

# Experimental design

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With thanks to:

Elisa van der Plas

Mona Garvert

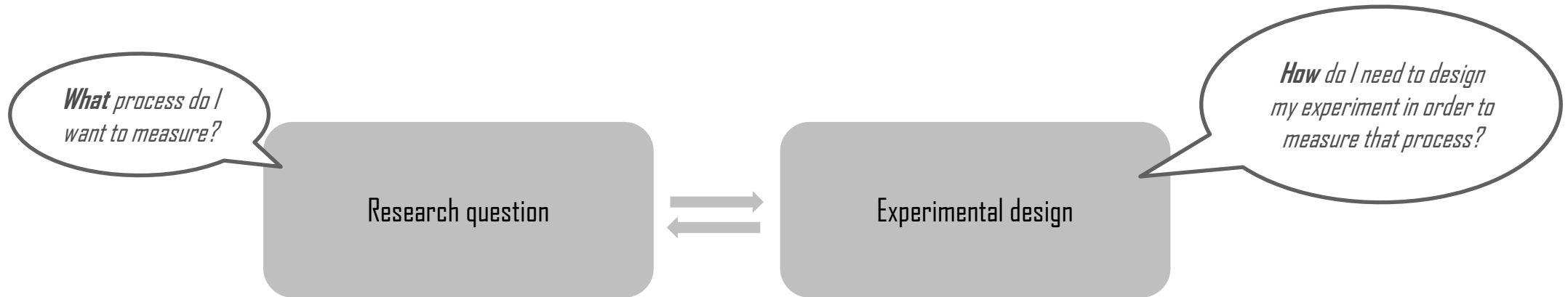
Sara Tomiello

Sara Bengtsson

Christian Ruff

Rik Henson

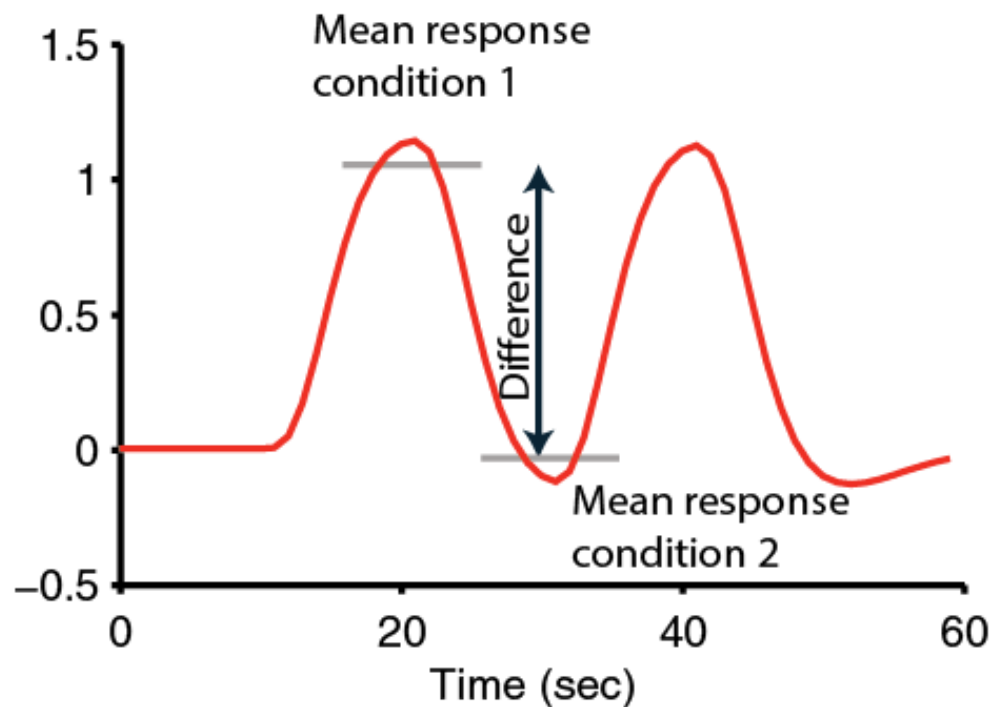
# It all starts with a good design!



## Why is that?

The BOLD signal does NOT provide you with an absolute measure of neural activity

Therefore, you need to compare activity across conditions



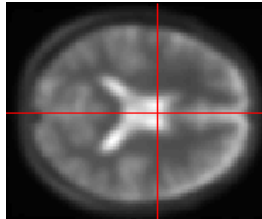
The sensitivity of your design depends on maximizing the relative change between conditions

# SPM processing hierarchy



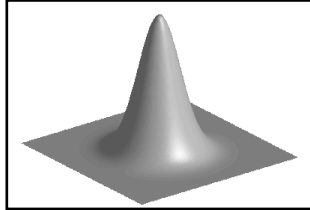
At the very top...

Image time-series



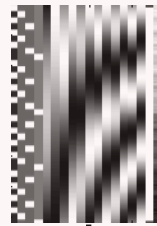
Realignment

Kernel



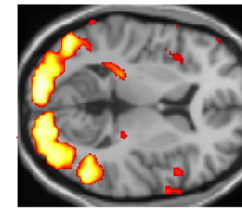
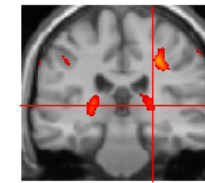
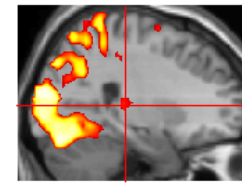
Smoothing

Design matrix



General linear model

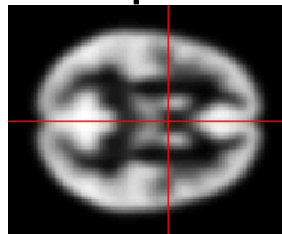
Statistical parametric map (SPM)



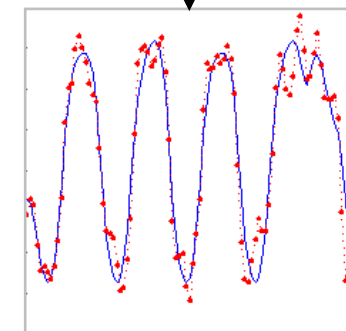
Statistical inference

Gaussian field theory

Normalisation



Template



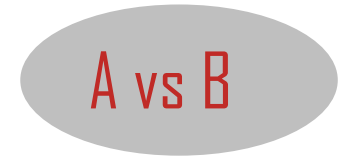
Parameter estimates

$p < 0.05$

## 1. Categorical designs

- Subtraction
- Conjunction

Pure insertion, evoked / differential responses  
Testing multiple hypotheses



## 2. Parametric designs

- Linear
- Nonlinear

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



## 3. Factorial designs

- Categorical
- Parametric

Interactions and pure insertion  
Linear and nonlinear interactions  
Psychophysiological Interactions (PPI)



# Cognitive subtraction

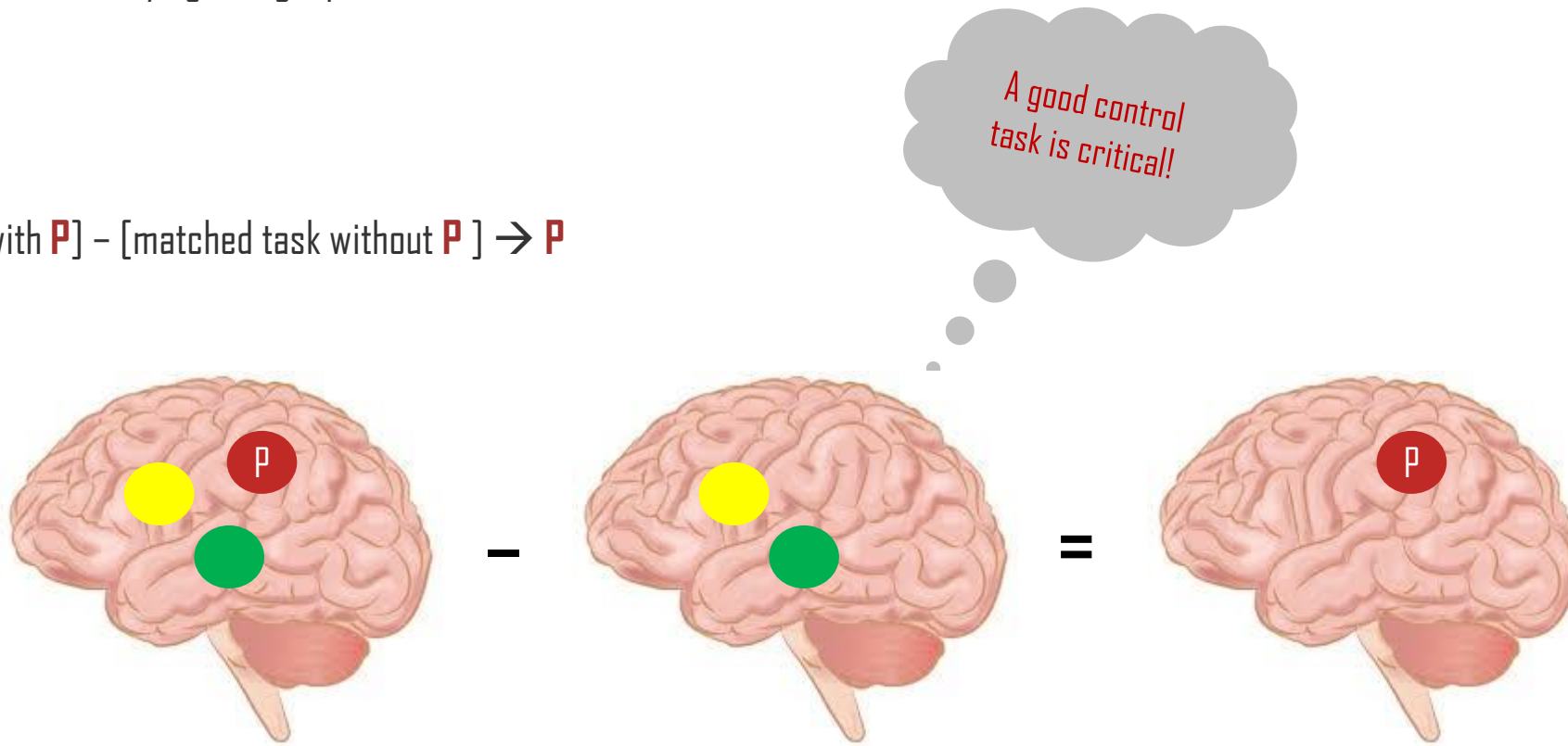
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## Aim

Neuronal structures underlying a *single* process **P**

## Procedure

Contrast: [Task with **P**] - [matched task without **P**]  $\rightarrow$  **P**



However...

