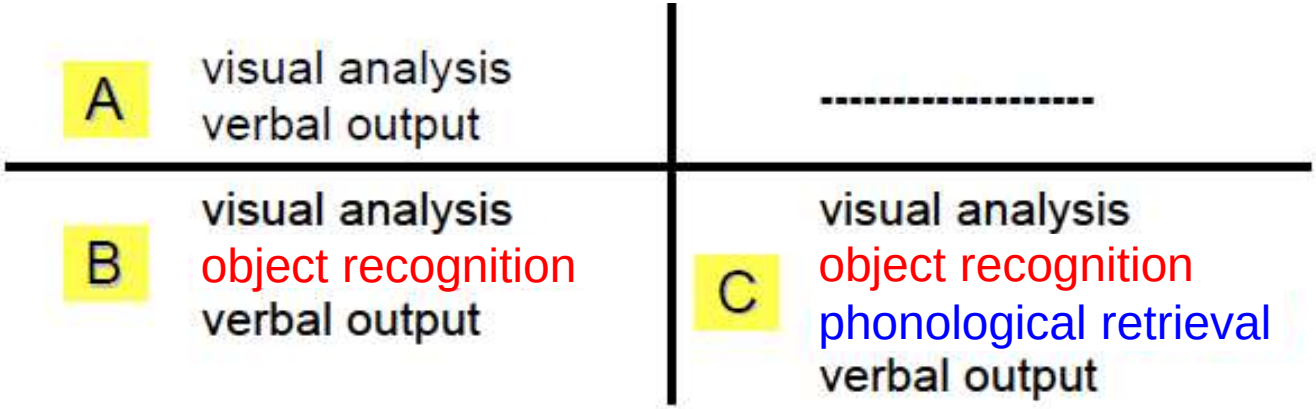
⇒ yes

C name concrete object
(*vis. analysis, object recognition, phonological retrieval, verbal output*)

⇒ butterfly

Friston et al. (1997)

Categorical designs



B - A ⇒ significant IT activation ⇒ object recognition!

C - B ⇒ no significant IT activation ⇒ no evidence for IT involvement in phonological retrieval!

Problem: unjustified assumption that IT response to object recognition is context independent!

more likely, one process modulates another

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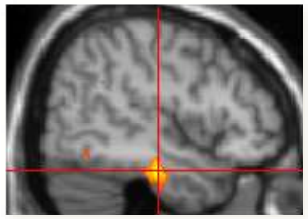
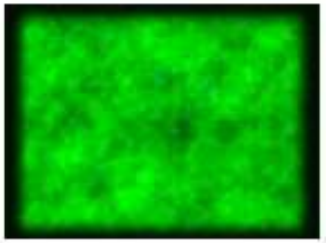
- Paradigm timing



Factorial designs

D Name colour of abstract image

(*vis. analysis, phonological retrieval, verbal output*)



⇒ green

	no phonolog. retrieval	phonolog. retrieval
no object recogn.	**A** visual analysis verbal output	**D** visual analysis phonological retrieval verbal output
object recognit.	**B** visual analysis object recognition verbal output	**C** visual analysis object recognition phonological retrieval verbal output

Interaction: (C - D) – (B - A) ⇒ significant IT activation

- phonological retrieval modulates IT response to object recognition
  ⇒ IT also involved in phonological retrieval!

Friston et al. (1997)

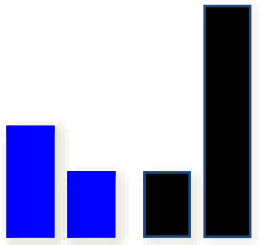
Factorial designs

Interactions

- The task is more than the sum of its (interdependent) processes
- A modulates B
- Test by varying A and B independently

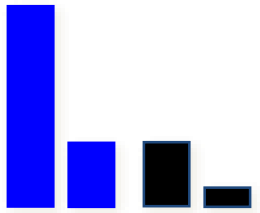
- May alternatively find only main effects – if so, serial subtraction and factorial designs give same answer

cross-over



and

simple



We can selectively inspect our data for one or the other by masking during inference

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Conjunction design

One way to minimize 'the baseline problem' is to isolate the same cognitive process by two or more separate contrasts, and inspect the resulting simple effects for commonalities.

Conjunctions can be conducted across different contexts:

- tasks
- stimuli
- senses (vision, audition)

etc.

Note: requirement for contrasts to be independent depends on which null hypothesis we test about conjunctions

Conjunction design

Two task pairs

- B – viewing concrete objects and saying “yes”
- C – naming concrete objects

Difference = phonological retrieval PLUS interaction with object recognition

- B2 – viewing coloured shapes saying “yes”
- C2 – naming colour of coloured shapes

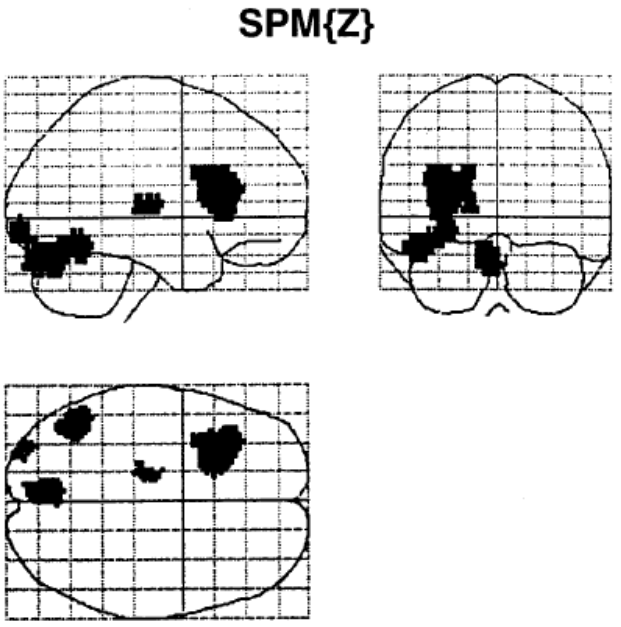
Diff = phonological retrieval PLUS interaction with visual analysis

