Experimental design

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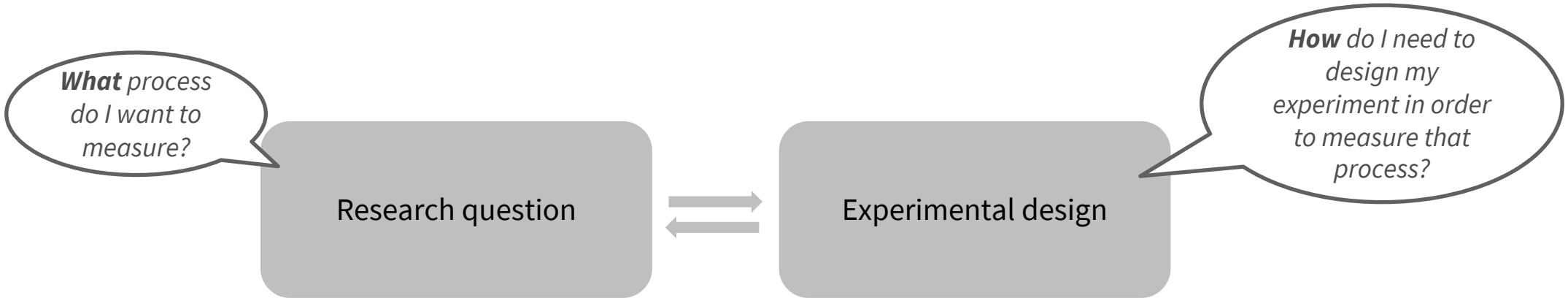
With thanks to:

Elisa van der Plas
Mona Garvert
Sara Tomiello
Sara Bengtsson
Christian Ruff
Rik Henson

The most important slide of this talk

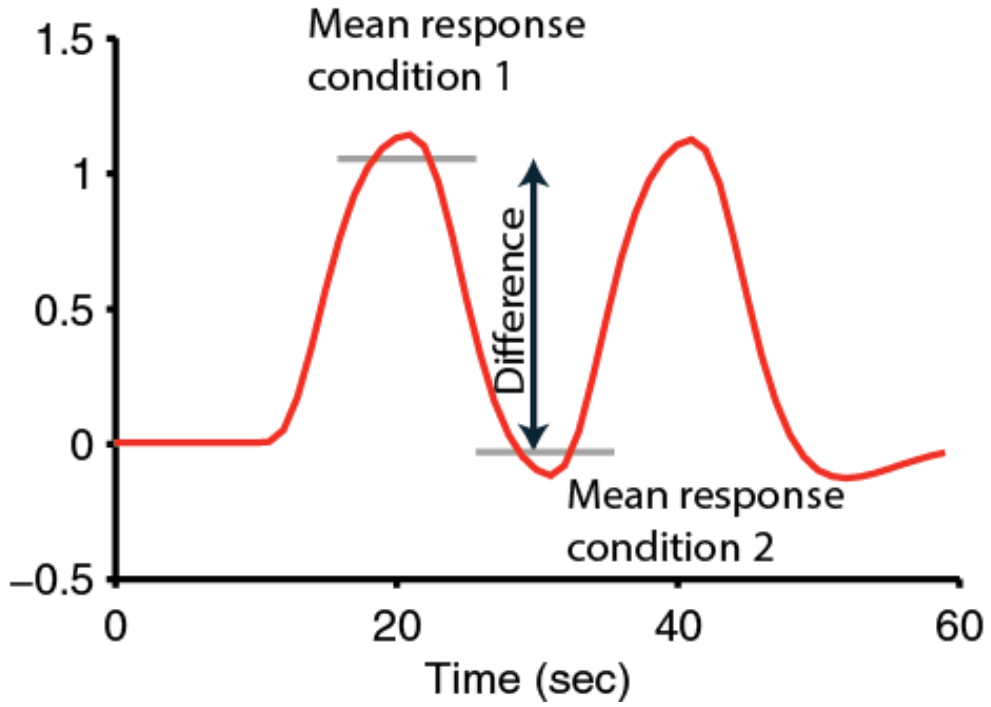
It all starts with a good design!



Why is that?

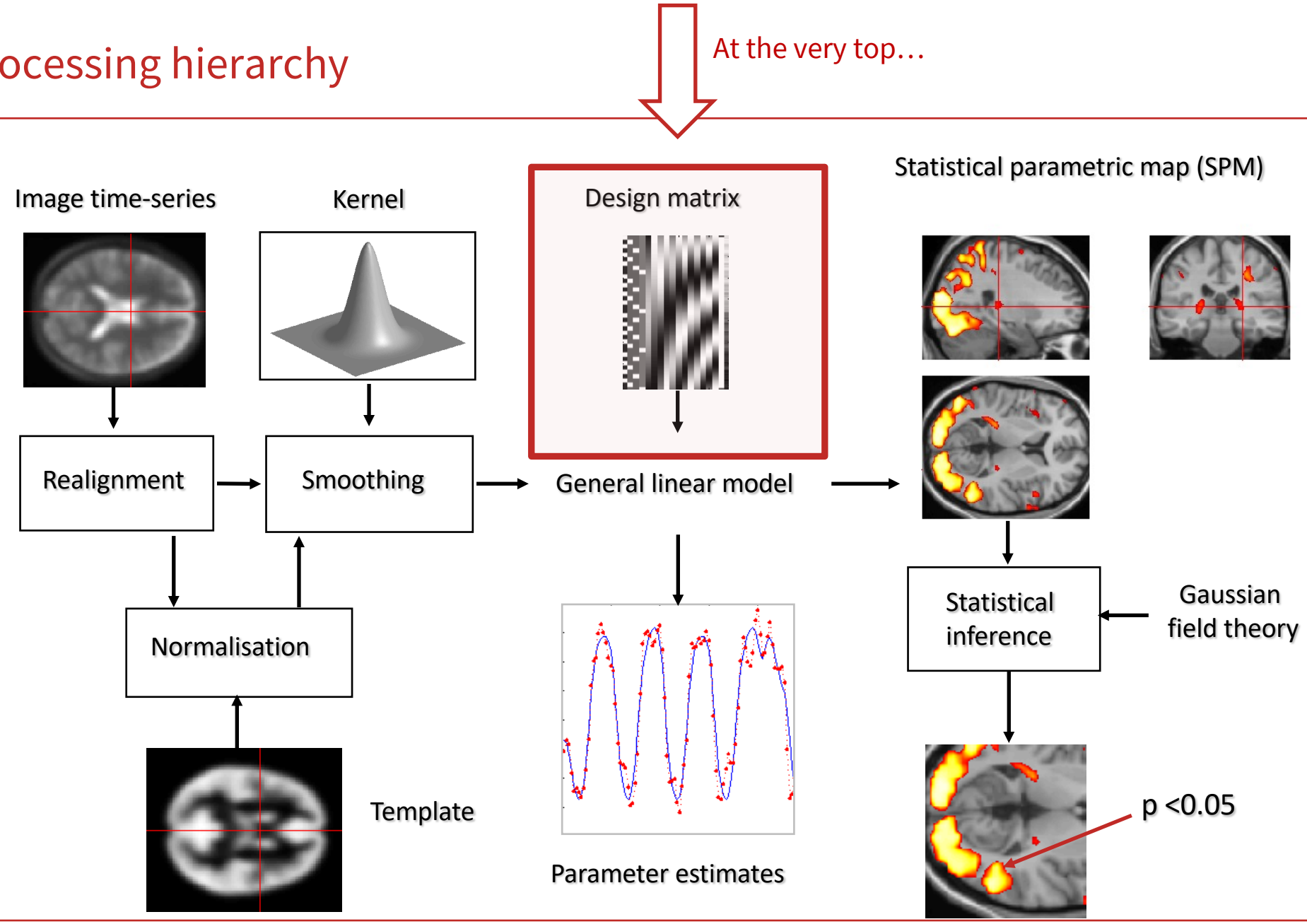
The BOLD signal does NOT provide you with an absolute measure of neural activity