## The critical assumption of pure insertion

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*Pure insertion assumption:* Assumption that adding components does not affect other processes



Pretty close to pure insertion...

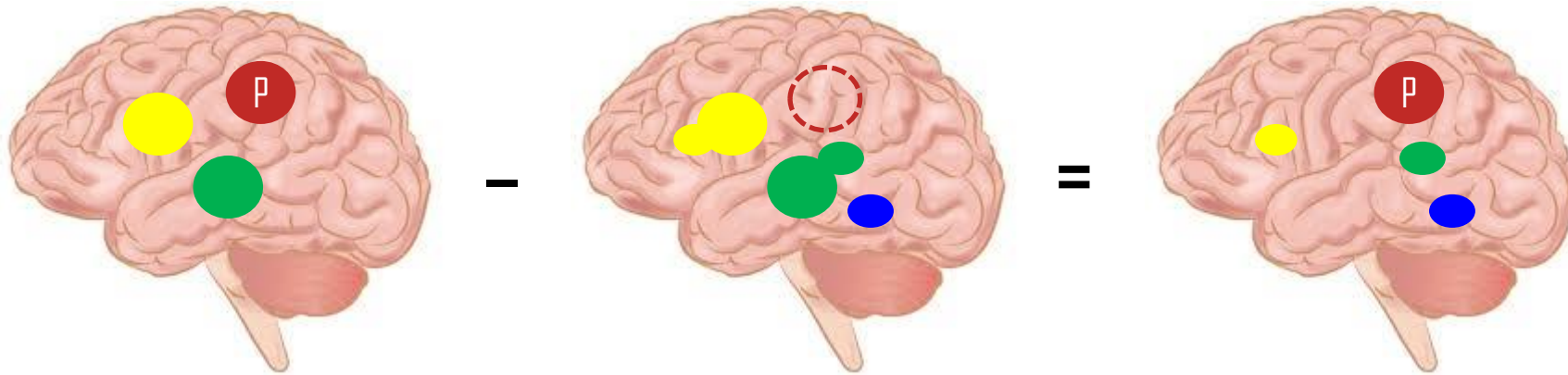


...this one not...

... the assumption of pure insertion is not realistic for brain processes.

## The critical assumption of pure insertion

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"Adding" or "removing" a process might change  
other processes  
→ non-linearity, i.e. interactions



**Question:** Which neural structures support **face recognition**?



What is a good control task?

**Aim:** Isolation of a cognitive process

**Method:** Compare the neural signal for a task that activates the cognitive process of interest (P) and a second task that controls for all but the process of interest (P)

# Choosing your baseline

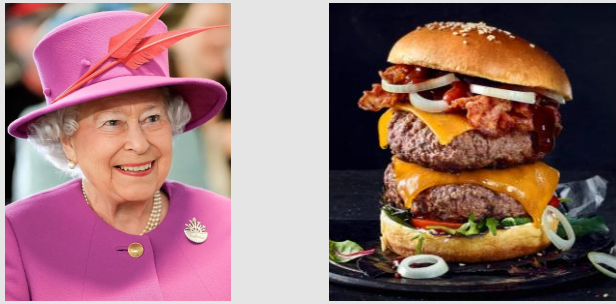
**Problem:** Difficulty of finding baseline tasks that activate all but the process of interest

Different stimuli and task



'Ah, that's the Queen' vs. 'I am so hungry...'

Different stimulus, same task



Name: 'The Queen' vs. Name: 'A burger'


Several components differ (visual-perceptual, cognitive, ...) → not good control tasks

# Choosing your baseline

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**Problem:** Difficulty of finding baseline tasks that activate all but the process of interest

Related stimuli, same task




vs.

Famous? - yes

Famous? - hm, wait, maybe... somewhat familiar...

Process P implicit in control task?  
Difficulty matched?

Same stimulus, different tasks



vs.

Name the person!

Name the gender!

Process P cancelled out (highly specific naming-related activity)?  
Interaction of task and stimuli?

# Choosing your baseline

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Different stimuli and task



'Ah, that's the Queen'    'I am so hungry...'

Different stimulus, same task



Name: 'The Queen'    Name: 'A burger'

Related stimuli, same task



Famous? - yes    Famous? - hm, wait, maybe...  
somewhat familiar...

Same stimulus, different tasks



Name the person!    Name the gender!

Depending on your choice of the control condition, you will answer very different questions!

# An example of cognitive subtraction

## Experimental design

Face viewing: F

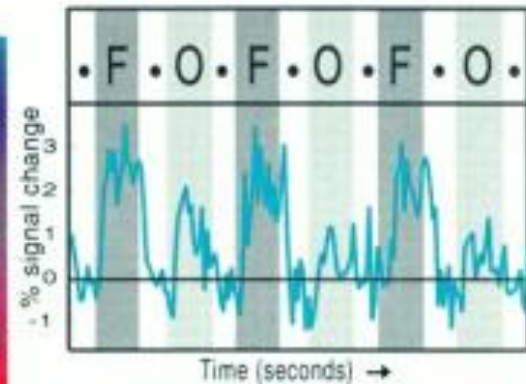
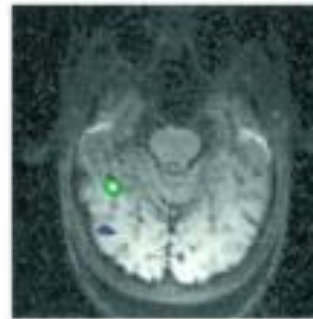
Object viewing: O

F - O = Face recognition

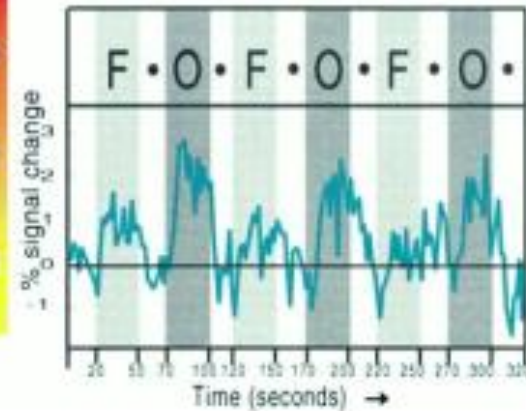
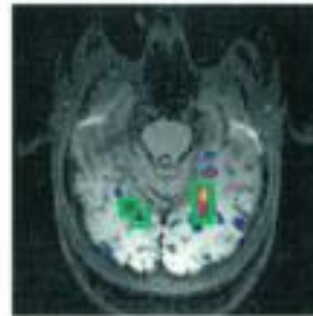
O - F = Object recognition

