

Experimental design

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With thanks to:

Elisa van der Plas

Mona Garvert

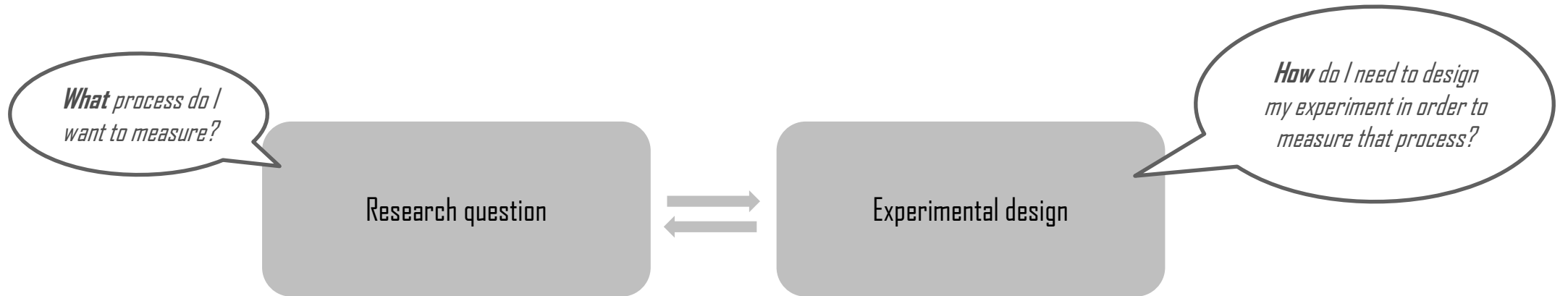
Sara Tomiello

Sara Bengtsson

Christian Ruff

Rik Henson

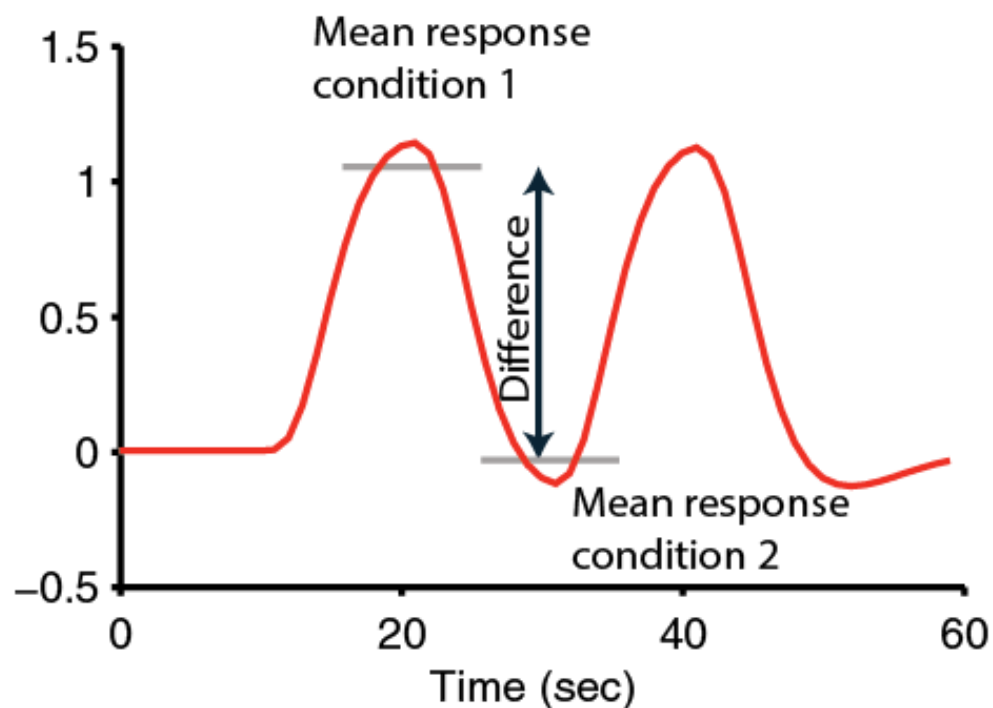
It all starts with a good design!



Why is that?

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

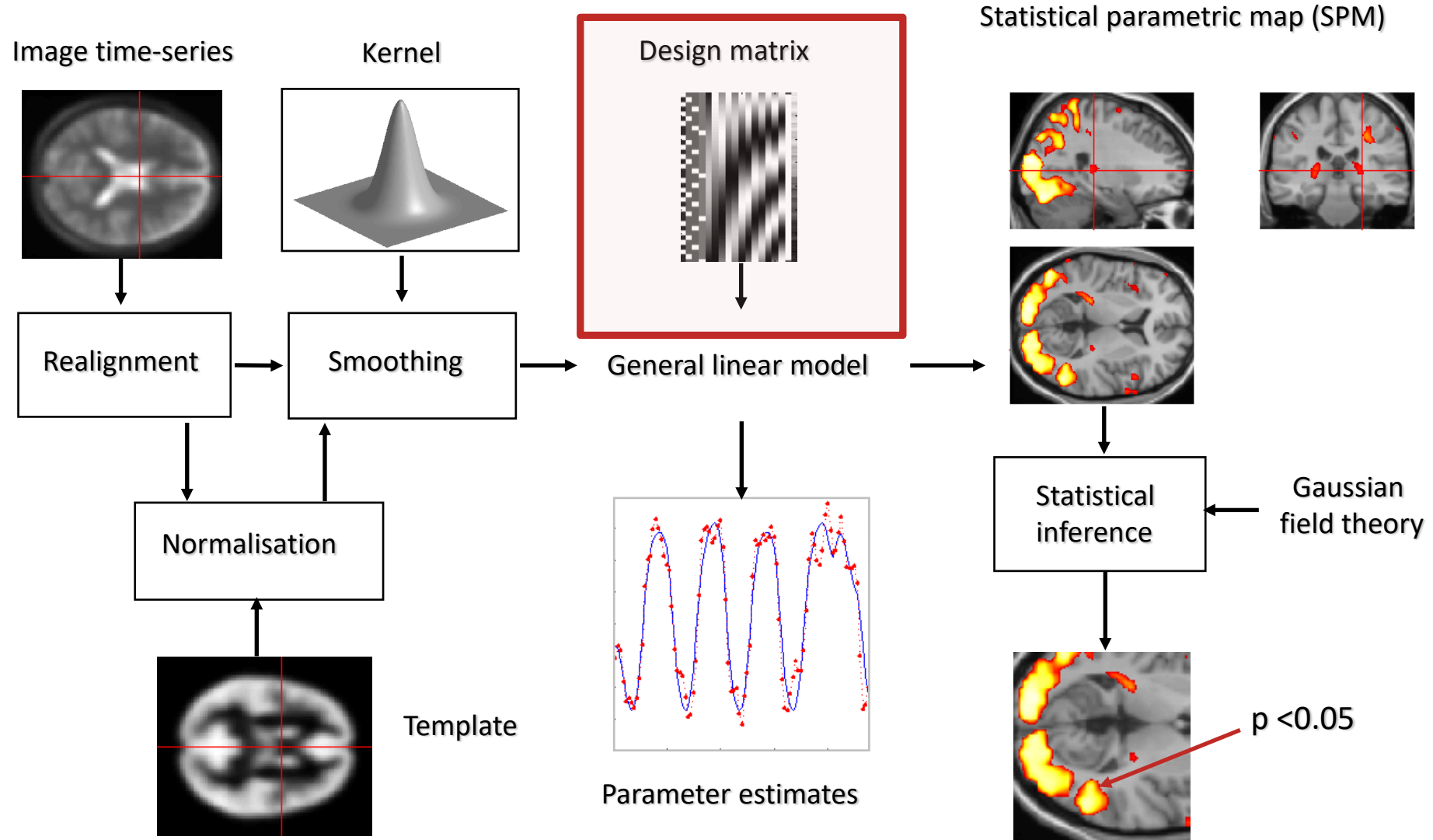
Therefore, you need to compare activity across conditions



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

SPM processing hierarchy

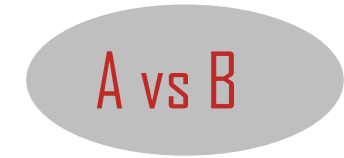
At the very top...



1. Categorical designs

- Subtraction
- Conjunction

Pure insertion, evoked / differential responses
Testing multiple hypotheses



2. Parametric designs

- Linear
- Nonlinear

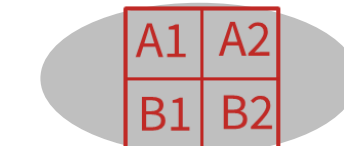
Adaptation, cognitive dimensions
Polynomial expansions, neurometric functions
Model-based regressors