Extending example from Friston et al. (1997)

Conjunction design

Overlap isolates the process of interest

- Phonological retrieval
- NOT its interactions with visual processing



Overlap of 4 subtractions

Price & Friston (1997)

Conjunction statistical tests

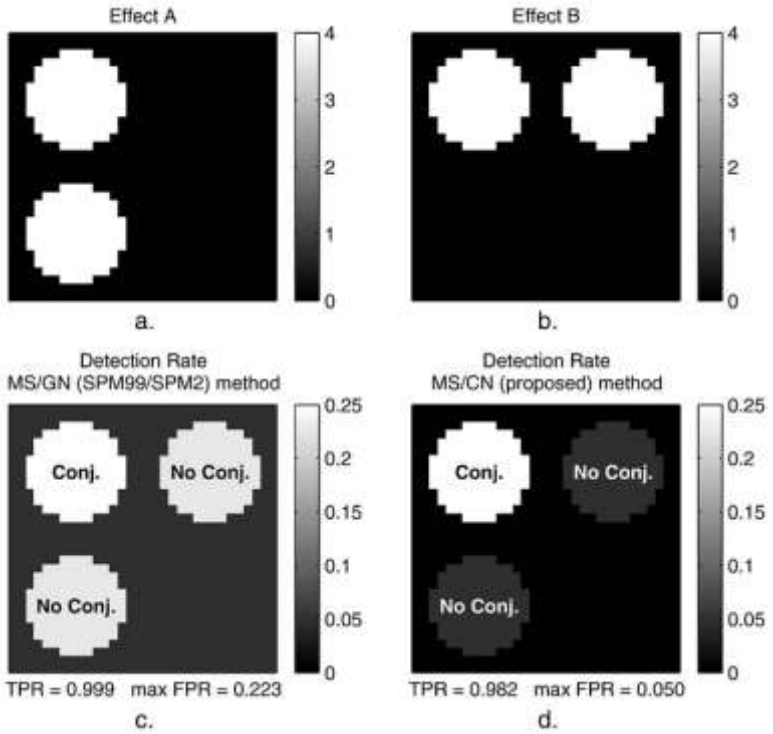
SPM12 offers two general ways to test the significance of conjunctions.

- Test of global null hypothesis (c): Significant set of consistent effects

"which voxels show effects of similar direction (but not necessarily individual significance) across contrasts?"
Requires independent contrasts

- Test of conjunction null hypothesis (d): Set of consistently significant effects

"which voxels show, for each specified contrast, effects > threshold?"
Works for dependent contrasts



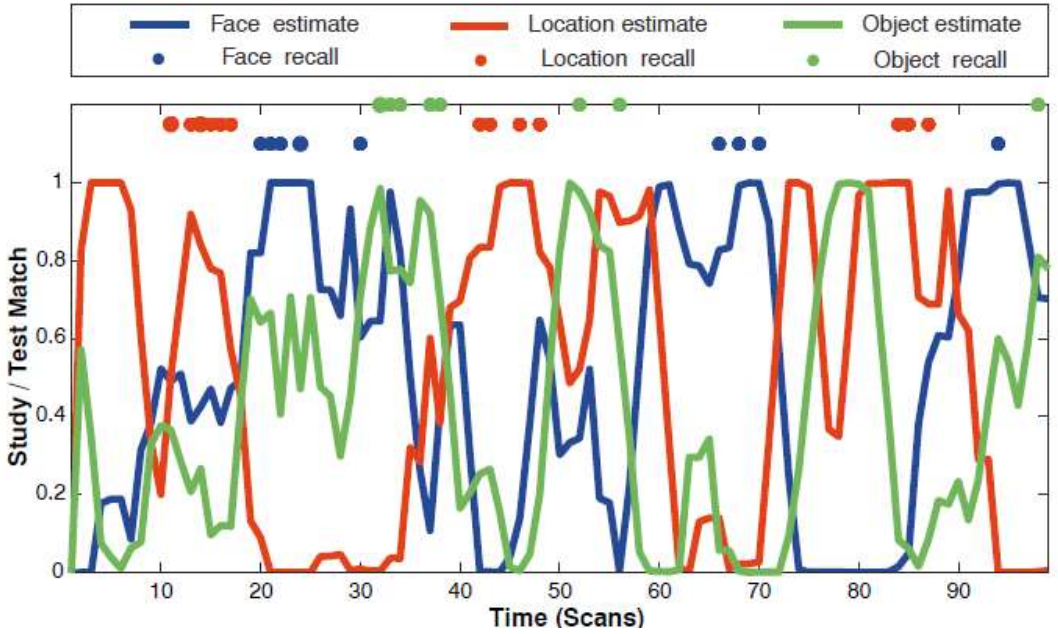
Friston et al., (2005). *Neuroimage,* 25:661-7.

Nichols et al., (2005). *Neuroimage,* 25:653-60.