Therefore, you need to compare activity across conditions



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

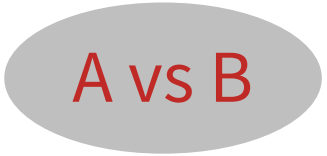
SPM processing hierarchy



Overview

1. Categorical designs

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

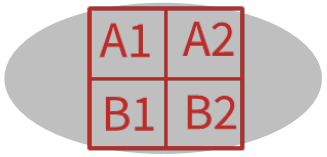


2. Parametric designs

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

3. Factorial designs

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



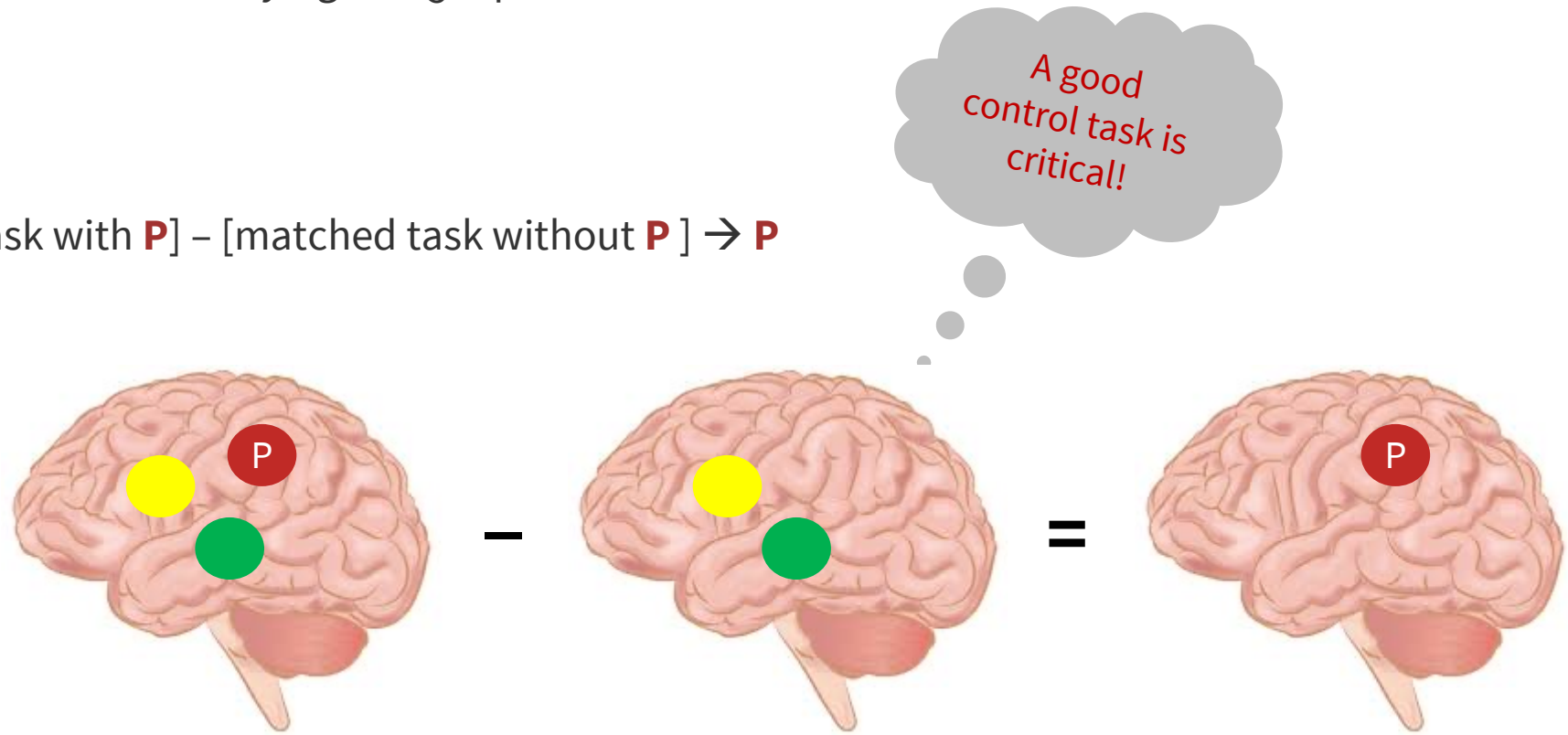
Cognitive subtraction

Aim

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

Procedure

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



However…

The critical assumption of pure insertion

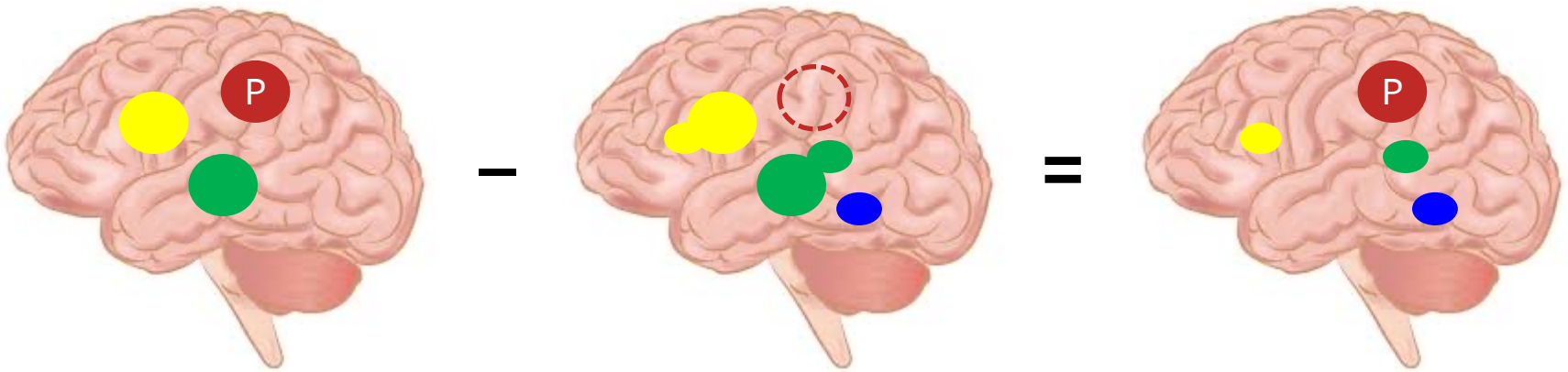
Pure insertion assumption: Assumption that adding components does not affect other processes

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

Simple subtraction

Question: Which neural structures support face recognition?

What is a good control task?

Aim: Isolation of a cognitive process

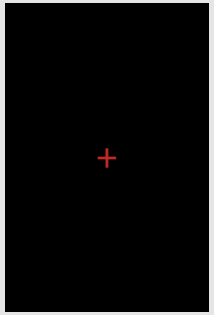
Method: Compare the neural signal for a task that activates the cognitive process of interest (P) and a second task that controls for all but the process of interest (P)

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

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!

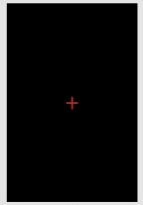
Name the gender!

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

Choosing your baseline

Different stimuli and task

vs.



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

Different stimulus, same task

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

Related stimuli, same task

vs.

Famous? - yes Famous? – hm, wait, maybe… somewhat familiar…

Same stimulus, different tasks

vs.

Name the person! Name the gender!