3. Factorial designs

- Categorical
- Parametric

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



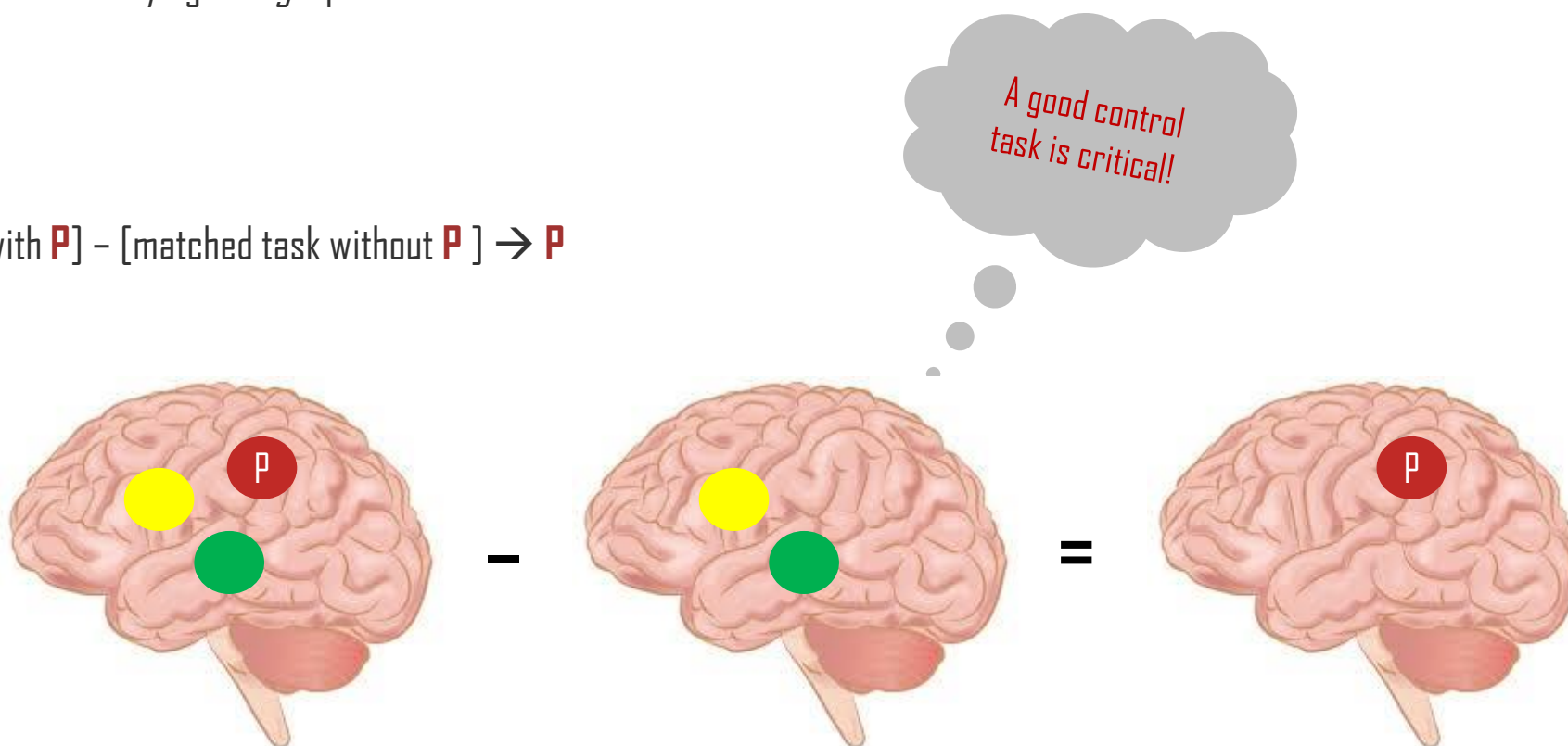
Cognitive subtraction

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

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



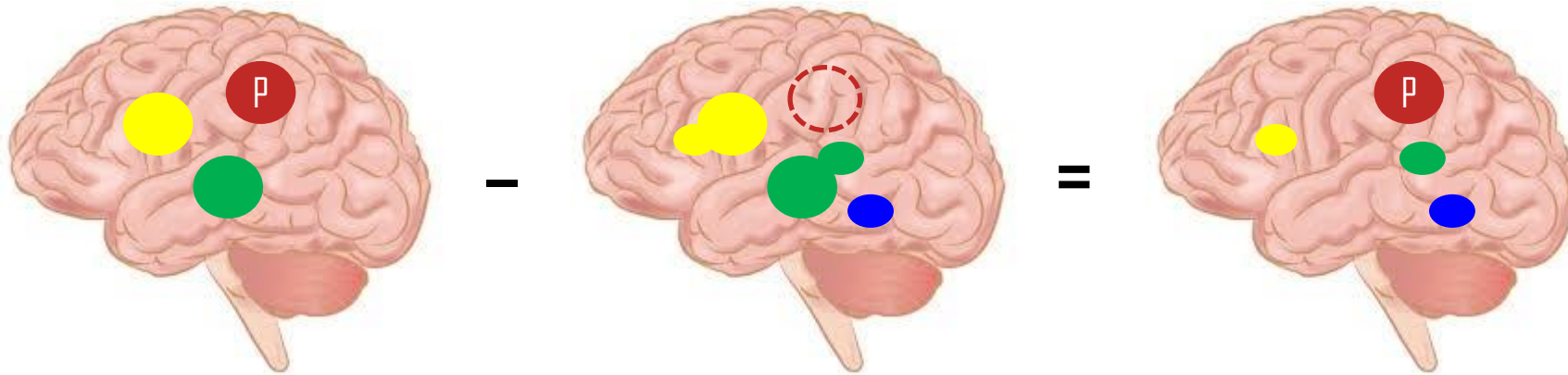
Pretty close to pure insertion...



...this one not...

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

The critical assumption of pure insertion



"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

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

Different stimulus, same task

	
Name: 'The Queen'	Name: 'A burger'

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

Choosing your baseline

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

Related stimuli, same task



Famous? - yes

vs.



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

Process P implicit in control task?
Difficulty matched?

Same stimulus, different tasks



Name the person!

vs.



Name the gender!

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

Choosing your baseline

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

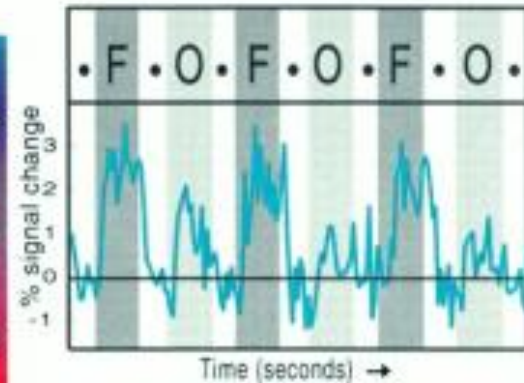
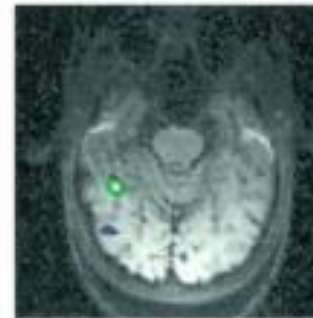
Object viewing: O

F - O = Face recognition

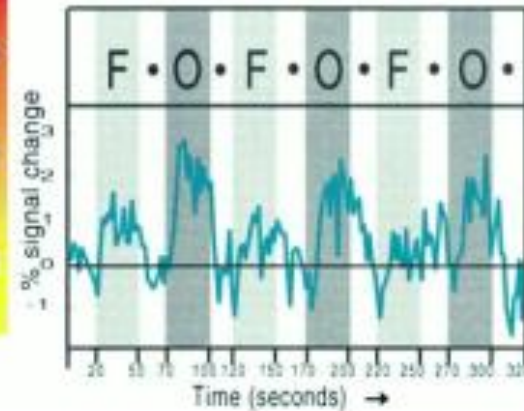
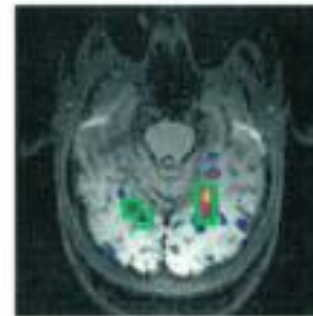
O - F = Object recognition

...under assumption of pure insertion

1a. Faces > Objects



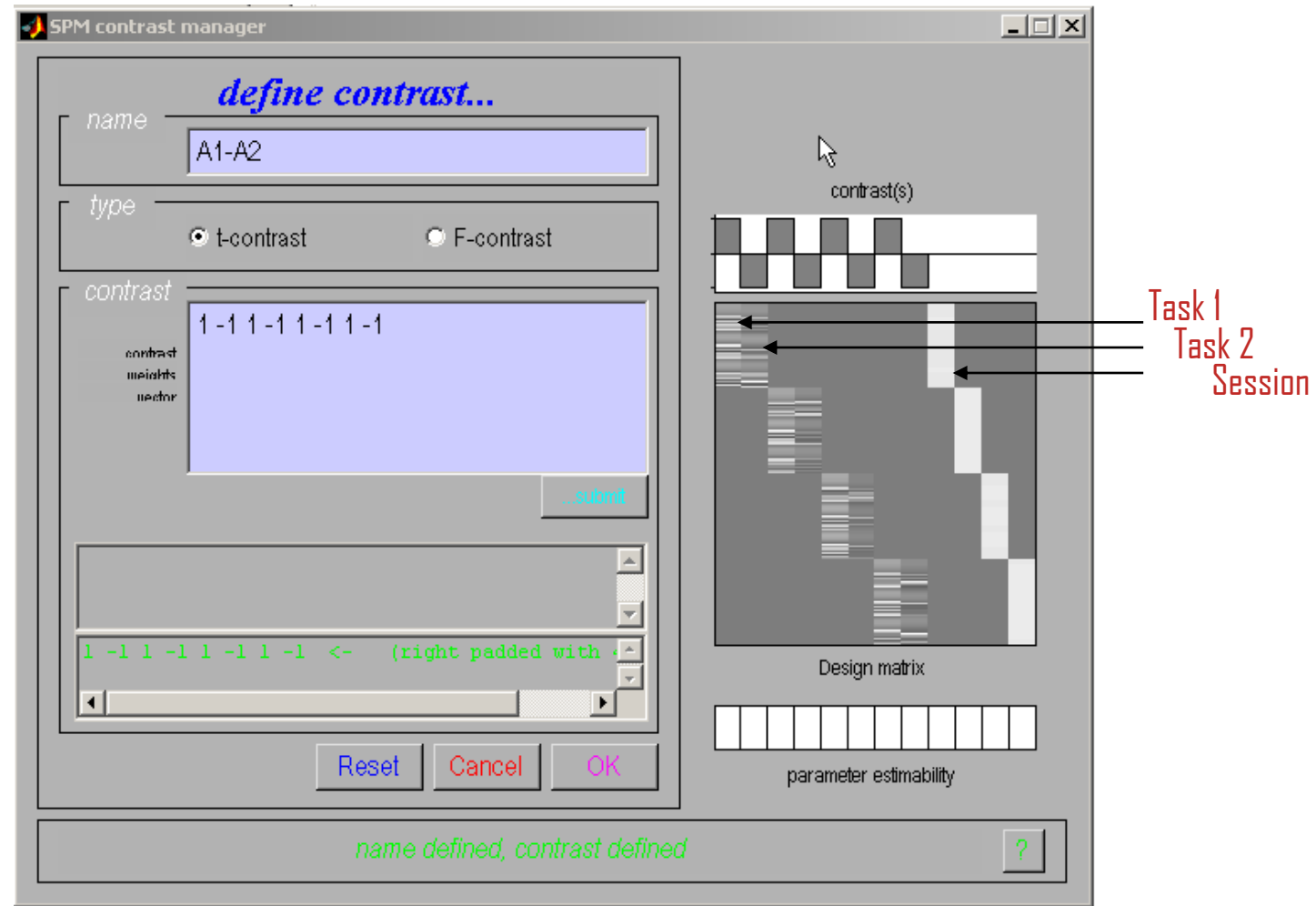
1b. Objects > Faces



Kanwisher et al., 1997, J. Neurosci.

Categorical responses

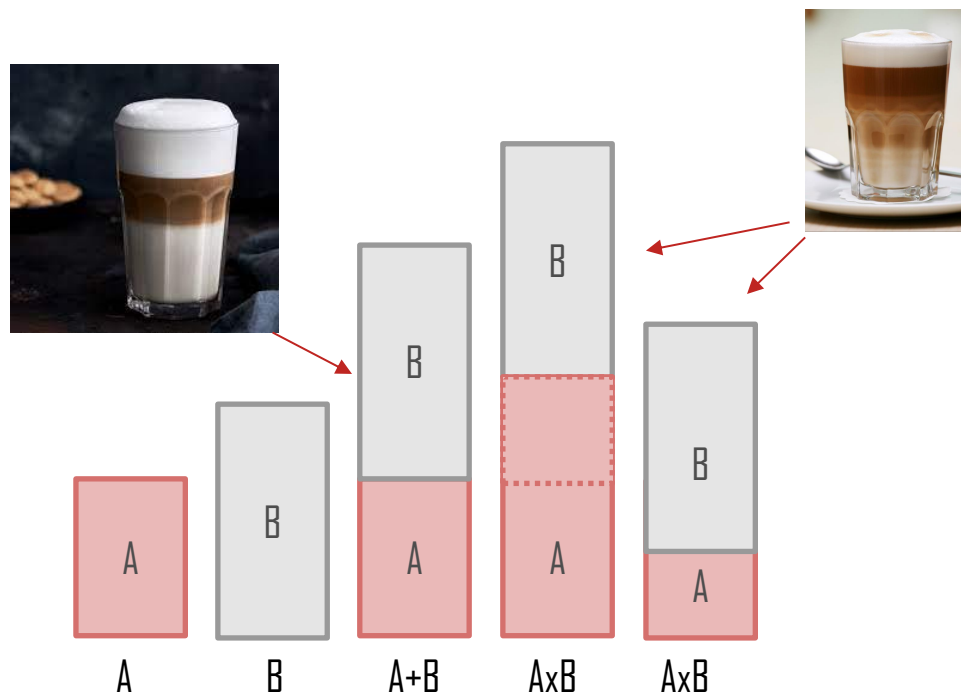
SPM interface



The problem of cognitive subtraction

Problems:

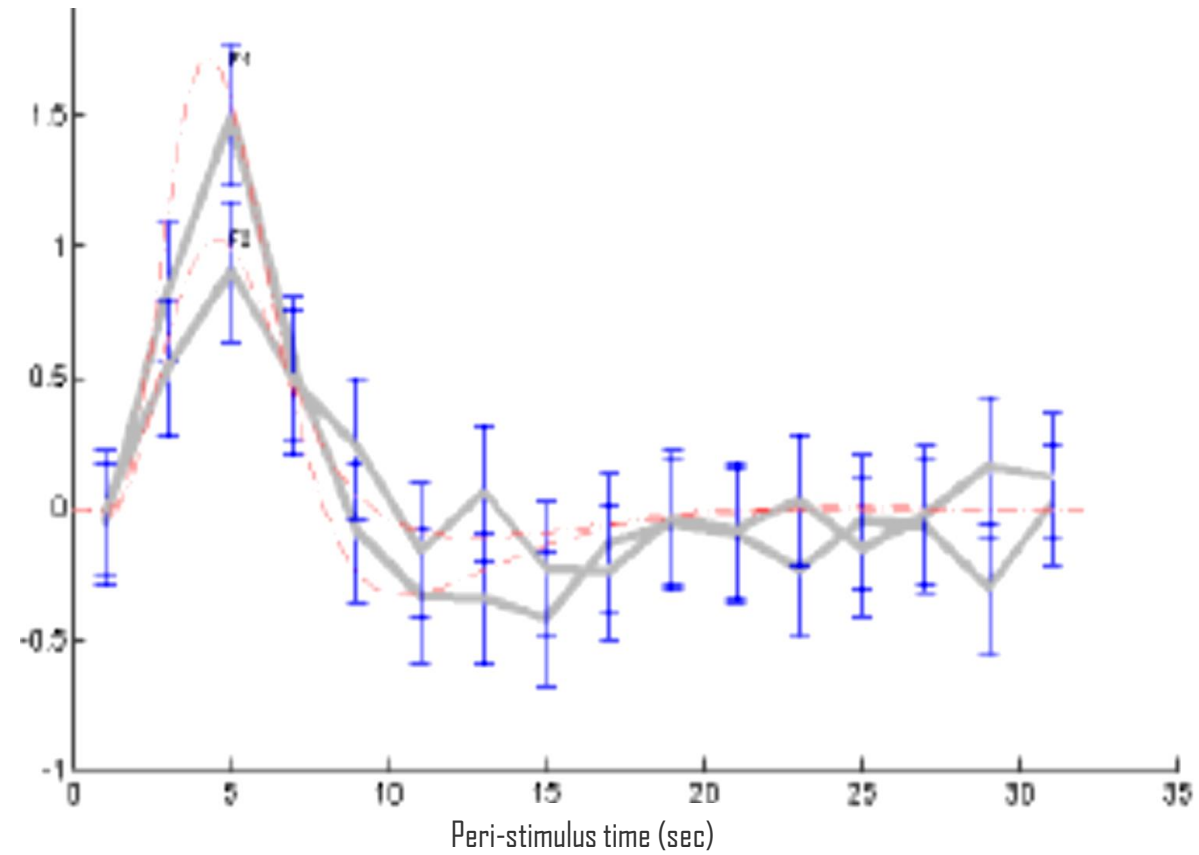
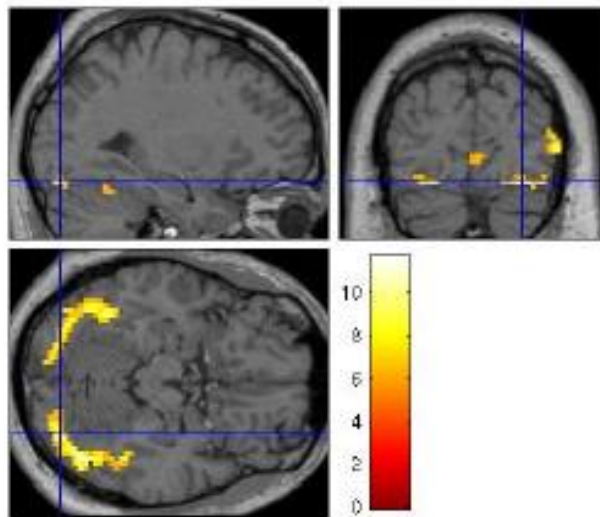
- Difficulty of finding baseline tasks that activate all but the process of interest (the “baseline problem”)
- Subtraction depends on the assumption of “pure insertion” (an extra cognitive component can be inserted without affecting the pre-existing components)



Friston et al., (1996)

fMRI adaptation as an example of neural interaction

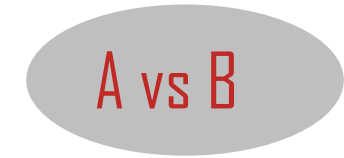
Famous faces: 1st time vs 2nd time



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2. Parametric designs

- Linear
- Nonlinear

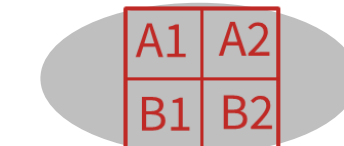
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3. Factorial designs

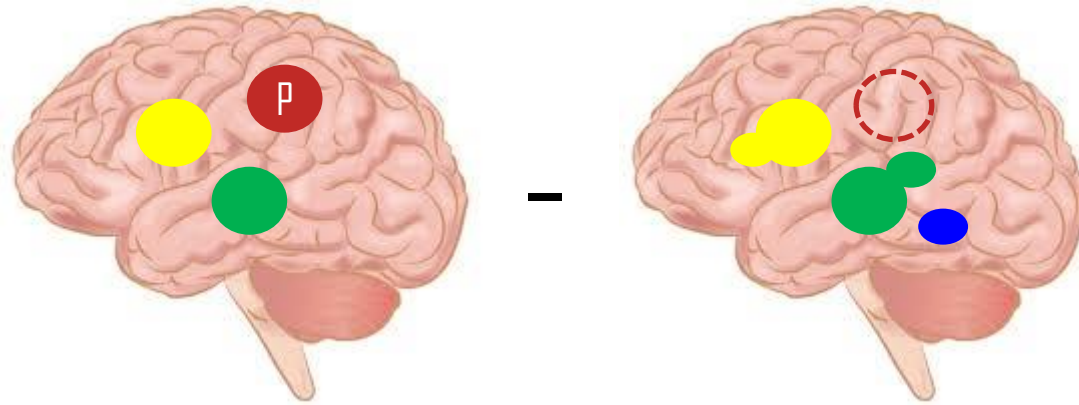
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Interactions and pure insertion
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Psychophysiological Interactions (PPI)

