Taxonomy of Experimental Design

Thomas Nichols

With thanks to:
Sara Bengtsson
Christian Ruff
Rik Henson
Daniel Glaser

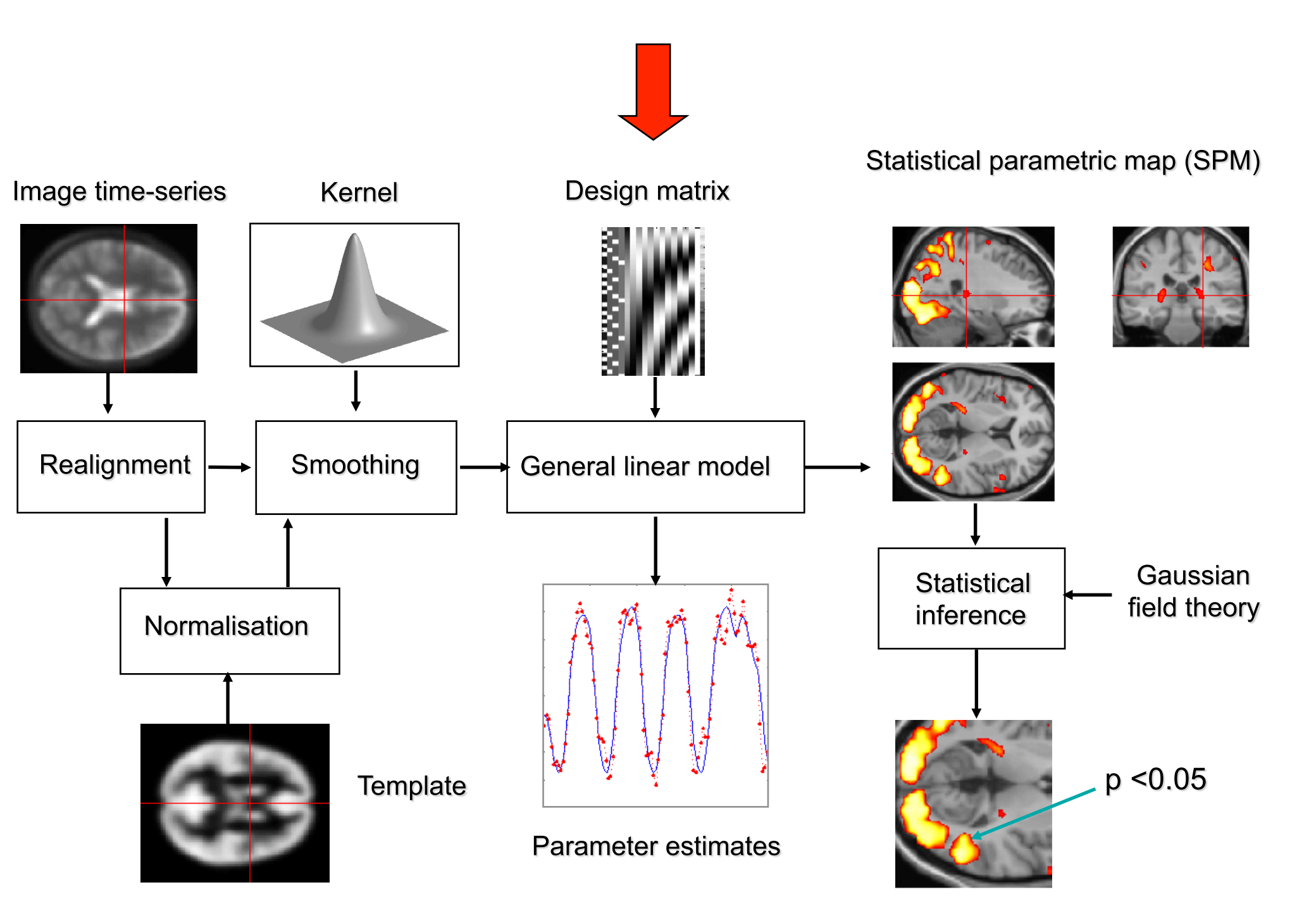


Image time-series
Kernel
Design matrix
Statistical parametric map (SPM)
Realignment
Smoothing
General linear model
Normalisation
Statistical inference
Gaussian field theory
Template
Parameter estimates
p <0.05

Overview

Categorical designs

Task A – Task B

Subtraction - Pure insertion, evoked / differential responses

Conjunction - Testing multiple hypotheses

Parametric designs

a A A A A

Linear - Adaptation, cognitive dimensions

Nonlinear - Polynomial expansions, neurometric functions

- Model-based regressors

Factorial designs

Categorical - Interactions and pure insertion

Parametric - Linear and nonlinear interactions

- Psychophysiological Interactions (PPI)

Cognitive subtraction

Aim

Neuronal structures underlying a *single* process P

Procedure

Contrast: [Task with P] – [matched task without P] → P

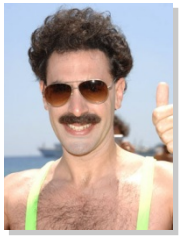
>> The critical assumption of „pure insertion“

Cognitive subtraction: Interpretations

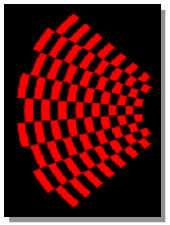
Question

Which neural structures support face recognition?

Distant stimuli

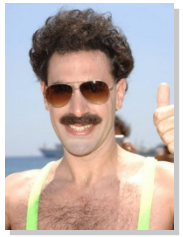


vs.



→ Several components differ!

Related stimuli



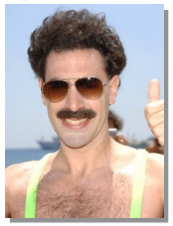
Borat

vs.

Mum?!

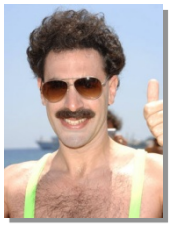
→ P implicit in control task?

Same stimulus, different tasks



Name the person!

vs.



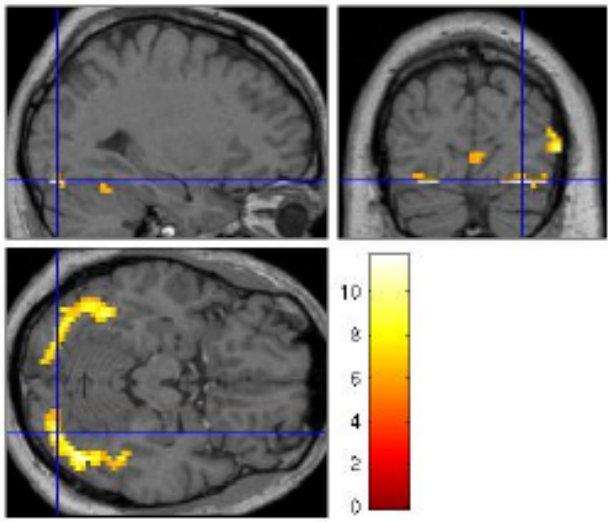
Name gender!

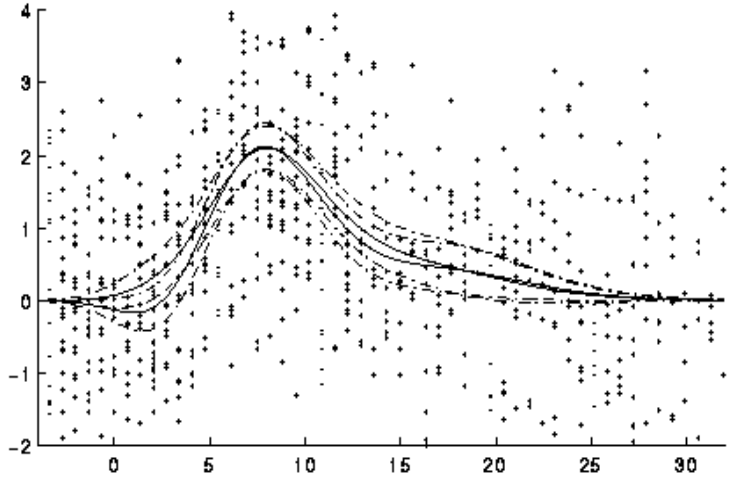
→ Interaction of process and task?