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

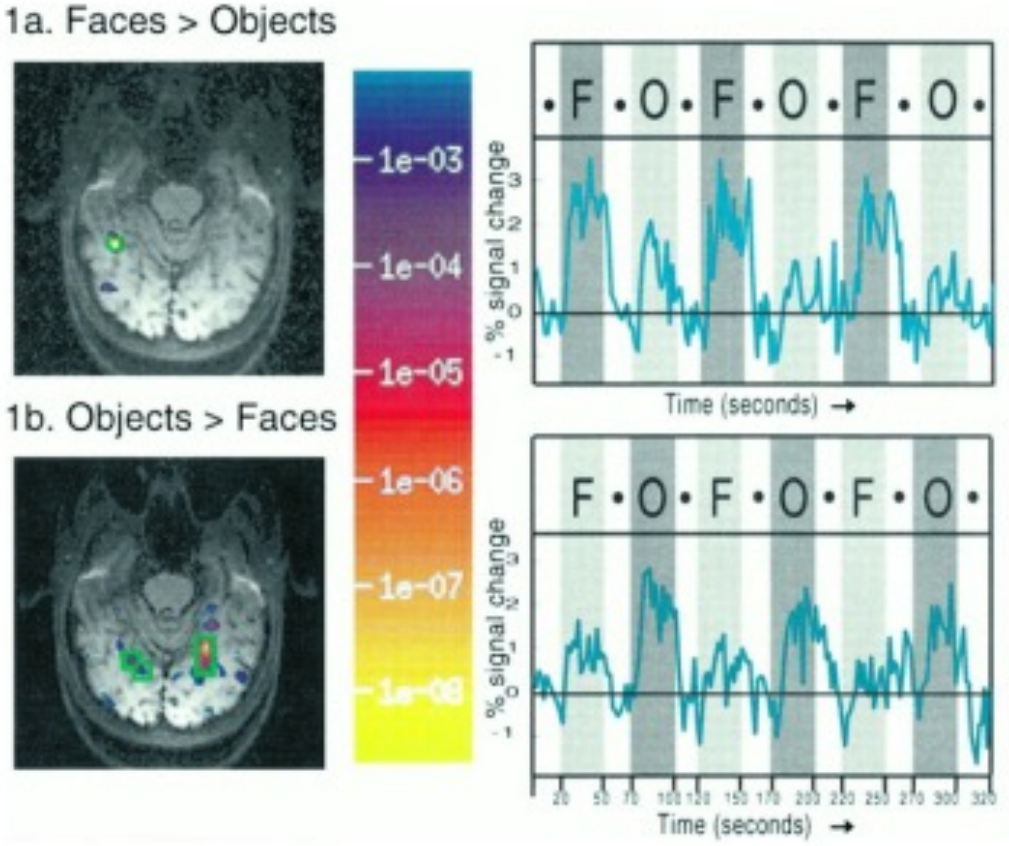
An example of cognitive subtraction

Experimental design

Face viewing: F
Object viewing: O

F - O = Face recognition
O - F = Object recognition

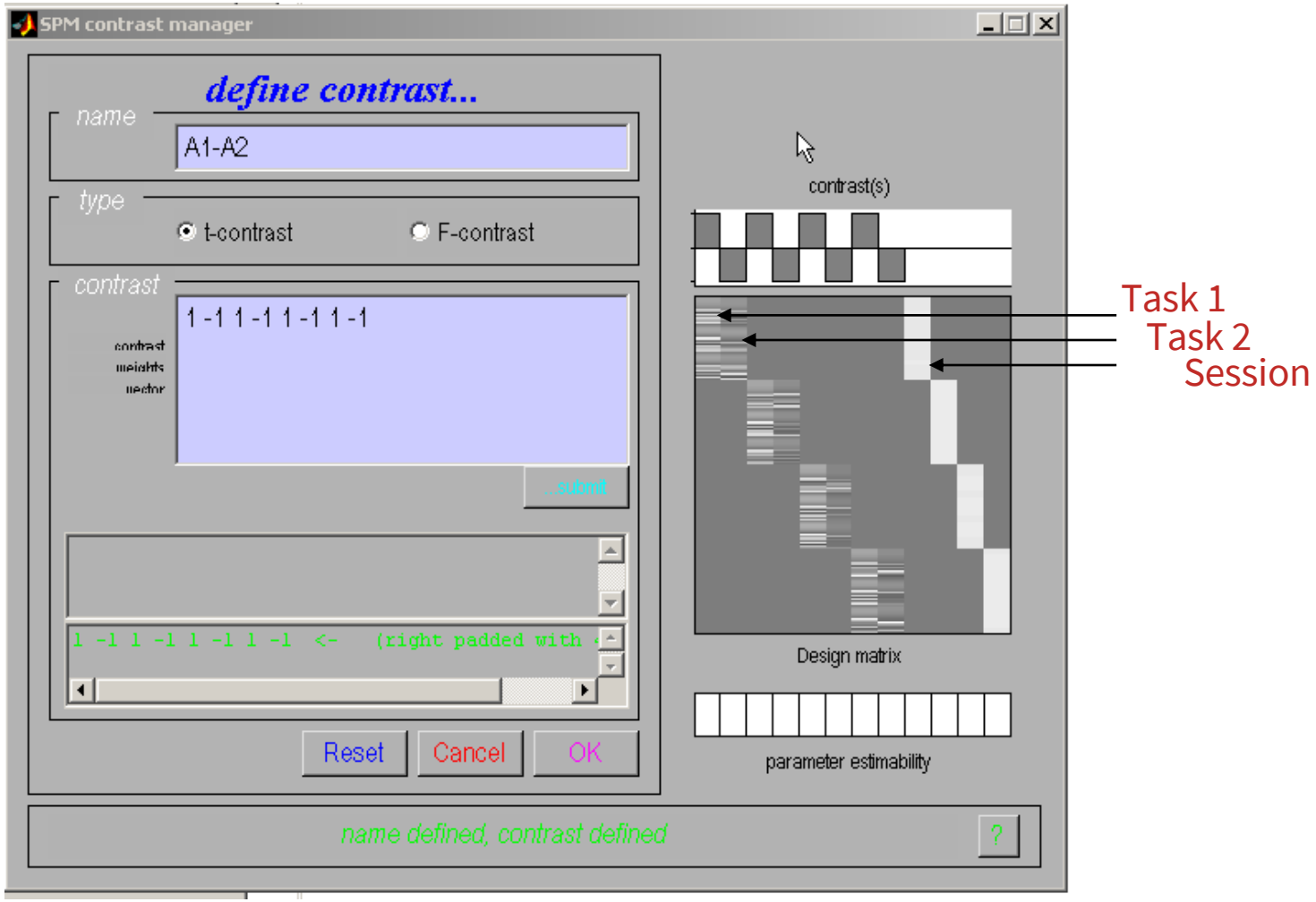
...under assumption of pure insertion



Kanwisher et al., 1997, J. Neurosci.

Categorical responses

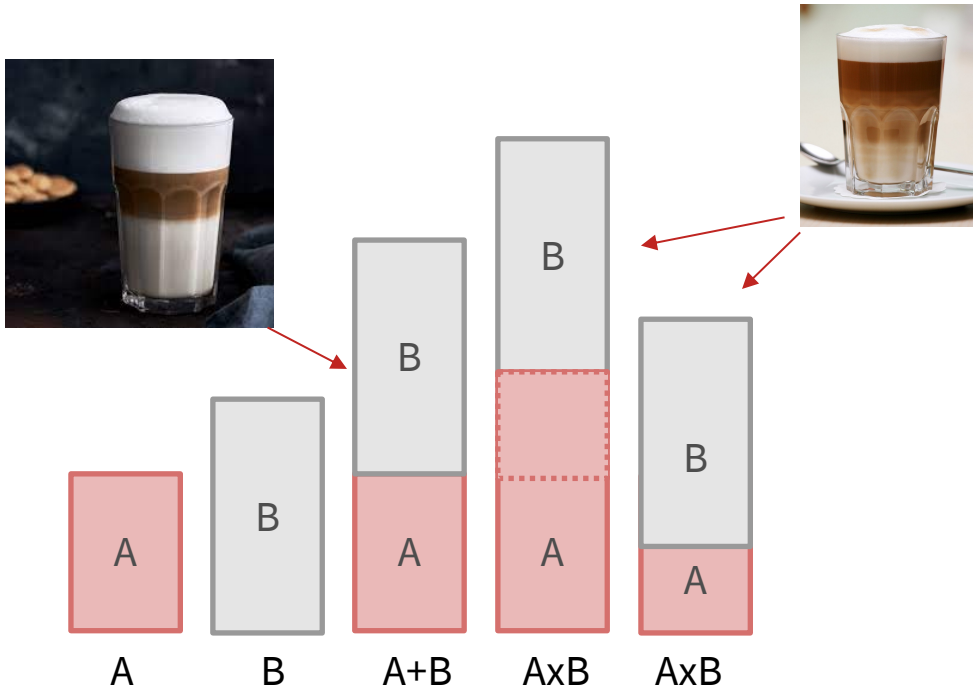
SPM interface



The problem of cognitive subtraction

Problems:

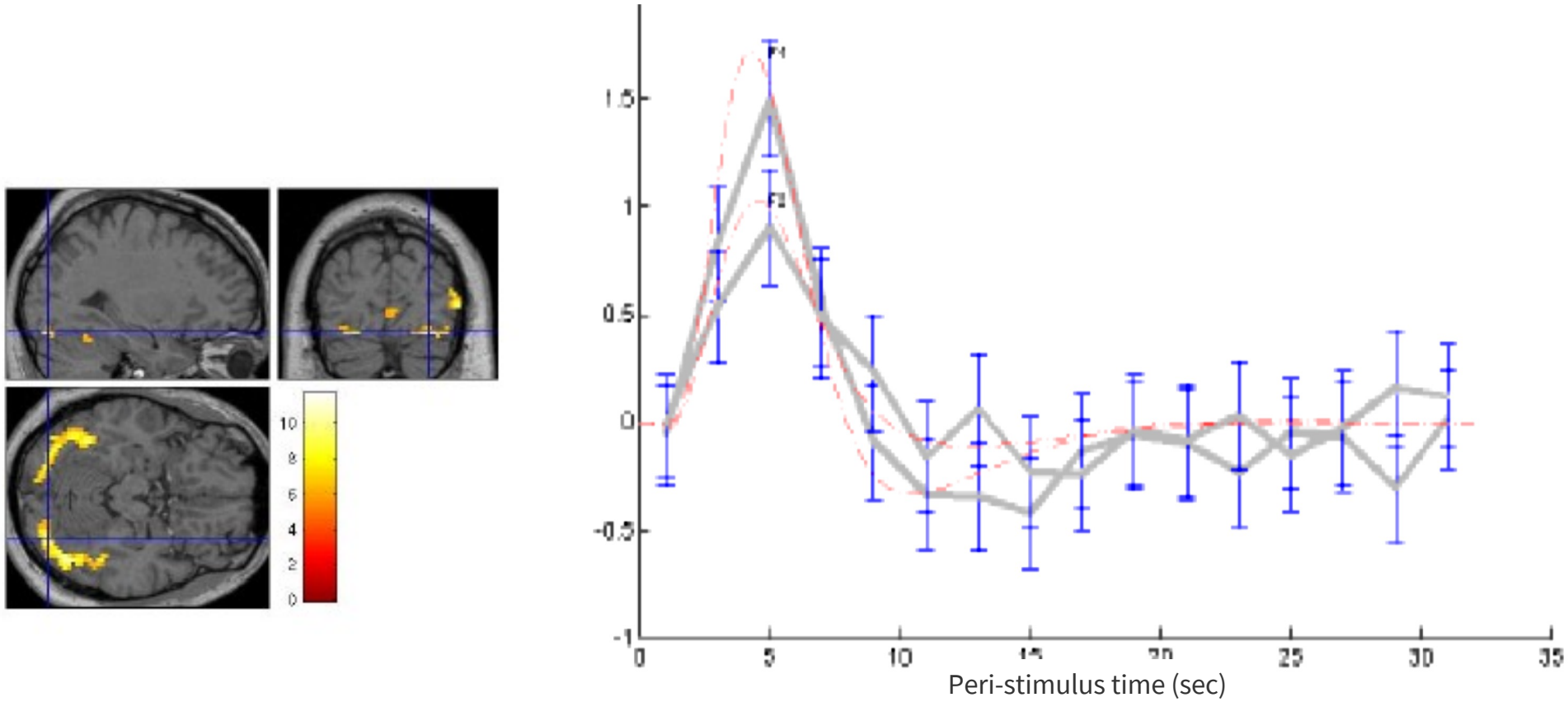
- Difficulty of finding baseline tasks that activate all but the process of interest (the “baseline problem”)
- Subtraction depends on the assumption of “pure insertion” (an extra cognitive component can be inserted without affecting the pre-existing components)