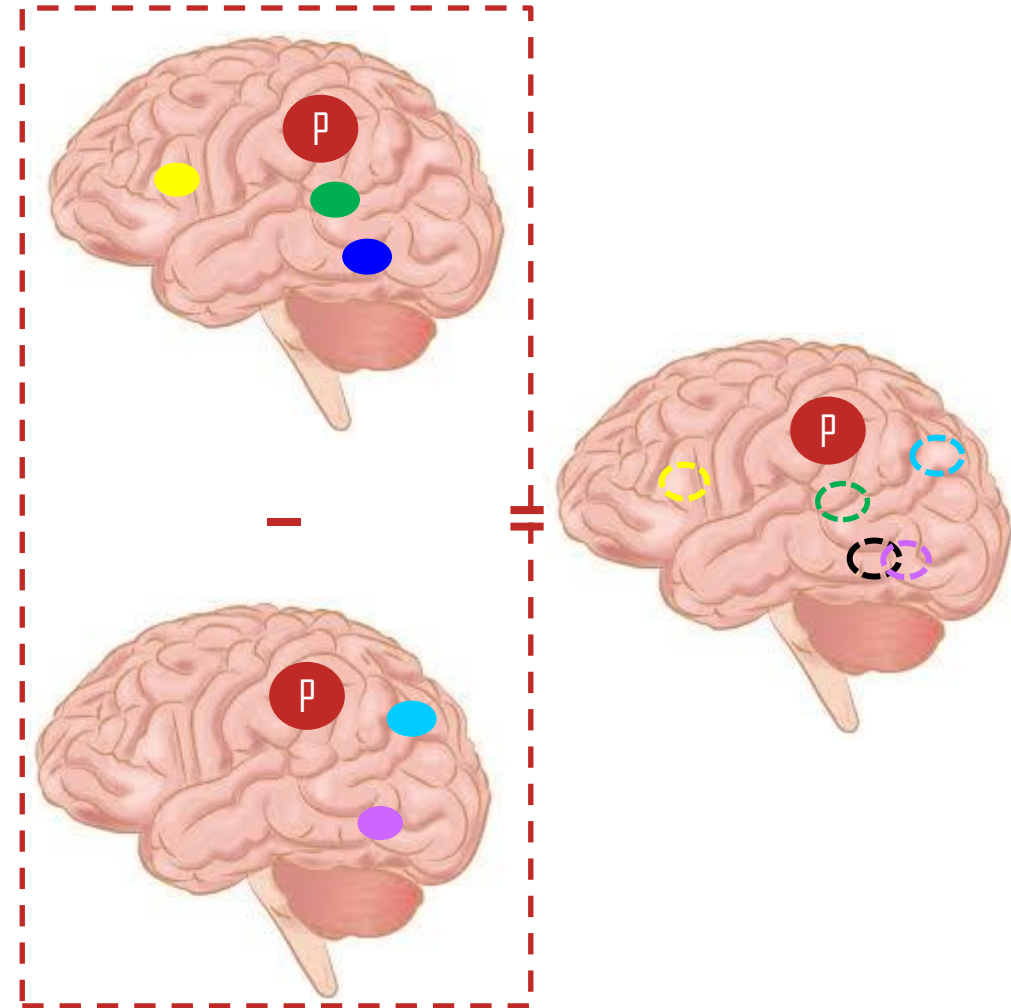


Tackling the baseline problem

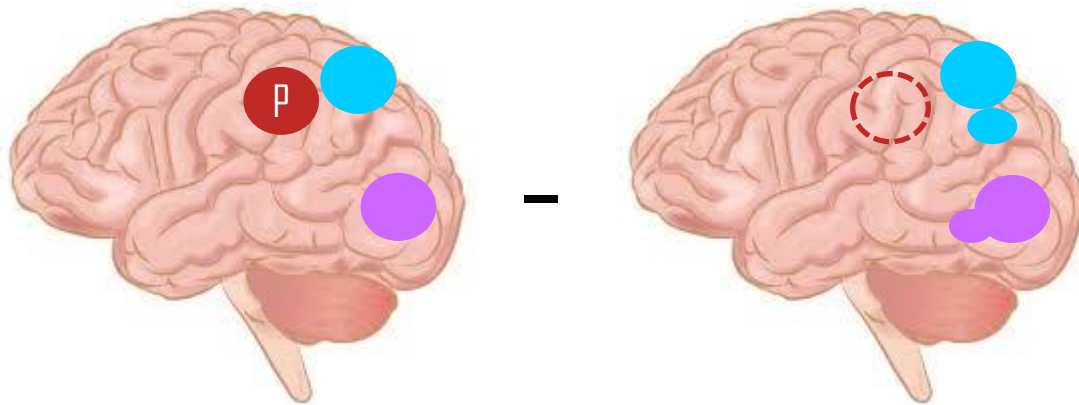
Contrast 1: condition A – condition B



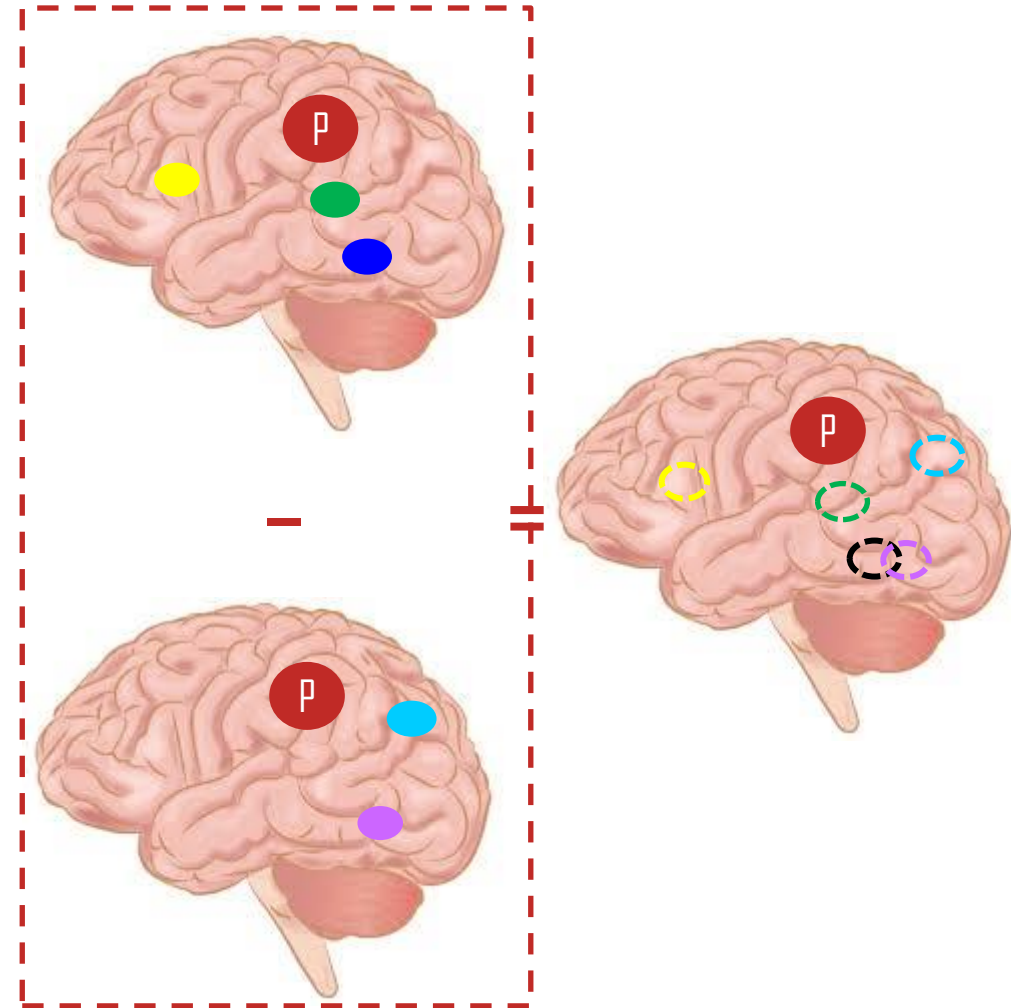
=



Contrast 2: condition C – condition D



=



Conjunction

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

Subtraction

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

Conjunction analysis

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

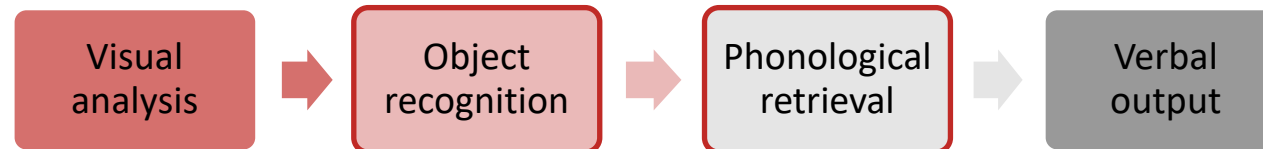
Only the process of interest (here: P4) is common to all task pairs.

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)

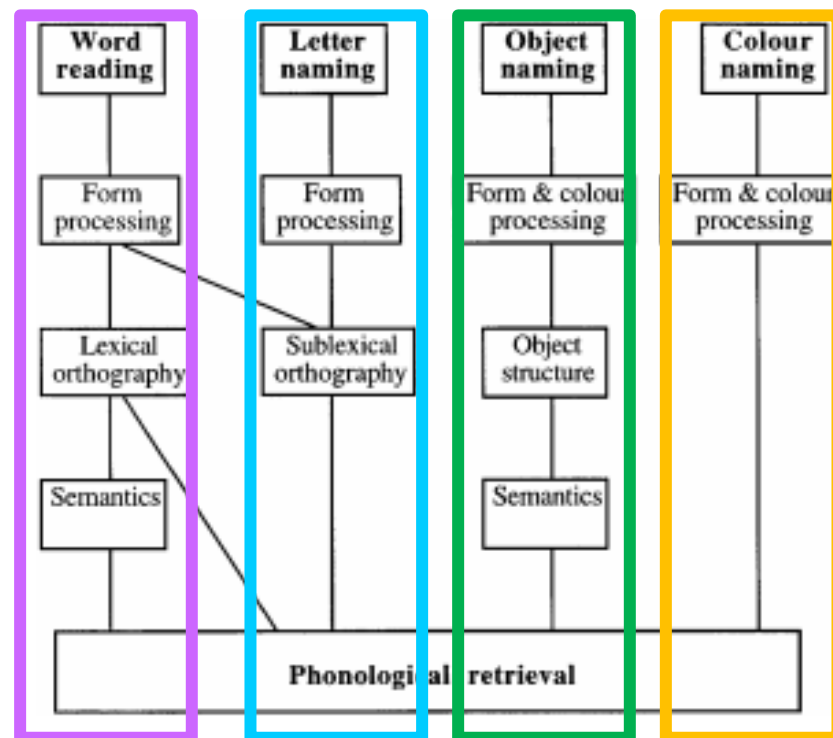
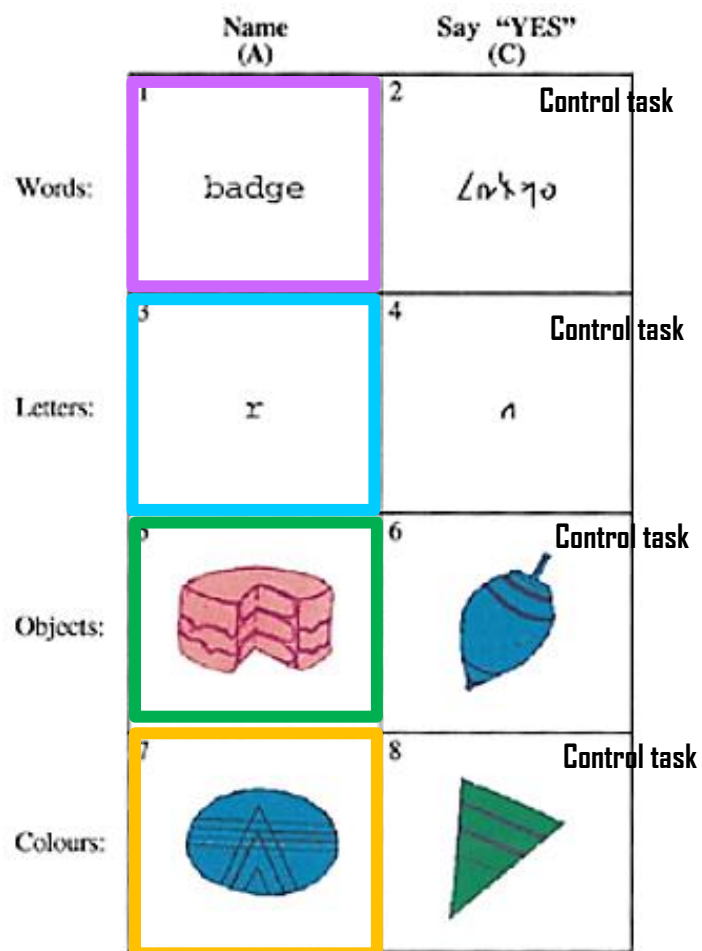
An example...

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



Conjunction analysis

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



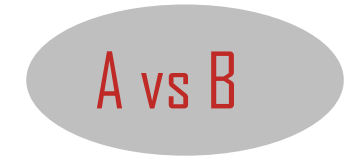
Phonological retrieval is the only cognitive component common to all task pair differences.

Price & Friston (1996)

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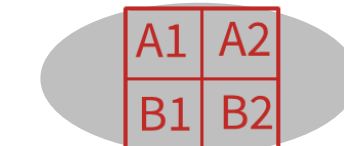
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Parametric designs

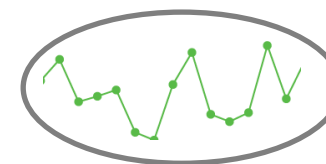
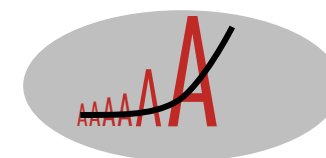
Does activity vary systematically with a continuously varying parameter?

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)

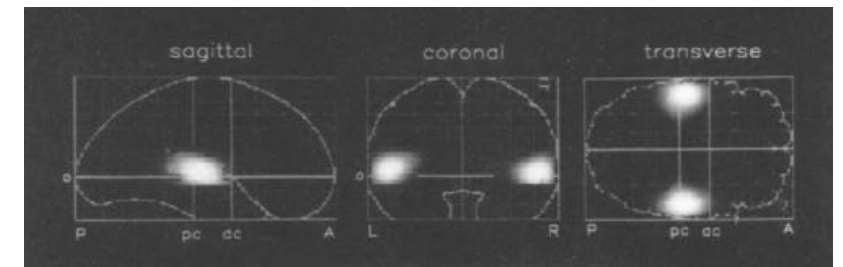
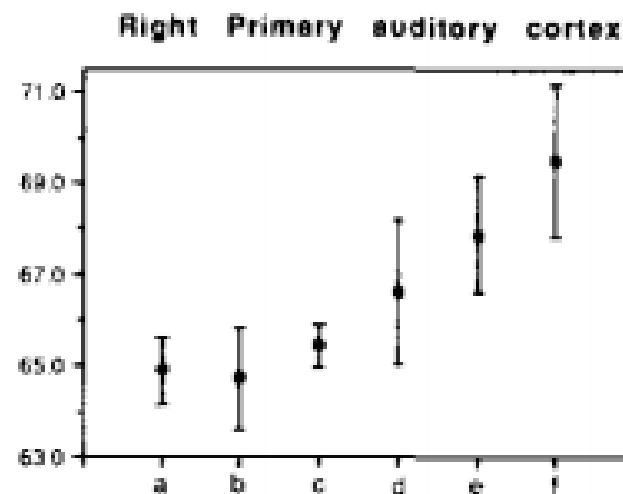
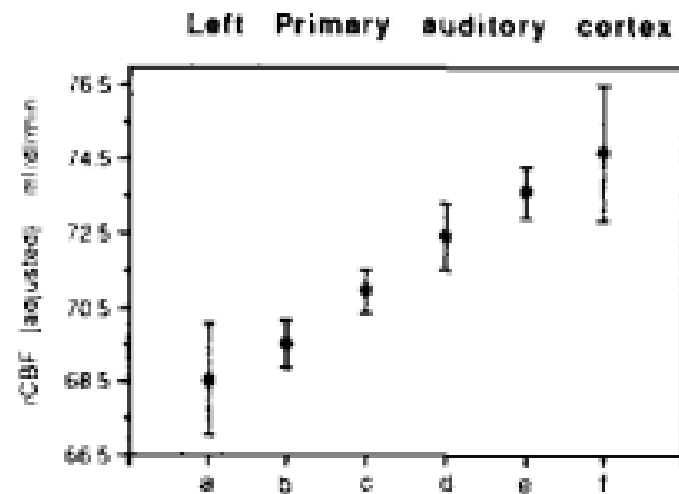
Avoids pure insertion but does assume no qualitative change in processing.