Evoked responses

SPM{F} testing for evoked responses

Faces vs. baseline 'rest'





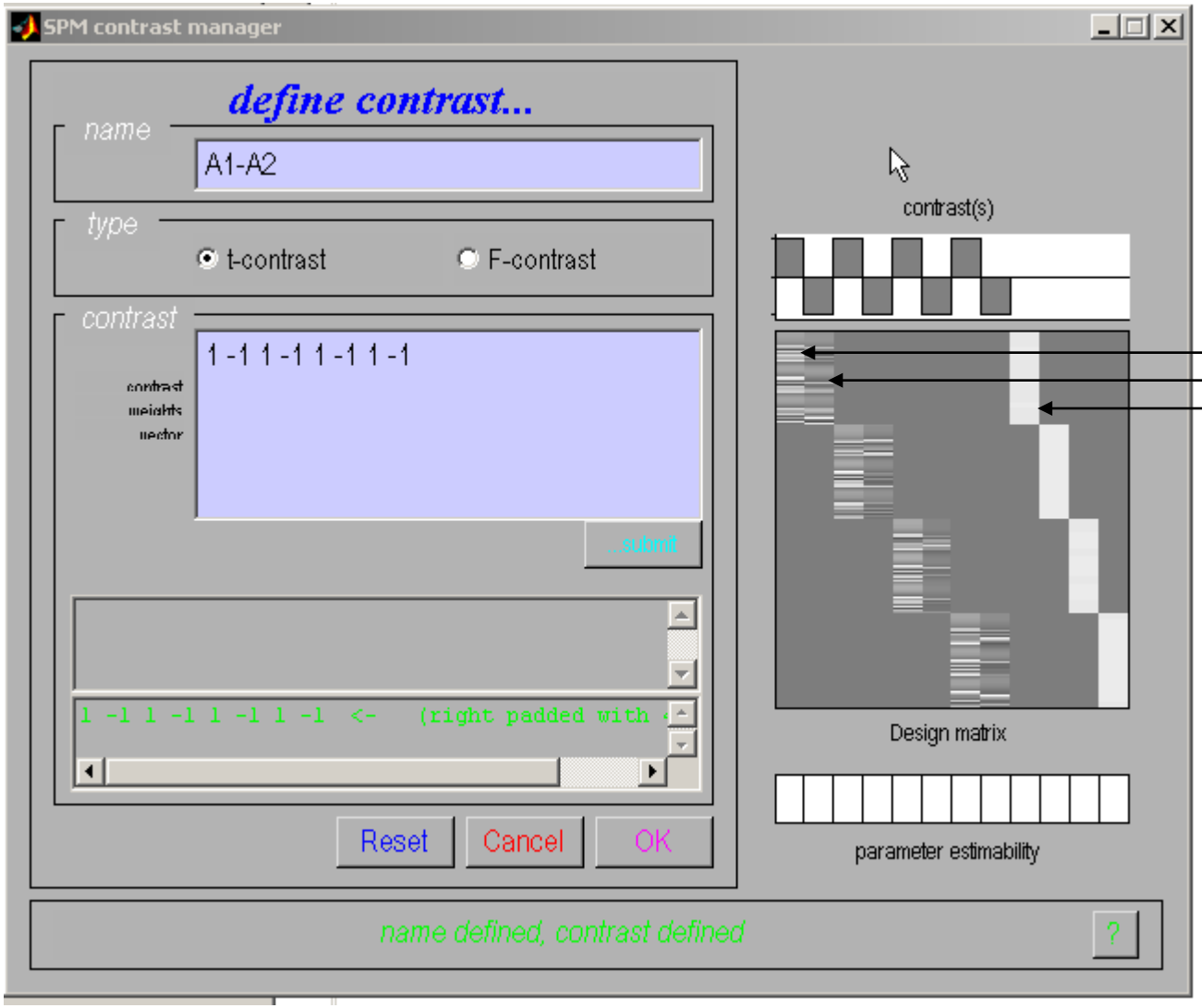
Peri-stimulus time {sec}

"Cognitive" interpretation hardly possible, but useful to define regions generally involved in the task.

Null events or long SOAs essential for estimation, which may result in an inefficient design.

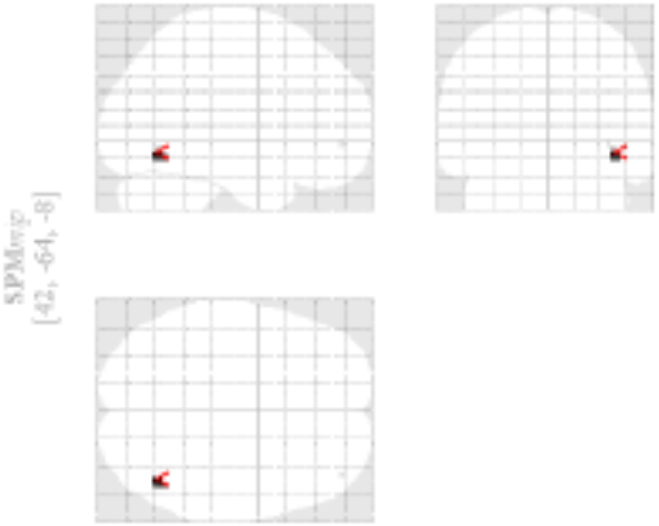
Can be useful as a mask to define regions of interests.

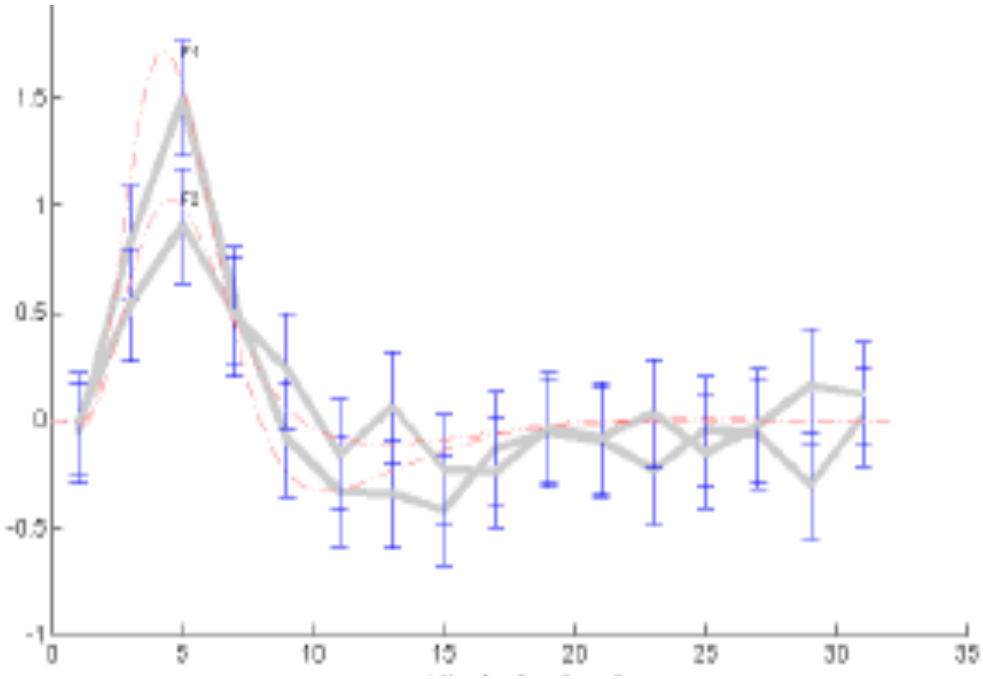
Categorical responses



Categorical response

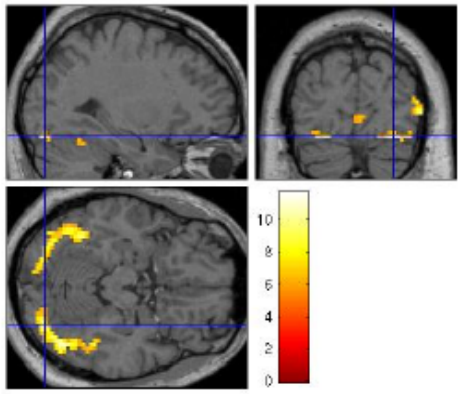
Famous faces: 1st time vs. 2nd time





Peri-stimulus time {sec}

Mask:
Faces vs. baseline.



Henson et al., (2002)

Overview

Categorical designs

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

Parametric designs

Linear	- Adaptation, cognitive dimensions
Nonlinear	- Polynomial expansions, neurometric functions
	- Model-based regressors

Factorial designs

Categorical	- Interactions and pure insertion
Parametric	- Linear and nonlinear interactions
	- Psychophysiological Interactions

Conjunction

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

Conjunctions can be conducted across different contexts:

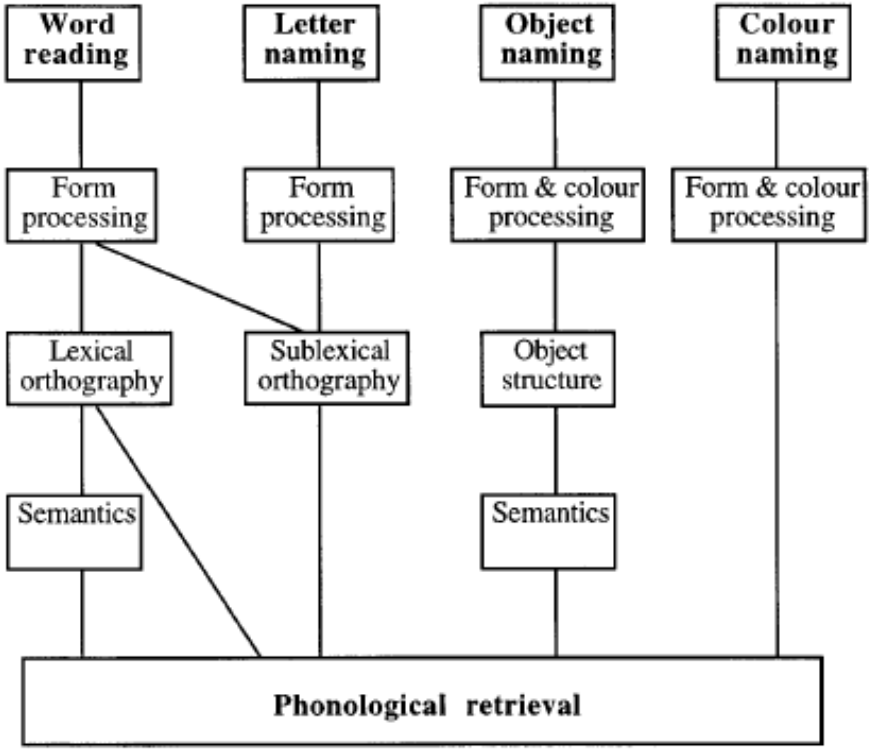
- tasks
- stimuli
- senses (vision, audition)

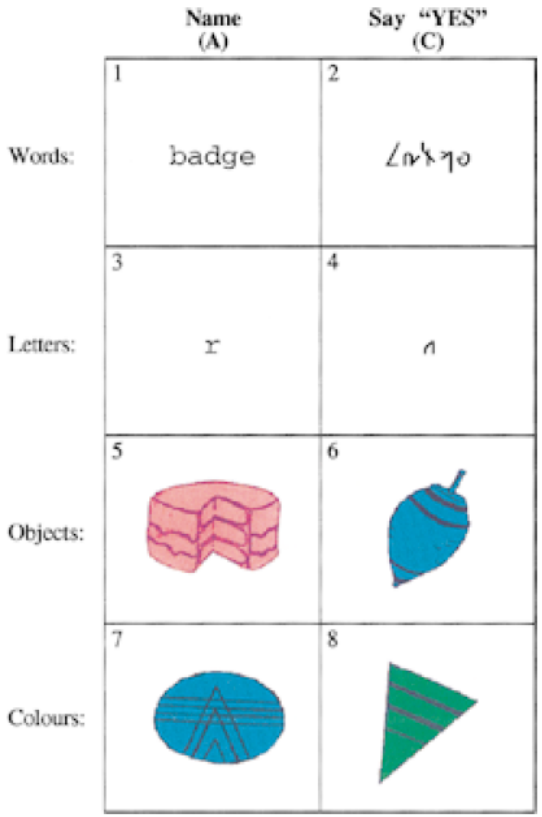
etc.

Conjunction: Example

Question

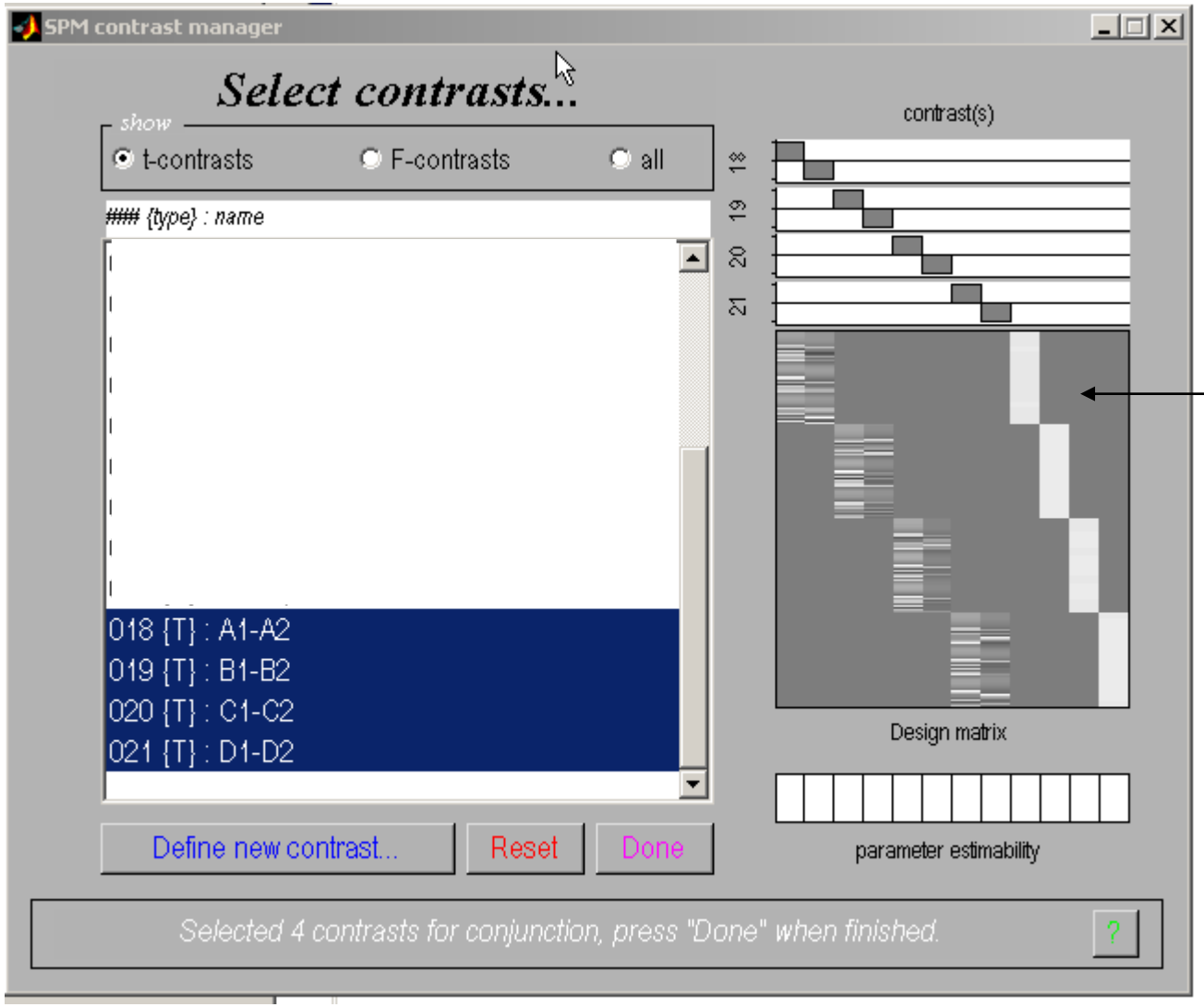
Which neural structures support phonological retrieval, independent of item?



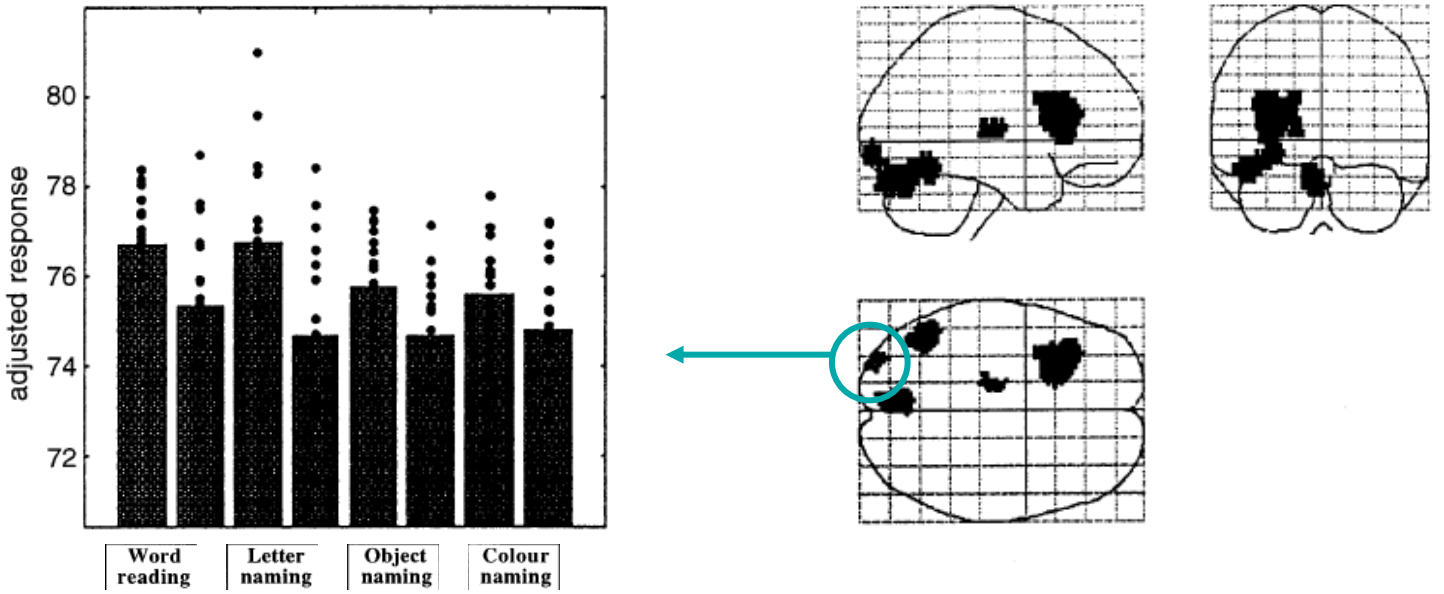


Price et al., (1996); Friston et al., (1997)

Conjunction specification



Conjunction: Example



Friston et al., (1997)

Conjunction: 2 ways of testing for significance

SPM8 offers two general ways to test the significance of conjunctions.