Conjunction design

Detecting overlapping processing

- Experiencing ‘events’ involving faces, scenes, objects
- Reactivation of same regions when these categories of memories were retrieved
- Multivariate pattern analysis (Advanced course)



MVPA recall study

Polyn et al. (2005)

Summary

- Categorical designs involve simple, or serial, subtraction and assume pure insertion
- Factorial designs do not need to assume pure insertion and examine interactions between cognitive variables
- Conjunction designs examine regions which engage the same processes in multiple contrasts, and can avoid issues with violations of pure insertion

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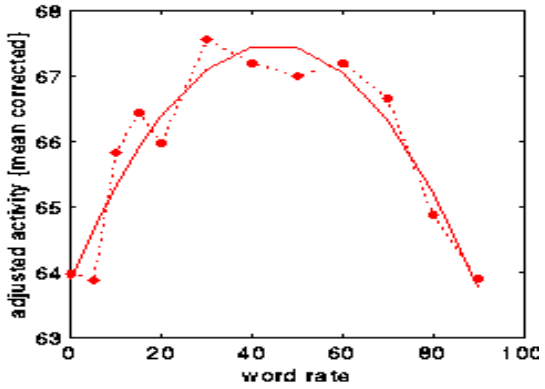
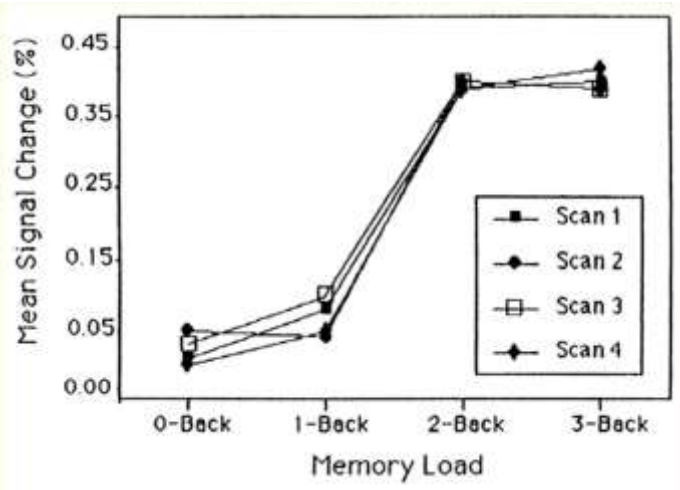
Parametric designs

A continuously varying parameter

- Detects systematic variation in activity with a process which is engaged to varying degrees
- Avoids pure insertion but does assume no qualitative change in this processing over levels of the task
- To investigate this, need to be more specific, e.g. Linear?
- BUT: often less sensitive

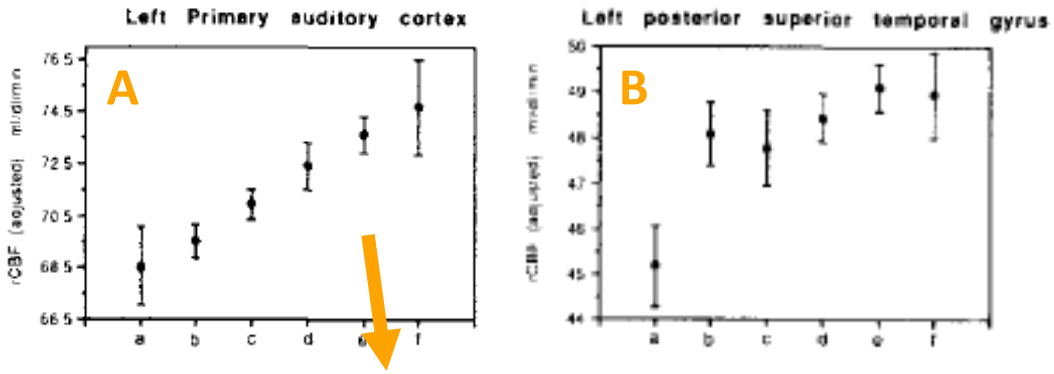
Buchel et al. (1996)



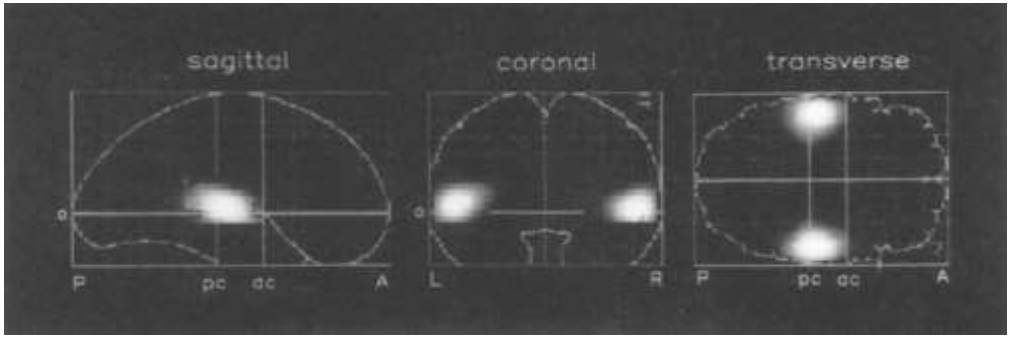


Cohen et al. (1996)

Parametric designs



Rest + 5 rates of auditory word presentation



Price et al. (1992)

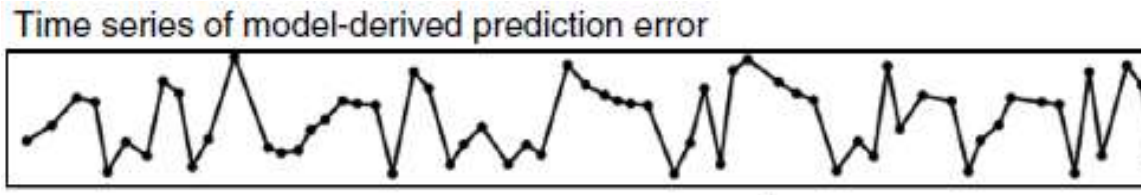
PET study

- Auditory words
- Linear relationship of presentation rate with activity in primary auditory cortex
- (Can also extend to factorial design)
- Implement using contrasts
- Or, the SPM12 GUI supports parametric modulation regressors in design
- Tuesday & Wednesday!