...under assumption of pure insertion

1a. Faces > Objects



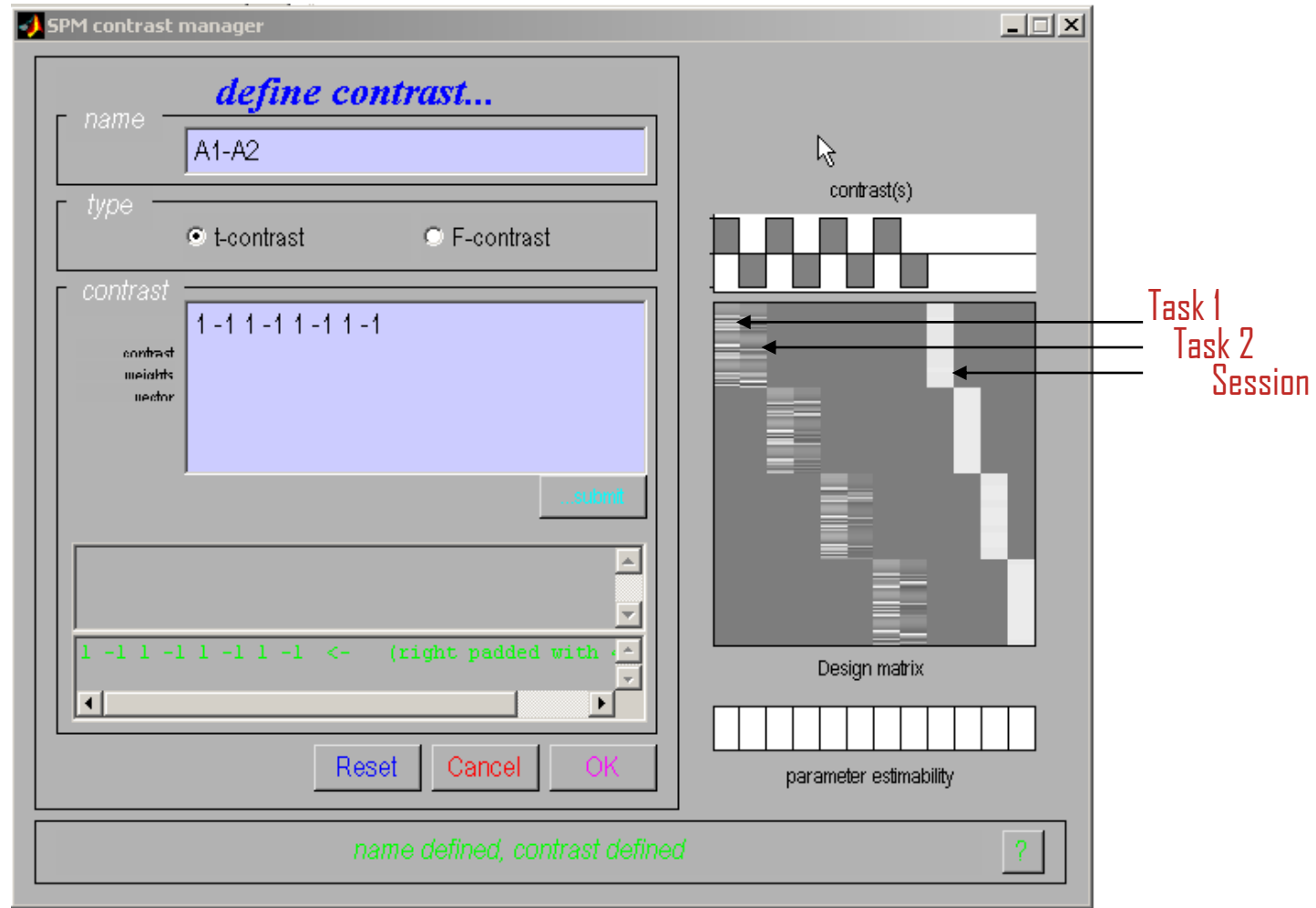
1b. Objects > Faces



Kanwisher et al., 1997, J. Neurosci.

# Categorical responses

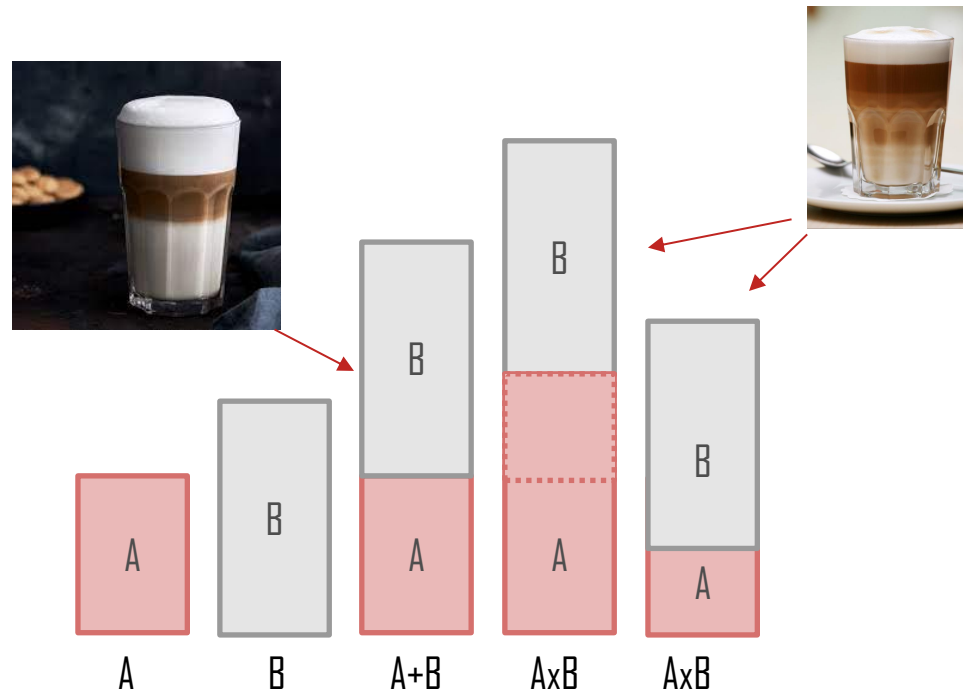
SPM interface



# The problem of cognitive subtraction

Problems:

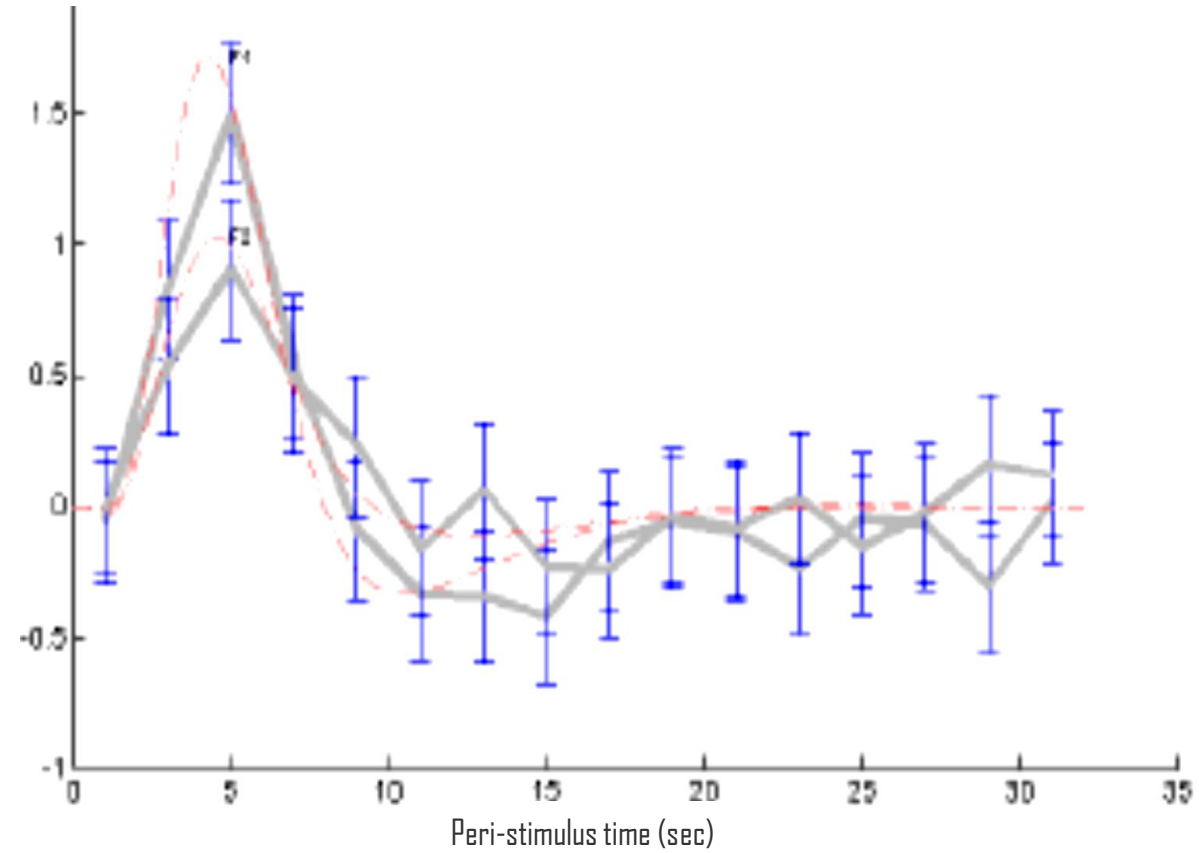
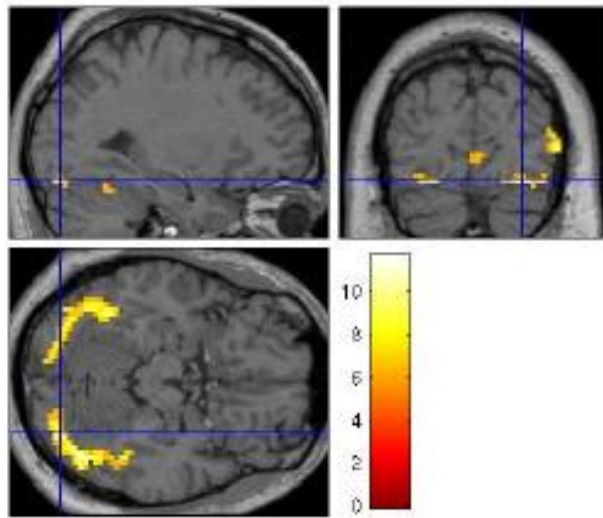
- Difficulty of finding baseline tasks that activate all but the process of interest (the “baseline problem”)
- Subtraction depends on the assumption of “pure insertion” (an extra cognitive component can be inserted without affecting the pre-existing components)



Friston et al., (1996)

# fMRI adaptation as an example of neural interaction

Famous faces: 1<sup>st</sup> time vs 2<sup>nd</sup> time

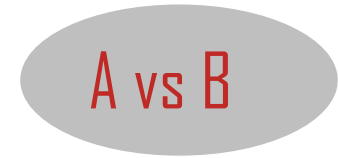




## 1. Categorical designs

- Subtraction
- **Conjunction**

Pure insertion, evoked / differential responses  
**Testing multiple hypotheses**