- Test of global null hypothesis:
  Significant set of consistent effects

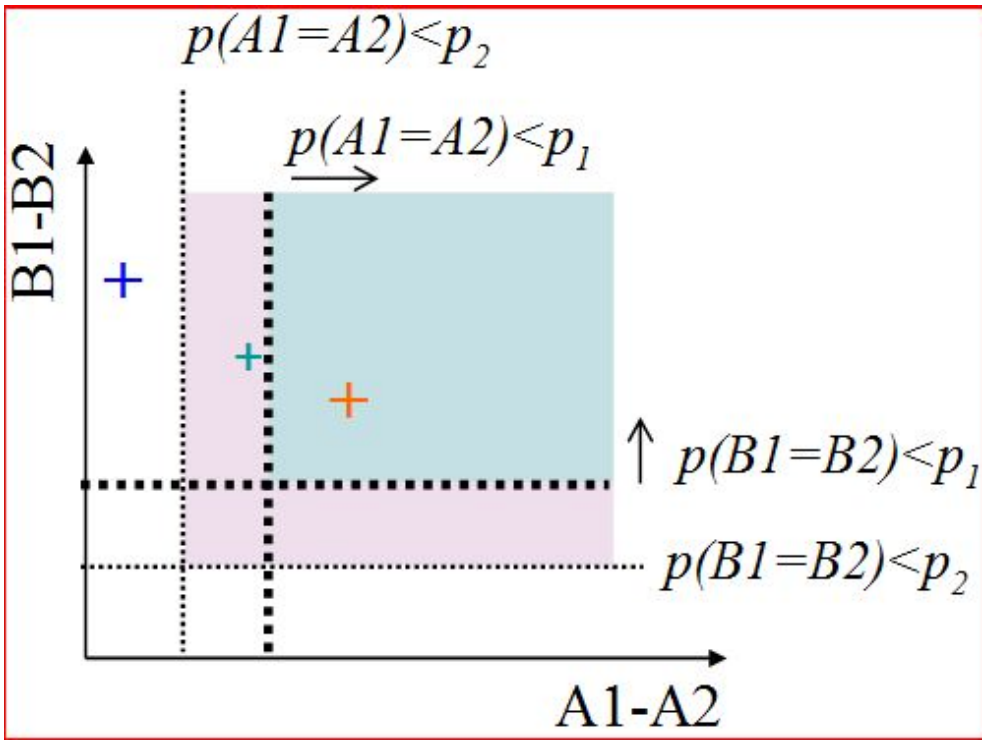
"which voxels show effects of similar direction (but not necessarily individual significance) across contrasts?"

The contrasts entering a global null conjunction have to be independent.

- Test of conjunction null hypothesis:
  Set of consistently significant effects

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

No independence requirement.



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

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

Overview

Categorical designs

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

Parametric designs

Linear	- Adaptation, cognitive dimensions
Nonlinear	- Polynomial expansions, neurometric functions
	- Model-based regressors

Factorial designs

Categorical	- Interactions and pure insertion
Parametric	- Linear and nonlinear interactions
	- Psychophysiological Interactions

Parametric Designs

Varying the stimulus-parameter of interest on a continuum, in multiple (n>2) steps...

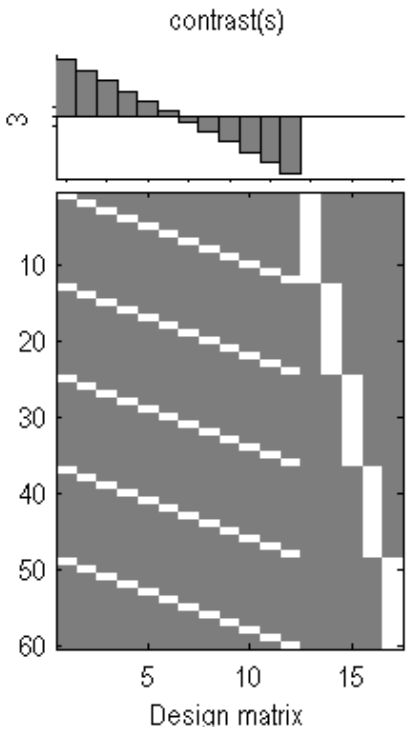
... and relating BOLD to this parameter

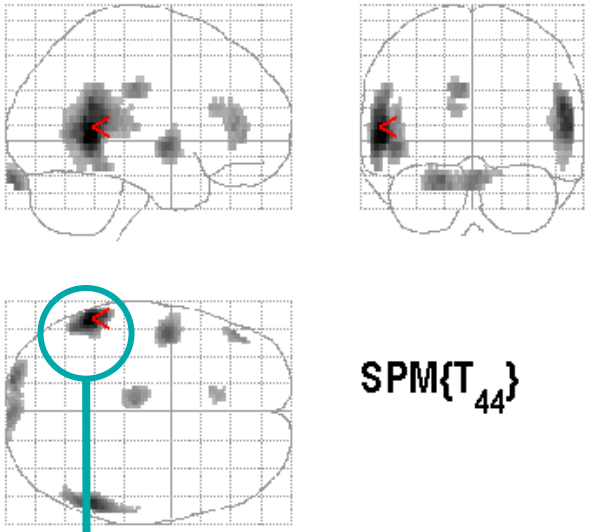
Possible tests for such relations are manifold:

- » Linear
- » Nonlinear: Quadratic/cubic/etc.
- » „Data-driven“ (e.g., neurometric functions, computational modelling)

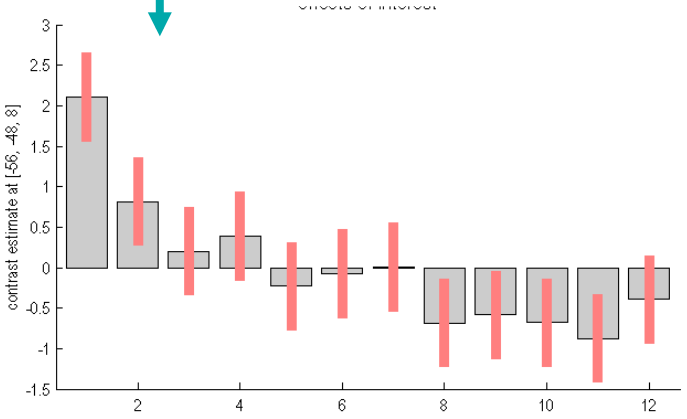
A linear parametric contrast

Linear effect of time

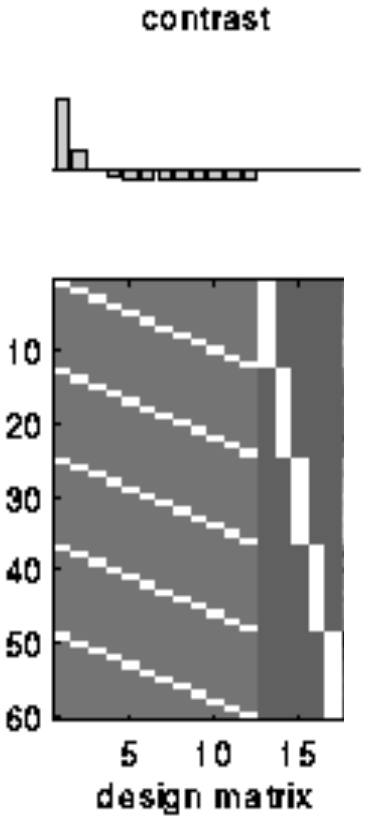




SPMresults: .\Spm2\PET_fluency\12ConStats
Height threshold T = 3.29
Extent threshold k = 0 voxels



Non-linear effect of time



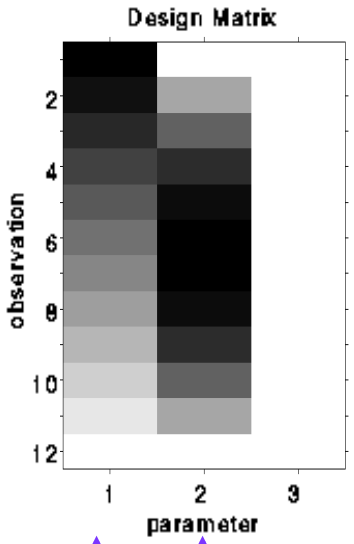
A non-linear parametric design matrix

Polynomial expansion:

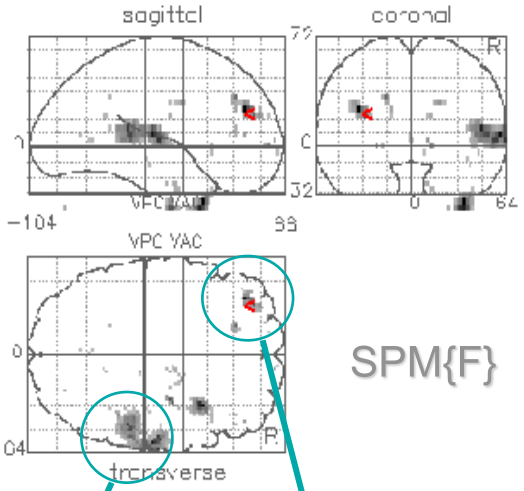
$f(x) \sim b_1 x + b_2 x^2 + \ldots$

...up to (N-1)th order for N levels

SPM8 GUI offers polynomial expansion as option during creation of parametric modulation regressors.

