Experimental design for Cognitive fMRI

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Edinburgh SPM course 2019

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

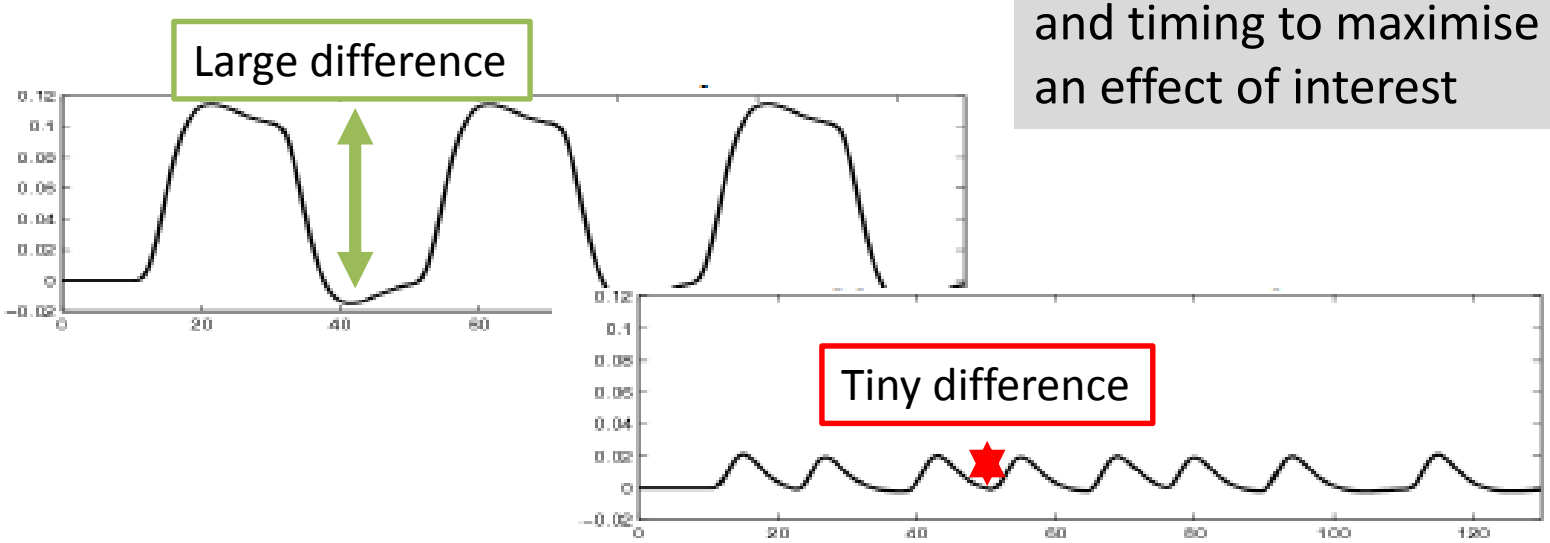
UNIVERSITY OF SUSSEX

Aim

- BOLD fMRI does not give an absolute measure of activity

→ Always compare activity across conditions using contrasts

Design task, conditions and timing to maximise an effect of interest



Overview

02 Experimental design (this lecture)

- fMRI for activation
- Design taxonomy
- fMRI for information

04 Design constraint & optimisation

- fMRI constraints
- Paradigm timing

Activation fMRI

- Measure the involvement of a region in a process
- Activation, activity, involvement, engagement…

= how mean BOLD signal varies with task condition

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"

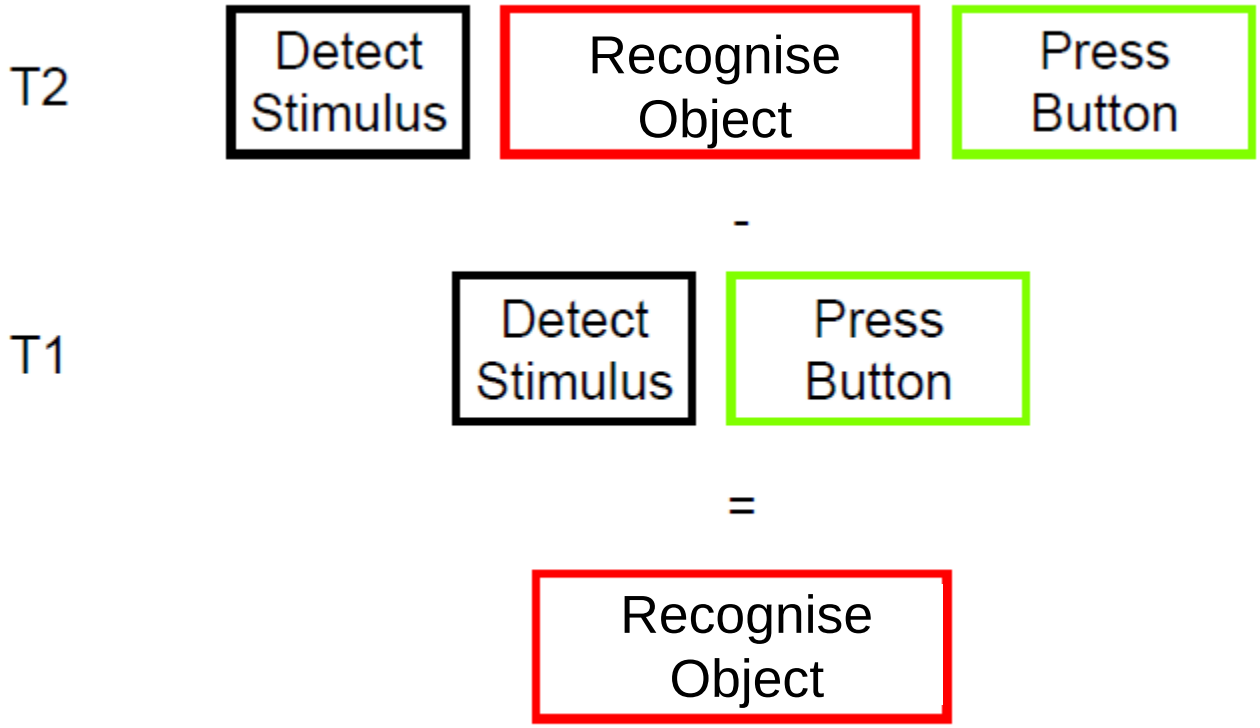
Donders (1898-9)

- Need: a meaningful cognitive question

"What is this?"

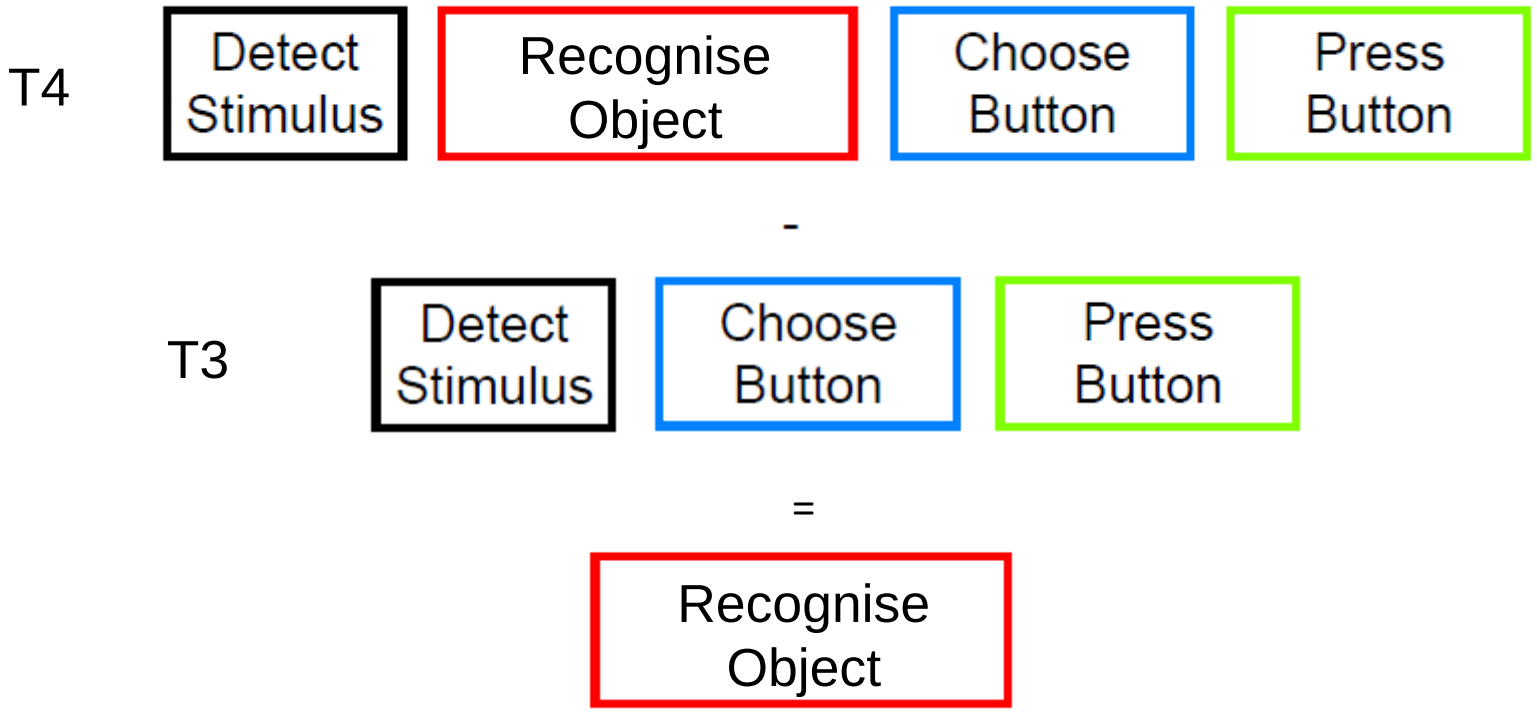
Cognitive subtraction

Use a simple reaction time task to isolate a process



Cognitive subtraction

Use a choice reaction time task – get the same results



Design taxonomy

- Categorical designs
- Factorial designs
- Conjunction designs
- Parametric designs