## 2. Parametric designs

- Linear
- Nonlinear

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



## 3. Factorial designs

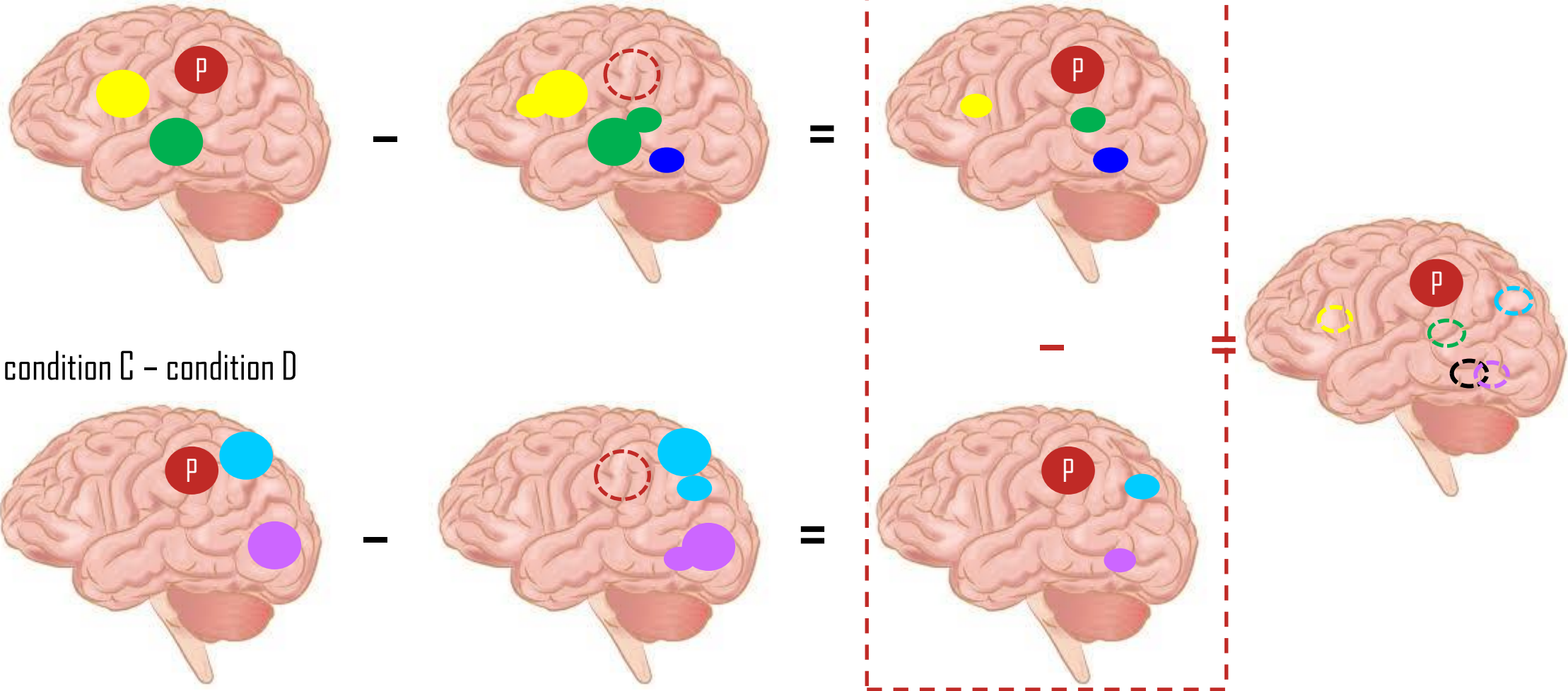
- Categorical
- Parametric

Interactions and pure insertion  
Linear and nonlinear interactions  
Psychophysiological Interactions (PPI)



# Tackling the baseline problem

Contrast 1: condition A - condition B



# Conjunction

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Minimization of “the baseline problem” by isolating the same cognitive process by two or more separate contrasts

**Subtraction**

	Task A	Task B
Process 1	Grey	Grey
2	Grey	Grey
3	Grey	Grey
4 (PI)	Black	White
5	Grey	Grey

**Conjunction analysis**

	Task Pair I		Task Pair II	
	A	B	A	B
Process 1	Grey	Grey	White	White
2	Grey	White	Grey	Grey
3	White	White	Grey	White
4 (PI)	Black	White	Black	White
5	Grey	Grey	White	White

Only the process of interest (here: P4) is common to all task pairs.

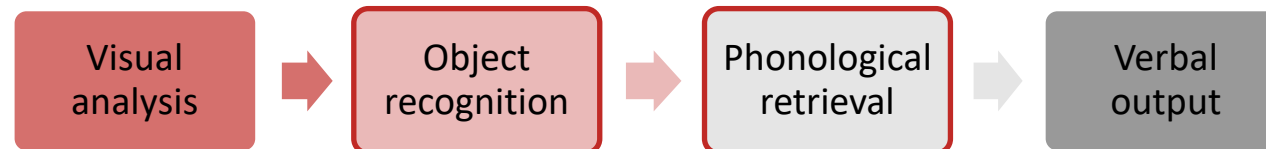
Conjunctions can be conducted across different contexts: tasks, stimuli, senses (vision, audition), ...

**Note:** The contrasts entering a conjunction have to be **independent** (i.e. they must be orthogonal, which is ensured automatically by SPM)

## An example...

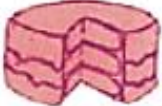



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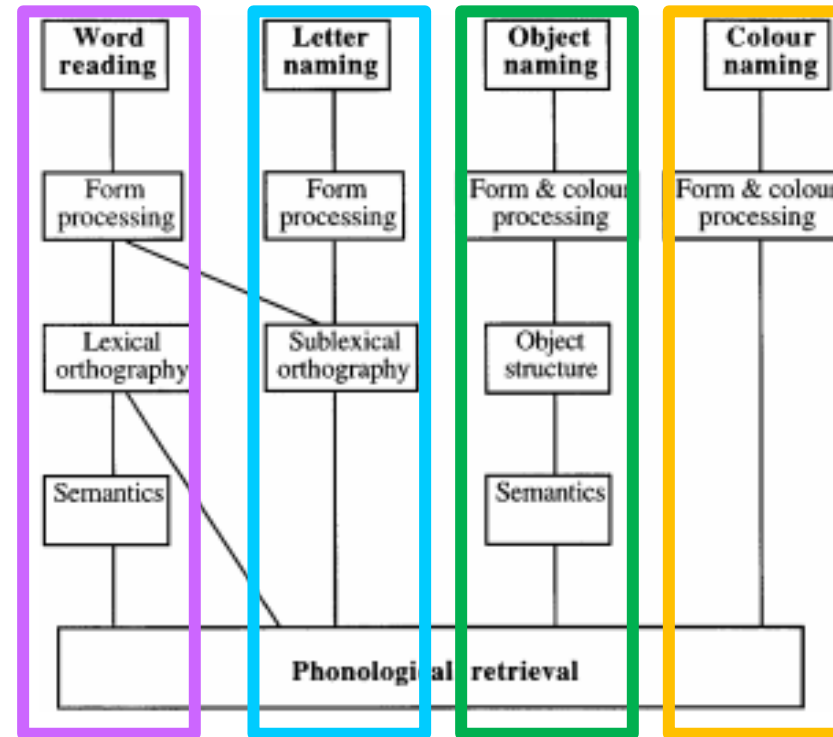
**Question:** Which neural structures support **phonological retrieval**, independent of item?



# Conjunction analysis

**Question:** Which neural structures support **phonological retrieval**, independent of item?

	Name (A)	Say "YES" (C)	
Words:	1 badge	2 Control task Հոկո	
Letters:	3 շ	4 Control task ճ	
Objects:	5 	6 Control task 	
Colours:	7 	8 Control task 	



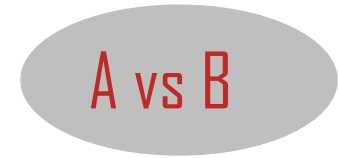
**Phonological retrieval** is the only cognitive component common to all task pair differences.

Price & Friston (1996)

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



## 2. Parametric designs

- Linear
- Nonlinear

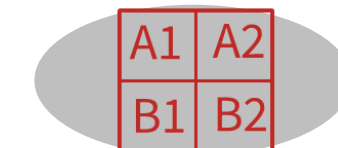
**Adaptation, cognitive dimensions**  
Polynomial expansions, neurometric functions  
Model-based regressors



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# Parametric designs

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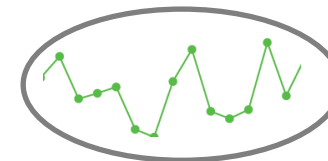
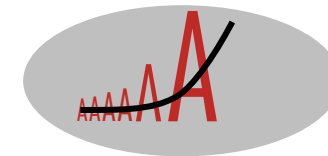
Does activity vary systematically with a continuously varying parameter?

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 :

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

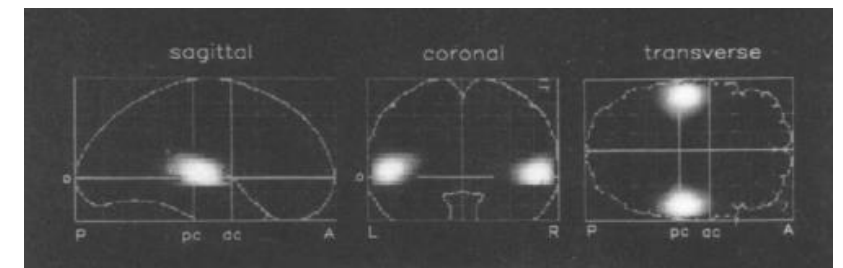
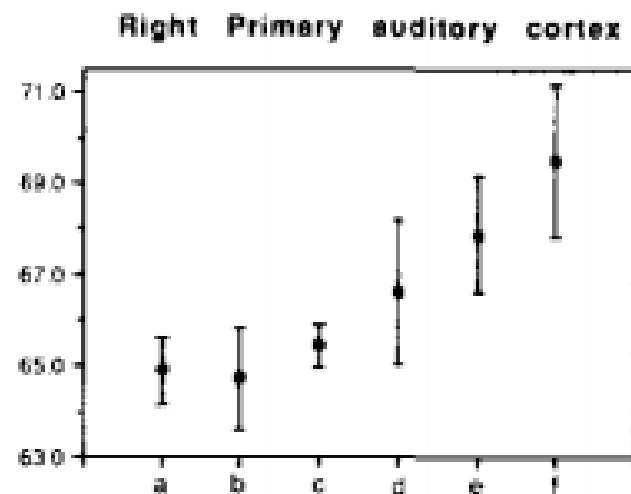
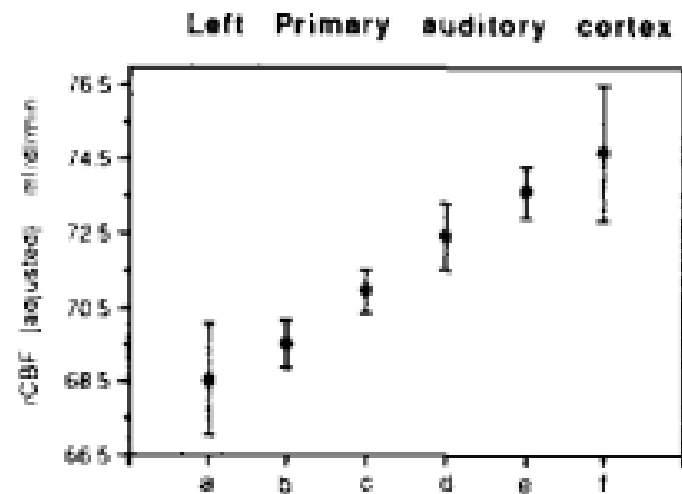
Avoids pure insertion but does assume no qualitative change in processing.