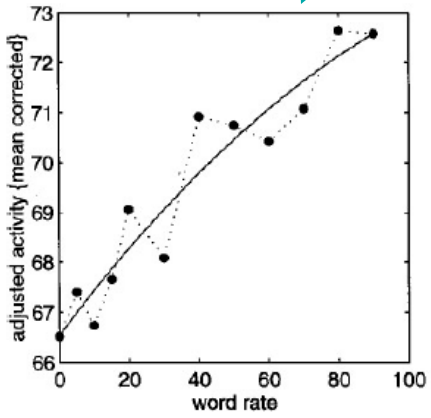


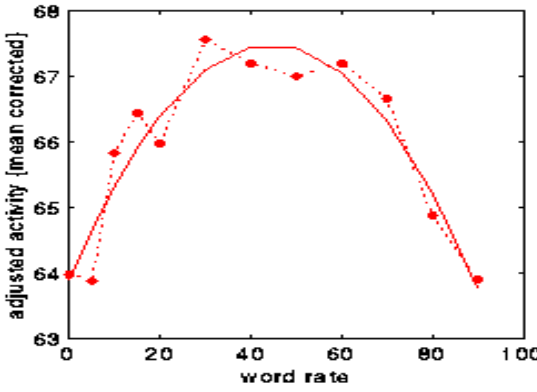
F-contrast [1 0] on linear param
F-contrast [0 1] on quadratic param



Linear

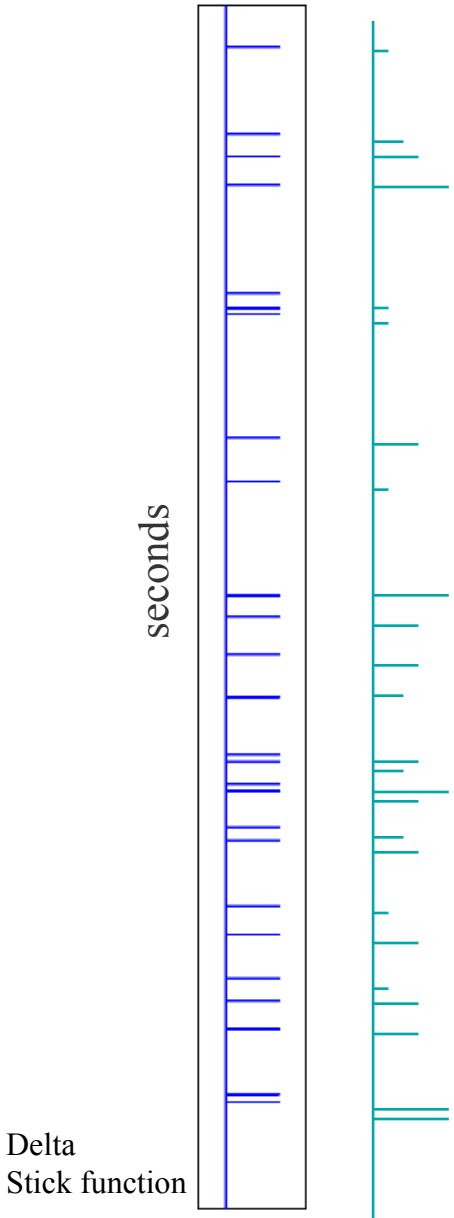
Quadratic





Buchel et al., (1996)

Parametric modulation



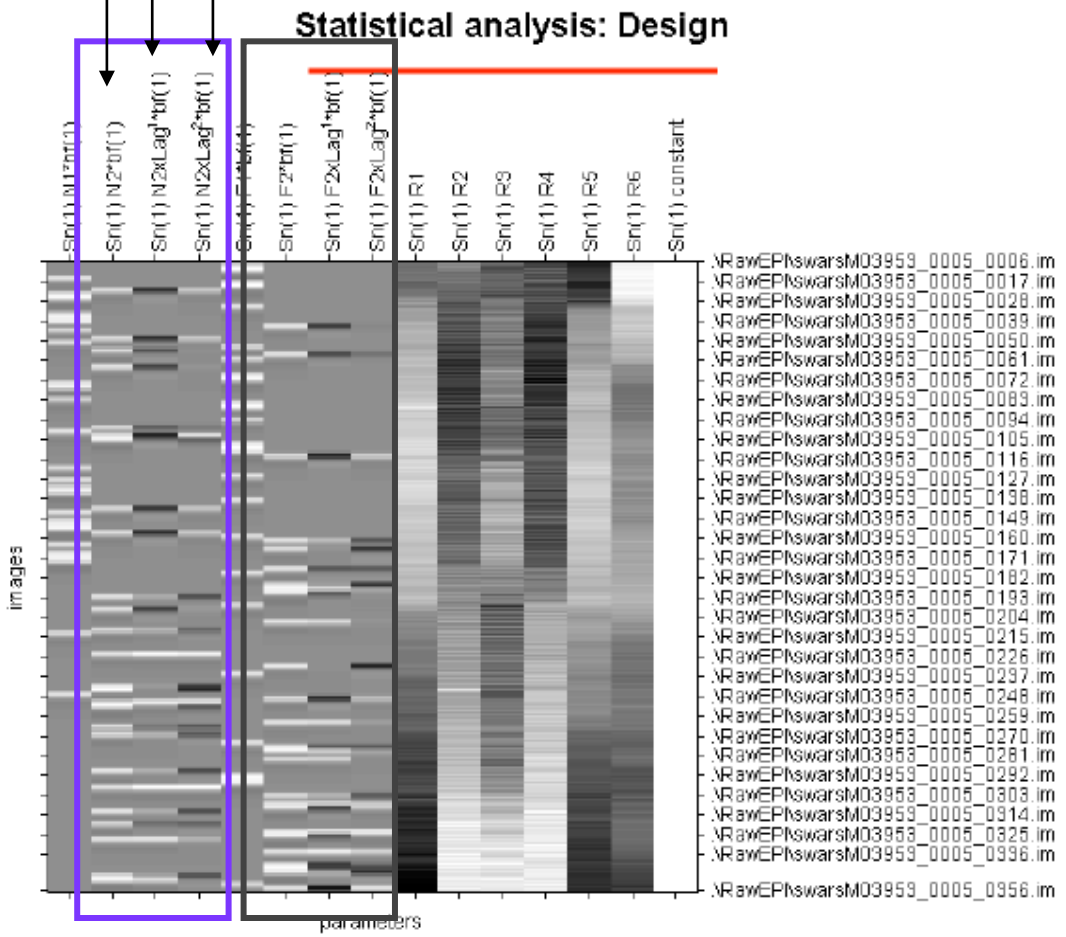
Delta
Stick function

Parametric
regressor

Quadratic param regress

Linear param regress

Delta function



Parametric design: Model-based regressors

In model-based fMRI, signals derived from a computational model for a specific cognitive process are correlated against BOLD from participants performing a relevant task, to determine brain regions showing a response profile consistent with that model.

The model describes a transformation between a set of stimuli inputs and a set of behavioural responses.

See e.g. O'Doherty et al., (2007) for a review.

Model-based regressors: Example

Question

Is the hippocampus sensitive to the probabilistic context established by event streams, rather than simply responding to the event itself?

The same question can be formulated in a quantitative way by using the information theoretic quantities ‘entropy’ and ‘surprise’.

- ‘surprise’ is unique to a particular event and measures its improbability.

$$I(x_i) = -\ln p(x_i);$$

- ‘entropy’ is the measure of the expected, or average, surprise over all events, reflecting the probability of an outcome before it occurs.