Friston et al., (1996)

fMRI adaptation as an example of neural interaction

Famous faces: 1st time vs 2nd time



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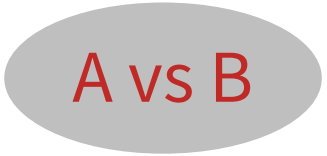

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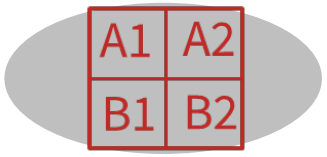
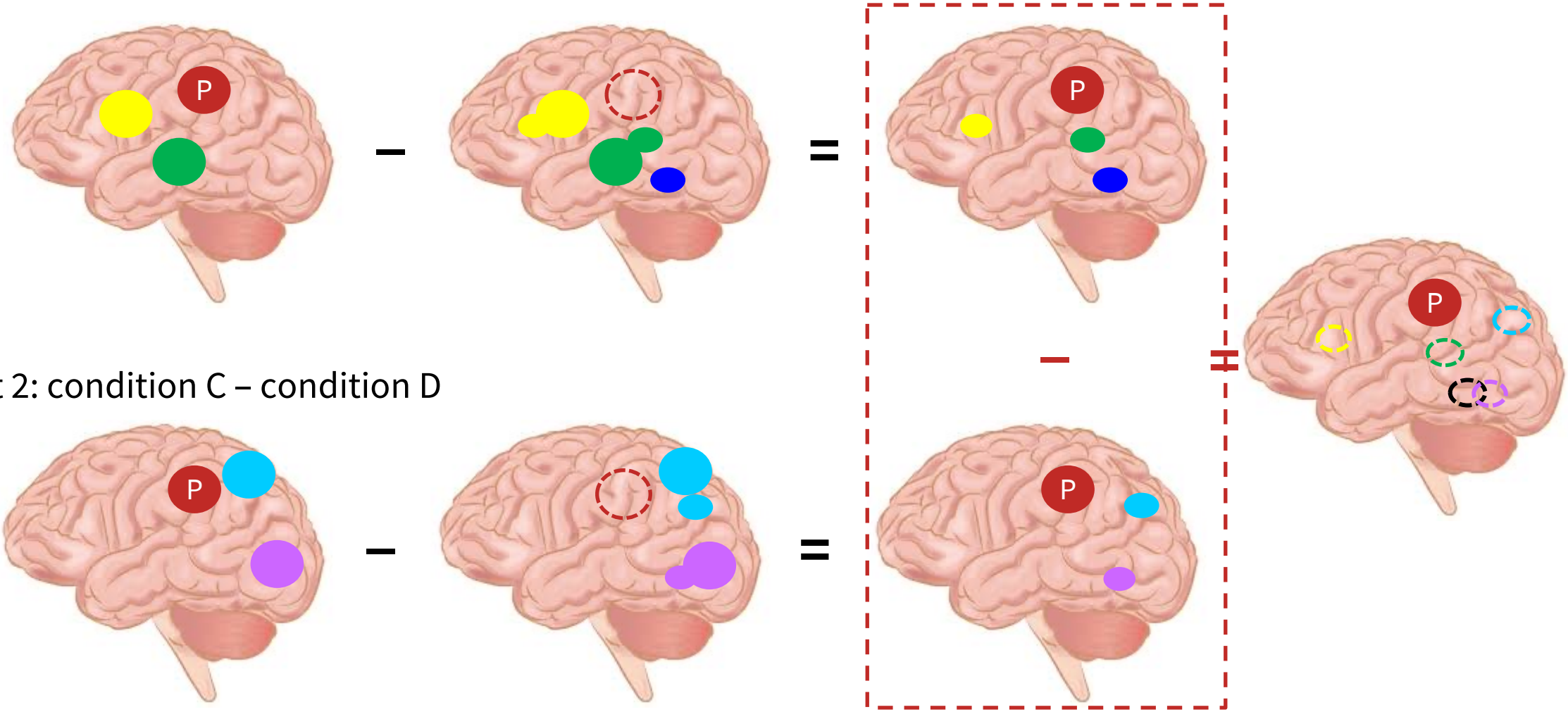


Tackling the baseline problem

Contrast 1: condition A – condition B

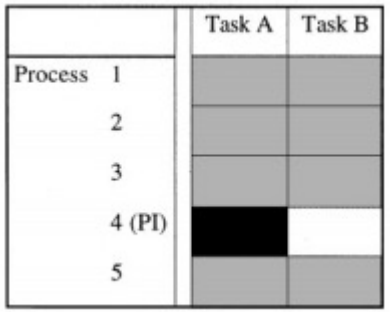


Contrast 2: condition C – condition D

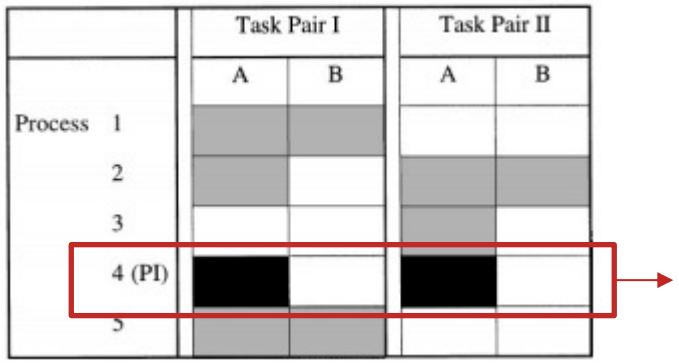
Conjunction

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

Subtraction



Conjunction analysis



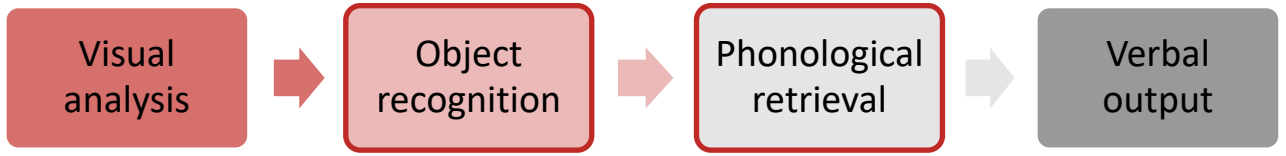
Only the process of interest (here: P4) is common to all task pairs.

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 ensure automatically by SPM)

An example…

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



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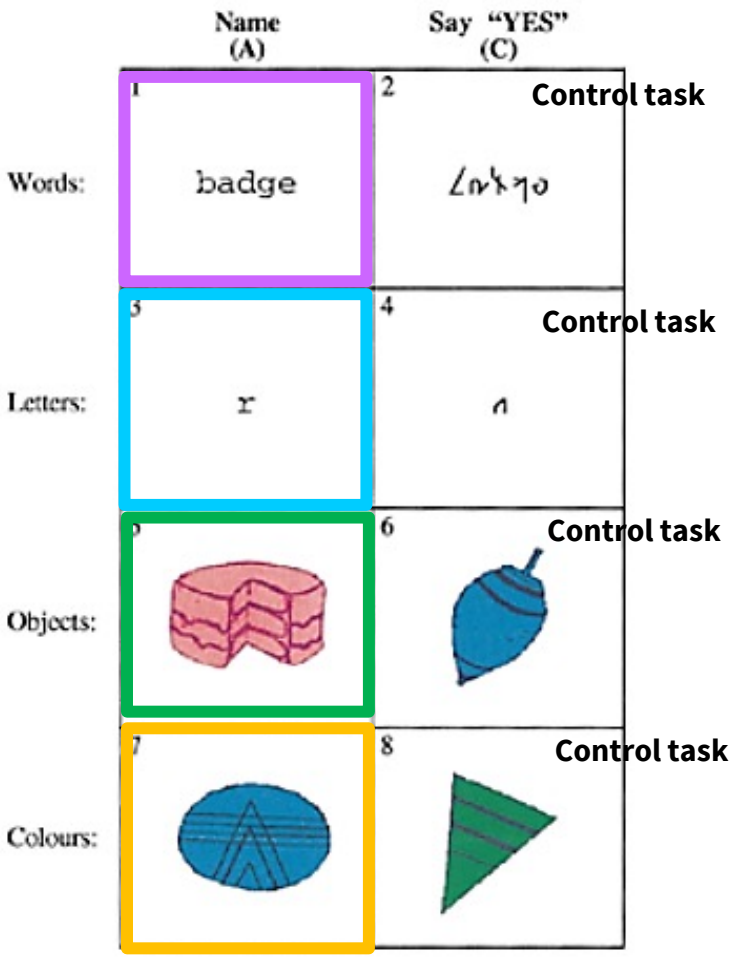
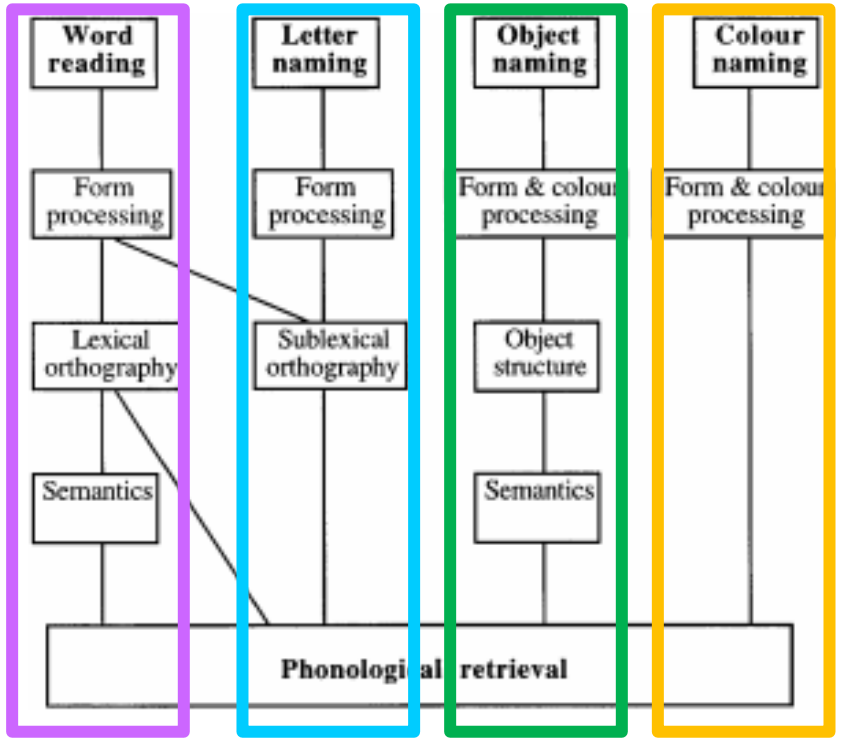