Parametric designs

Model based fMRI

- Computational model provides neurometric function e.g. Rescorla-Wagner prediction error
- Can also do model comparison



Glascher & O'Doherty (2010)

Overview

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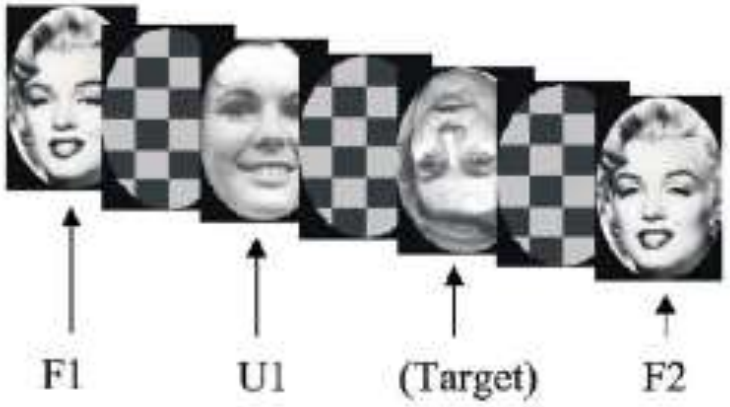
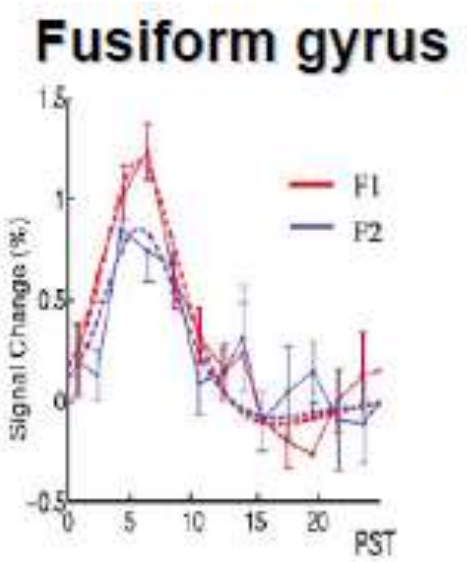
fMRI adaptation

- Repetition suppression
- = a reduced BOLD response to repeated stimuli
- Accompanies priming (behavioural)



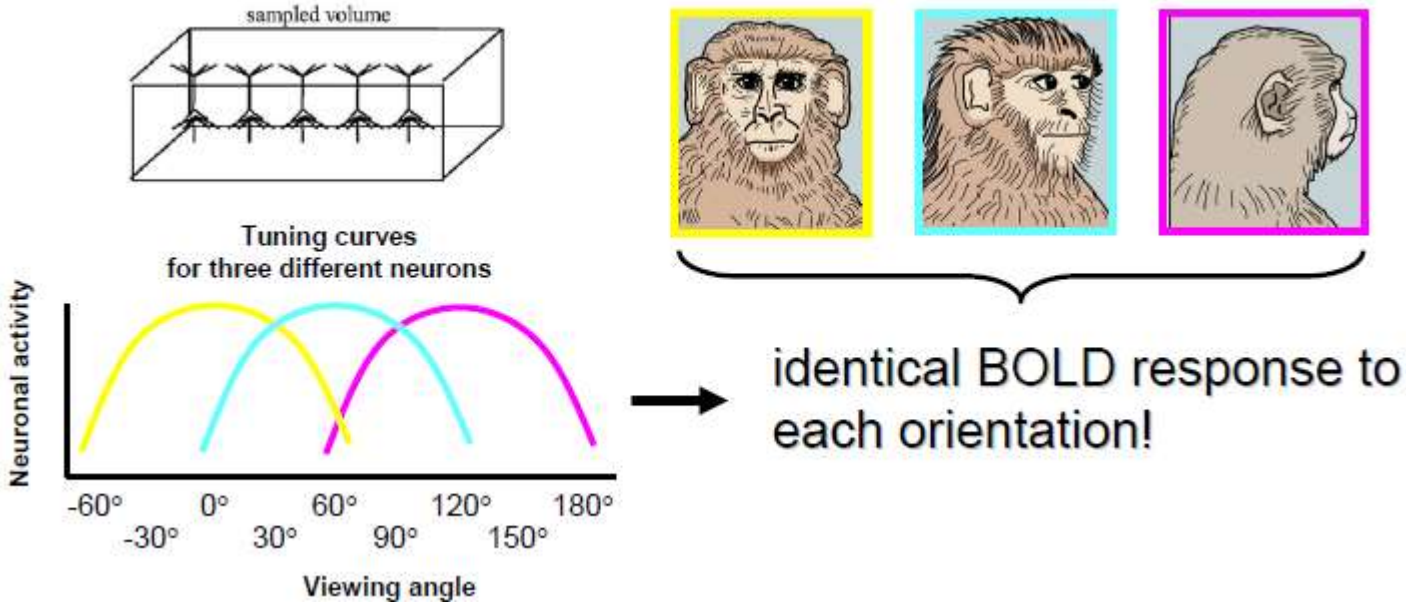


Henson et al. (2000)