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

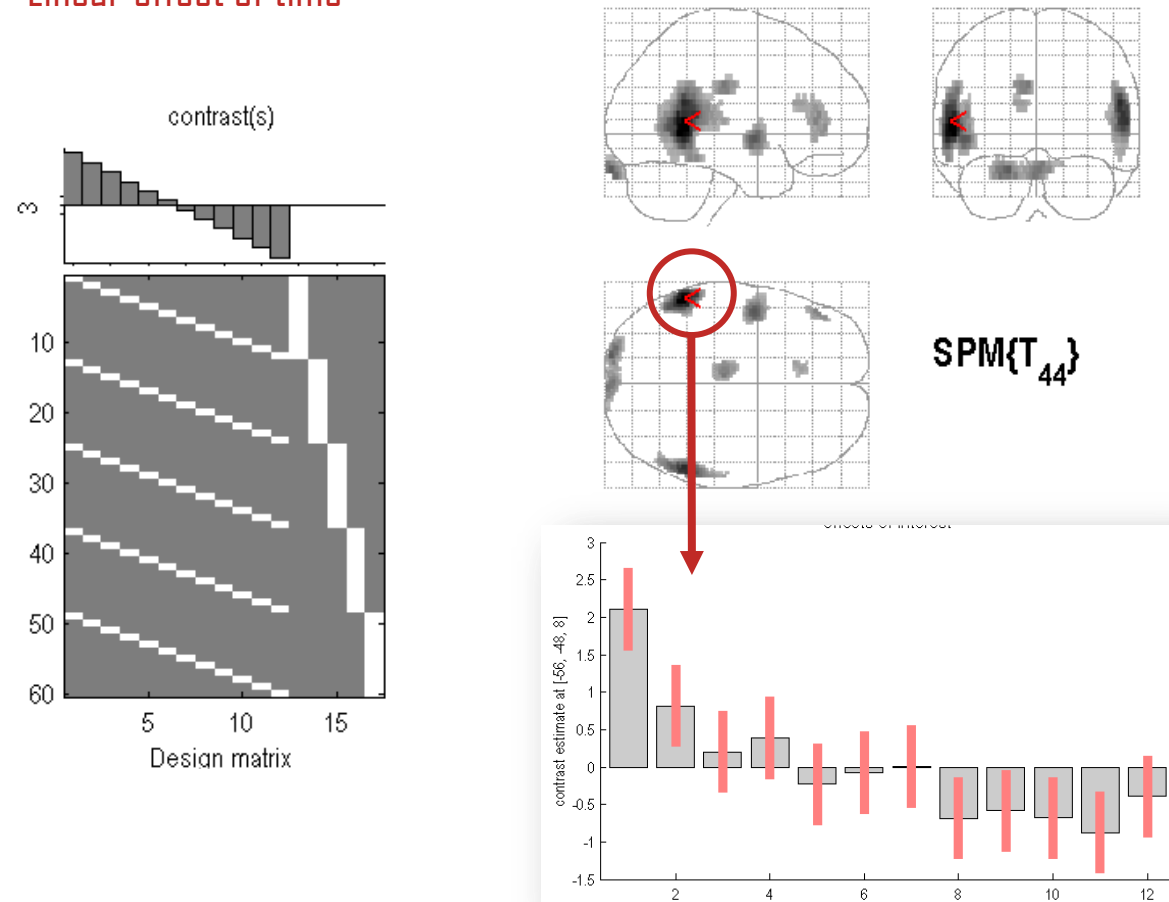


Price et al. 1992

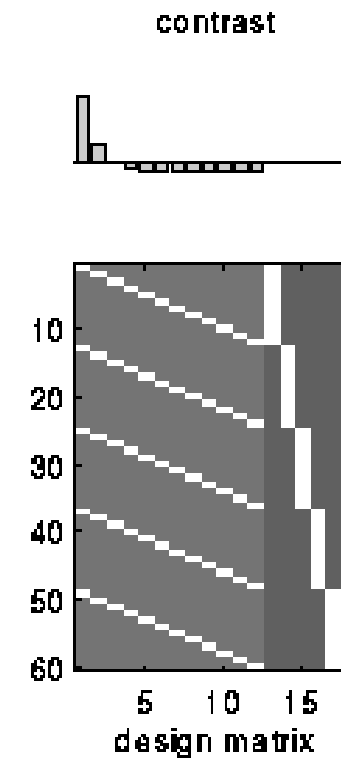
A linear parametric contrast

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

Linear effect of time



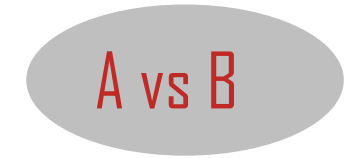
Non-linear effect of time



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- Linear
- **Nonlinear**

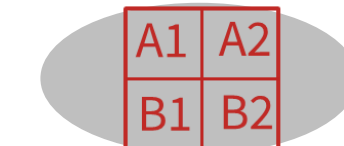
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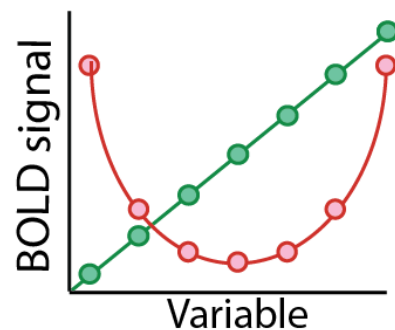
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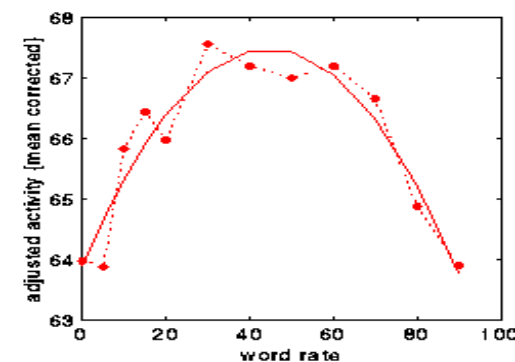
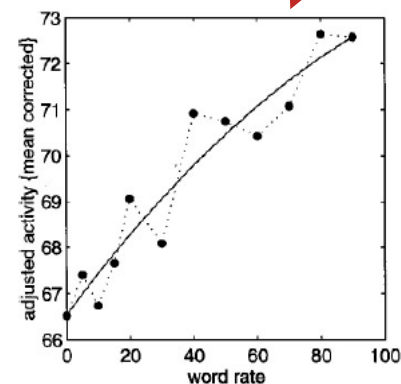
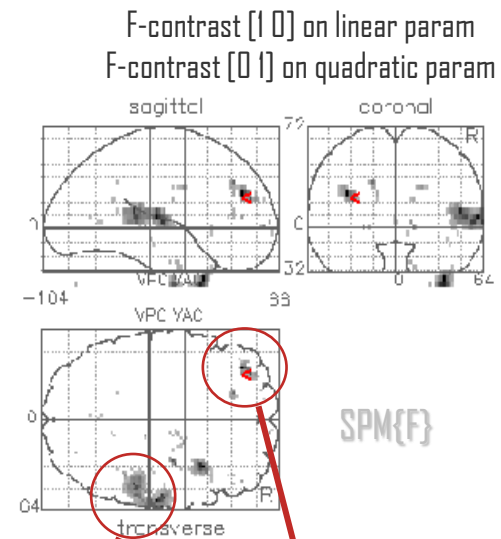
A non-linear parametric design matrix

Polynomial expansion:
 $f(x) = b_1 x + b_2 x^2 + \dots$
...up to $(N-1)^{\text{th}}$ order for N levels

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



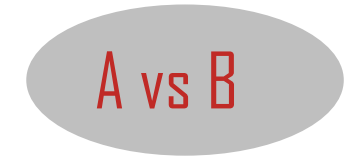
Büchel et al., (1996)



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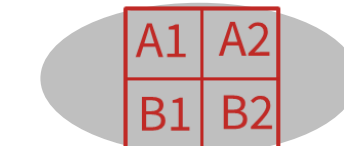
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3. Factorial designs

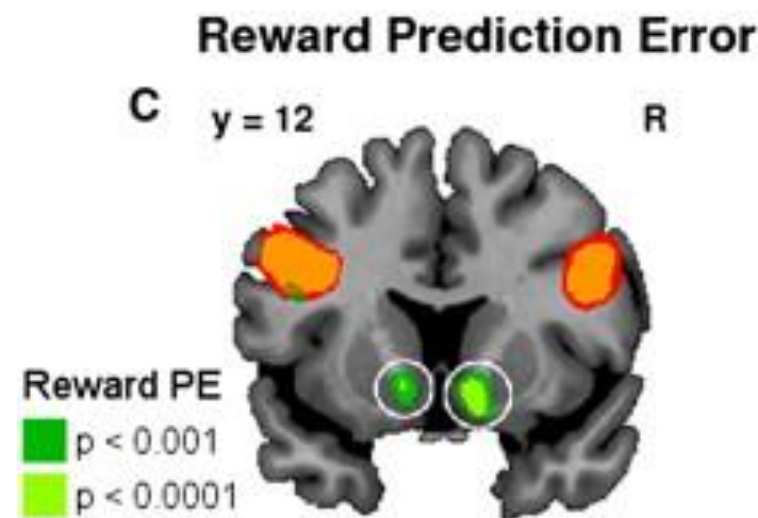
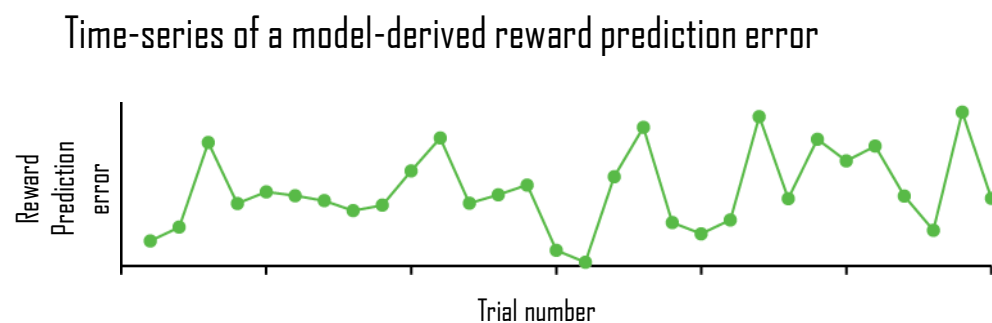
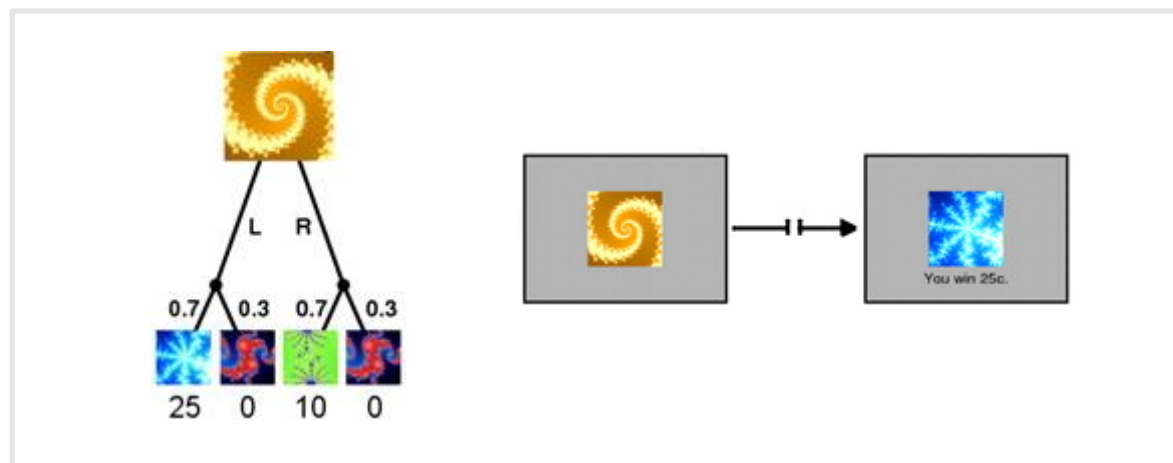
- Categorical
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Parametric design: Model-based regressors