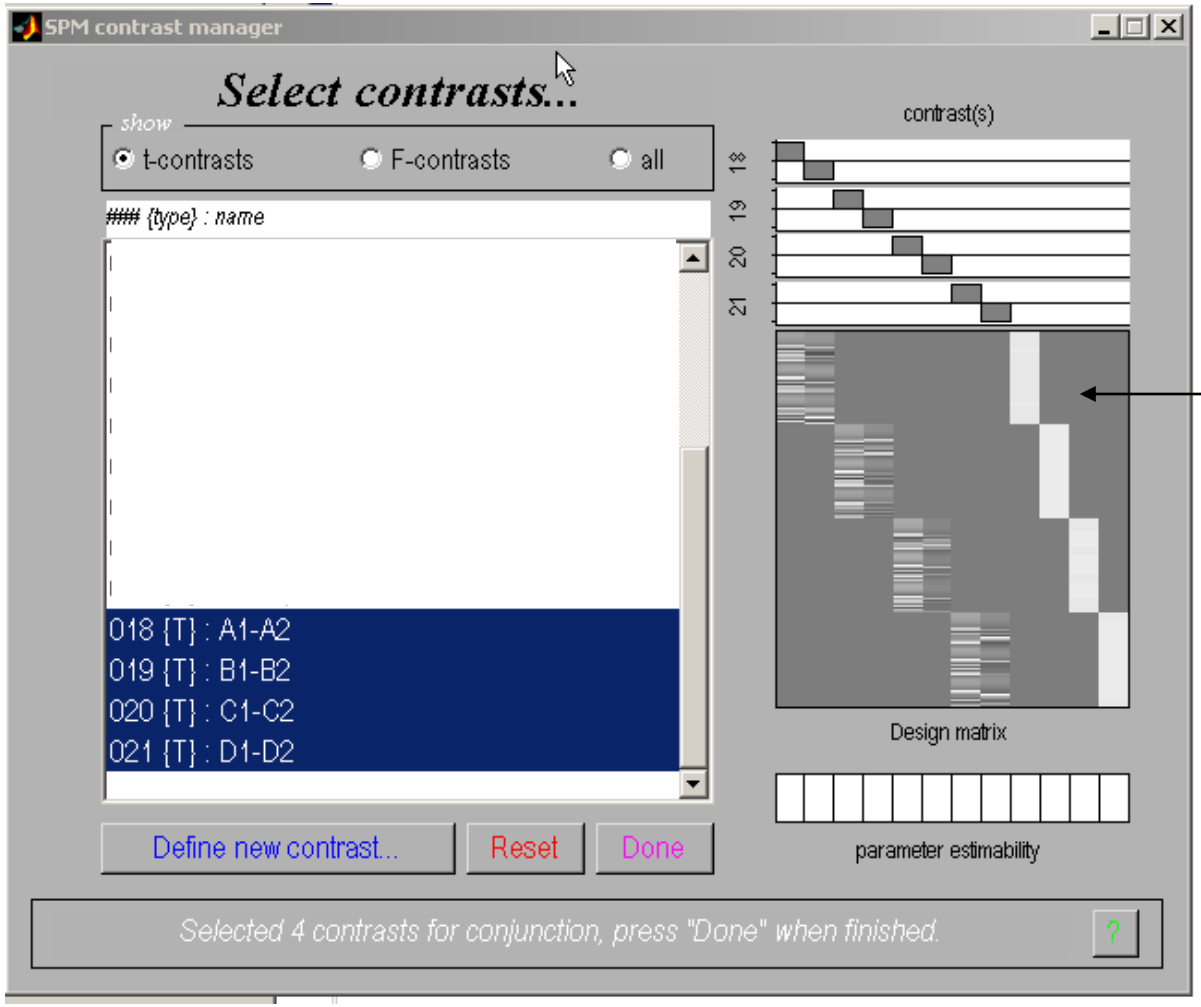


Phonological retrieval is the only cognitive component common to all task pair differences.

Price & Friston (1996)

Conjunction analysis

SPM

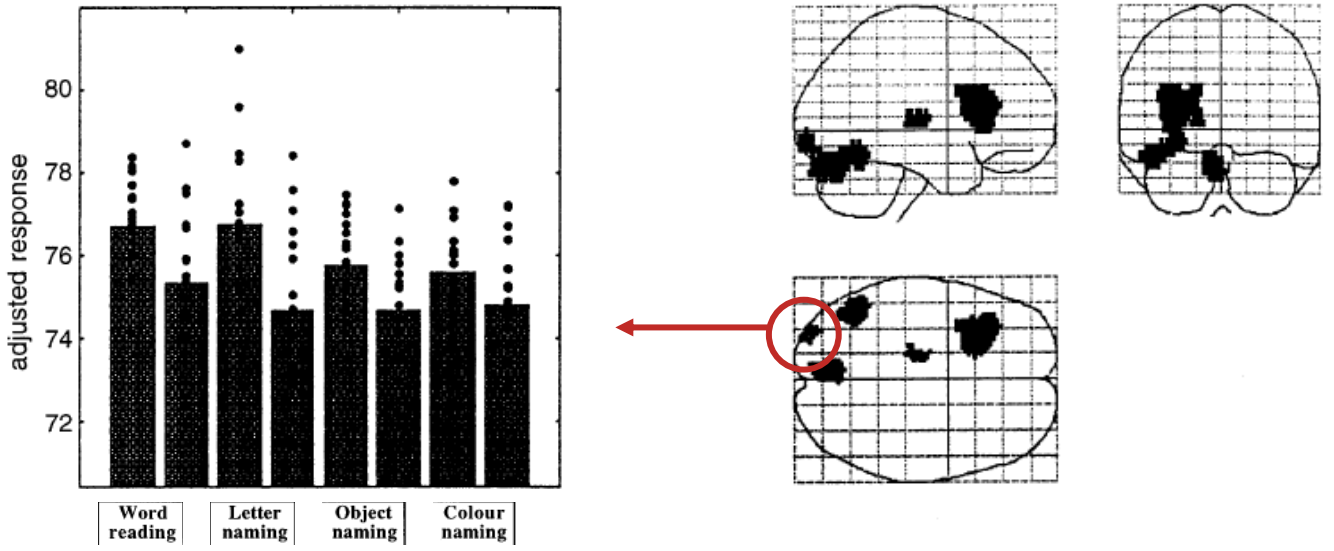


1 task/session

Conjunction analysis

Isolates the process of Phonological retrieval, no interaction with visual processing etc

Overlap of 4 subtractions



Price & Friston (1996)

Areas are identified in which task-pair effects are jointly significant (conjunction)

→ Associated with process of interest (phonological retrieval)