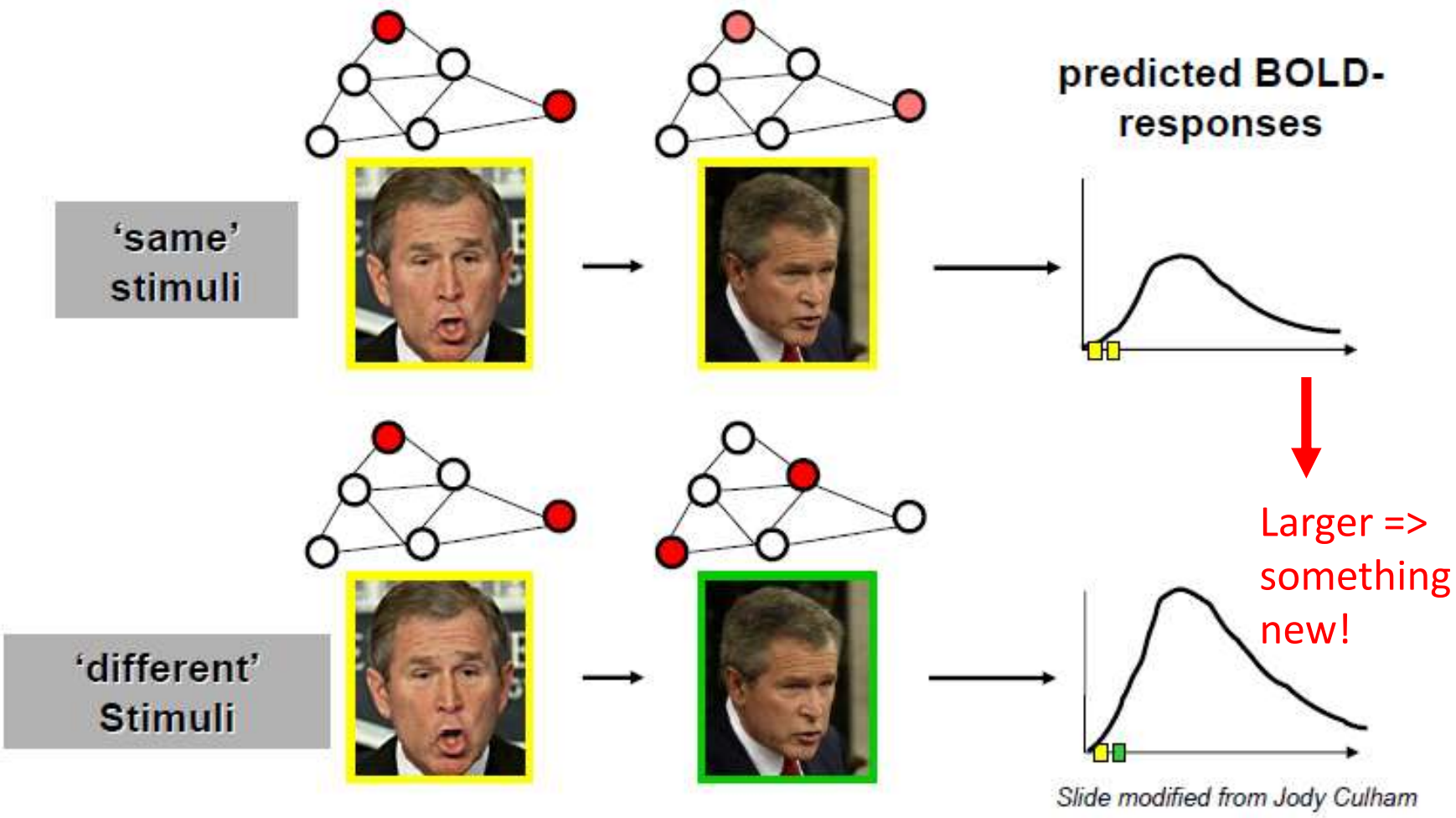
fMRI adaptation

Repetition suppression as a tool

- fMRI – typical voxel = 10,000s of neurons
- Is there a mix, tuned to diff. face orientations?
- Or: all viewpoint-invariant?



fMRI adaptation

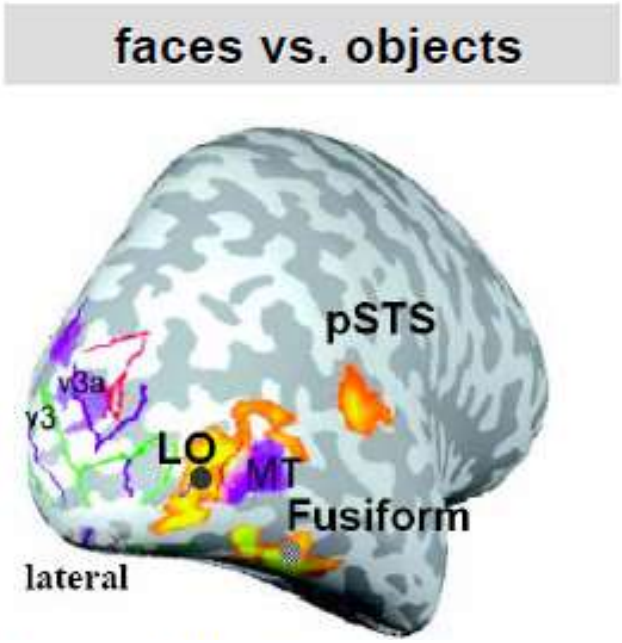


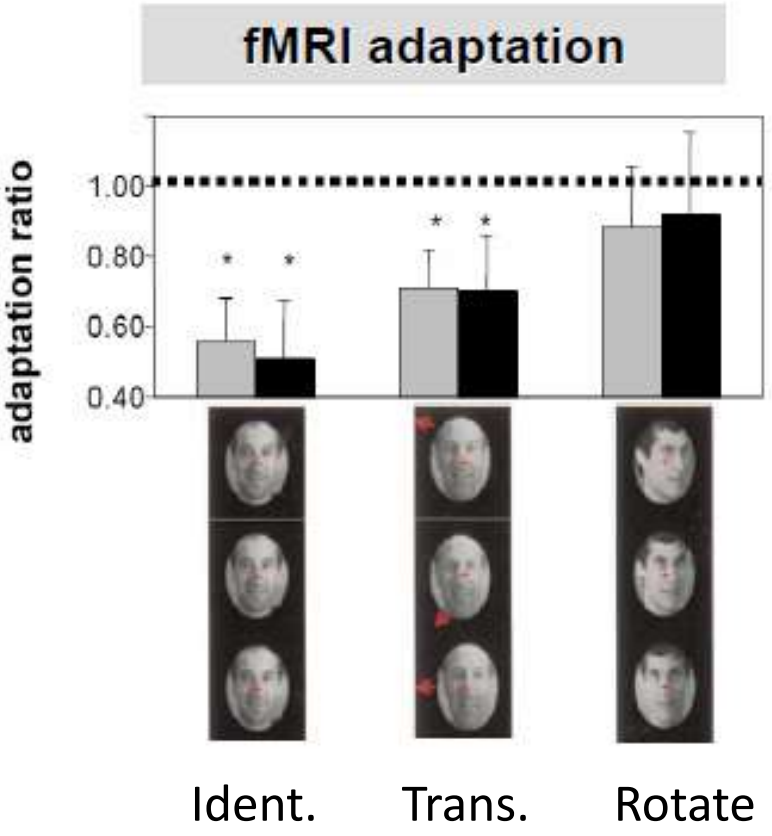
Release from adaptation => sensitivity to the changed feature

fMRI adaptation

Orientation tuning in human LOC (posterior Fusiform)