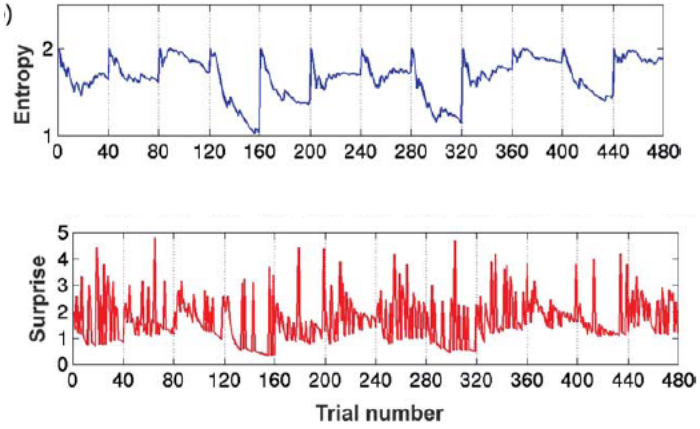
$$H(X) = \sum_i -p(x_i)\ln p(x_i) = \langle I(x_i)\rangle$$

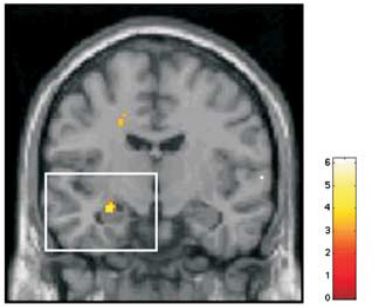
xi is the occurrence of an event. H(X) quantifies the expected info of events sampled from X.

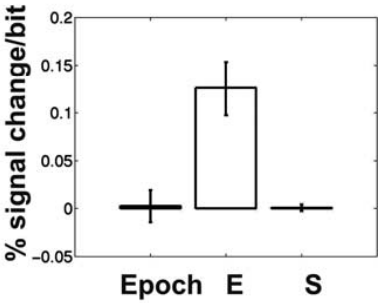
Thus, hippocampus would be expected to process ‘entropy’ and not ‘surprise’.

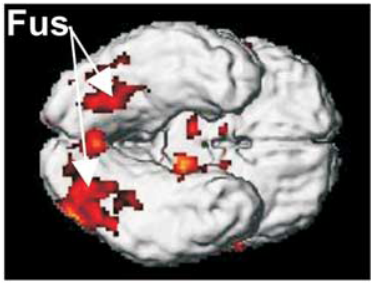
Model-based regressors: Example

Participants responded to the sampled item by pressing a key to indicate the position of that item in the row of alternative coloured shapes.
The participants will learn the probability with which a cue appears.









Strange et al., (2005)

Overview

Categorical designs

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

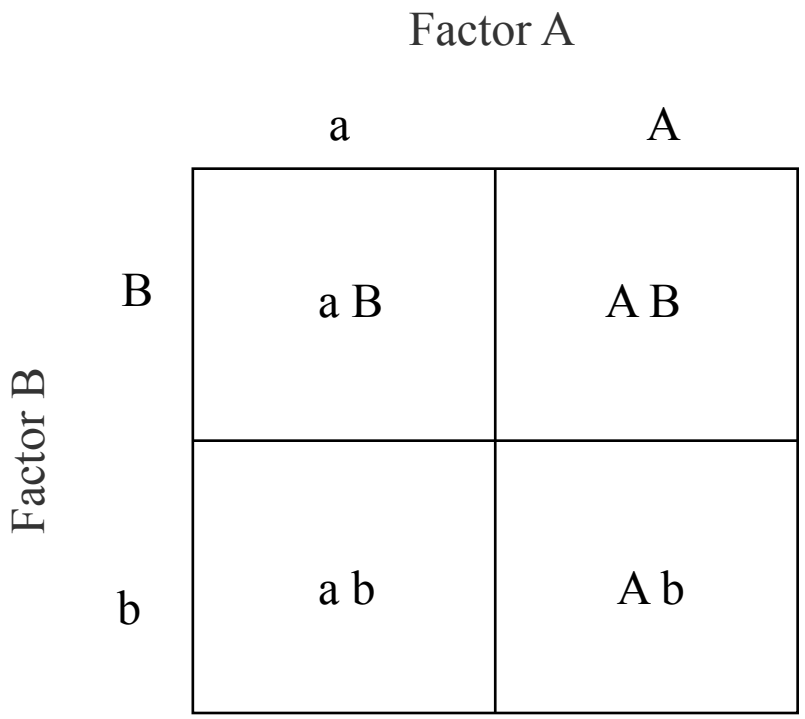
Parametric designs

Linear	- Adaptation, cognitive dimensions
Nonlinear	- Polynomial expansions, neurometric functions
	- Model-based regressors

Factorial designs

Categorical	- Interactions and pure insertion
Parametric	- Linear and nonlinear interactions
	- Psychophysiological Interactions

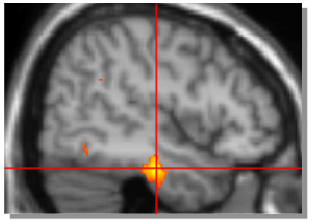
Factorial designs: Main effects and Interaction

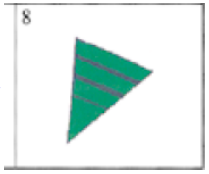
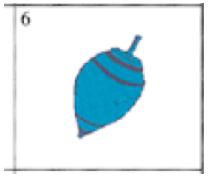
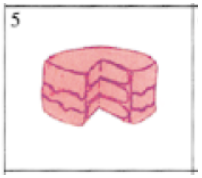


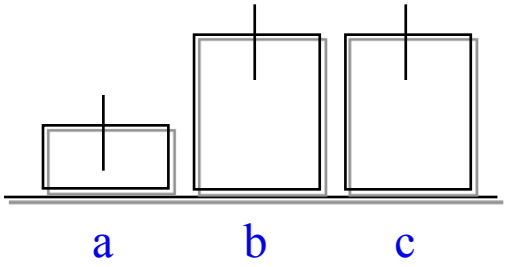
Factorial designs: Main effects and Interaction

Question

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

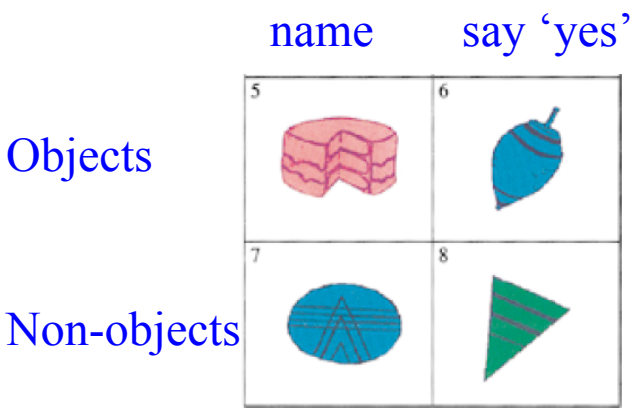


Non-object	say 'yes' 	a. Visual analysis and speech.
Object	say 'yes' 	b. Visual analysis, speech, and object recognition.
Object	name 	c. Visual analysis, speech, object recognition, and phonological retrieval.



Friston et al., (1997)

Factorial designs: Main effects and Interaction

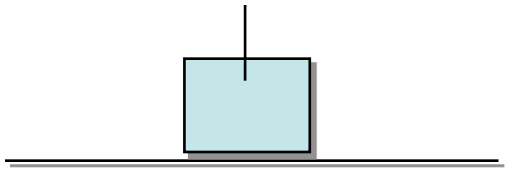


Main effect of task (naming): (O n + N n) – (O s + N s)

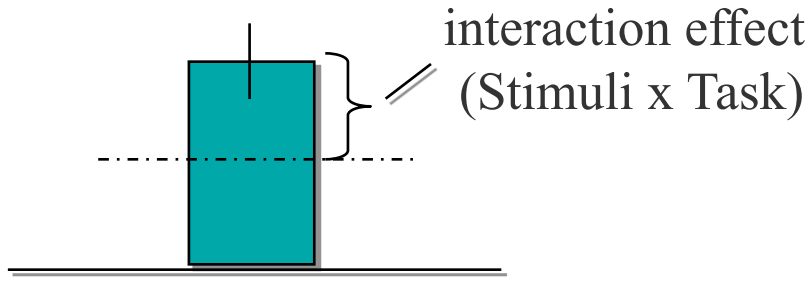
Main effect of stimuli (object): (O s + O n) – (N s + N n)

Interaction of task and stimuli: (O n - N n) – (O s - N s)

Can show a failure of pure insertion



'Say yes' [Object vs Non-objects]