# Parametric designs

## PET

- Auditory words presented at different rates (rest, 5 rates between 10wpm and 90 wpm)
- Activity in primary auditory cortex is linearly related to word frequency



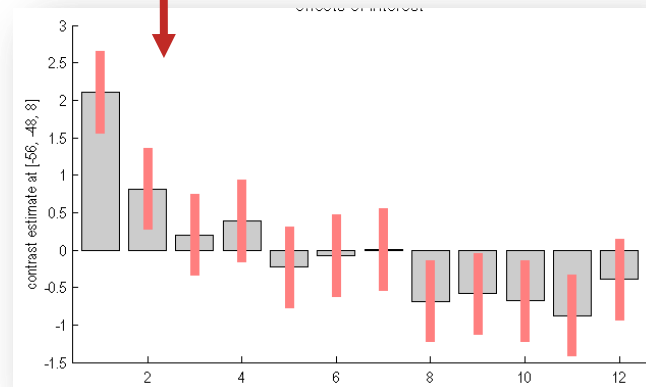
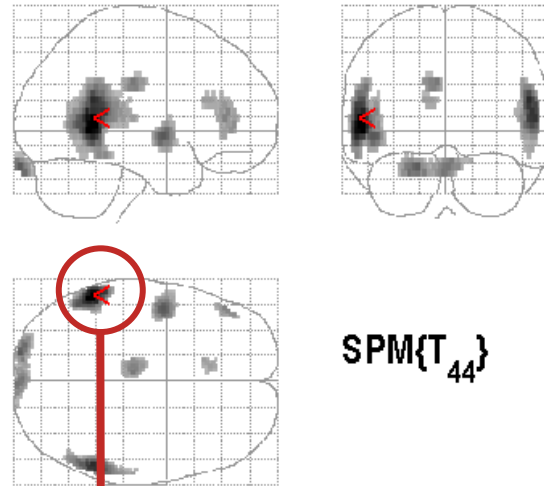
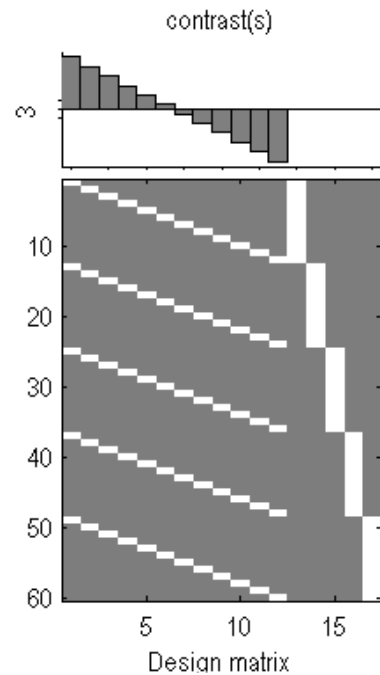
Price et al. 1992



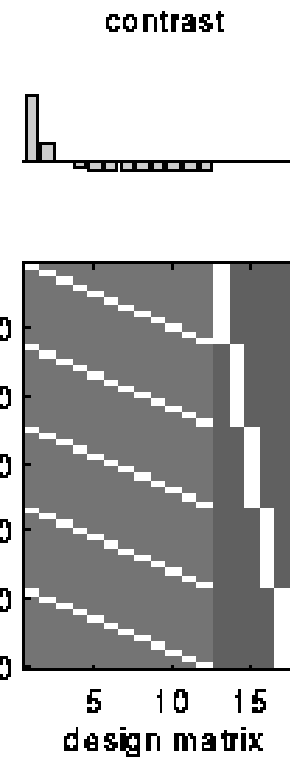
# A linear parametric contrast

Is there an adaptation effect if people listen to words multiple times?

## Linear effect of time



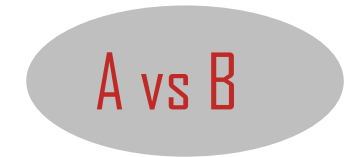
## Non-linear effect of time



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- Linear
- **Nonlinear**

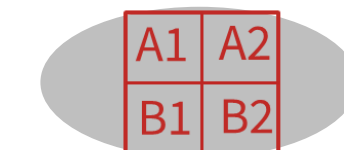
Adaptation, cognitive dimensions  
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## 3. Factorial designs

- Categorical
- Parametric

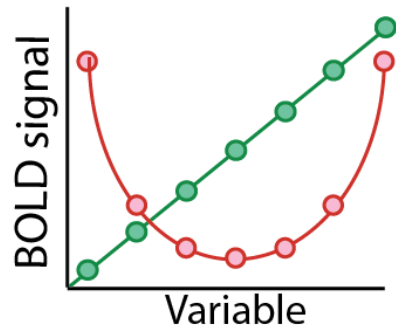
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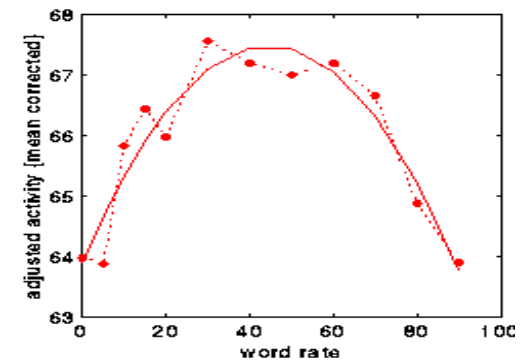
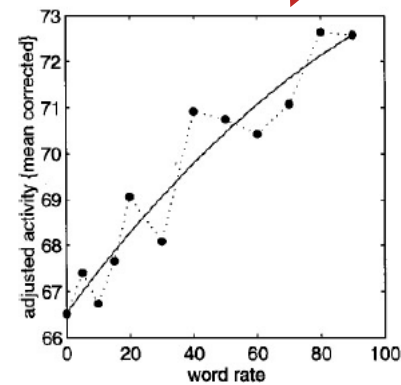
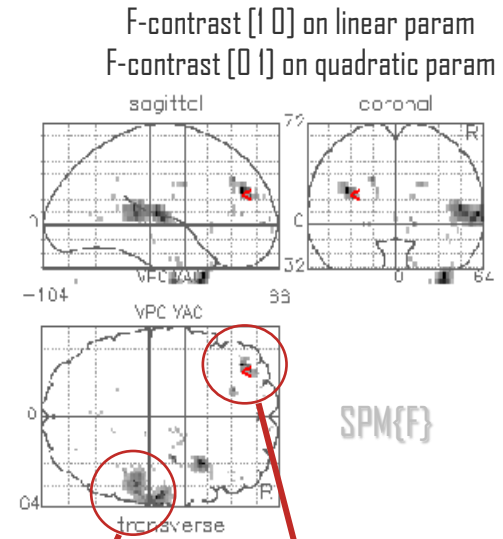
# A non-linear parametric design matrix

Polynomial expansion:  
 $f(x) = b_1 x + b_2 x^2 + \dots$   
...up to (N-1)<sup>th</sup> order for N levels

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



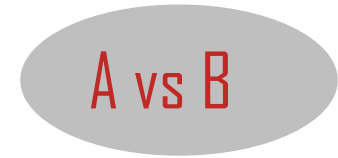
Büchel et al., (1996)



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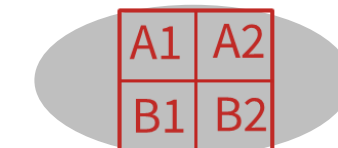
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## 3. Factorial designs