Conjunction: two ways of testing for significance

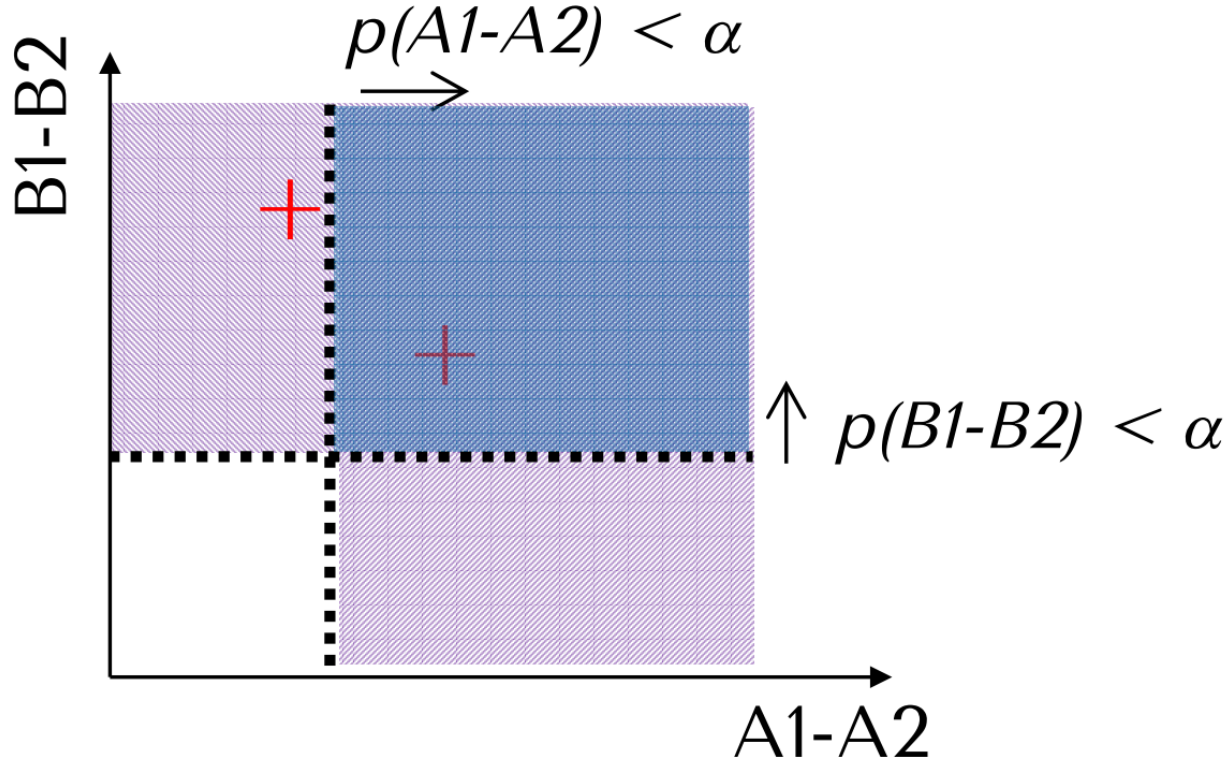
SPM offers two general ways to test the significance of conjunctions:

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

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

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

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



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

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

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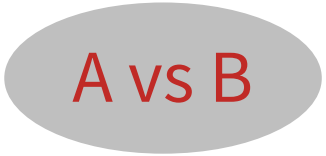

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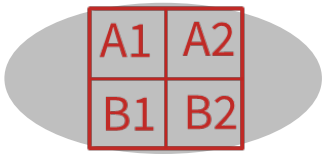


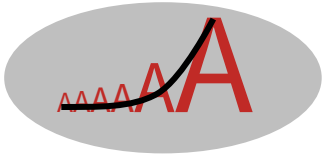
Parametric designs

Does activity vary systematically with a continuously varying parameter?

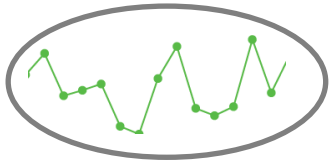
Varying the stimulus-parameter of interest on a continuum, in multiple (n>2) steps and relating BOLD to this parameter

Possible tests for such relations :

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



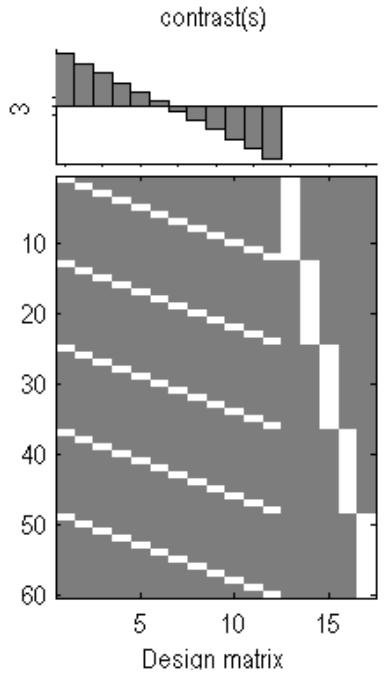
Avoids pure insertion but does assume no qualitative change in processing.

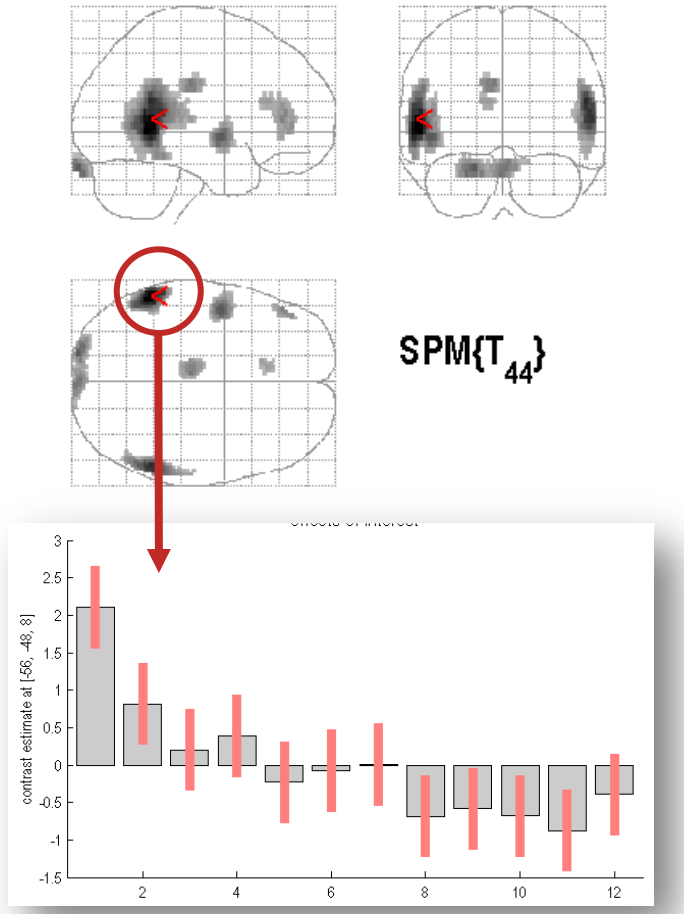


A linear parametric contrast

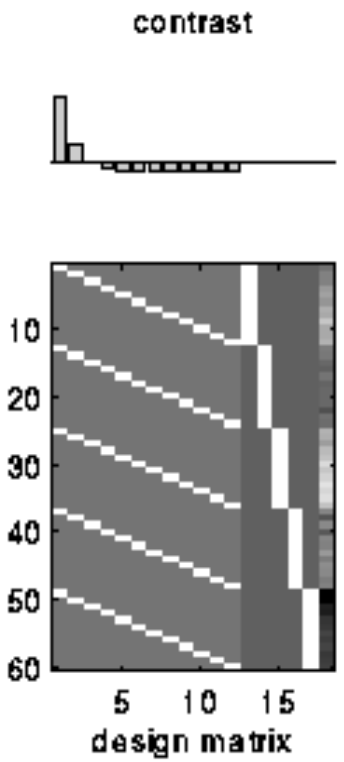
Is there an adaptation effect if people listen to words multiple times?

Linear effect of time





Non-linear effect of time



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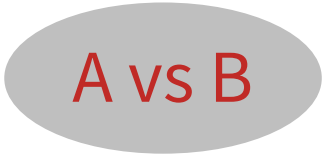

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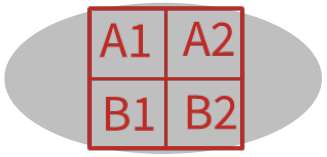
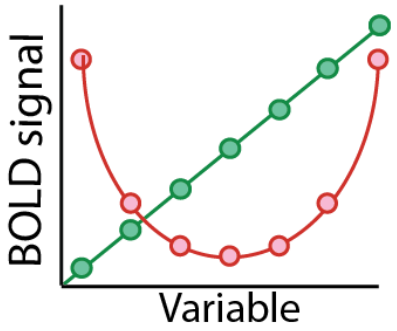


A non-linear parametric design matrix

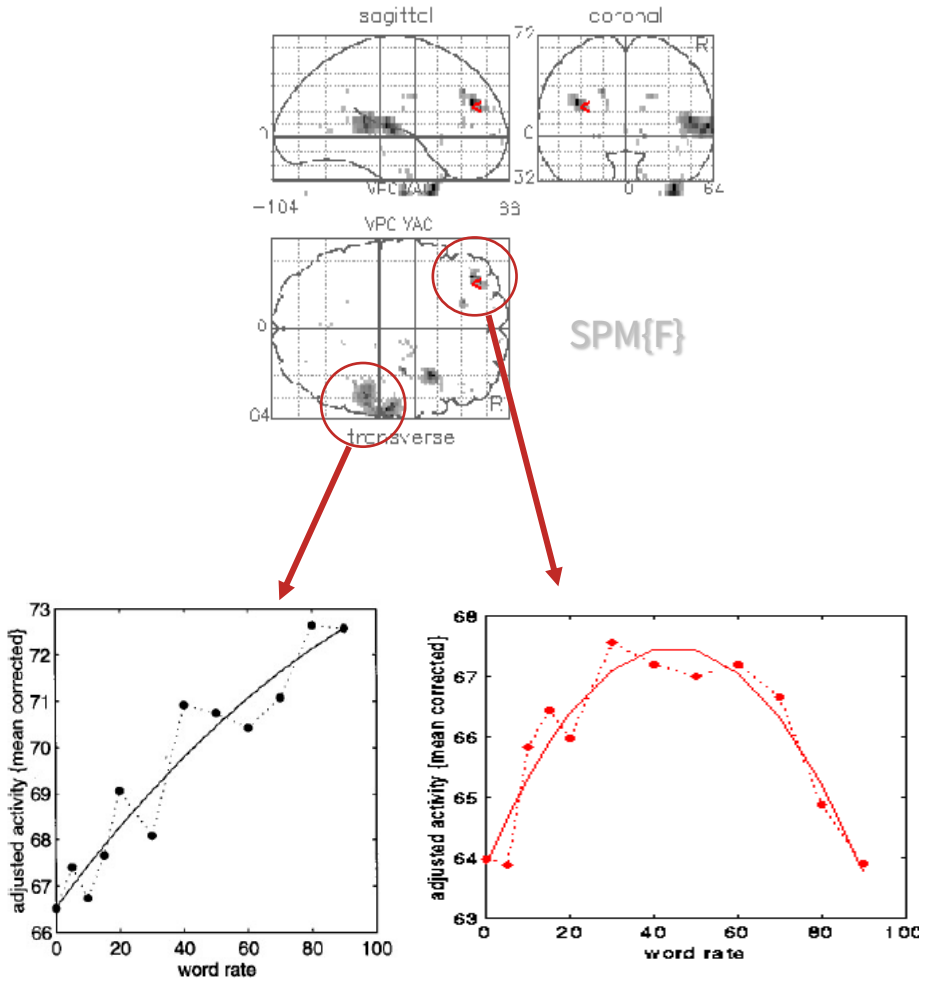
Polynomial expansion:
$f(x) = b_1 x + b_2 x^2 +$
...up to $(N-1)^{th}$ order for N levels