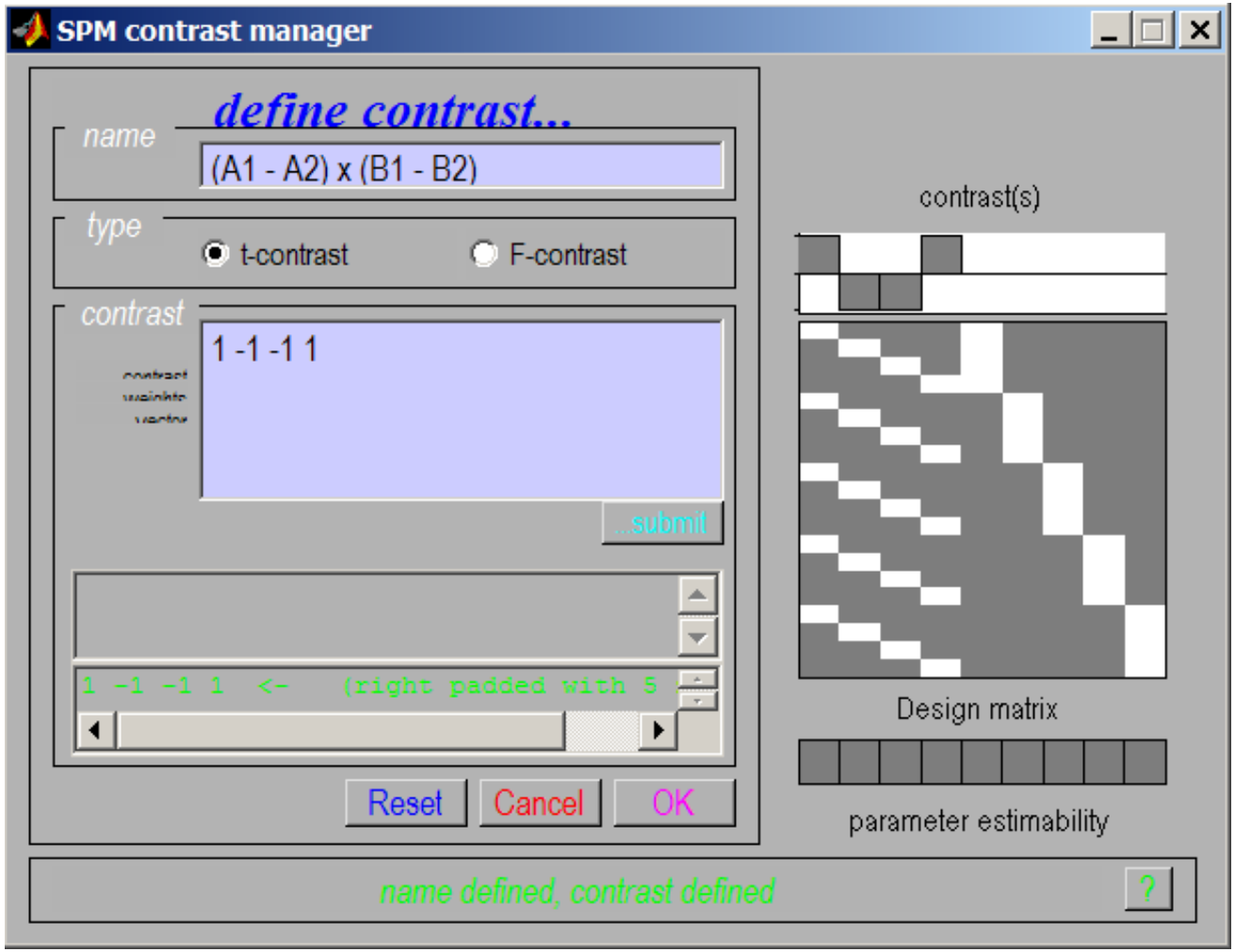


Phonological retrieval [Object vs Non-objects]

Inferotemporal (IT) responses do discriminate between situations where phonological retrieval is present or not. In the absence of object recognition, there is a *deactivation* in IT cortex, in the presence of phonological retrieval.

Friston et al., (1997)

Interaction and pure insertion

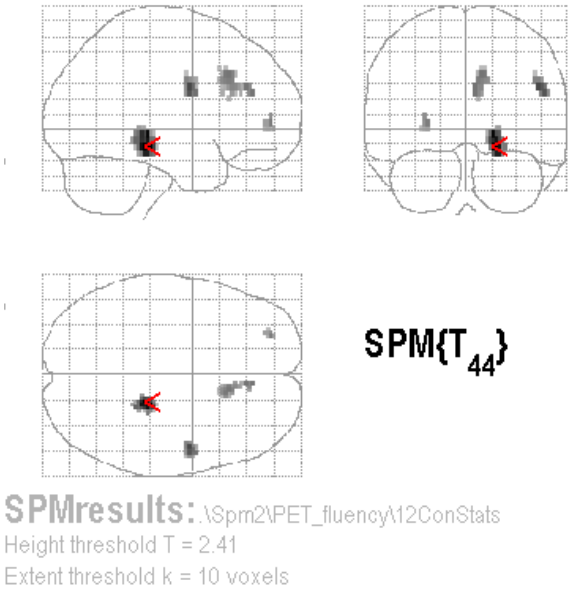


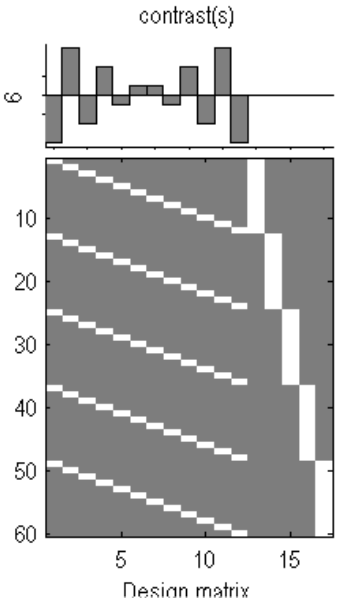
Linear Parametric Interaction

Question

Are there different kinds of adaptation for Word generation and Word repetition as a function of time?

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





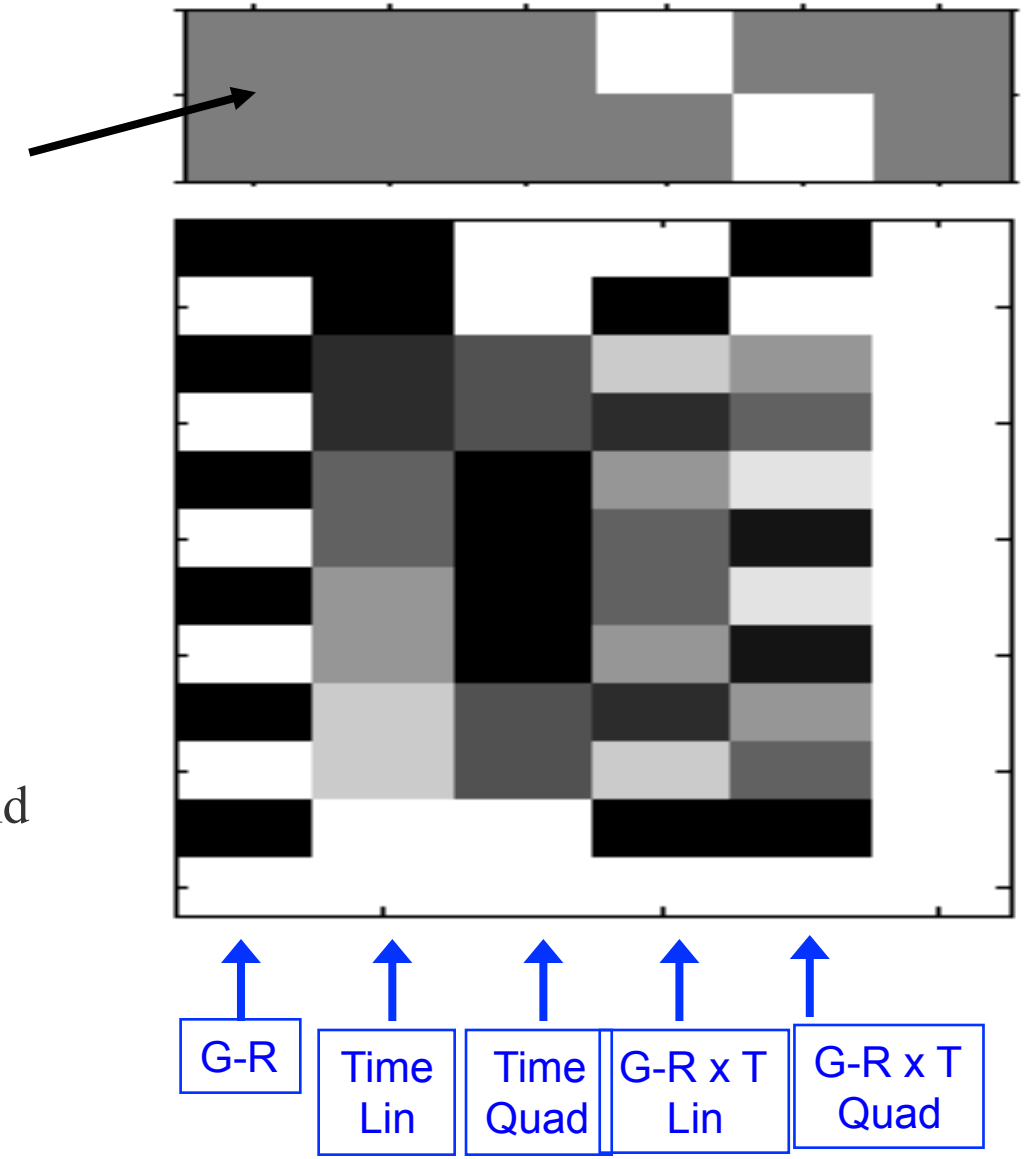
Contrast:

[5 3 1 -1 -3 -5](time) ⊗ [-1 1] (categorical)

= [-5 5 -3 3 -1 1 1 -1 3 -3 5 -5]

Non-linear 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…

Overview

Categorical designs

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

Parametric designs

Linear	- Adaptation, cognitive dimensions
Nonlinear	- Polynomial expansions, neurometric functions
	-Model-based regressors

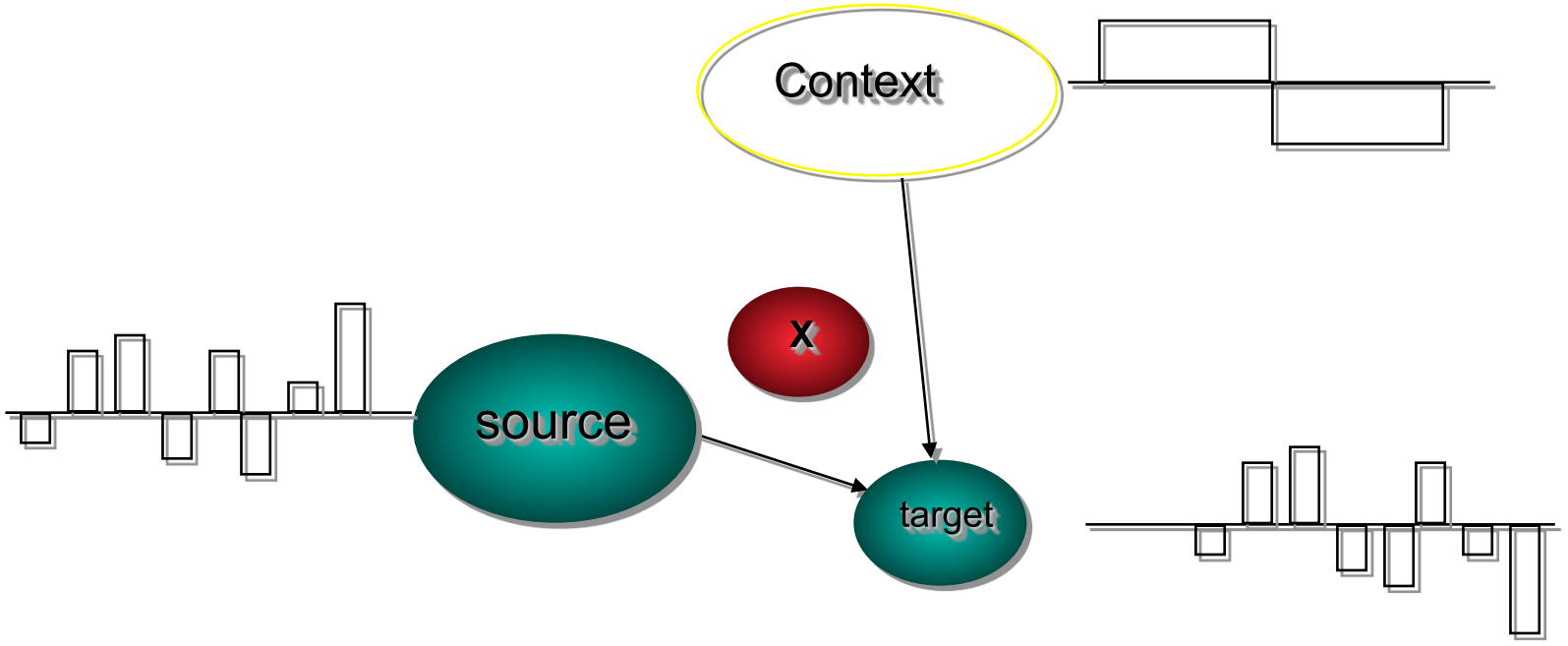
Factorial designs

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

Psycho-physiological Interaction (PPI)

Parametric, factorial design,
in which one factor is a psychological context

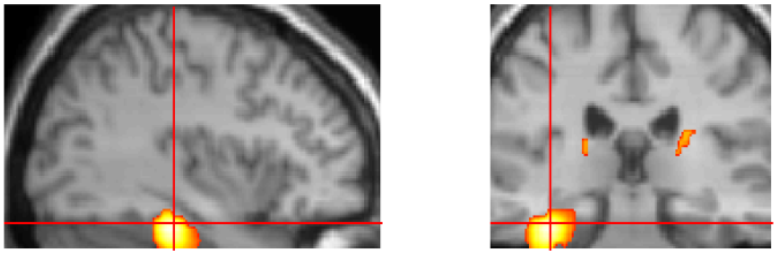
and the other is a physiological source
(activity extracted from a brain region of interest)

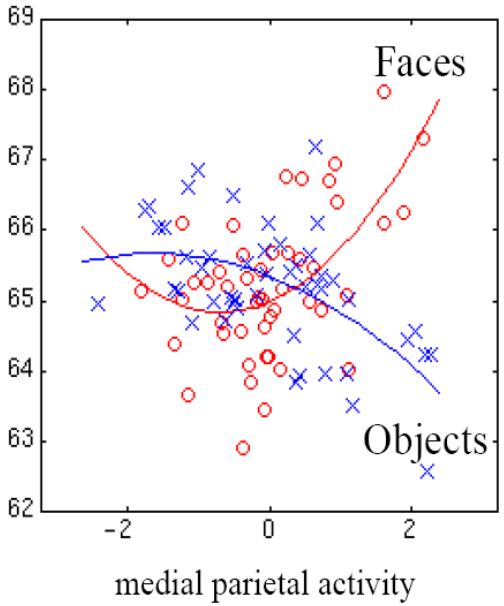


With PPIs we predict physiological responses in one part of the brain
in terms of an interaction between task and activity in another part of the brain.

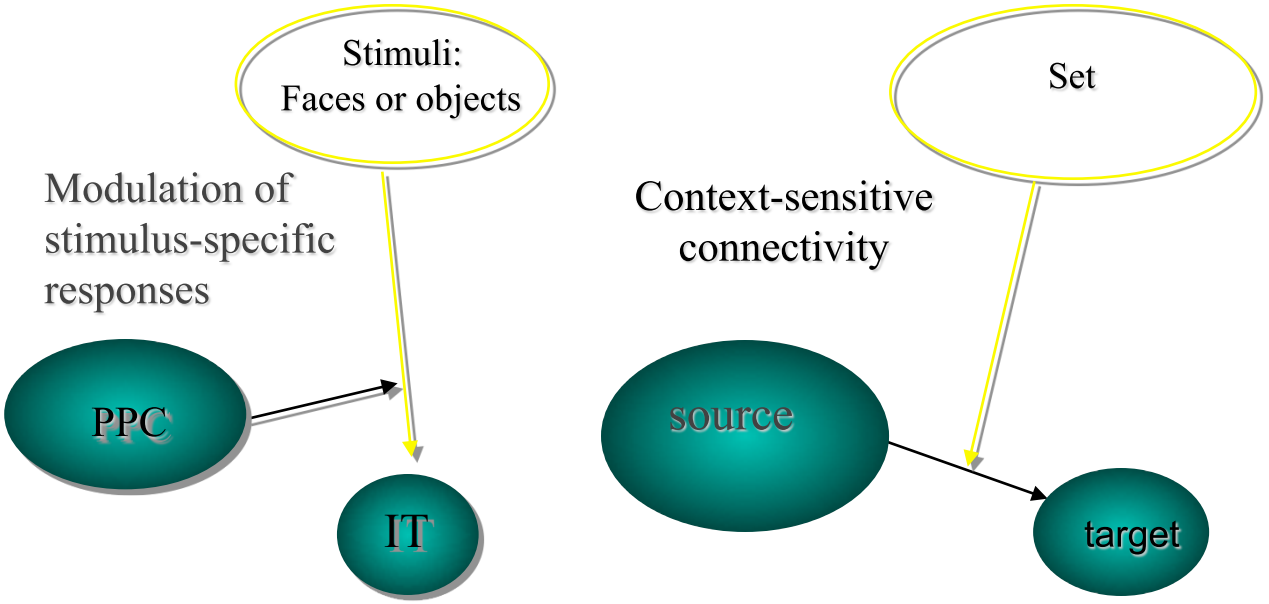
Psycho-physiological Interaction (PPI)

Psycho-physiological interactions
in the right infero-temporal region





Inferiotemporal cortex discriminates between faces and objects only when parietal activity is high.



Dolan et al., 1997

Overview

Categorical designs

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

Parametric designs

Linear	- Adaptation, cognitive dimensions
Nonlinear	- Polynomial expansions, neurometric functions
	- Model-based regressors

Factorial designs

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