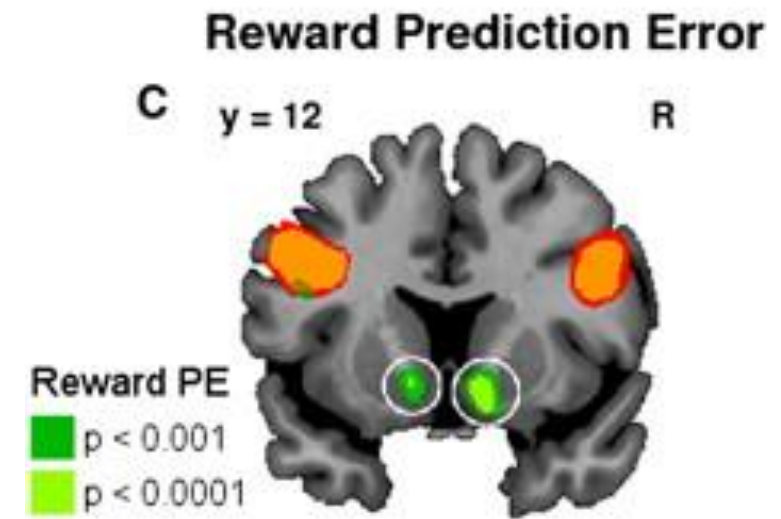
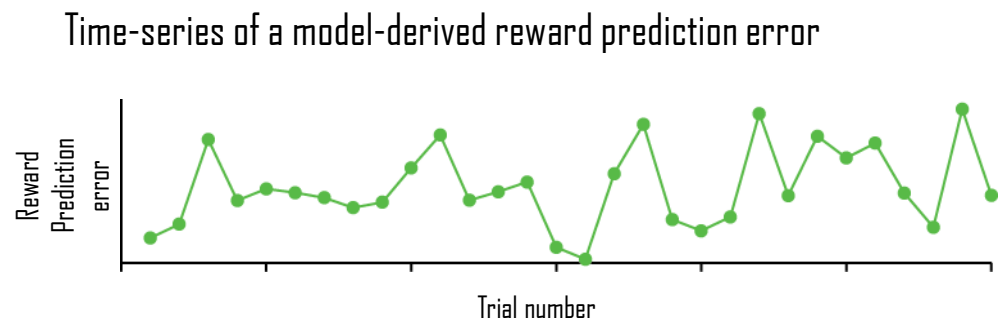
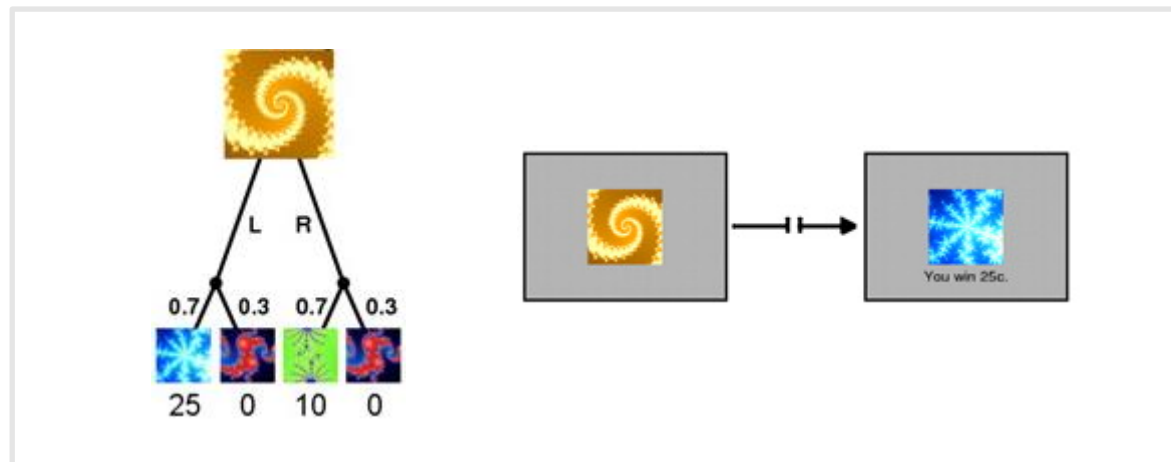
- Categorical
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## Parametric design: Model-based regressors

Signals derived from a **computational model** are correlated against BOLD, to determine brain regions showing a response profile consistent with the model, e.g. Rescorla-Wagner prediction error

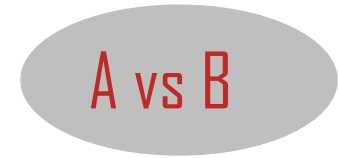


Gläscher & O'Doherty (2010)

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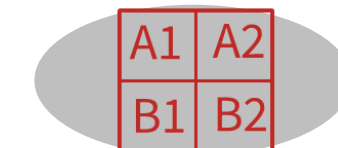
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- **Categorical**
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# Factorial design

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		Factor A	
		A	a
Factor B	B	A B	a B
	b	A b	a b

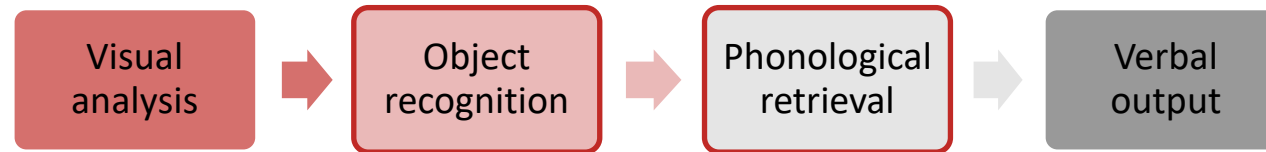
Highly efficient: Factorial designs allow for testing main effects and interactions!

We can address the “pure insertion” problem!

# Factorial design

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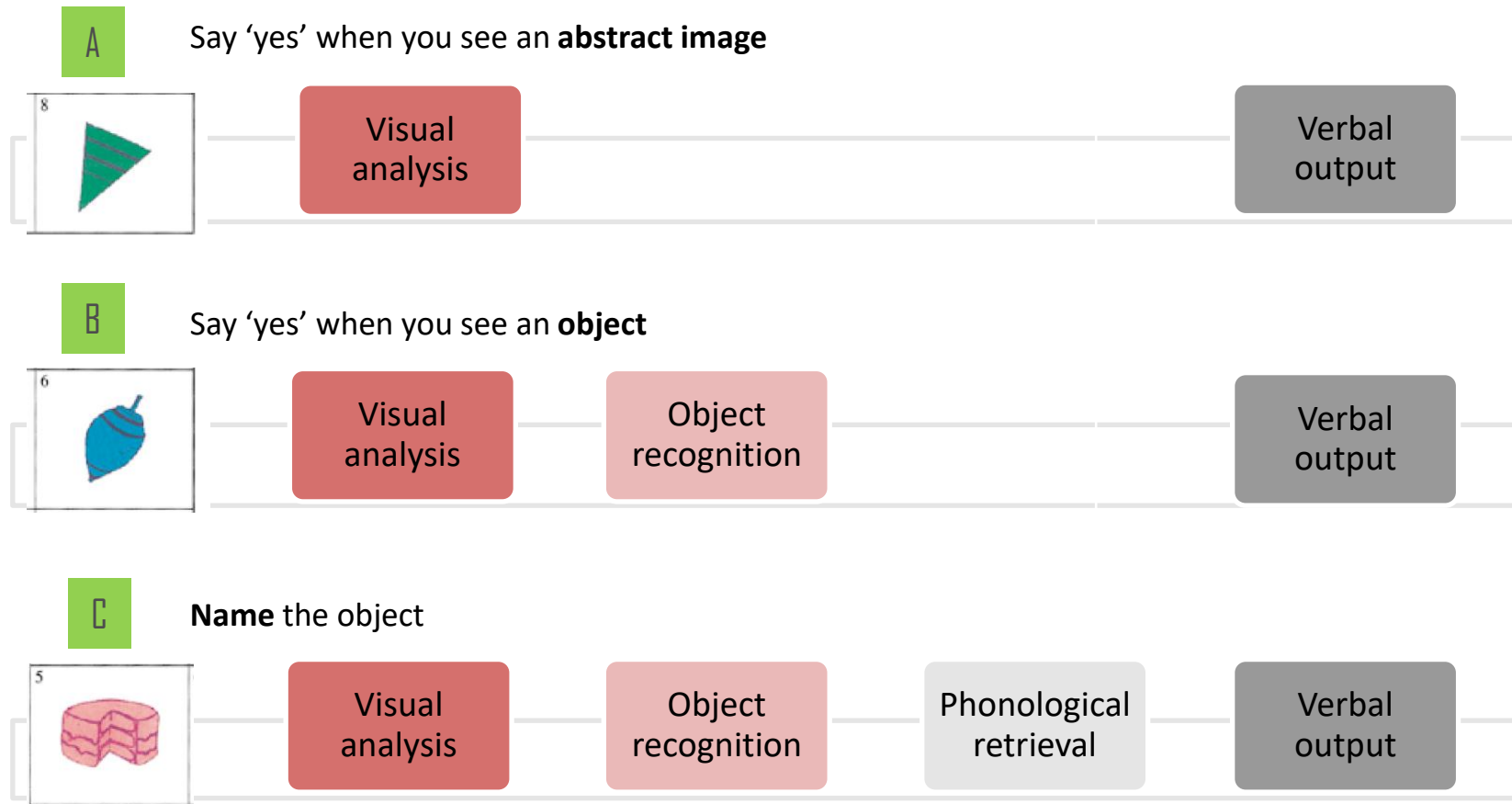
**Question:** Is the inferiotemporal cortex sensitive to both **object recognition** and **phonological retrieval** of object names?





# Factorial design


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



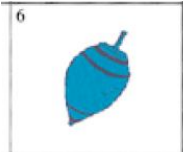
# Factorial design

**Question:** Is the inferotemporal cortex sensitive to both object recognition and phonological retrieval of object names?