- Recovery from adaptation when rotate faces





Grill-Spector et al. (2001)

Summary

- Parametric designs extend categorical designs, requiring weaker assumptions to detect effects of a cognitive variable over multiple levels

- fMRI adaptation uses repetition suppression to examine neural representations

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Paradigm timing

Separating signal from noise

- Absolute BOLD signal not interpretable, so always make a contrast of task conditions*
- Stopping and restarting the scanner resets the baseline, so keep comparisons within-session
- fMRI signal is weak: functionally significant changes <5% signal intensity so get all the signal you can

- Paradigm timing is also critical…
- your task-related changes of interest need to take place slowly but not too slowly

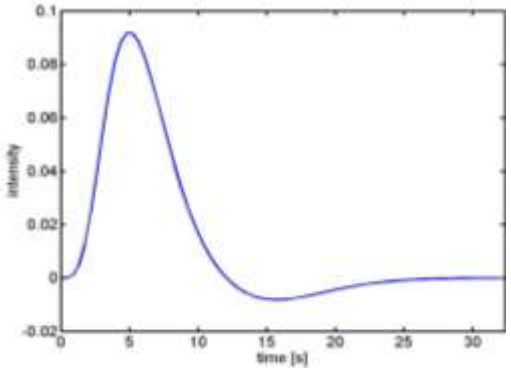
*although can measure connectivity, e.g. at rest

Separating signal from noise

- For adequate signal-to noise, must filter out large low frequency effects (e.g., scanner drift, aliased physiological rhythms) > ~0.01 Hz (1 cycle per 100 sec)
- To avoid removing effects of interest at the same time, need fairly high experimental design frequency

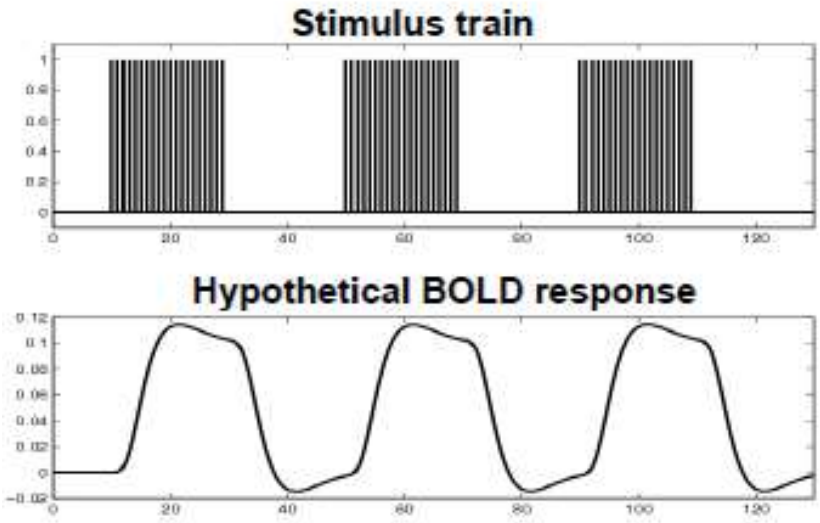
BUT

- 'Sluggish' BOLD response with slow response to neural changes effectively filters out high frequencies
- So also avoid very rapid experimental changes



Paradigm timing

Block Design

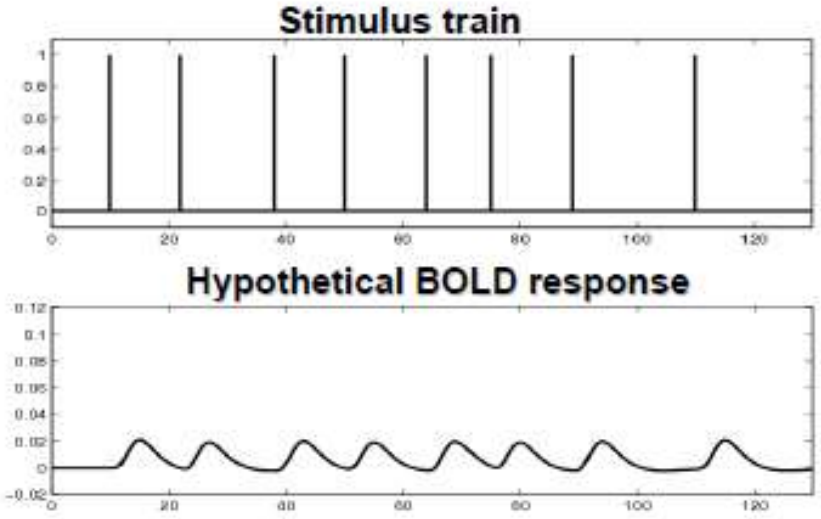


Analysis of whole block

Large effects (=efficient)

Optimal on-off cycle = 32 sec (sluggish BOLD response vs. low frequency confounds)