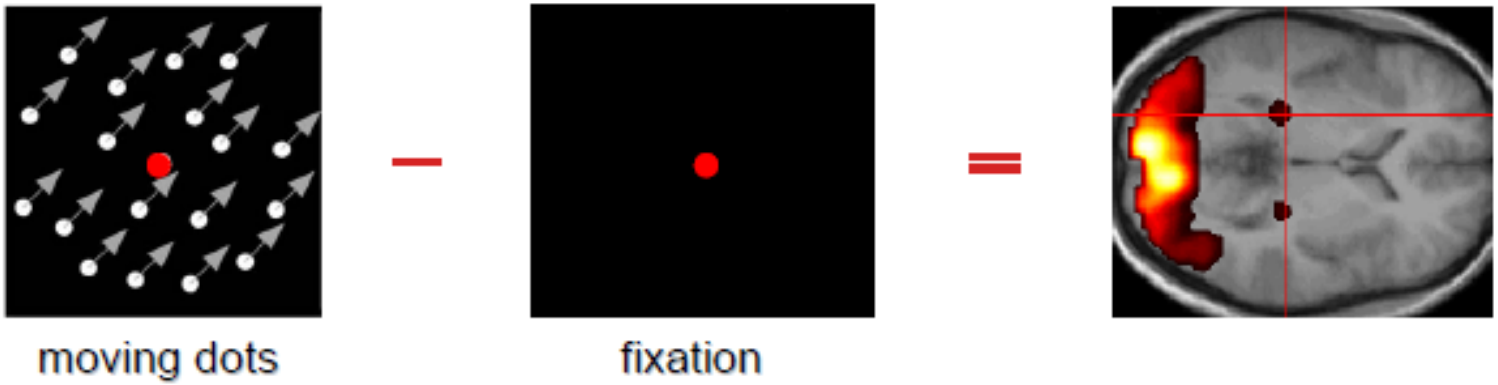
Categorical designs

Simple subtraction

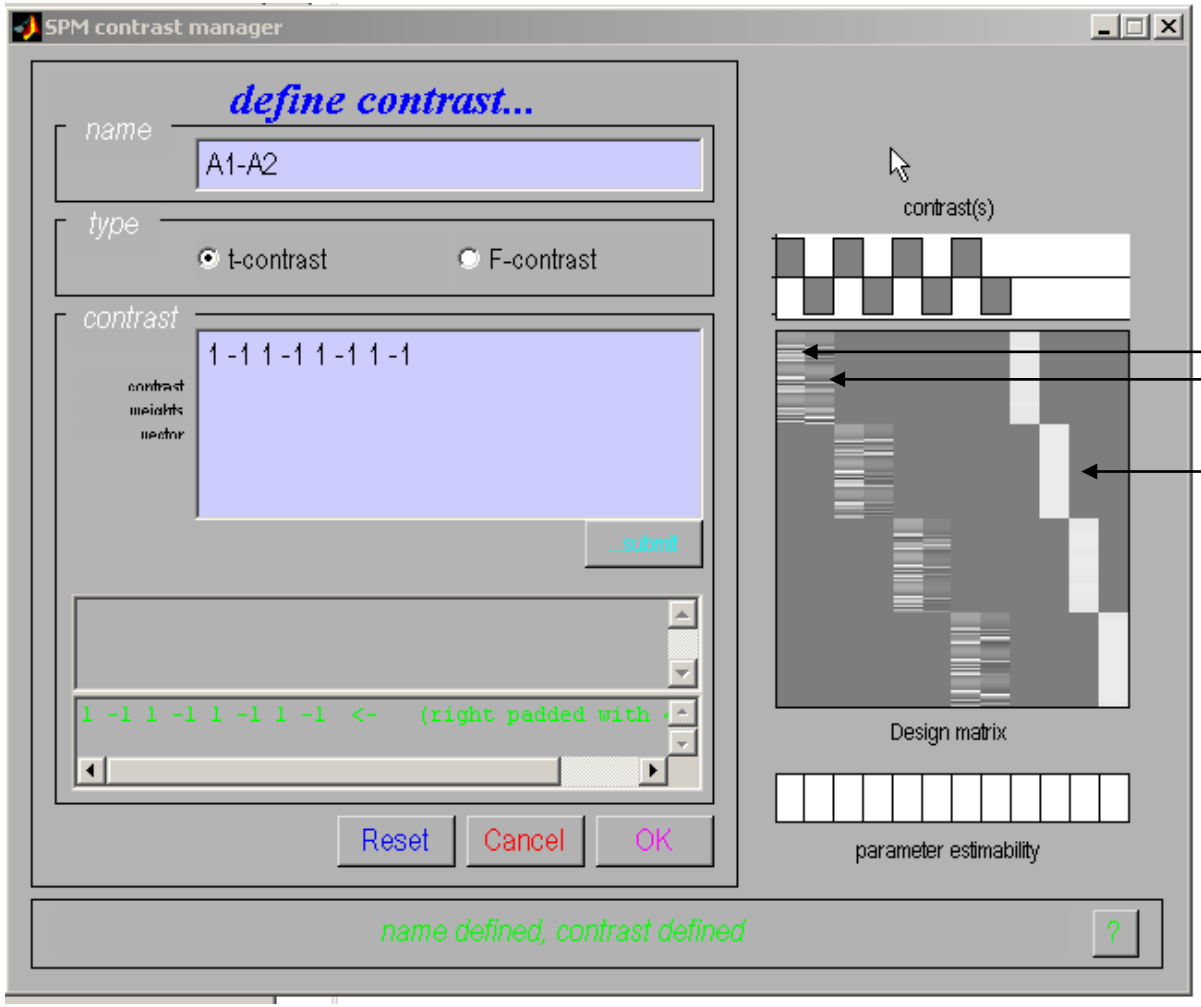
- Testing for activation difference

A. Which regions specialised for a function?

B. Do 2 tasks differ in processing?



In SPM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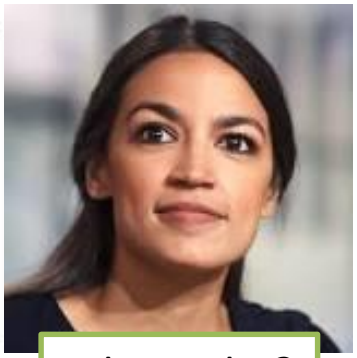
contrast(s)
Design matrix
parameter estimability
Condition 1
Condition 2
Constant for each session (run)

Control condition

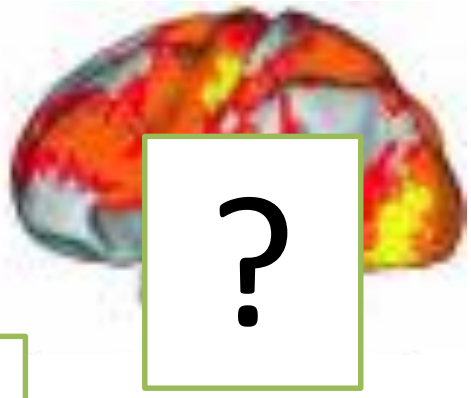
- Experimental task must engage the process
- Control task must engage everything else

- Is fixation the right control for face naming?



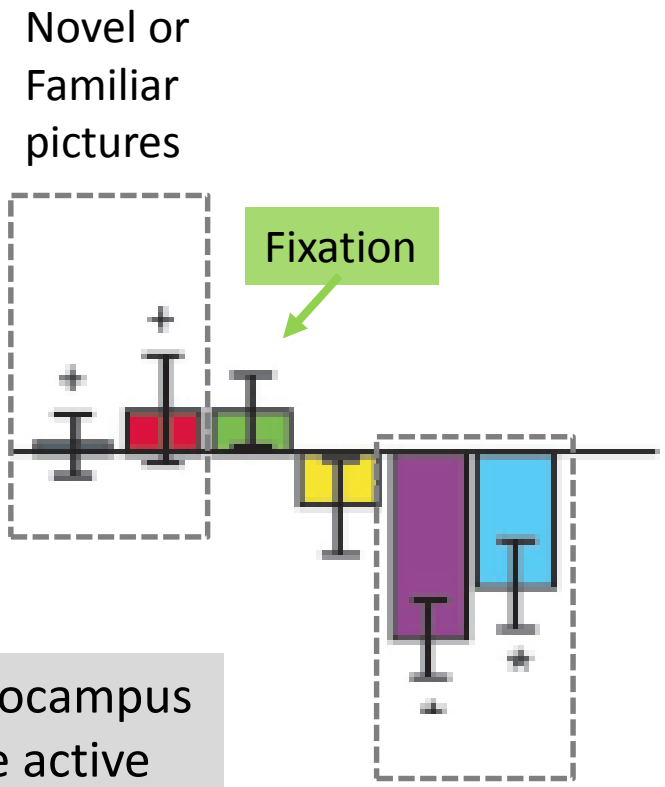
Who is she?

I need to eat after this scan…



Different stimulus, different task, different response…

Control condition



Hippocampus more active for fixation than noise detection/ digit decision tasks

Early "Failure to activate" the hippocampus during episodic memory tasks

Were studies of amnesia wrong?

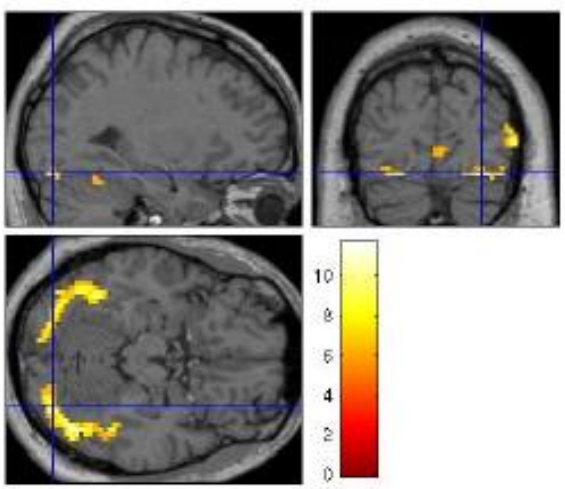
…only if we use fixation/ rest as the baseline

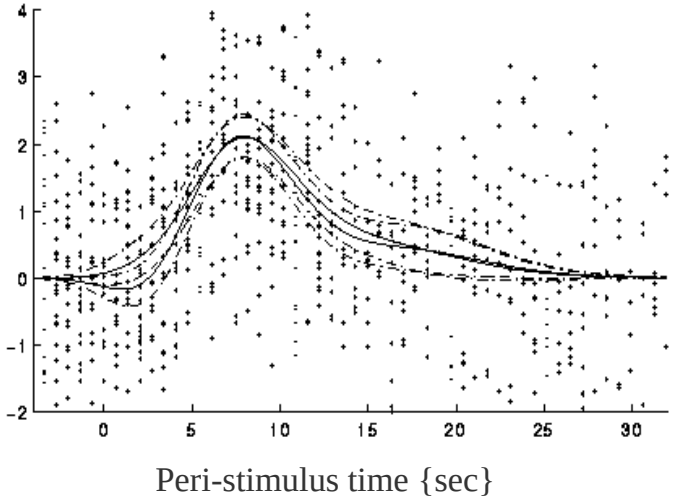
→ Choice of a baseline depends on your question!

Stark & Squire (2001) PNAS

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

"What is this?"