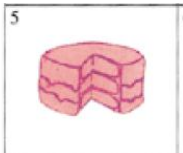
**A** Say 'yes' when you see an **abstract image**

8 

**B** Say 'yes' when you see an **object**

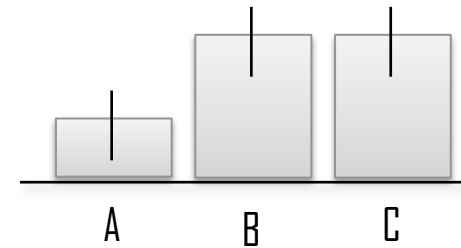
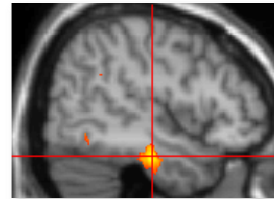
6 

**C** **Name the object**

5 

Friston et al., (1997)

Results in inferotemporal cortex:



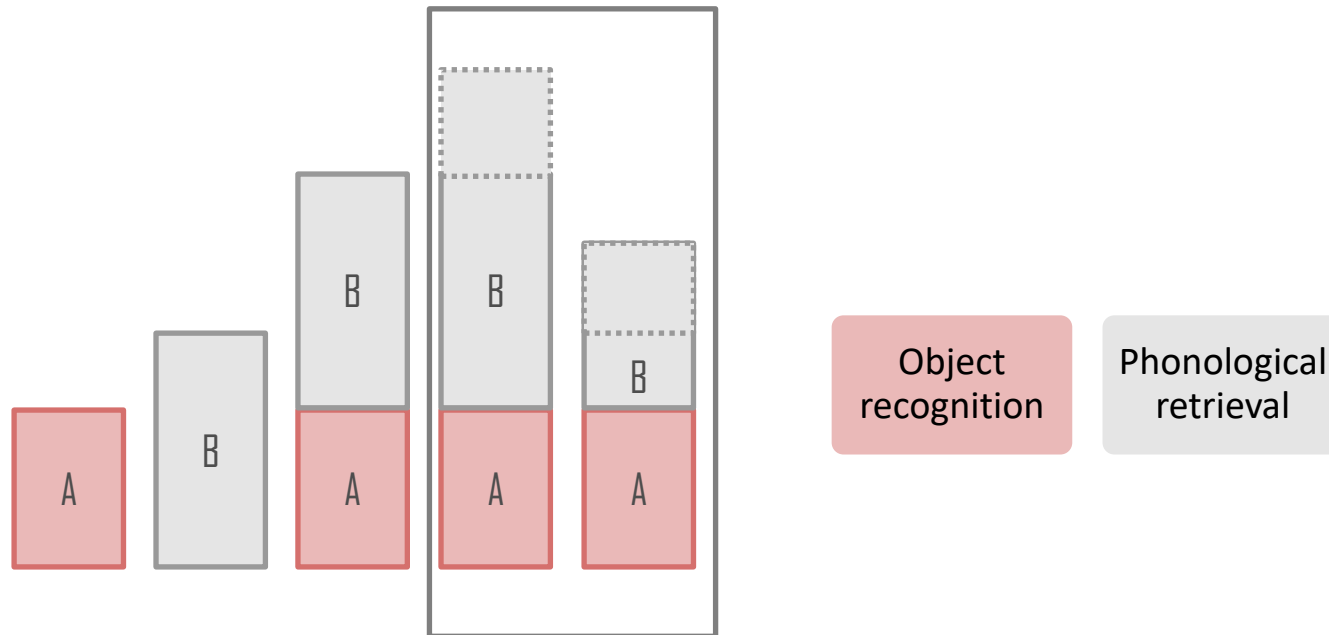
**B** > **A** Object recognition

**C** = **B** IT not involved in phonological retrieval?!

# Addressing interactions in factorial designs

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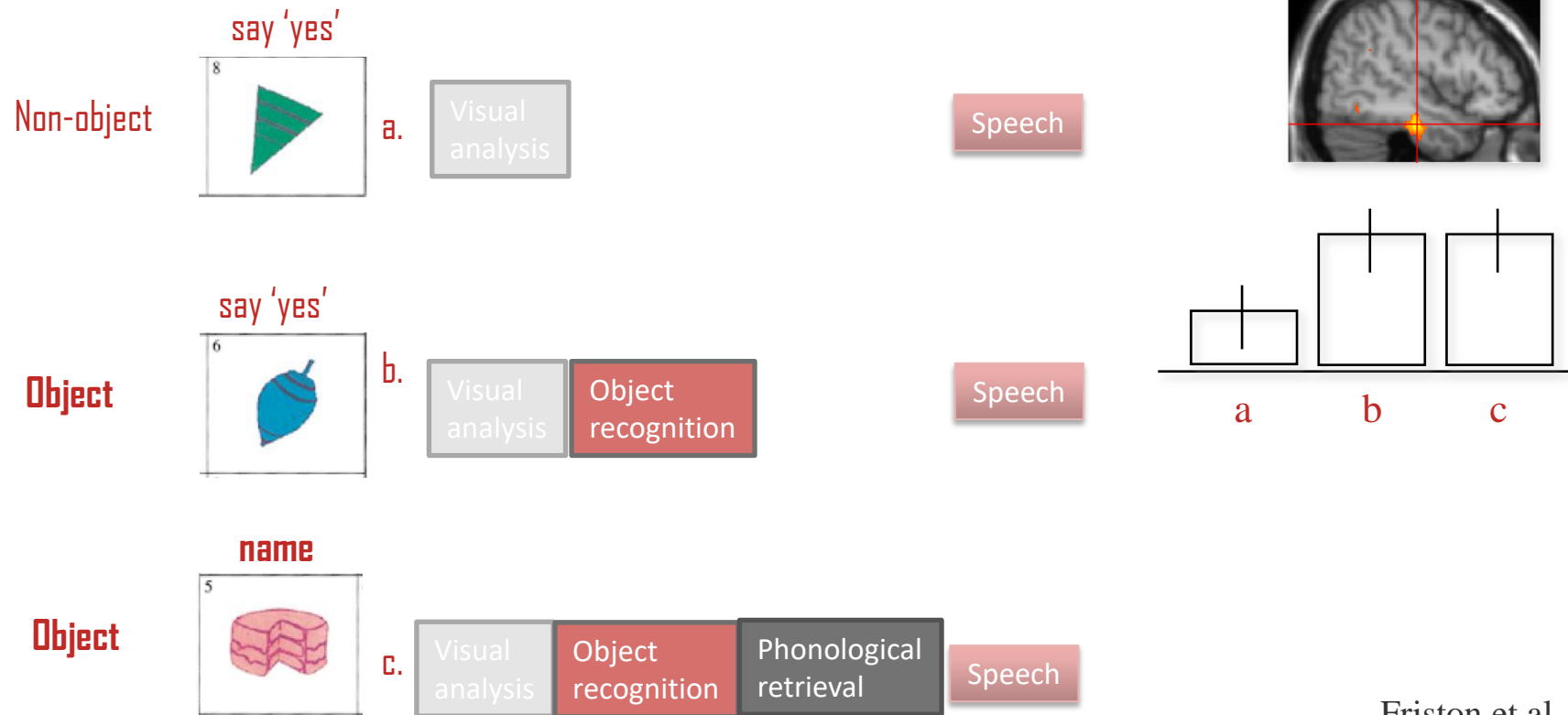
Is the task the sum of its component processes, or does A modulate B?



**Let's test the interaction explicitly!**  
**How?**  
**→ Vary A and B independently!**

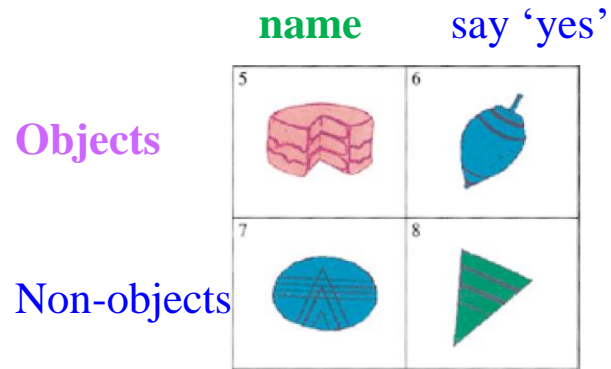
# Factorial designs: Main effects and interaction

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



Friston et al., (1997)