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

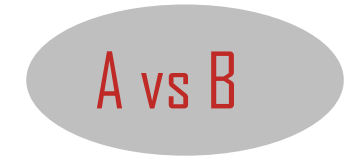


Gläscher & O'Doherty (2010)

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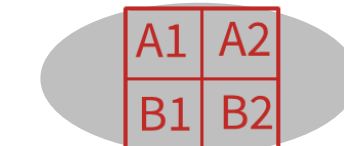
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Factorial design

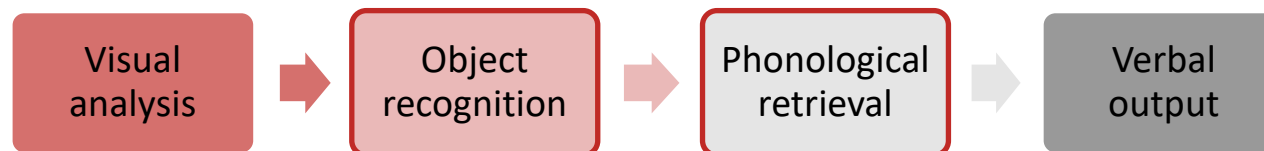
		Factor A	
		A	a
Factor B	B	A B	a B
	b	A b	a b

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

We can address the “pure insertion” problem!

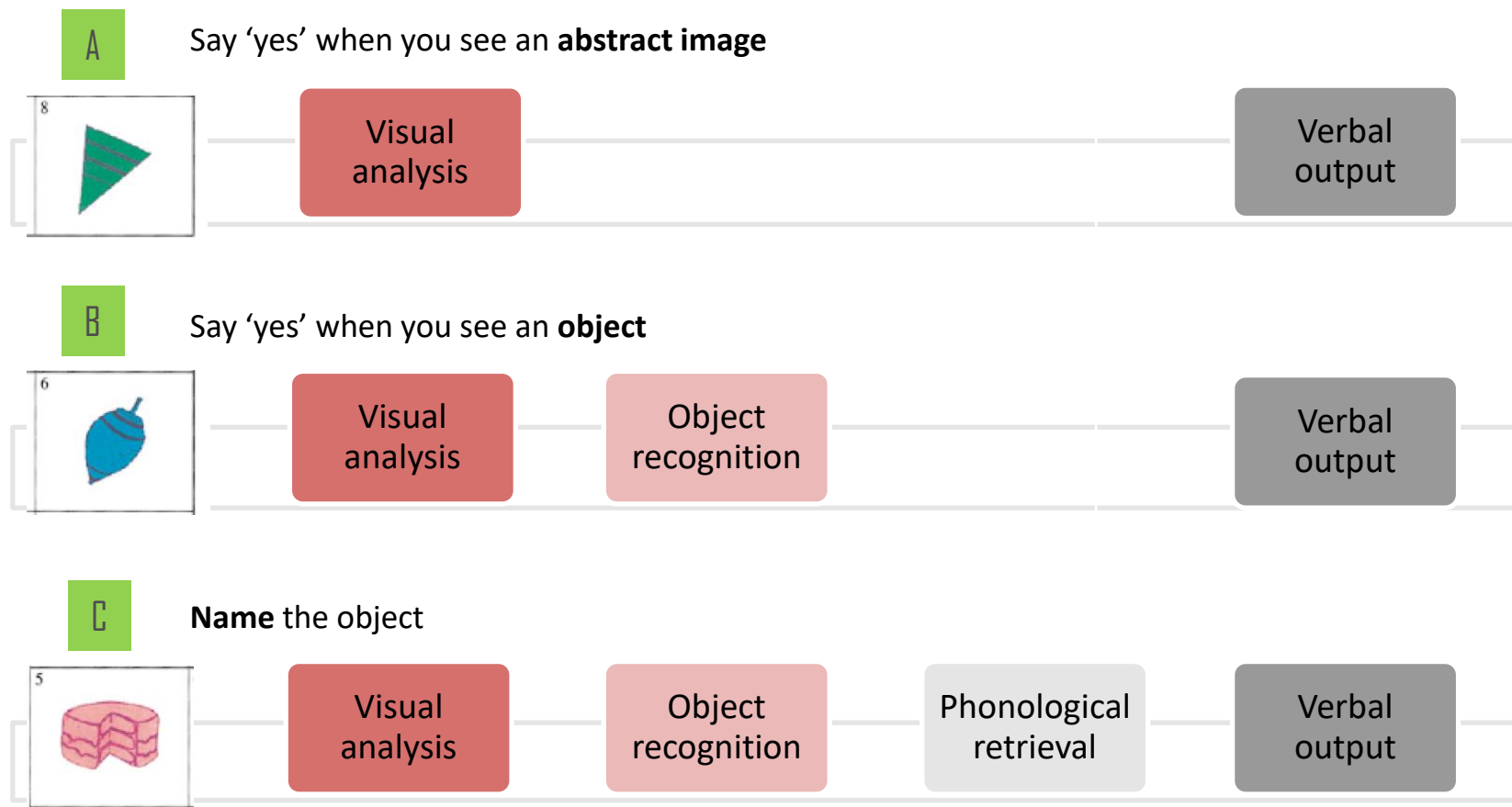
Factorial design

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?



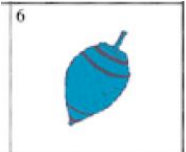
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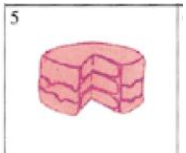
A Say 'yes' when you see an **abstract image**

8 

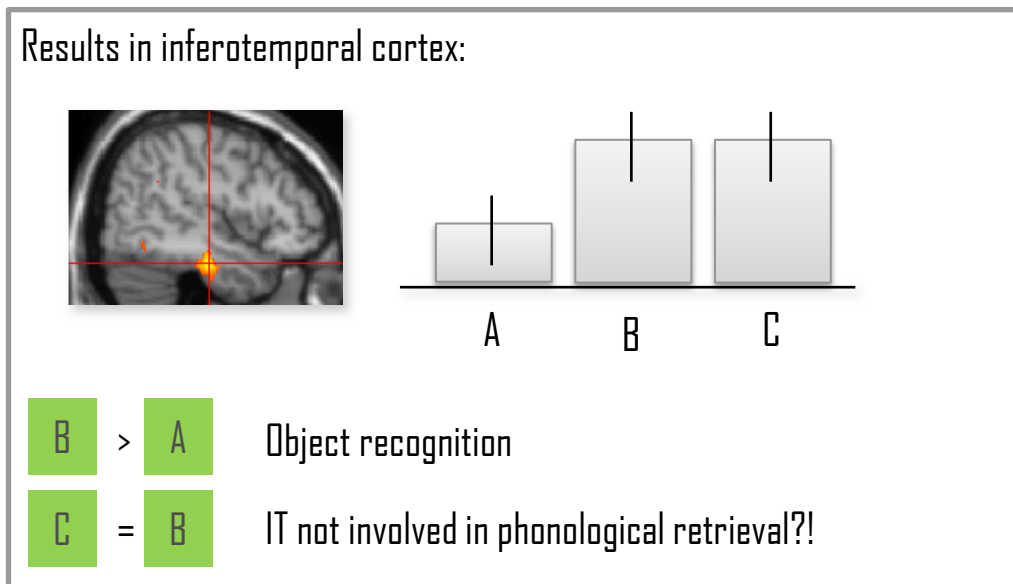
B Say 'yes' when you see an **object**

6 

C **Name** the object

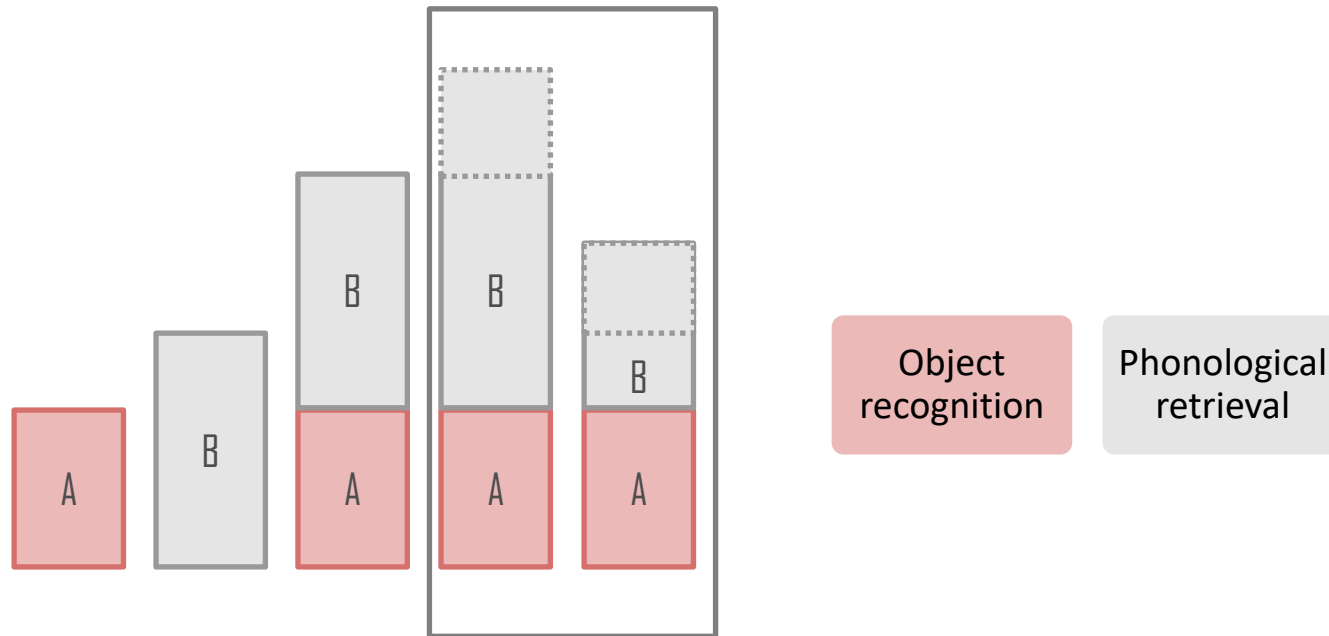
5 

Friston et al., (1997)