Object recognition

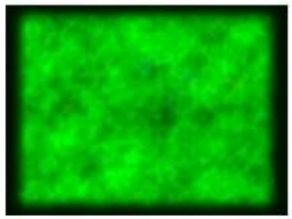
Phonological retrieval

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*)

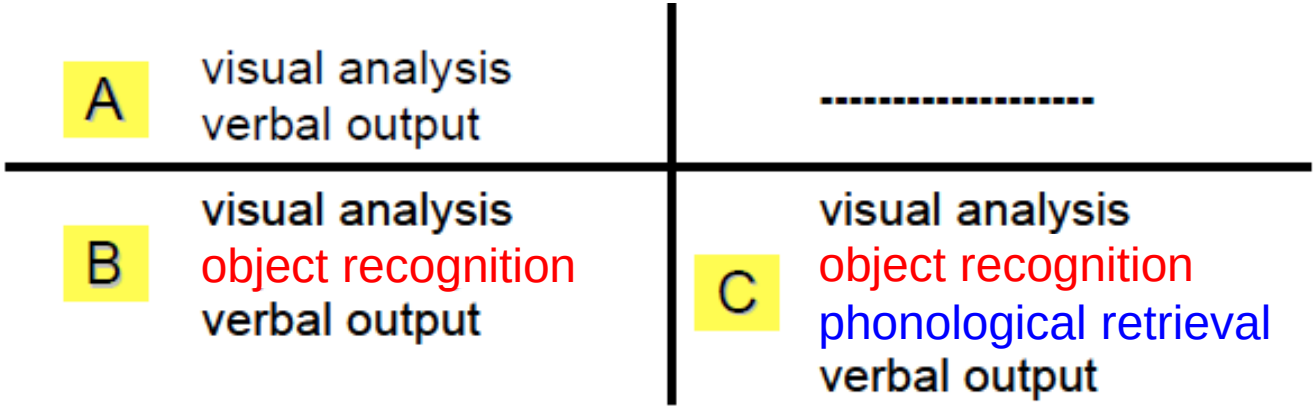
⇒ yes

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!

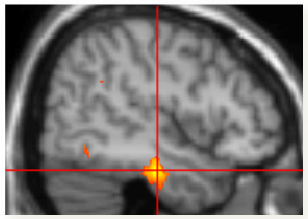
C - B ⇒ no significant IT activation ⇒ no evidence for IT involvement in phonological retrieval!

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

more likely, one process modulates another

Design taxonomy

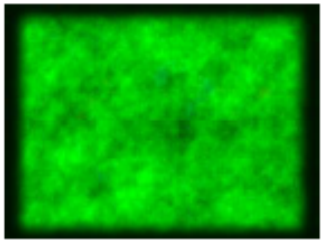
- Categorical designs
- Factorial designs
- Conjunction designs
- Parametric designs



Factorial designs

D Name colour of abstract image

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



⇒ green

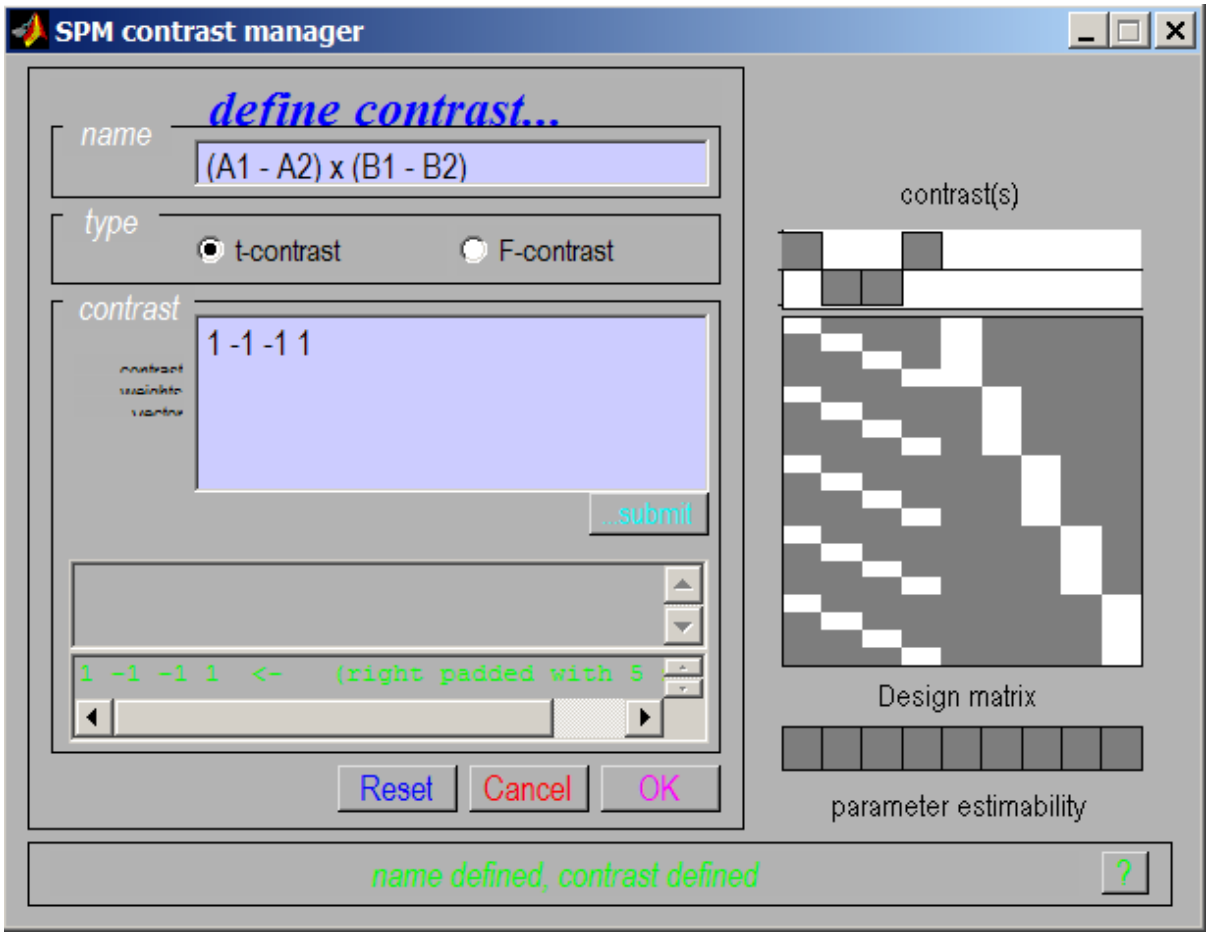
	no phonolog. retrieval	phonolog. retrieval
no object recogn.	**A** visual analysis verbal output	**D** visual analysis phonological retrieval verbal output
object recognit.	**B** visual analysis object recognition verbal output	**C** visual analysis object recognition phonological retrieval verbal output

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

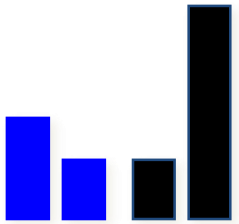
- phonological retrieval modulates IT response to object recognition
  ⇒ IT also involved in phonological retrieval!

Friston et al. (1997)

In SPM

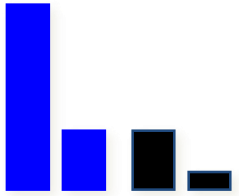


Interactions:



cross-over

vs.



simple

Selectively check data for one or the other by masking during inference

Design taxonomy

- Categorical designs
- Factorial designs
- Conjunction designs
- Parametric designs

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

First task pair (from previous):

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

D-C = phonological retrieval PLUS interaction with object recogn.

New task pair:

- D2 – viewing coloured shapes saying “yes”
- C2 – naming colour of coloured shapes

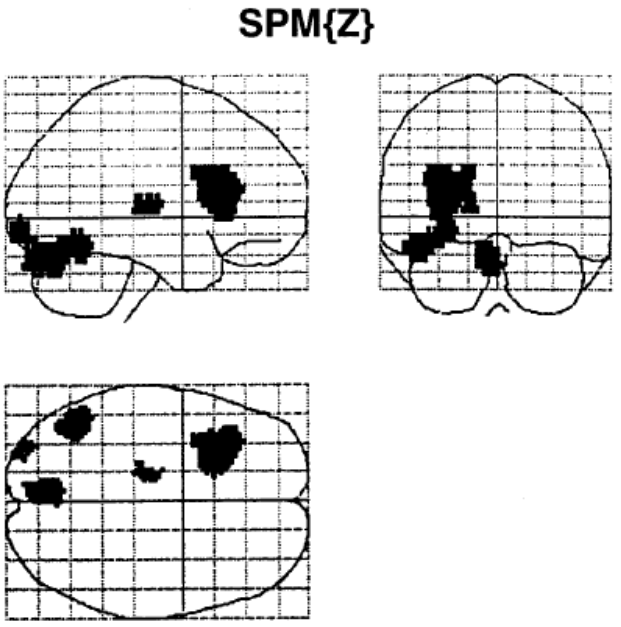
D2-C2 = phonological retrieval PLUS interaction w/ only vis. analysis

Extending example from Friston et al. (1997)

Conjunction design

Overlap isolates the process of interest

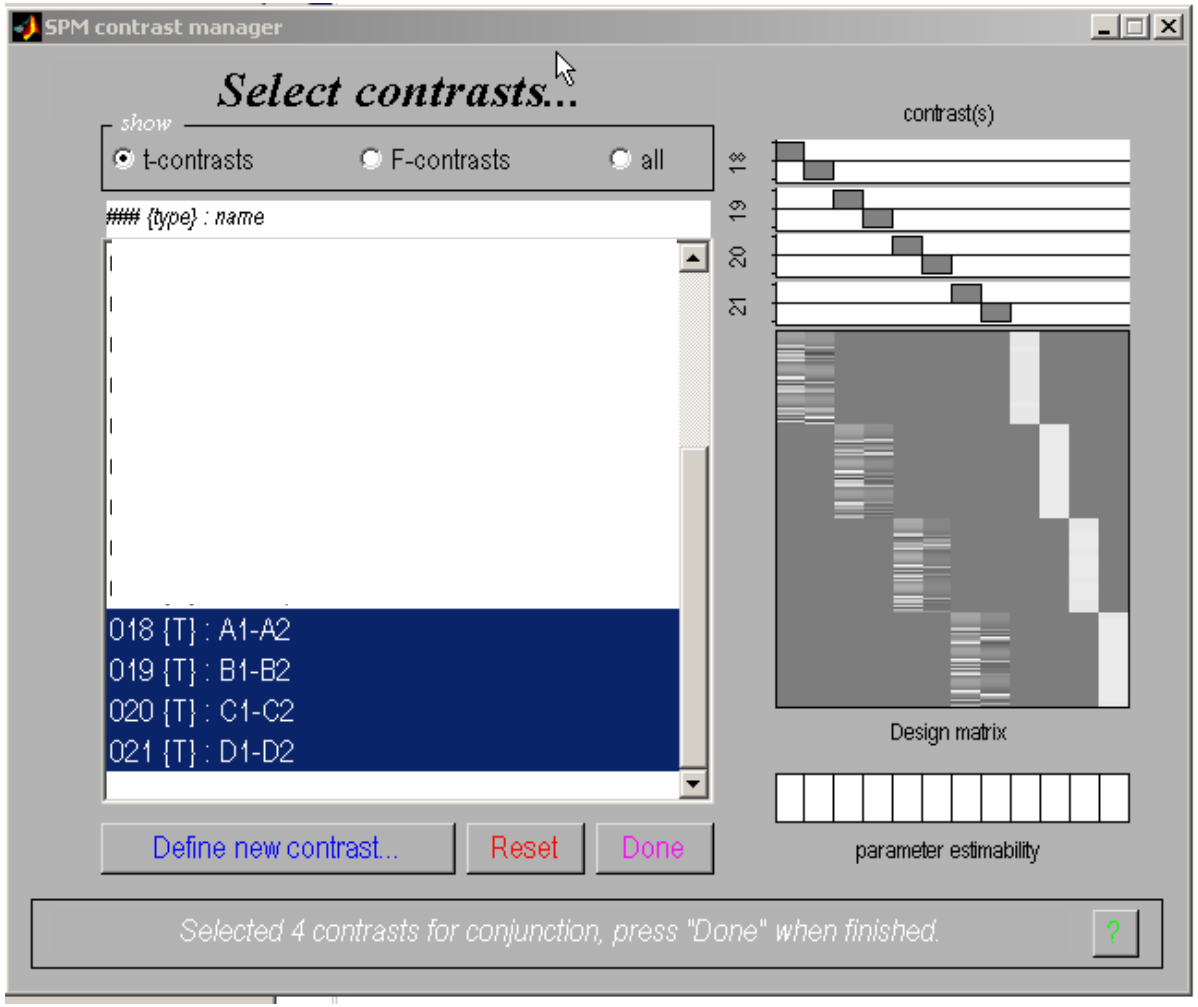
- Phonological retrieval
- NOT its interactions with visual processing