# Factorial designs: Main effects and interaction

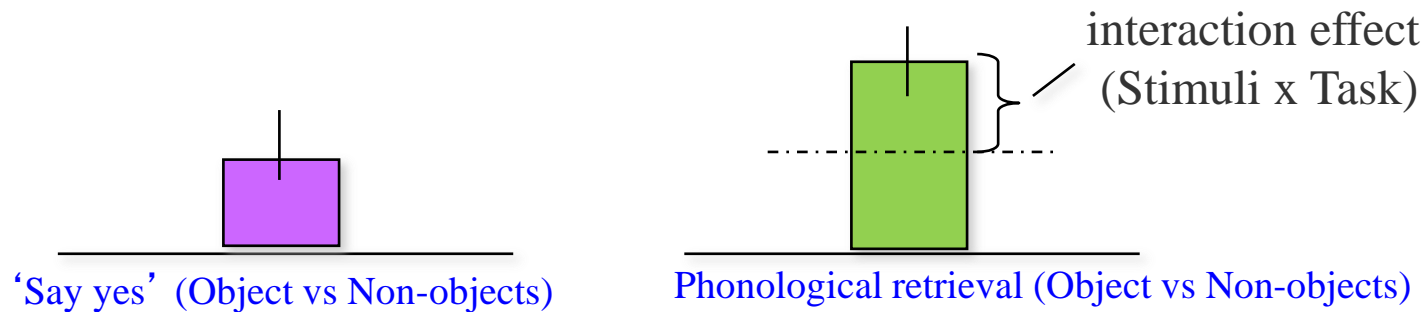


**Main effect** of task (naming):  $(\text{O}NAME + \text{N}NAME) - (\text{O}YES + \text{N}YES)$

**Main effect** of stimuli (object):  $(\text{O}YES + \text{O}NAME) - (\text{N}YES + \text{N}NAME)$

**Interaction** of task & stimuli:  $(\text{O}NAME + \text{N}YES) - (\text{O}YES + \text{N}NAME)$

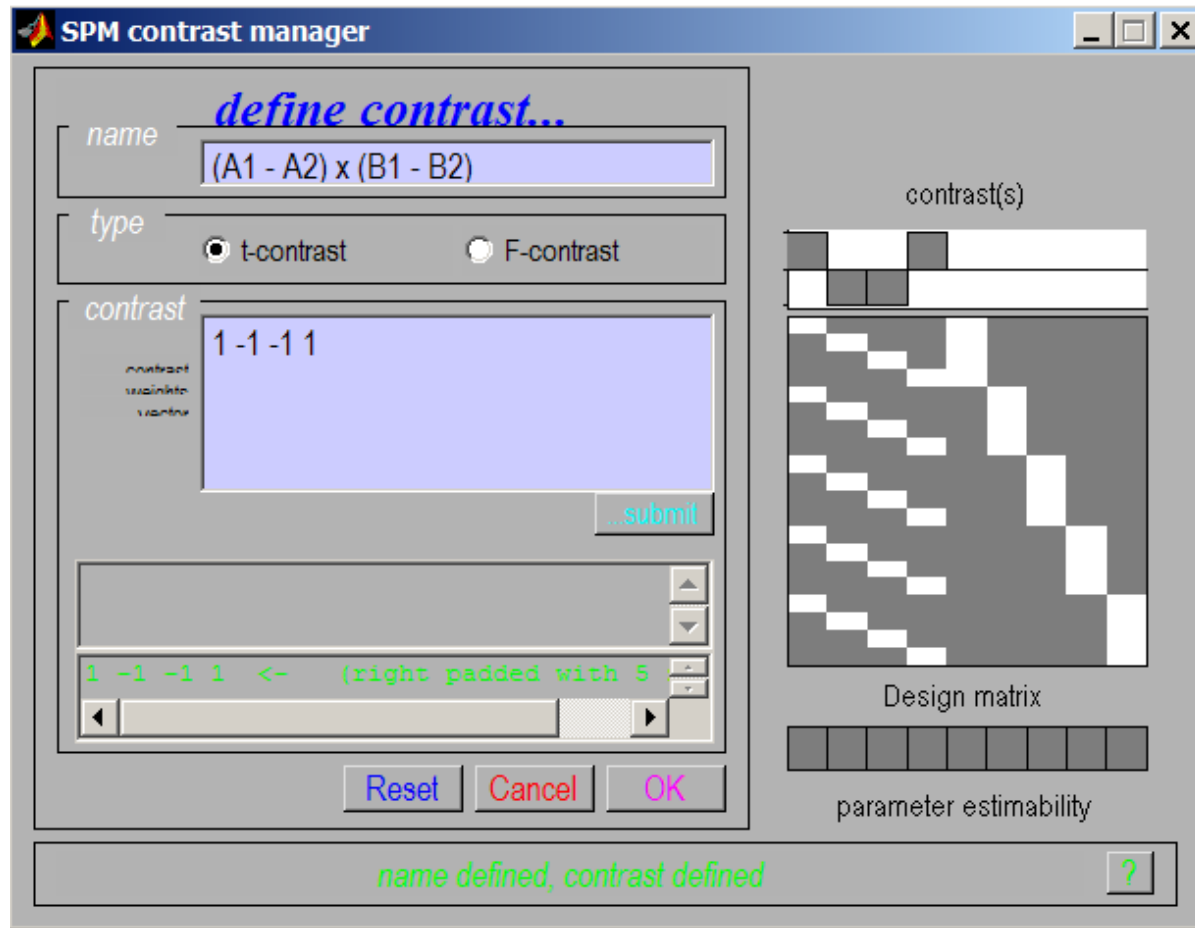
*Can show a failure of pure insertion*



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.

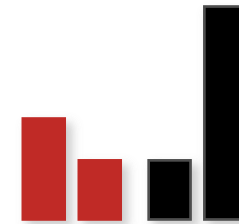
Friston et al., (1997)

# Interaction in SPM



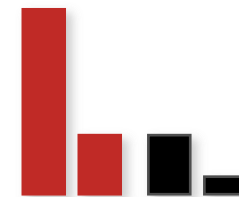
Interactions:

cross-over



and

simple

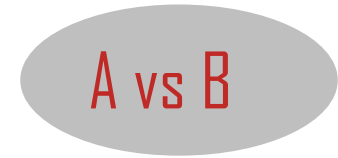


We can selectively inspect our data for one or the other by **masking** during inference

## 1. Categorical designs

- Subtraction
- Conjunction

Pure insertion, evoked / differential responses  
Testing multiple hypotheses



## 2. Parametric designs

- Linear
- Nonlinear

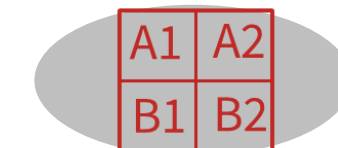
Adaptation, cognitive dimensions  
Polynomial expansions, neurometric functions  
Model-based regressors



## 3. Factorial designs

- Categorical
- **Parametric**

Interactions and pure insertion  
**Linear and nonlinear interactions**  
Psychophysiological Interactions (PPI)

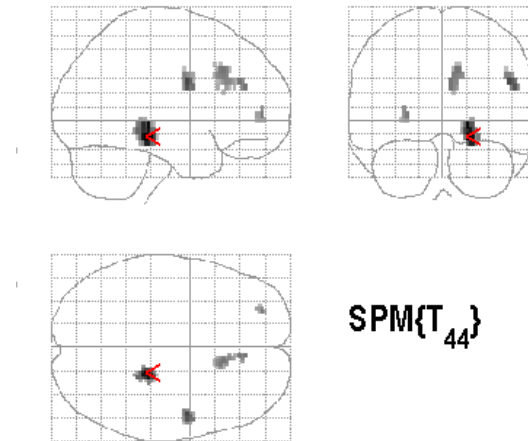


# Linear Parametric Interaction

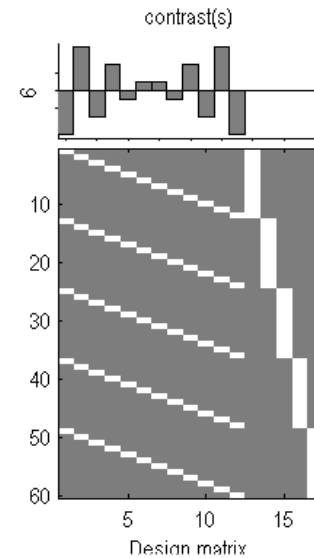
**Question:** Are there different kinds of adaptation for word generation and word repetition as a function of time?

A (Linear)  
Time-by-Condition

Interaction  
("Generation strategy"?)



SPMresults: \Spm2\PET\_fluency\12ConStats  
Height threshold T = 2.41  
Extent threshold k = 10 voxels



Contrast:

$$[5 \ 3 \ 1 \ -1 \ -3 \ -5](\text{time}) \otimes [-1 \ 1] (\text{categorical})$$

$$= [-5 \ 5 \ -3 \ 3 \ -1 \ 1 \ 1 \ -1 \ 3 \ -3 \ 5 \ -5]$$



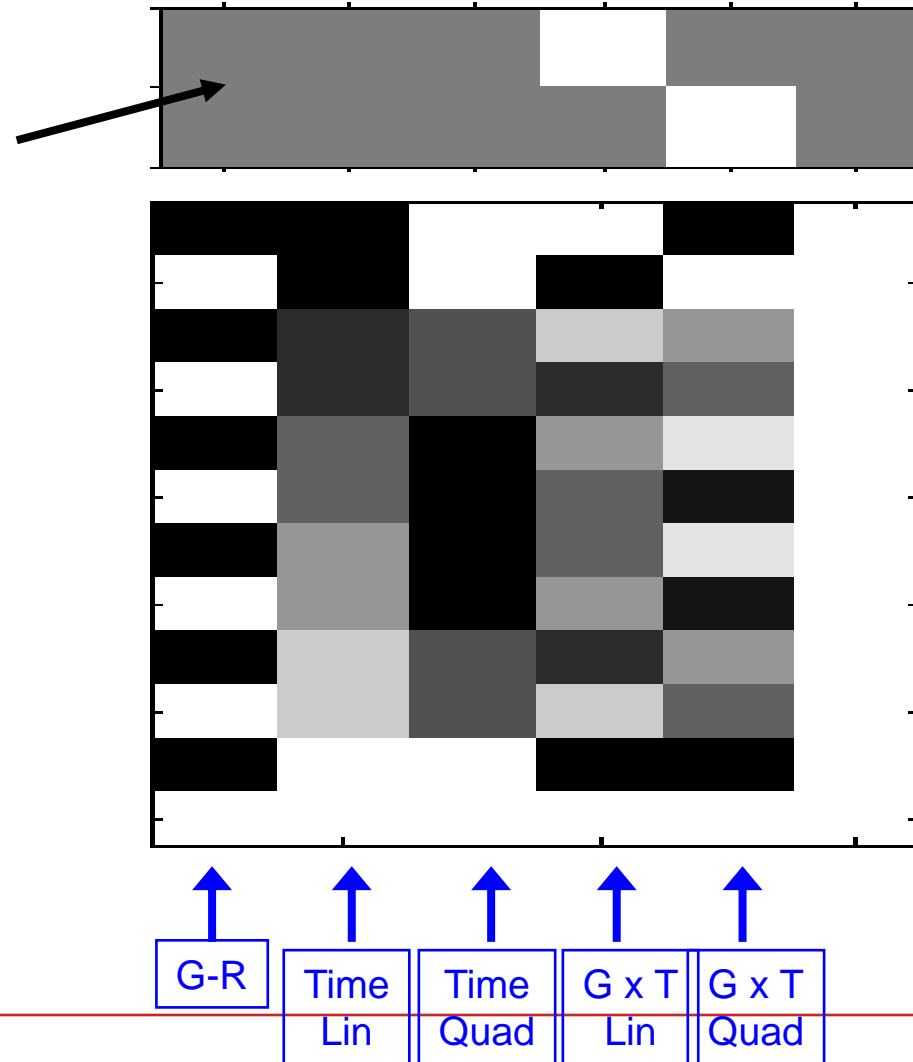
# Non-Linear Parametric Interaction

F-contrast tests for  
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...



Questions?

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