Addressing interactions in factorial designs

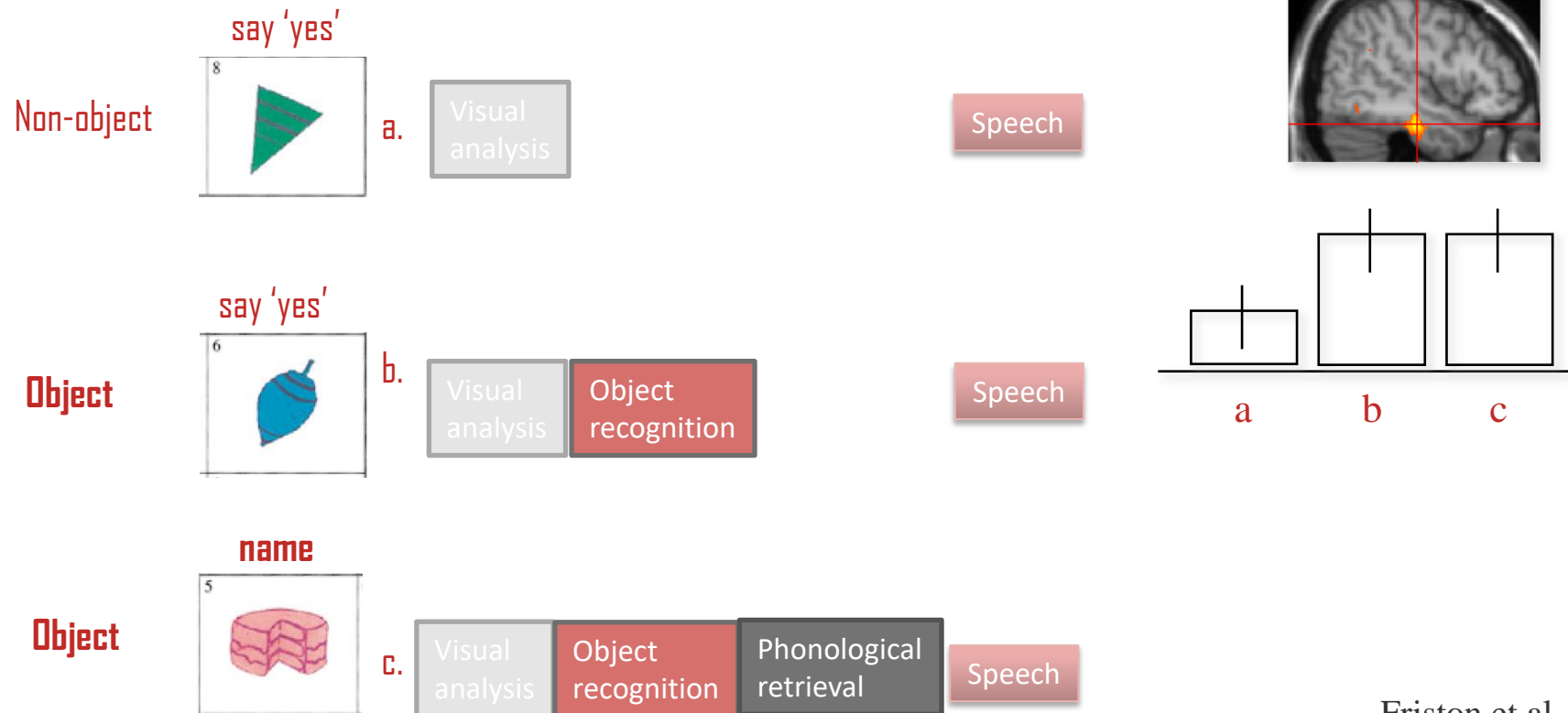
Is the task the sum of its component processes, or does A modulate B?



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

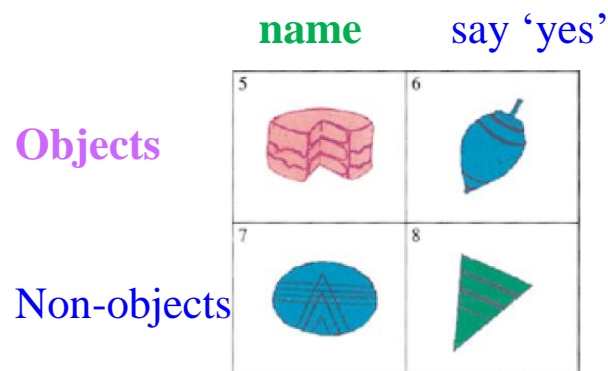
Factorial designs: Main effects and interaction

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

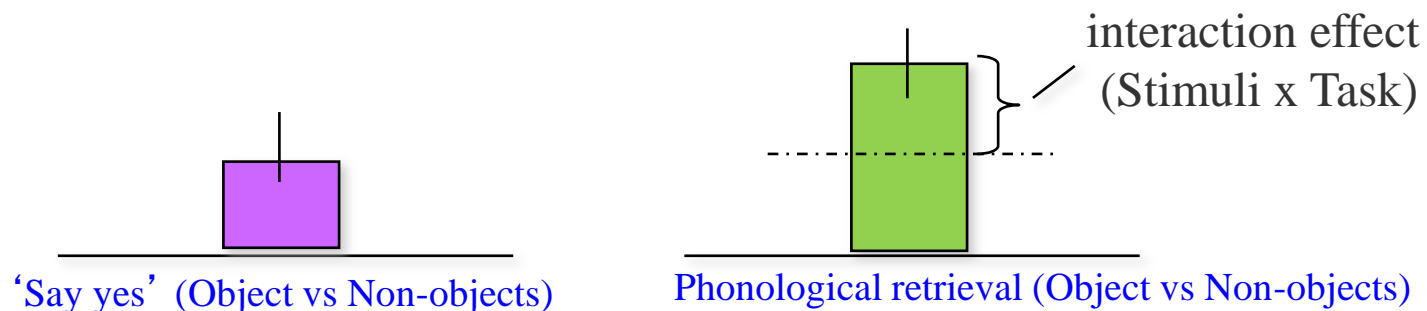


Main effect of task (naming): $(\text{O}NAME + \text{N}NAME) - (\text{O}YES + \text{N}YES)$

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

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

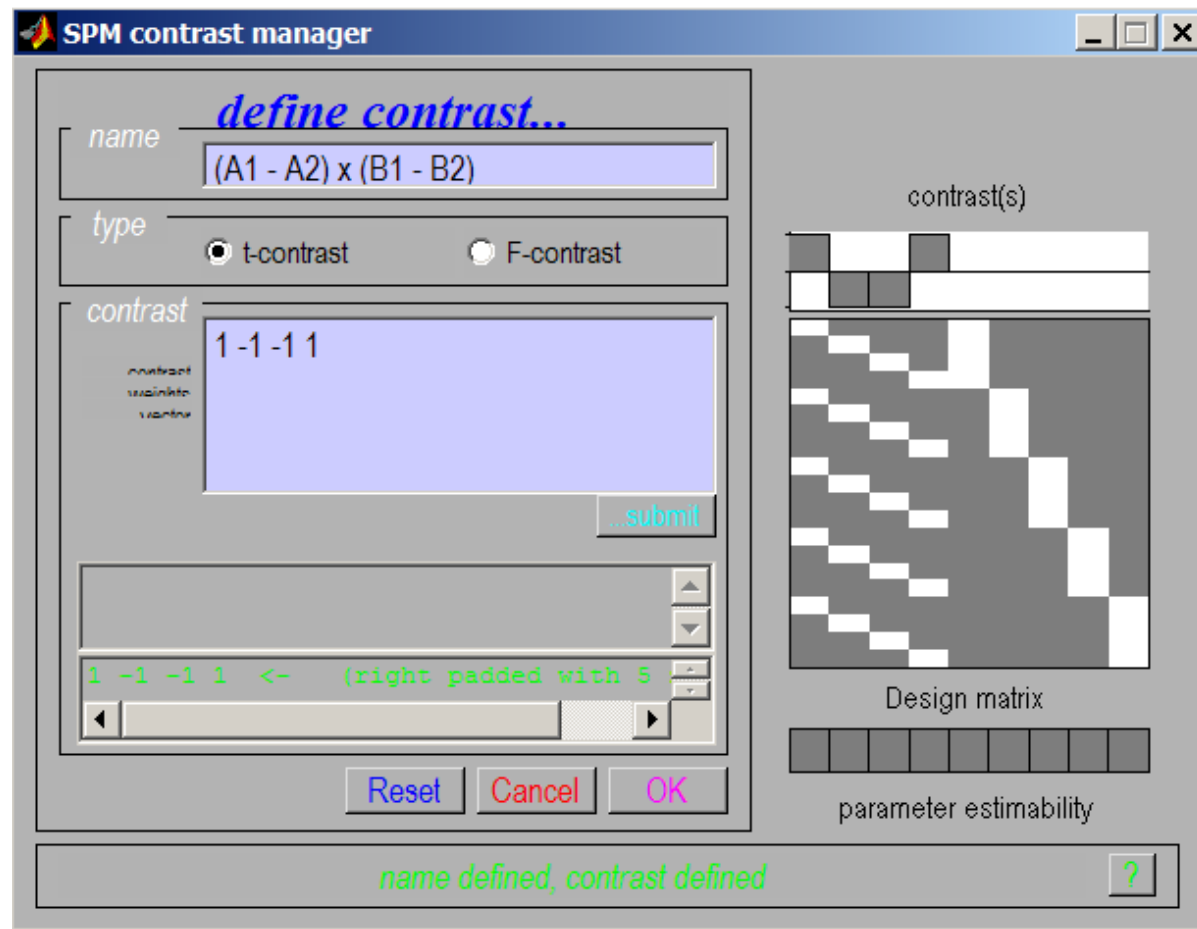
Can show a failure of pure insertion



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.

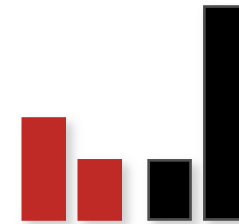
Friston et al., (1997)

Interaction in SPM



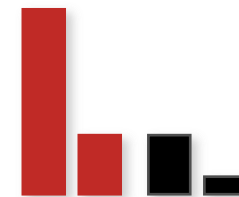
Interactions:

cross-over



and

simple

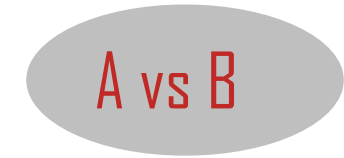


We can selectively inspect our data for one or the other by **masking** during inference

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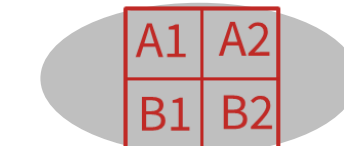
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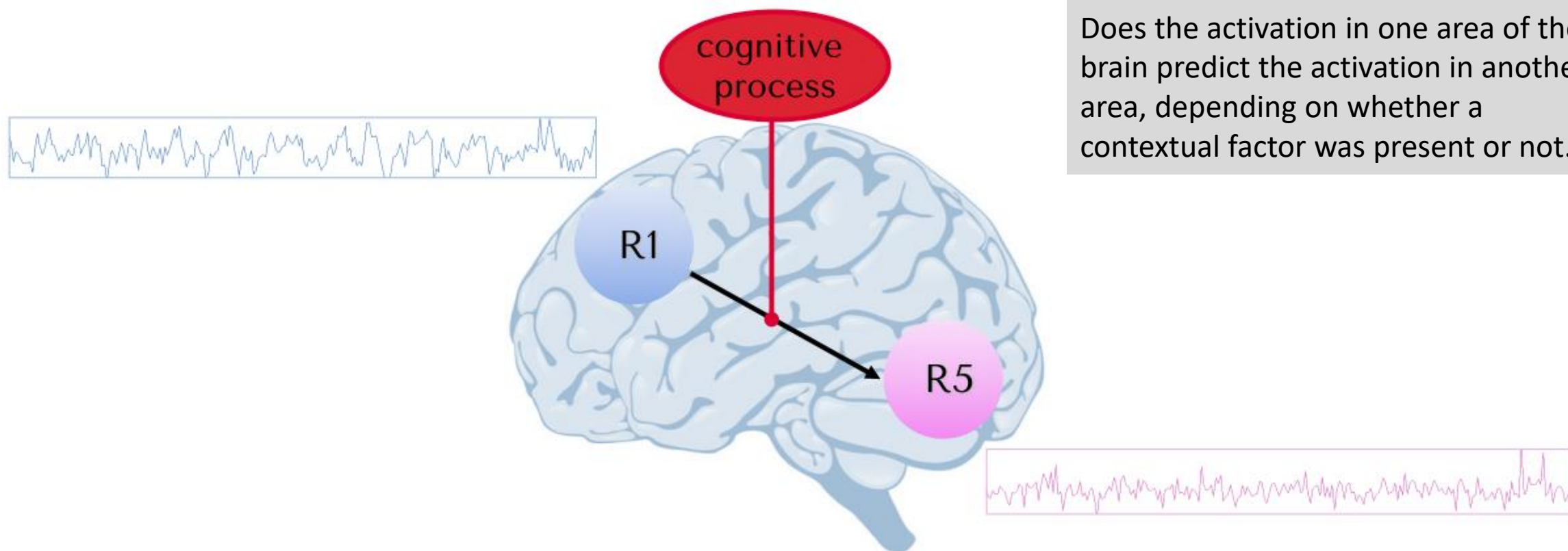
3. Factorial designs

- Categorical
- **Parametric**

Interactions and pure insertion
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Psycho-physiological Interaction (PPI)



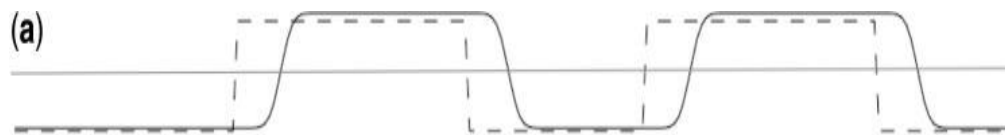
Question:

Does the activation in one area of the brain predict the activation in another area, depending on whether a contextual factor was present or not.