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



Büchel et al., (1996)

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



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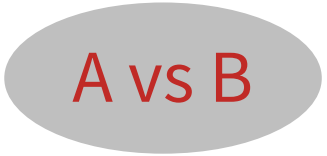

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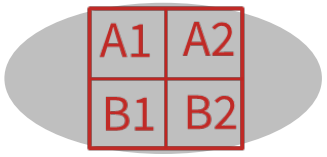
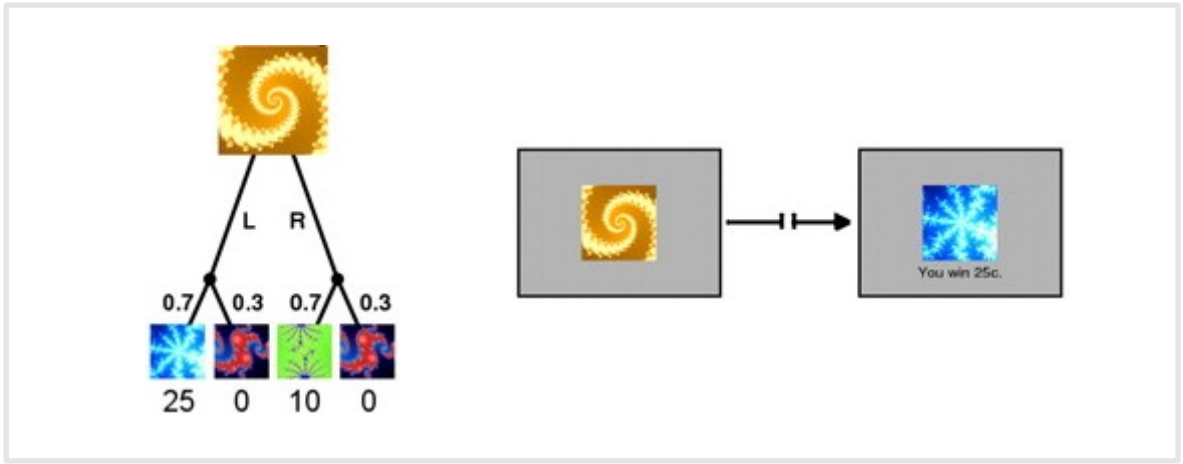
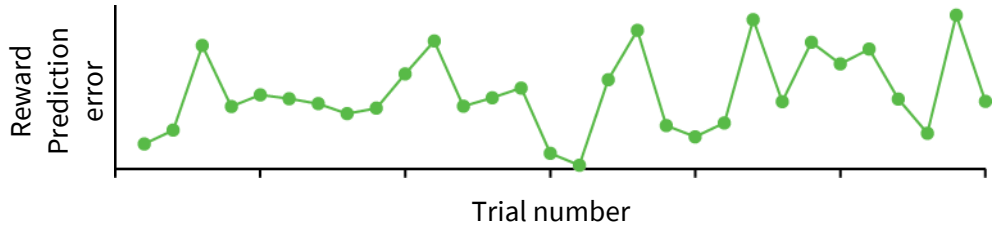


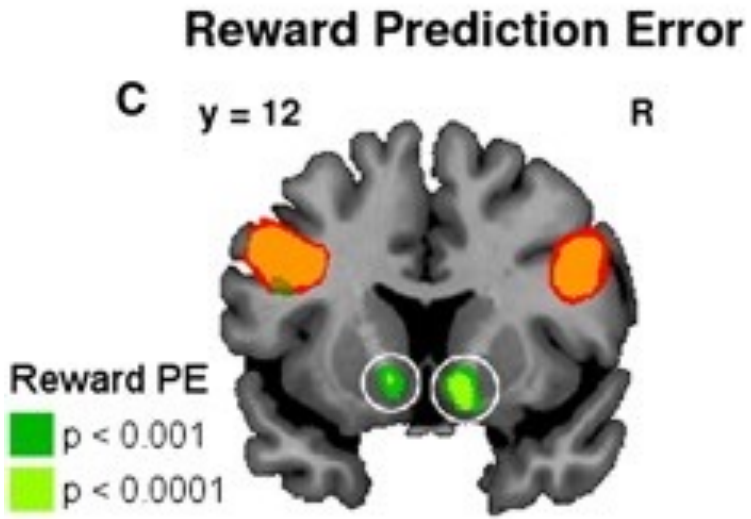
Parametric design: Model-based regressors

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



Time-series of a model-derived reward prediction error





Gläscher & O'Doherty (2010)

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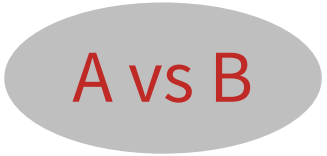

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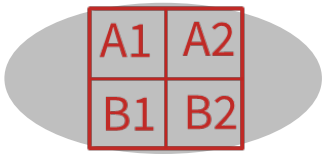
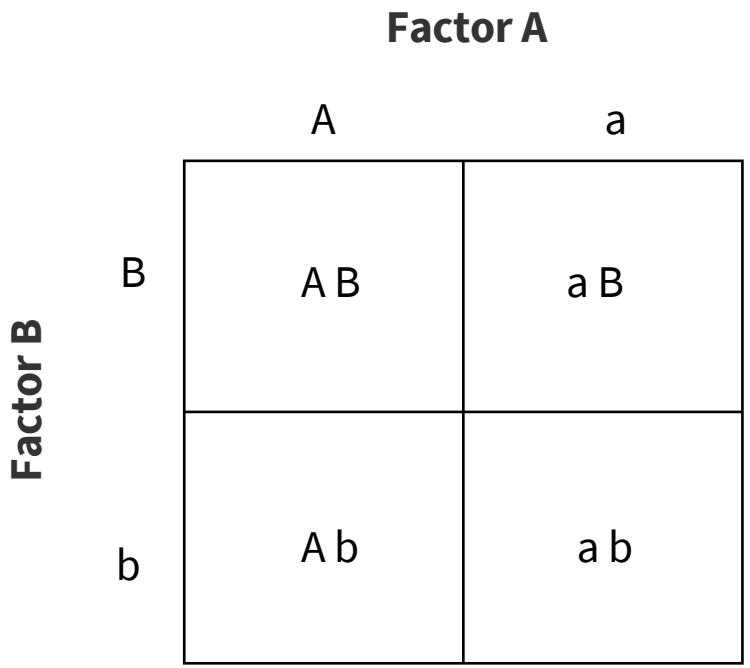


Factorial design

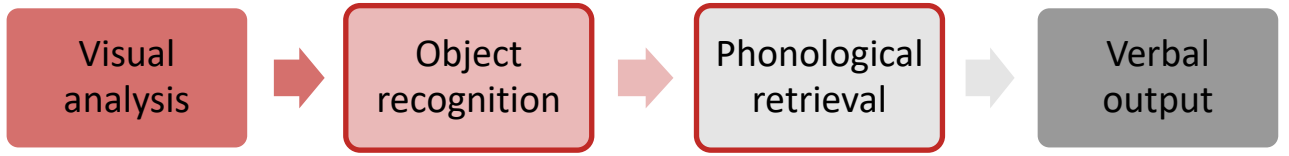


Highly efficient: Factorial designs allow for testing main effects and interactions!

We can address the “pure insertion” problem!