Overlap of 4 subtractions

Price & Friston (1997)

In SPM



Select multiple contrasts

Conjunction statistical tests

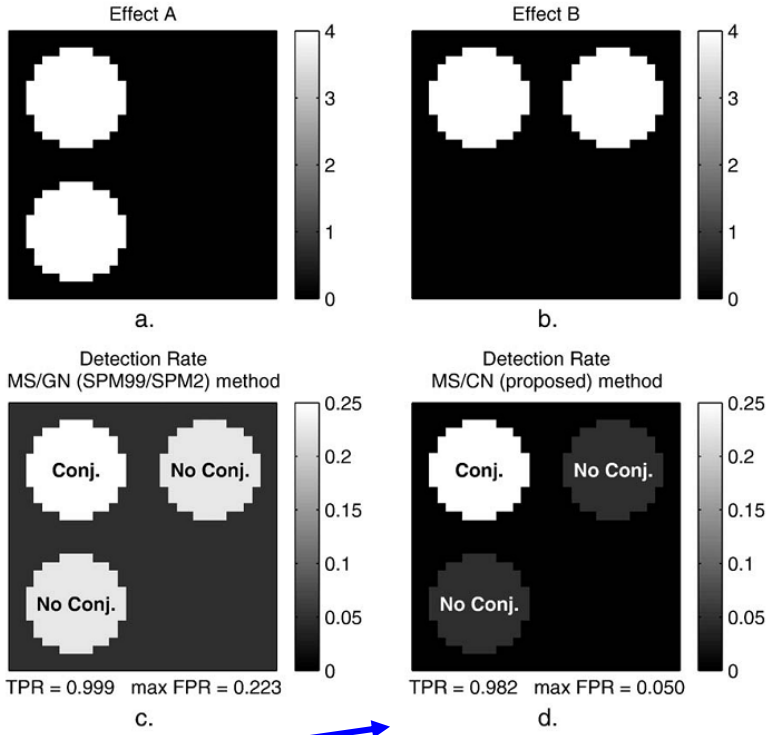
In SPM12, two ways to test the significance of conjunctions.

- 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



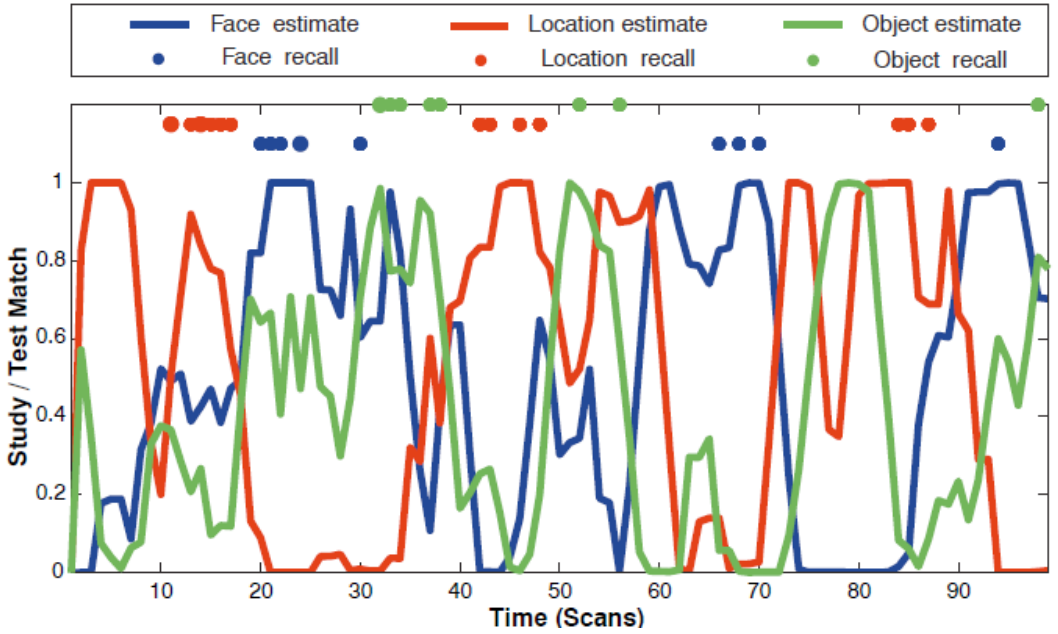
Friston et al., (2005). *Neuroimage,* 25:661-7.

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

Design taxonomy

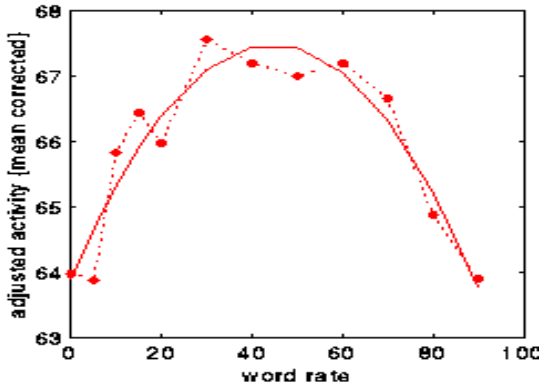
- Categorical designs
- Factorial designs
- Conjunction designs
- Parametric designs

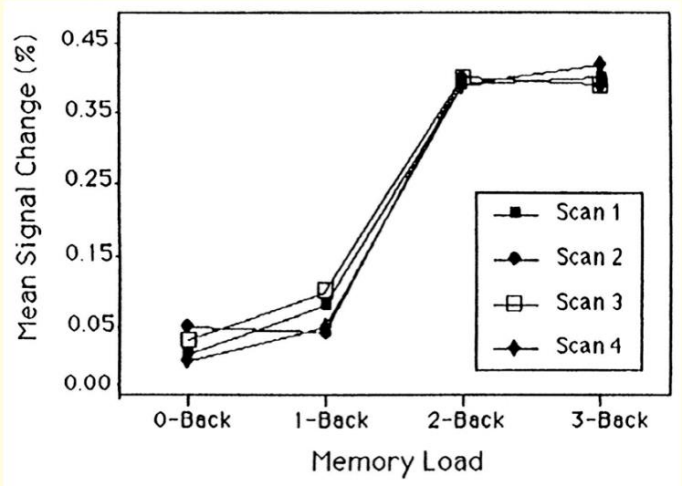
Parametric designs

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

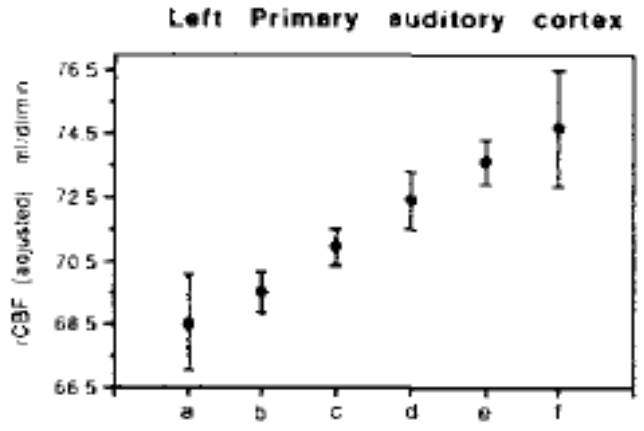
Buchel et al. (1996)



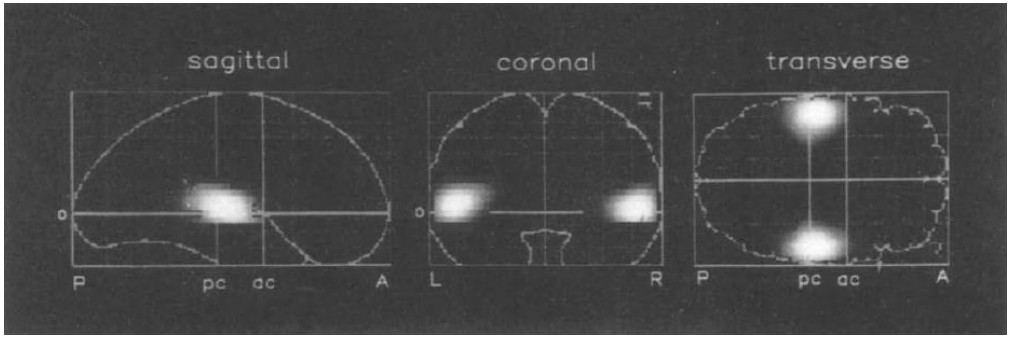


Cohen et al. (1996)

Parametric designs



Rest + 5 rates of auditory word presentation



Price et al. (1992)

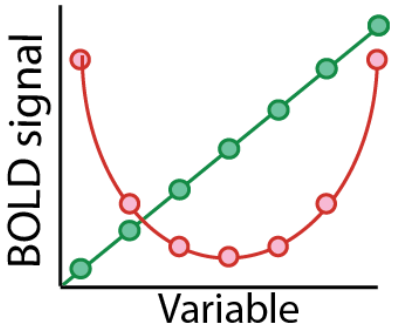
PET study

- Auditory words
- Linear relationship of presentation rate with activity in primary auditory cortex
- (Can also extend to factorial design)
- Implement using contrasts
- E.g. [-2 -1 0 1 2]
- weighting over 5 non-rest conditions