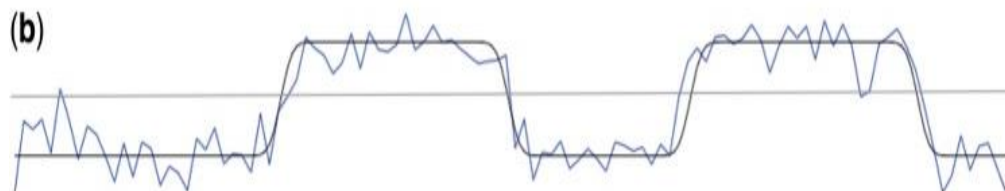
Psycho-physiological Interaction (PPI)

Does learning involve functional connectivity between parietal cortex and stimuli specific areas?

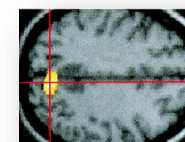
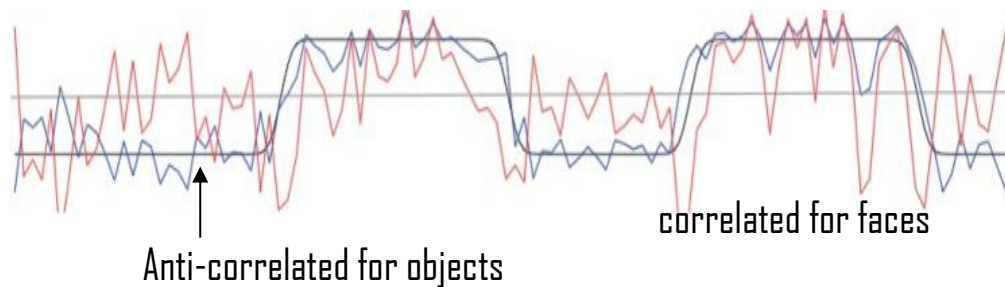
Main effect of task (Faces - objects)



Activity in parietal cortex (main effect learning)



PPI regressor = HRF convolved task x seed ROI regressors



Seed region

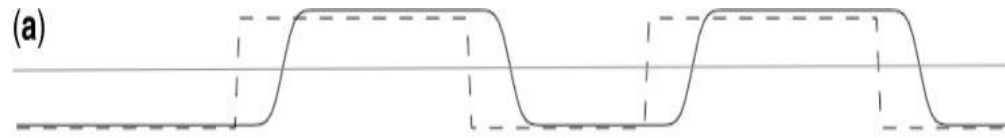


Whole brain

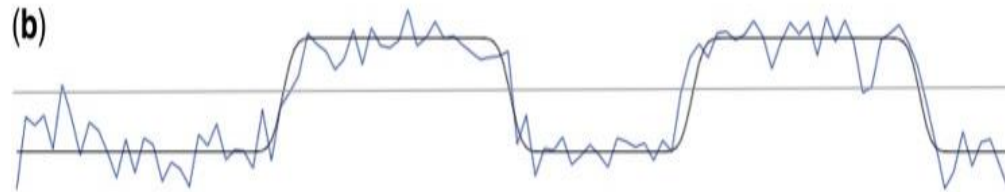
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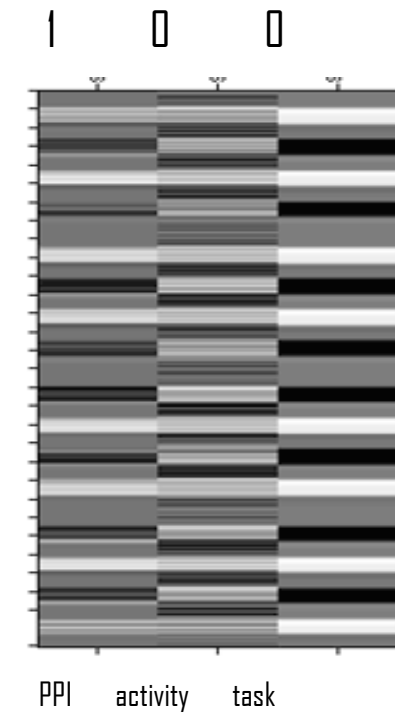
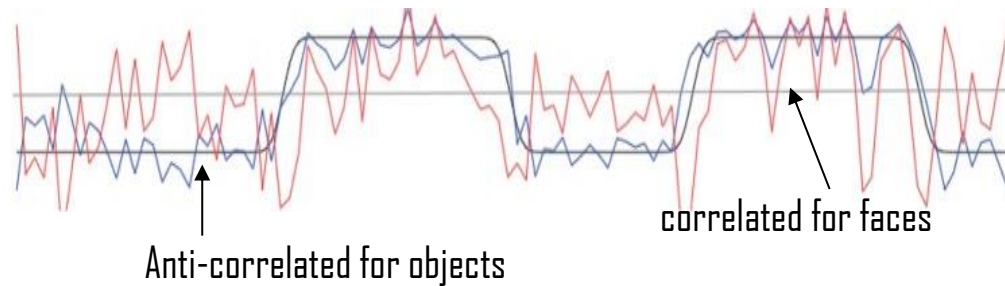
Main effect of task (Faces - Objects)



Activity in parietal cortex (main effect of learning)



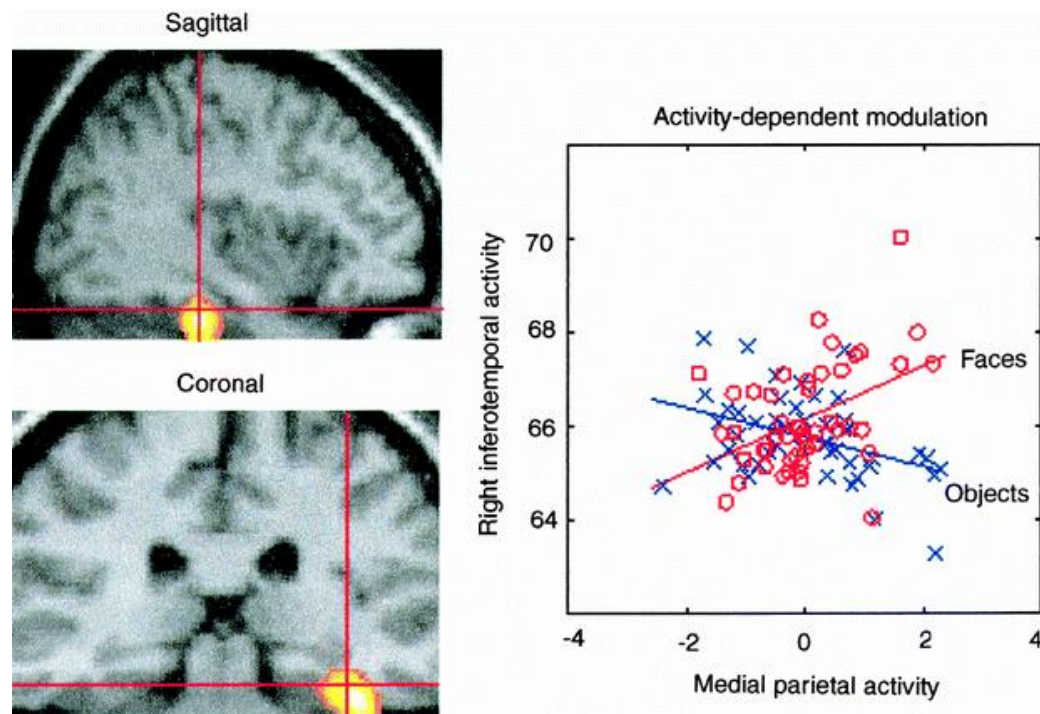
PPI regressor = HRF convolved task x seed ROI regressors



The interaction term should account for variance over and above what is accounted for by the main effect of task and physiological correlation

Psycho-physiological Interaction (PPI)

Coupling between ITC and parietal cortex depends on the stimulus



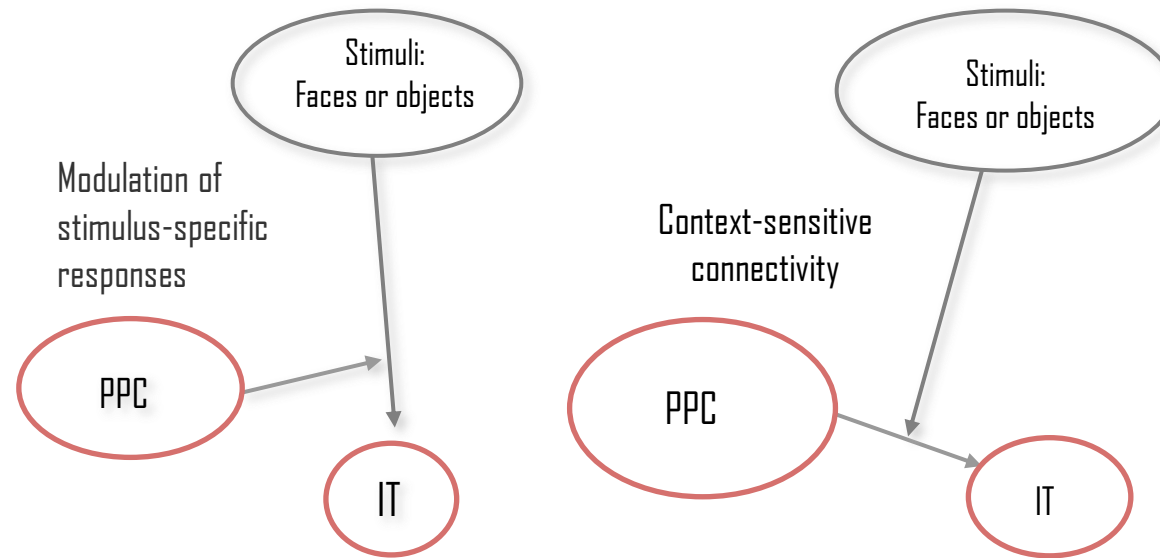
Coupling between the temporal face area and the medial parietal cortex when, and only when, faces were perceived

Suggests: ITC can differentiate between faces and objects only if parietal activity is high

Dolan et al., 1997

Psycho-physiological interactions (PPI)

A standard PPI analysis does not make inferences about the **direction** of information flow (causality)



Questions?