Event-Related Design



Analysis of single items

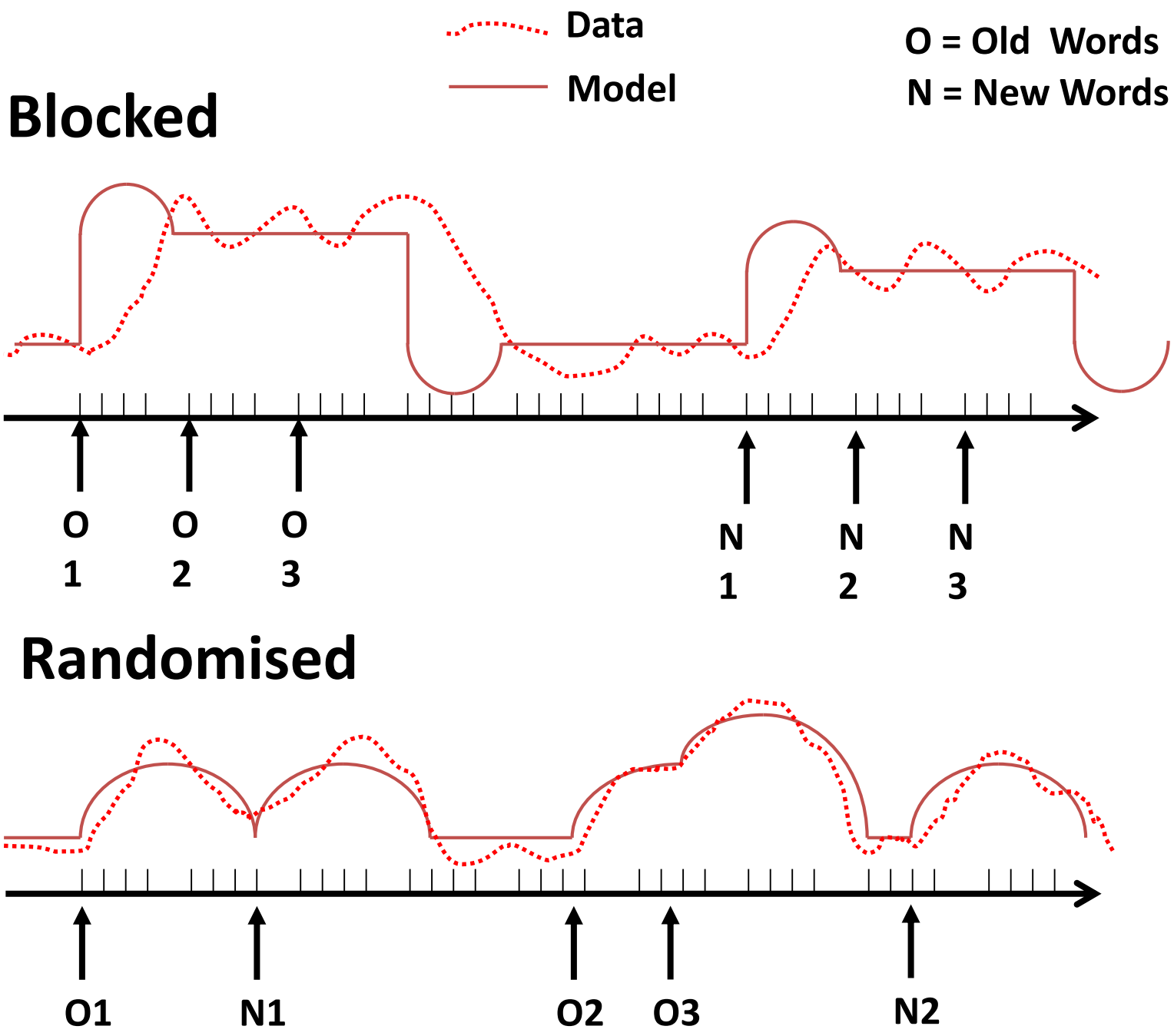
Smaller effects

SOA from min ~= 2 sec

Paradigm timing

Advantages of event-related design

- Intermixing of conditions avoids unwanted psychological effects e.g. habituation, expectancy, loss of concentration


Data
Model
O = Old Words
N = New Words
Blocked
O 1
O 2
O 3
N 1
N 2
N 3
Randomised
O1
N1
O2
O3
N2