Non-linear parametric design

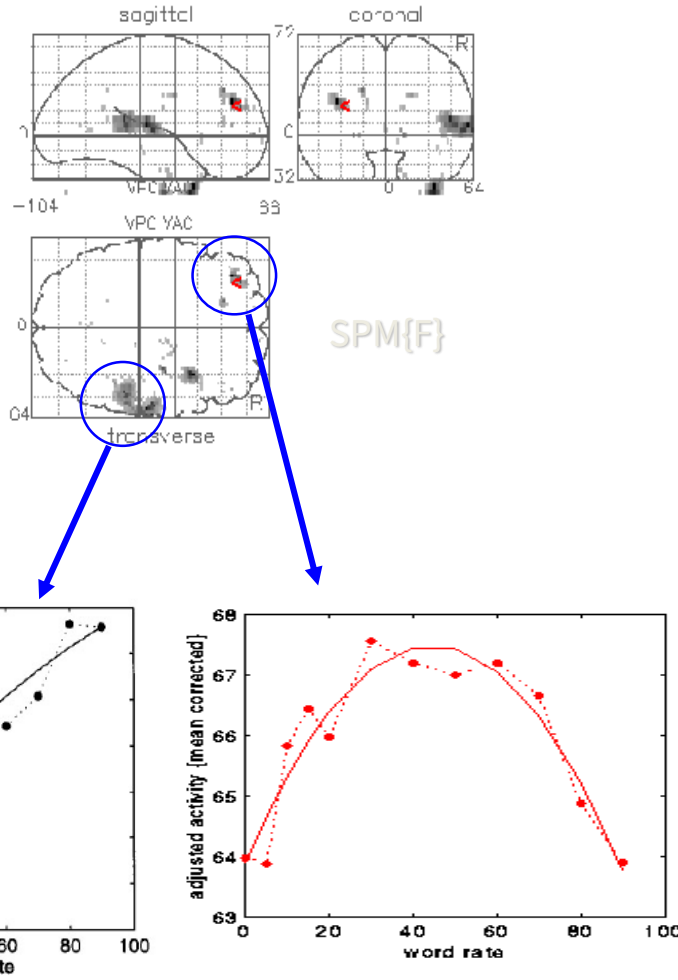
Polynomial expansion:
$f(x) = b_1 x + b_2 x^2 + \ldots$

Parametric modulator in SPM design
Add columns (regressors)



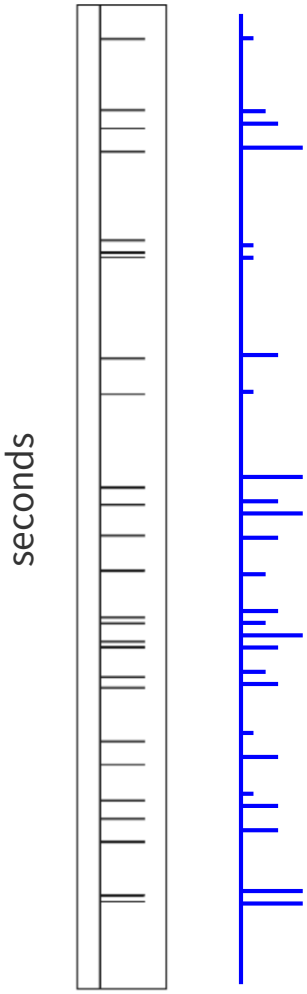
Test for regions specifically showing linear and/or quadratic effects

F-contrast [1 0] on linear param
F-contrast [0 1] on quadratic param



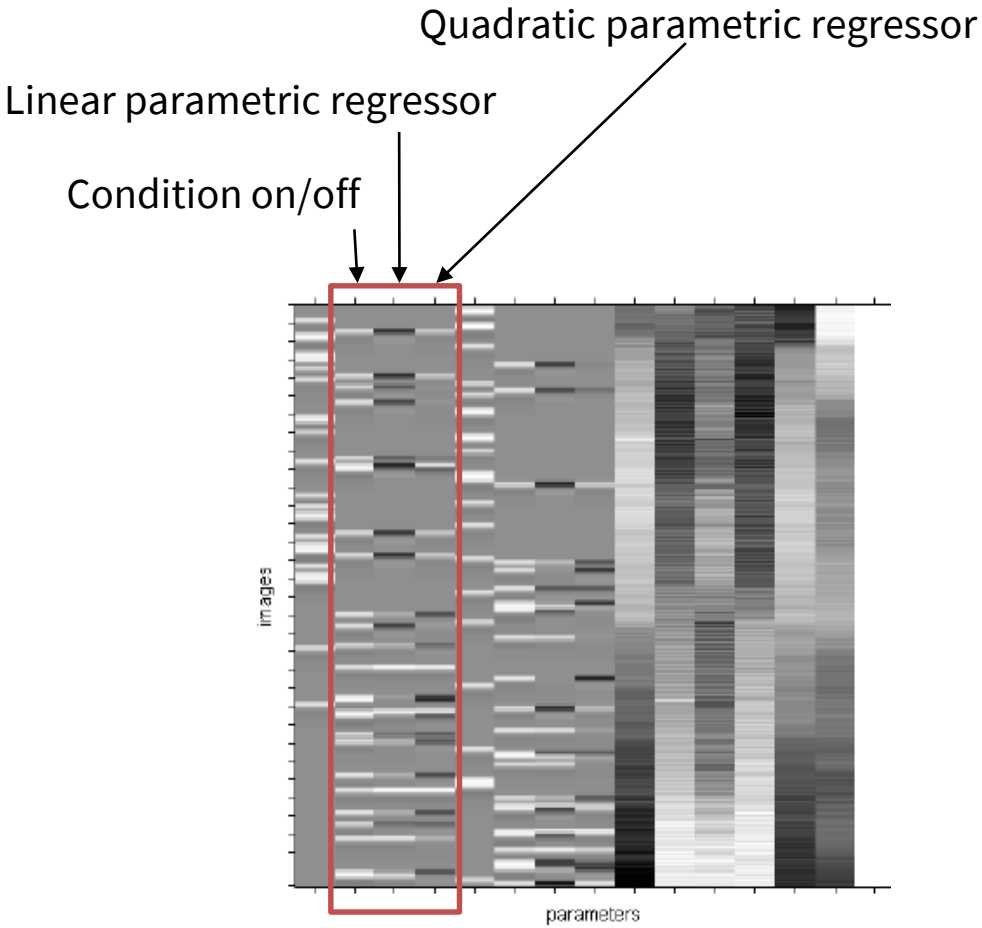
Büchel et al., (1996)

In SPM: parametric modulation



Delta
Stick function
= condition on/off

Parametric
Regressor = augmented
by function



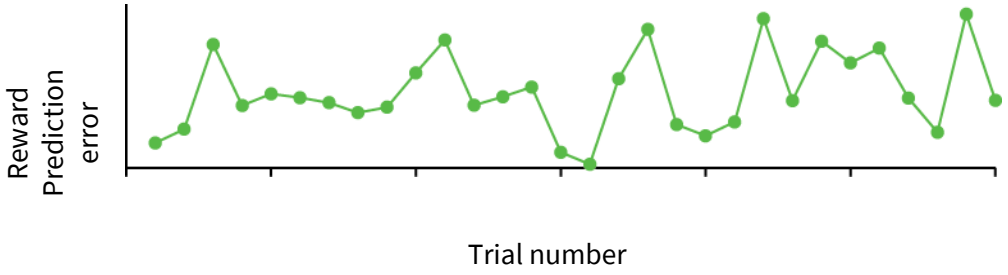
Model-based parametric design

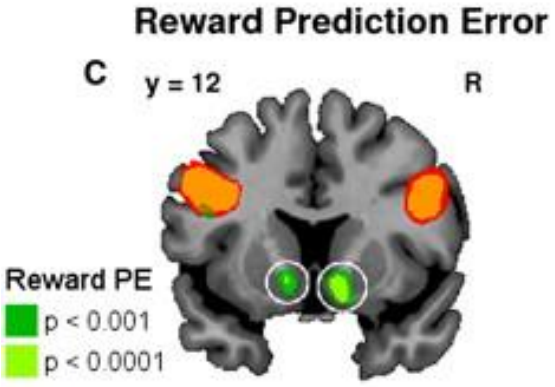
(Formal) model based fMRI

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

choices determine interim and outcome states, eventually reward

Time-series of a model-derived reward prediction error





Glascher & O'Doherty (2010)

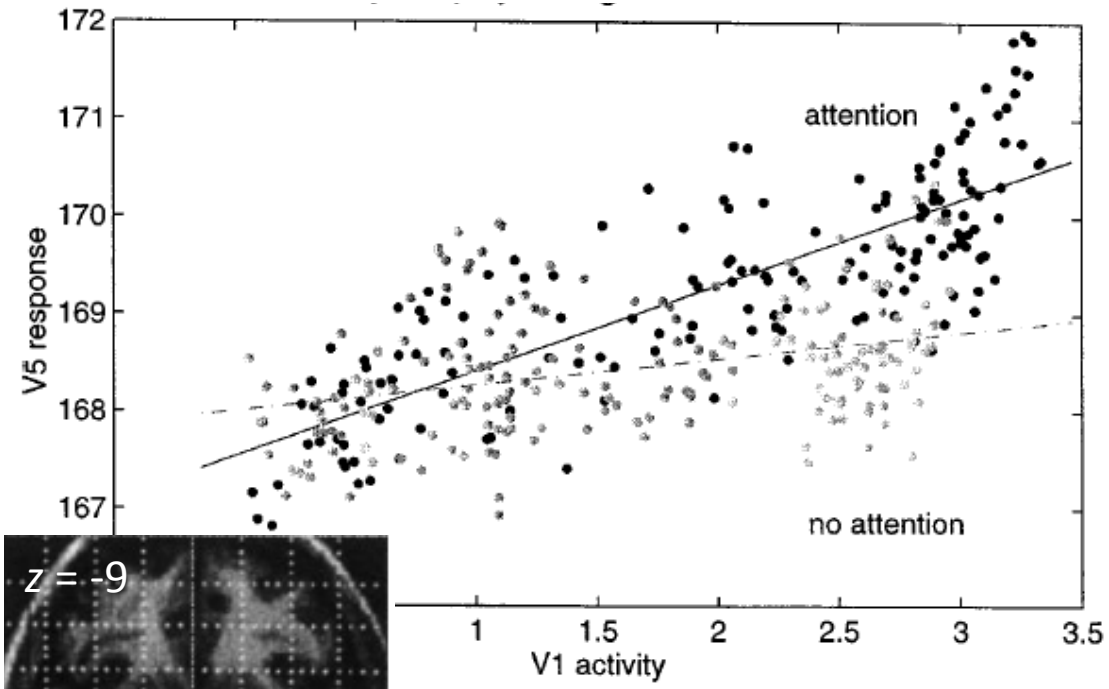
Parametric and factorial: PPI

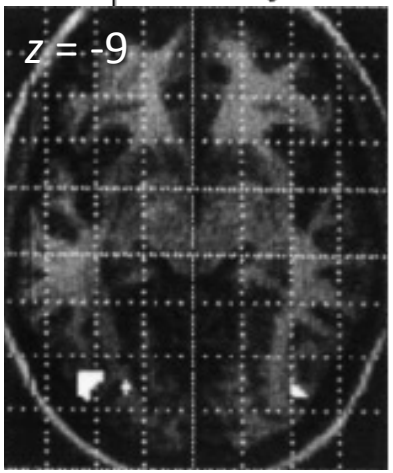
- Another parametric variant takes activity in a seed voxel as a predictor