Paradigm timing

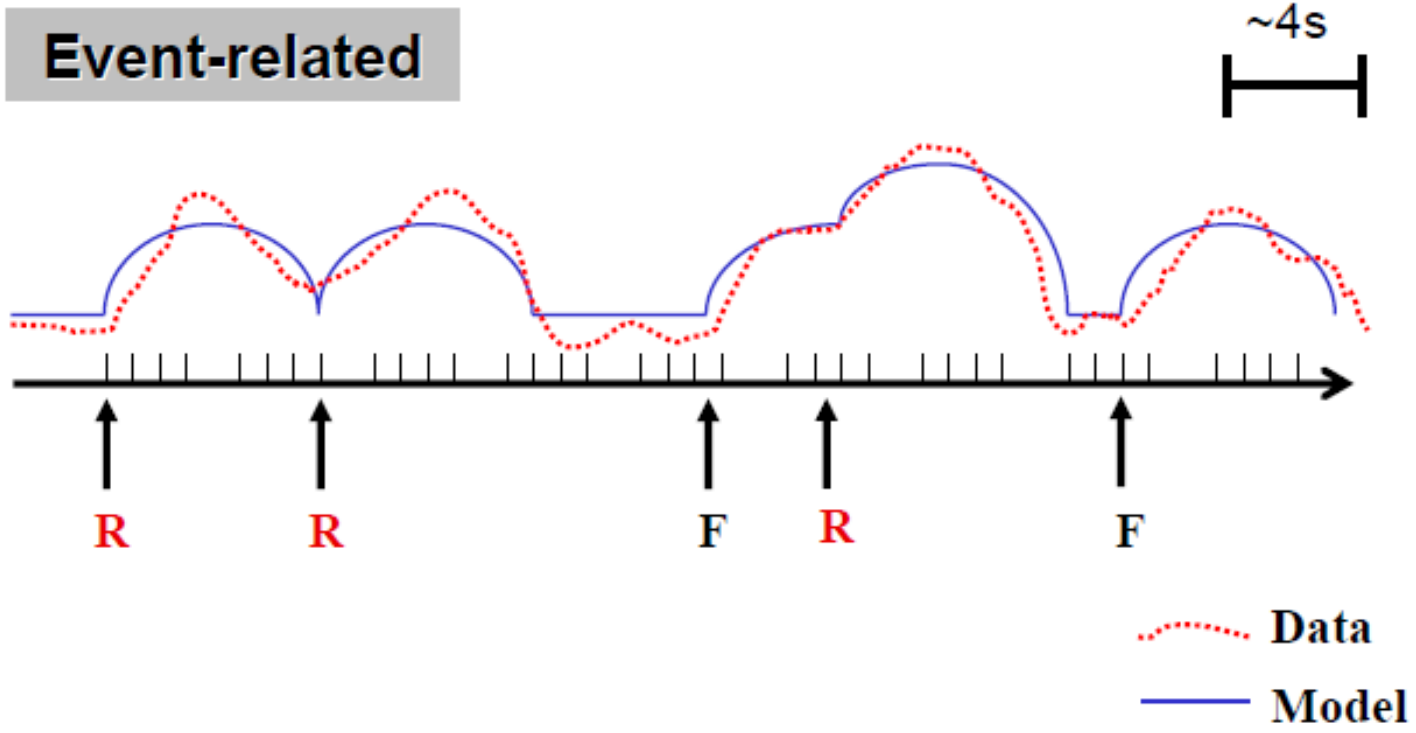
Advantages of event-related design

- Intermixing of conditions avoids unwanted psychological effects e.g. habituation, expectancy, loss of concentration
- Post-hoc classification of trials, e.g. Subsequent memory effect

Paradigm timing

R = Words Later Remembered

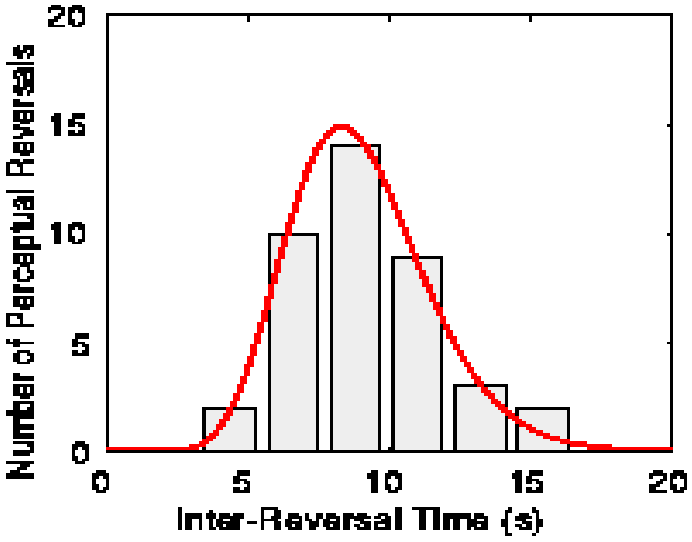
F = Words Later Forgotten

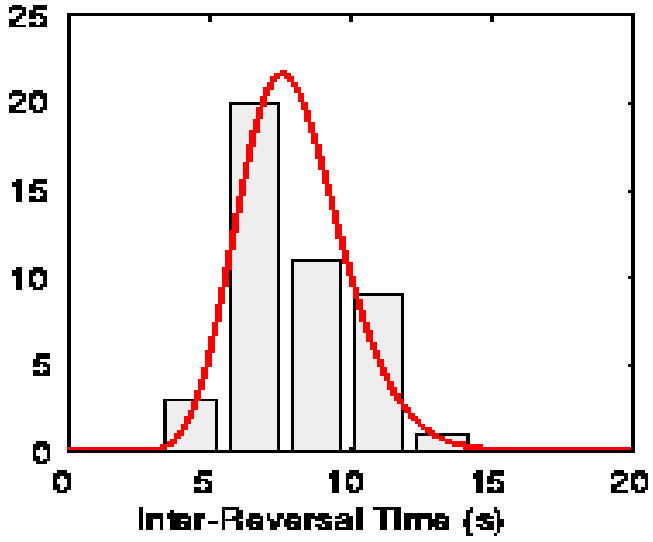


Paradigm timing

Advantages of event-related design

- Intermixing of conditions avoids unwanted psychological effects e.g. habituation, expectancy, loss of concentration
- Post-hoc classification of trials, e.g. Subsequent memory effect
- Some events can only be indicated by subject at particular time e.g. Spontaneous perceptual changes


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


0
5
10
15
20
25
Inter-Reversal Time (s)

Paradigm timing

Advantages of event-related design

- Intermixing of conditions avoids unwanted psychological effects e.g. habituation, expectancy, loss of concentration
- Post-hoc classification of trials, e.g. Subsequent memory effect
- Some events can only be indicated by subject at particular time e.g. Spontaneous perceptual changes
- Some events cannot be blocked, e.g. oddball

Summary

Main message: different designs for different questions

Don't forget

- Scan for as long as possible (lots of trials)
- Never contrast trials very far apart in time (low f noise)
- Never contrast conditions run in different scanner sessions (i.e., scanner stopped and restarted)

Want to know more?

- Temporal design efficiency
- Design optimisation
- http://imaging.mrc-cbu.cam.ac.uk/imaging/DesignEfficiency

Design taxonomy

Categorical designs

Task A – Task B

- Subtraction - Pure insertion, evoked / differential responses
- Conjunction - Testing multiple hypotheses or for overlap

Parametric designs

a A A A A

- Linear - Adaptation, cognitive dimensions
- Nonlinear - Polynomial expansions, neurometric functions
- Model-based fMRI (model parameters)

Factorial designs

- Categorical - Interactions/ test pure insertion
- Parametric - Linear and nonlinear interactions
- Psychophysiological Interactions (PPI)