  = a form of effective connectivity analysis

  A model-based directional test of connectivity between regions
- PPI = psychophysiological interaction

Psychophysiological interaction

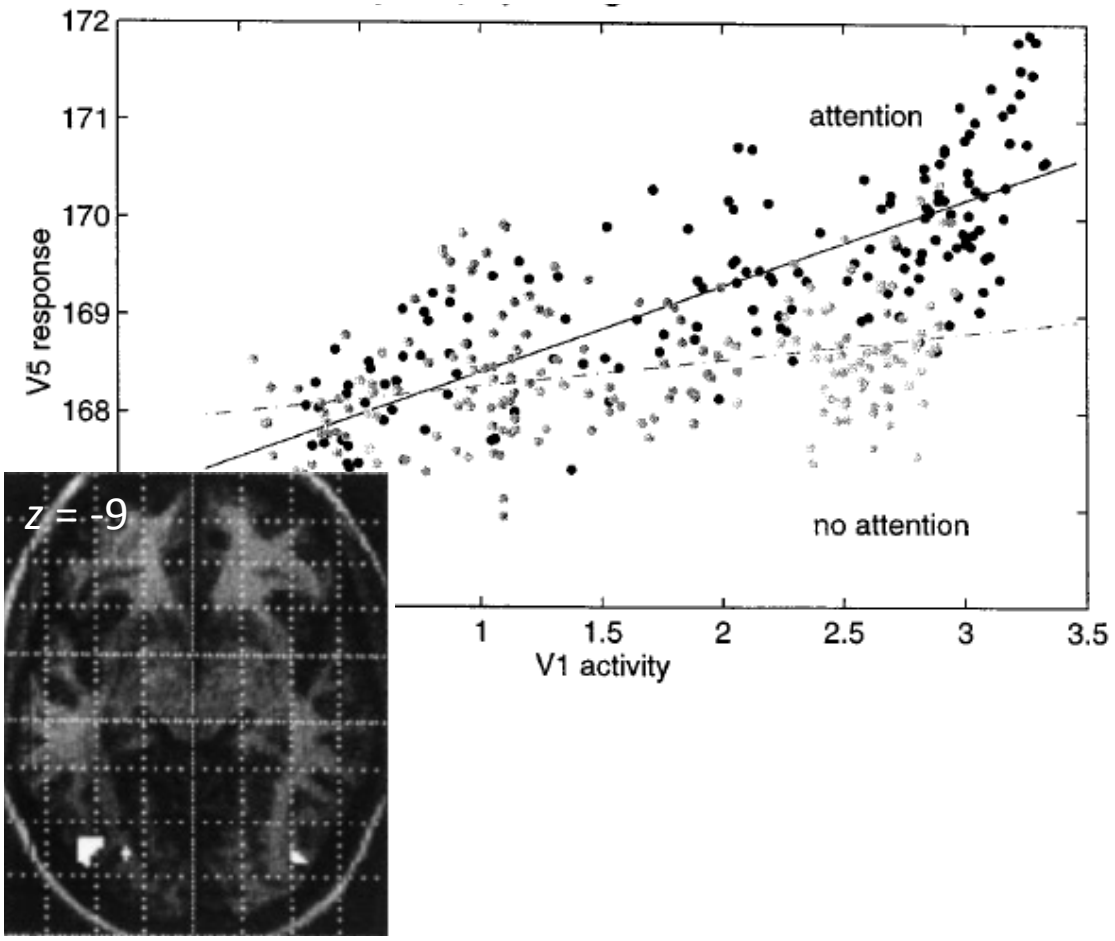




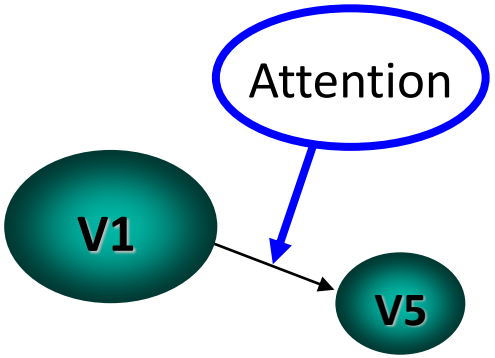
Friston et al., 1997
NeuroImage

- Primary visual cortex V1 activity = parametric physiological predictor
- If V1 predicts V5 over time => connectivity
- Attention vs. no-attention to motion = categorical psychological predictor
- Interaction = test of difference in connectivity
- Significant effects in V5 'visual motion area'

Psychophysiological interaction



- Attention augments the contribution of **V1** to **V5**



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)

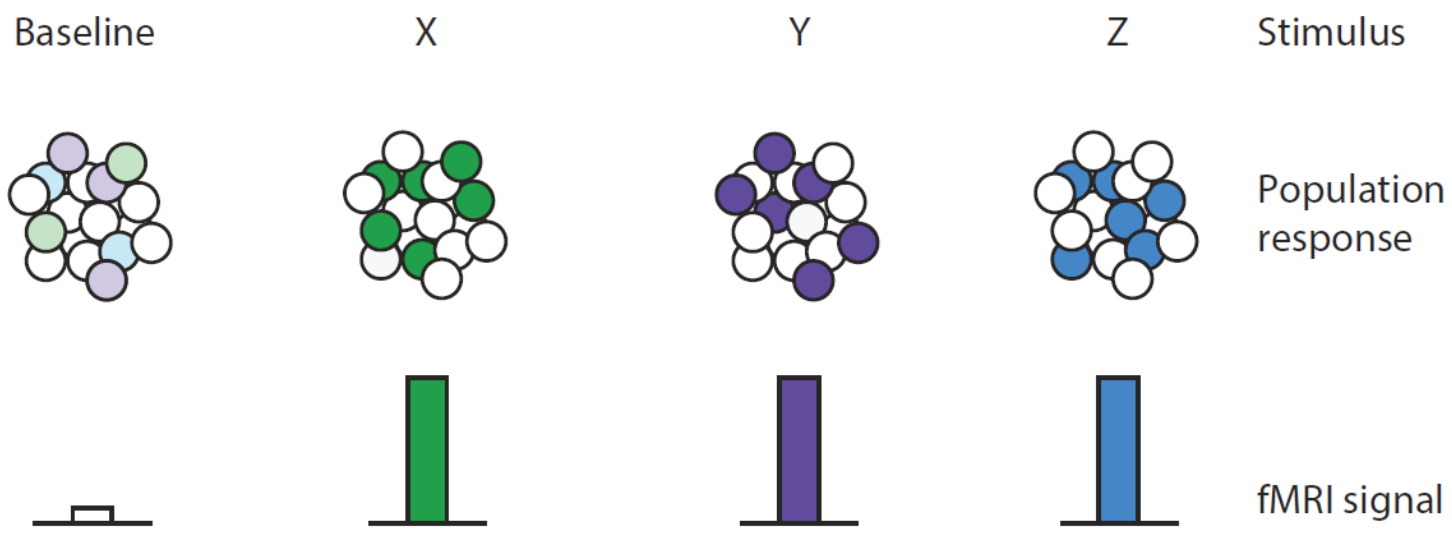
Overview

02 Experimental design (this lecture)

- fMRI for activation
- Design taxonomy
- fMRI for information

Representational brain imaging

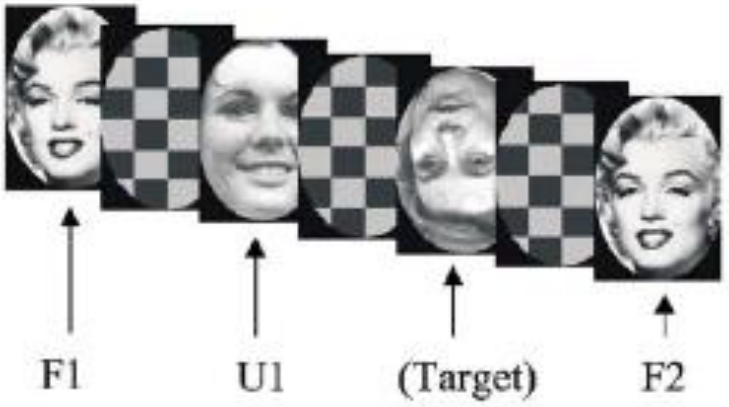
- So far we have tested for involvement of regions in processes
- fMRI can also be used to study the representational content of regions or voxels

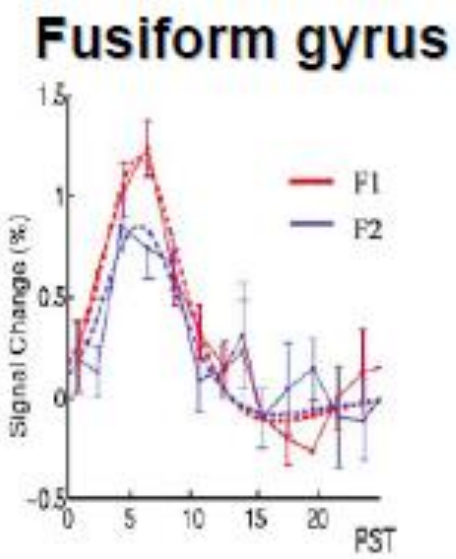


Barron, Garvert & Behrens 2016

fMRI adaptation

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



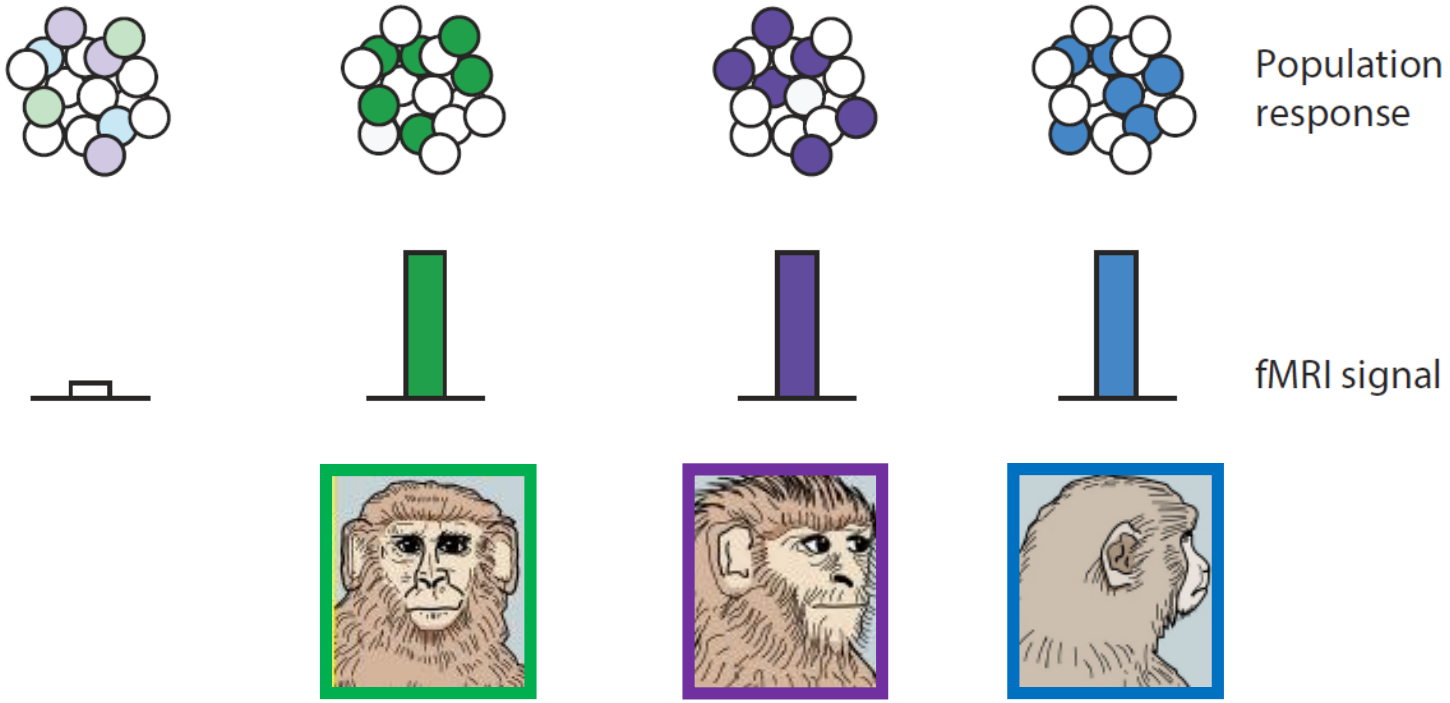


Henson et al. (2000)

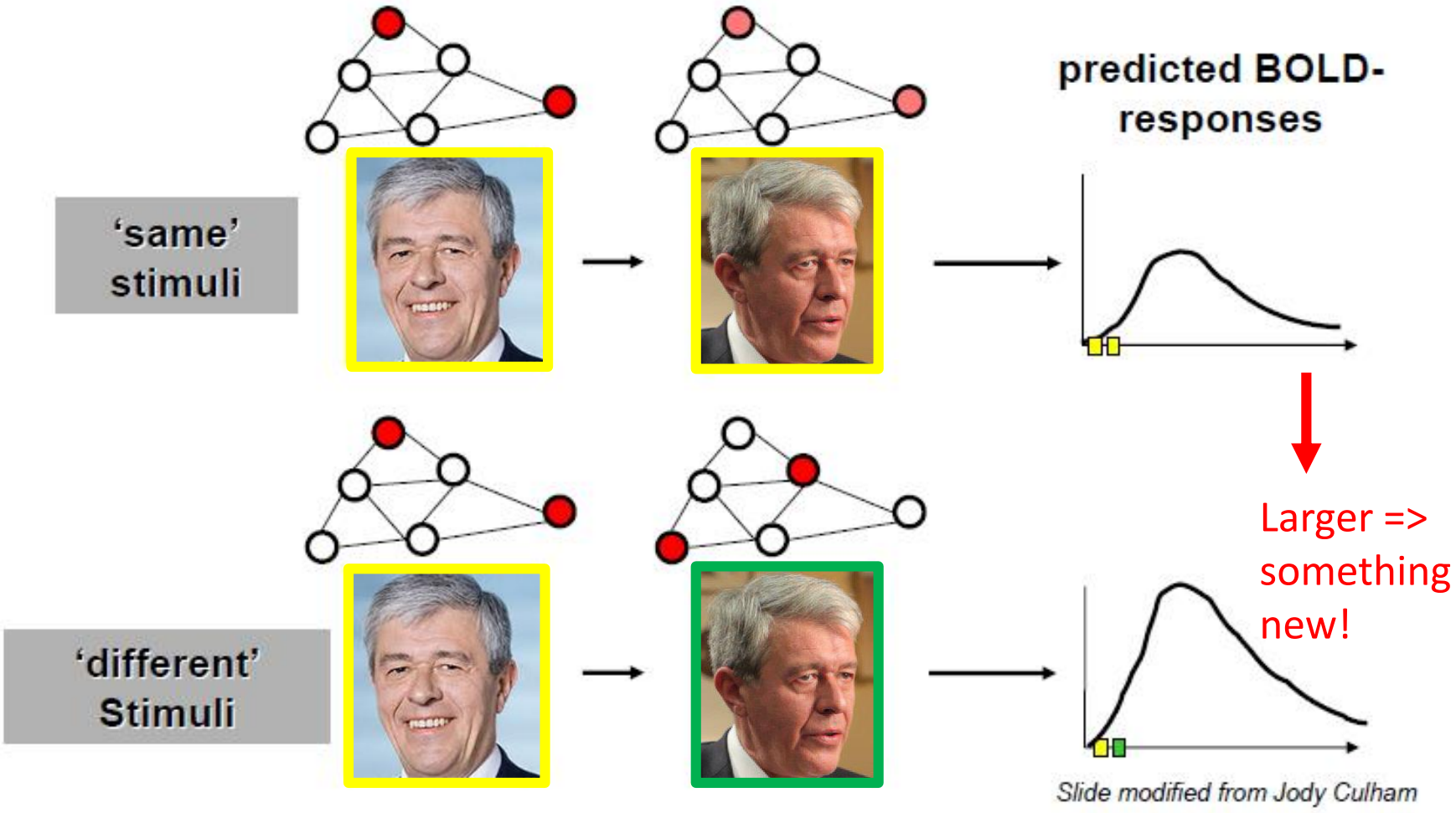
fMRI adaptation

Repetition suppression as a tool

- Maybe: mix of neurons tuned to different face orientations?
- Or: all viewpoint-invariant?



fMRI adaptation

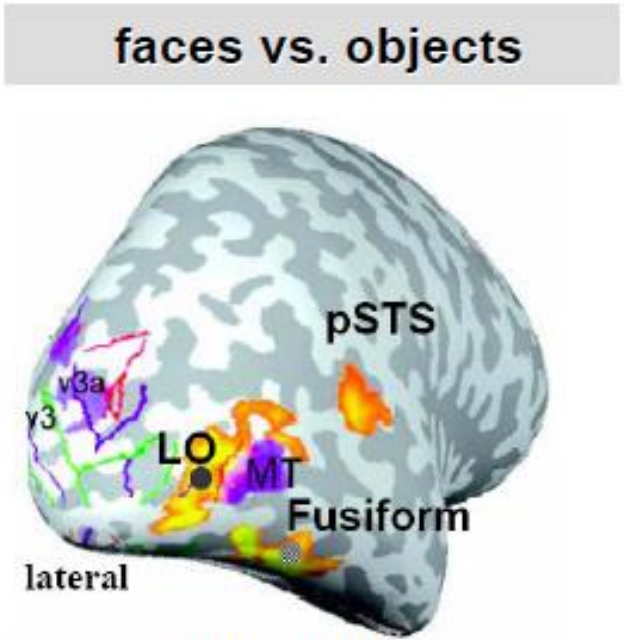


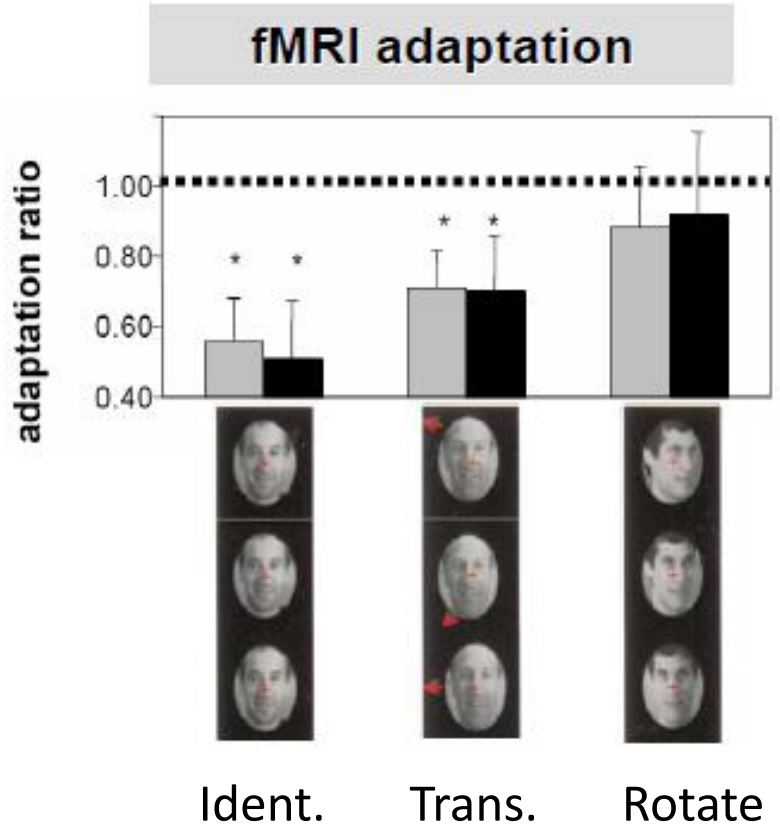
Release from adaptation => sensitivity to the changed feature

fMRI adaptation

Orientation tuning in human LOC (posterior Fusiform)

- Recovery from adaptation when rotate faces





Grill-Spector et al. (2001)

Interim summary

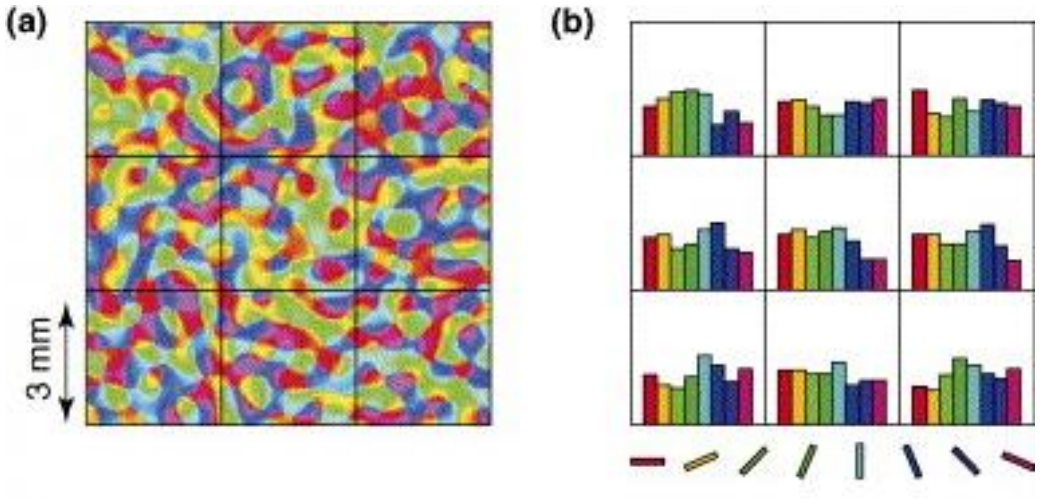
- fMRI adaptation uses repetition suppression to examine neural representations

Multivariate pattern analysis

Multivariate methods for studying representational content

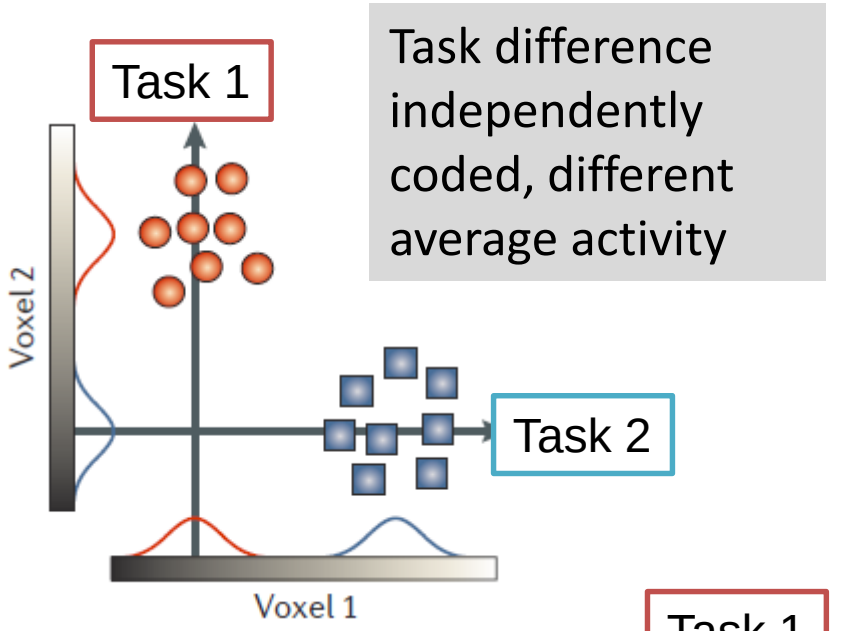
- If information is represented in a distributed fashion

… we may have fine-grained spatial structure across voxels

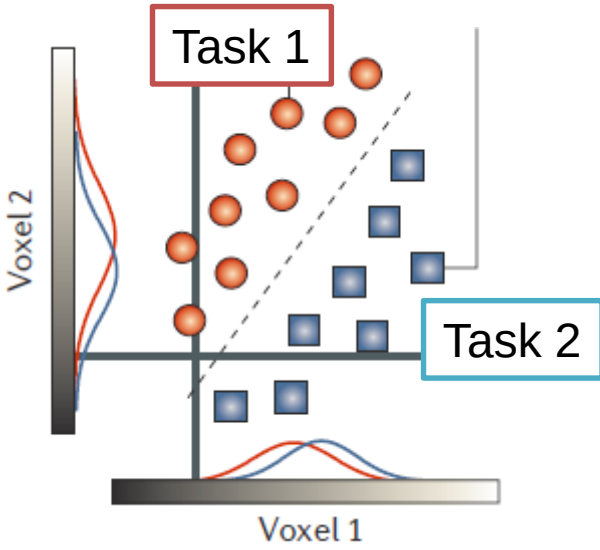


Multivariate pattern analysis

- In traditional Statistical Parametric Mapping, each voxel is analysed with a separate statistical test
- But brain regions not operate separately
- Classification of task by algorithm which has learned feature boundary

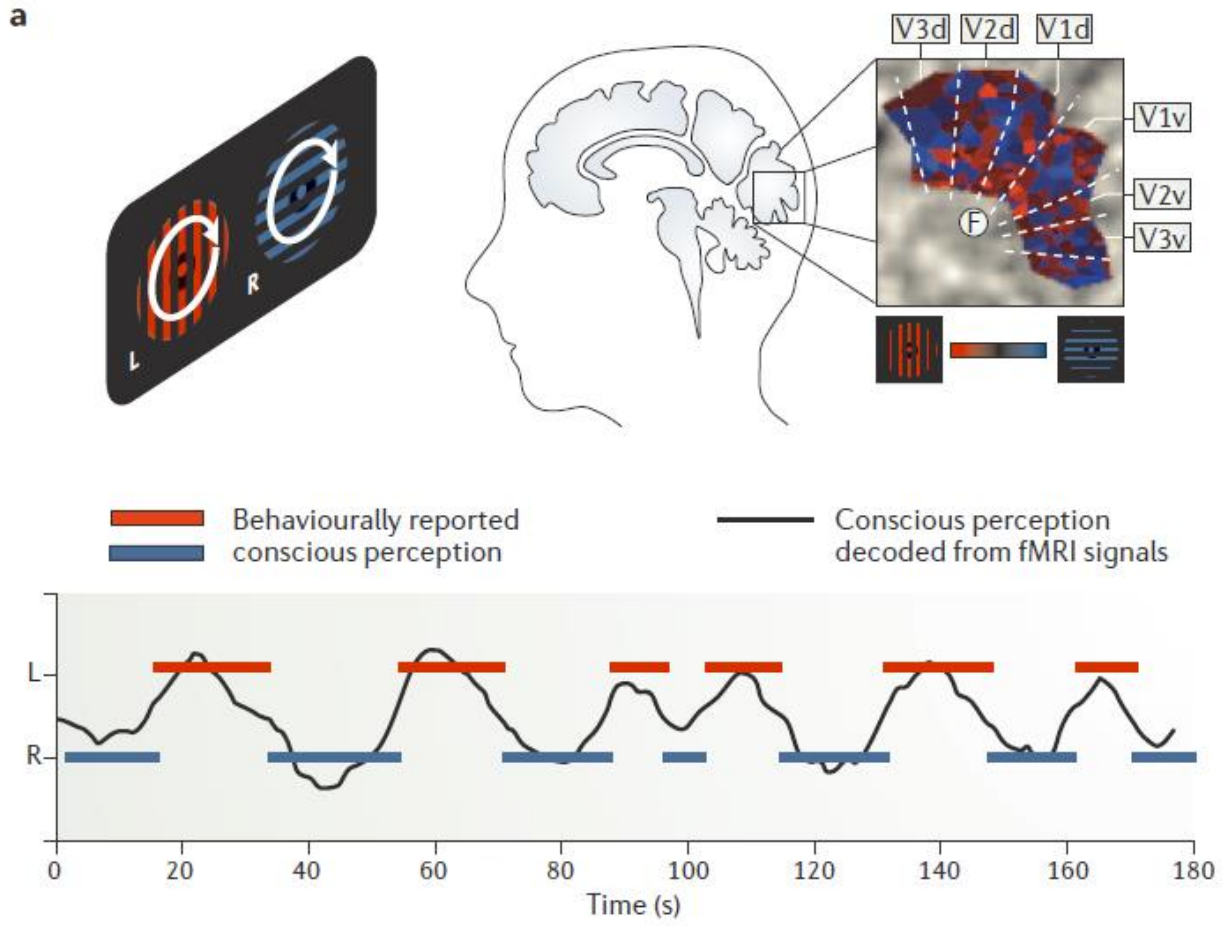


Task difference independently coded, different average activity



Task difference jointly coded between voxels

‘Decoding’ conscious experience



Binocular rivalry - spontaneously changing percept with no overt behaviour

Train a classifier algorithm on multivoxel data with known labels: red or blue perception

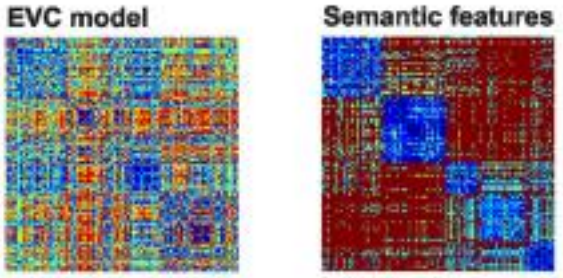
Then predict perception using independent dataset

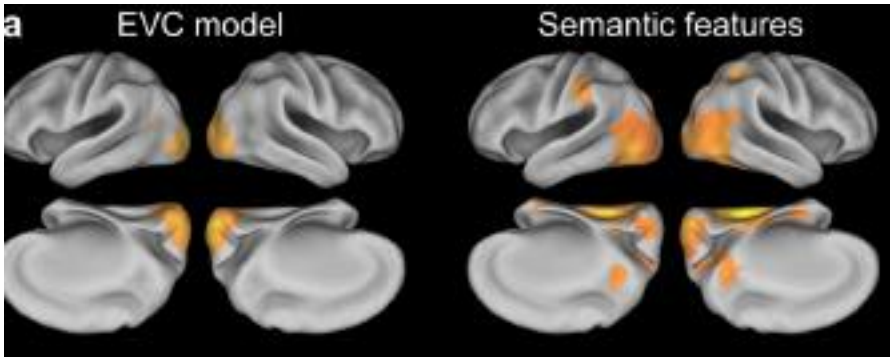
Haynes & Rees (2005; see 2006)

Representational similarity analysis

- Estimate similarity over stimuli/ conditions, multivoxel data
- Compare representational models of data similarity

Clarke & Tyler (2014): semantic versus visual confusability of objects





Kriegeskorte et al. (2008)

Interim summary

- Multivariate analysis can reveal more/ address different questions
- Simple classification study is like a categorical design, e.g. Haynes & Rees (2005)
- Similarity can be used like a conjunction, e.g. Polyn et al. (2005), encoding-retrieval similarity in memory
- More in Advanced course!

Conclusions

- Activation measures the involvement of a region in a process
- Design taxonomy supports tests of questions about
  - Processes differing between tasks
  - Modulation of one process by another
  - Overlap between tasks
  - Involvement in continuously varying quantities
- Adaptation and multivariate approaches focus on information content of activity, and representation
- Also concerned with difference and similarity, and (increasingly) with model comparison