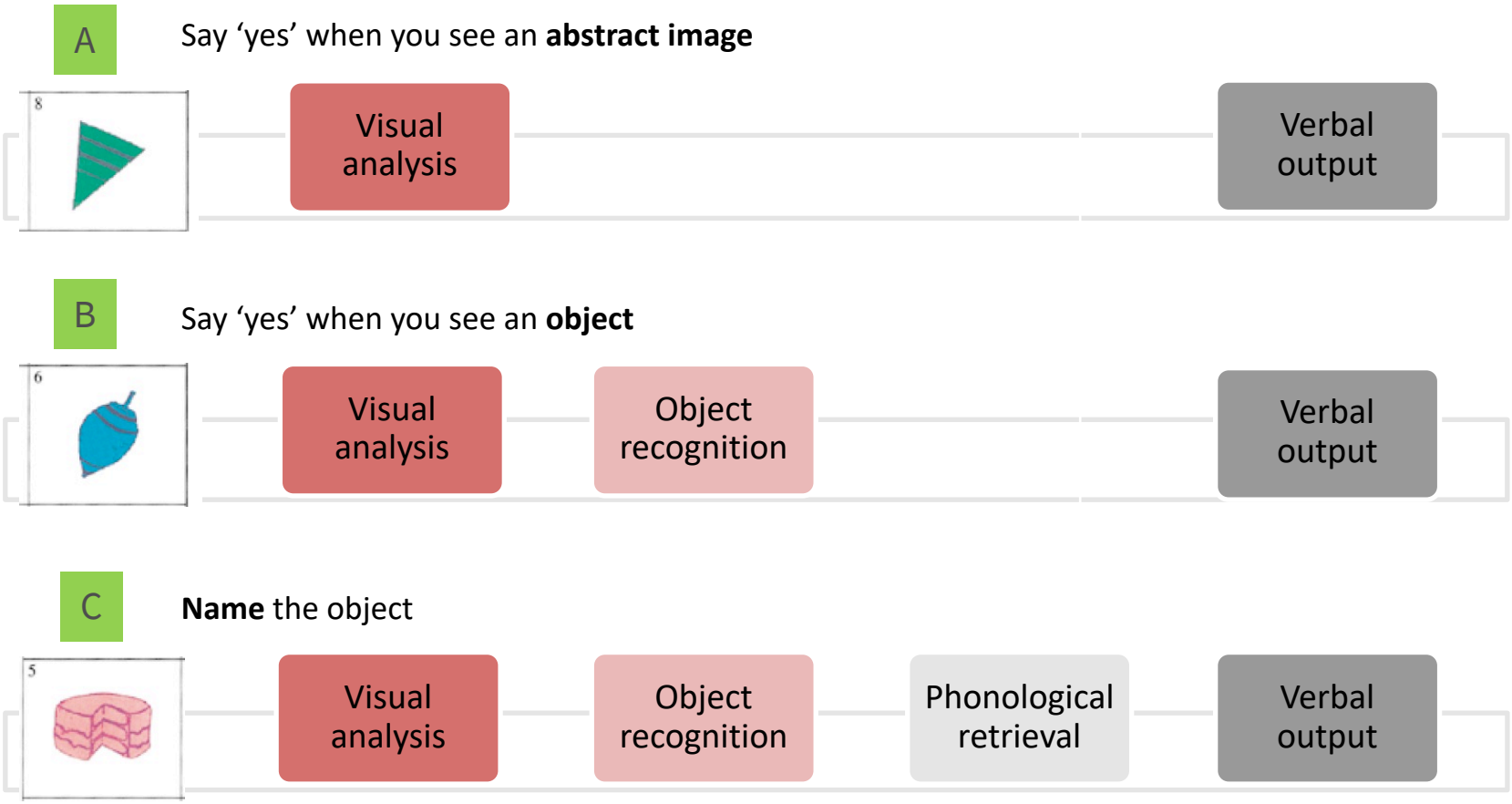
Factorial design

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?

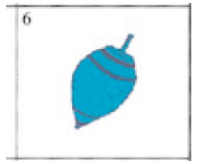


Factorial design

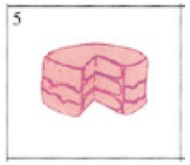
Question: Is the inferiotemporal cortex sensitive to both object recognition and phonological retrieval of object names?

A — Say ‘yes’ when you see an **abstract image**

B — Say ‘yes’ when you see an **object**

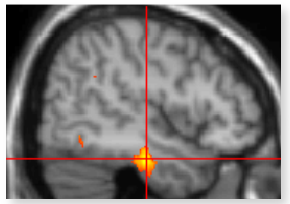


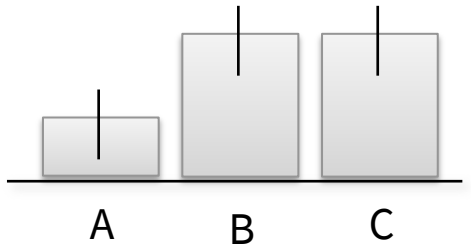
C — **Name** the object



Friston et al., (1997)

Results in inferotemporal cortex:



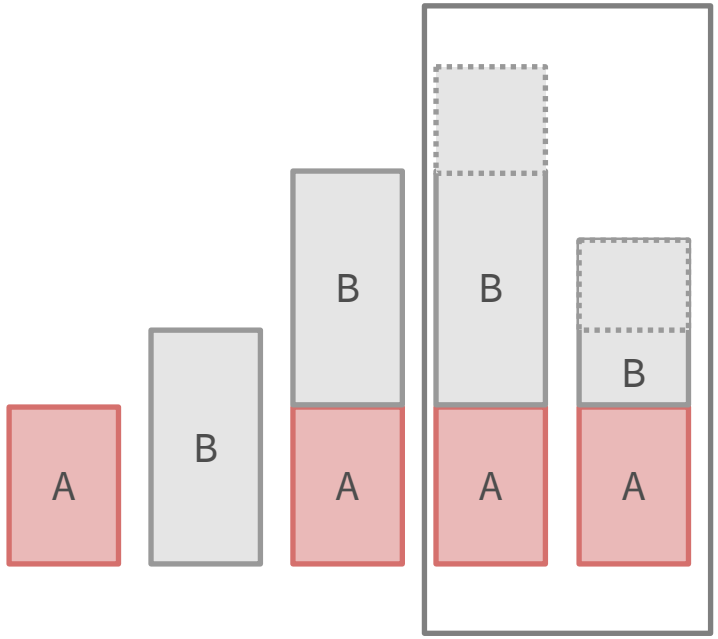


B > A Object recognition

C = B IT not involved in phonological retrieval?!

Addressing interactions in factorial designs

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



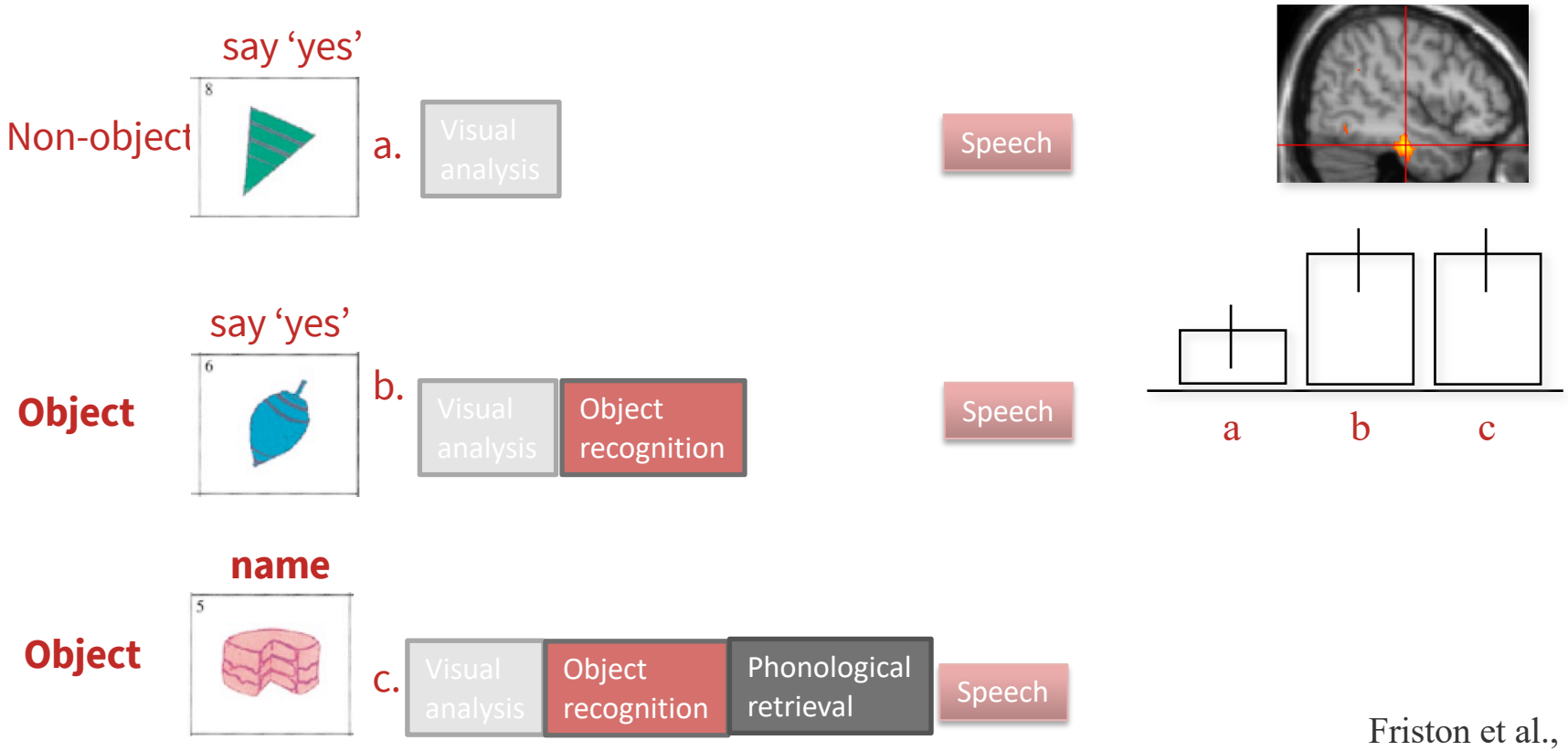
Object recognition

Phonological retrieval

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

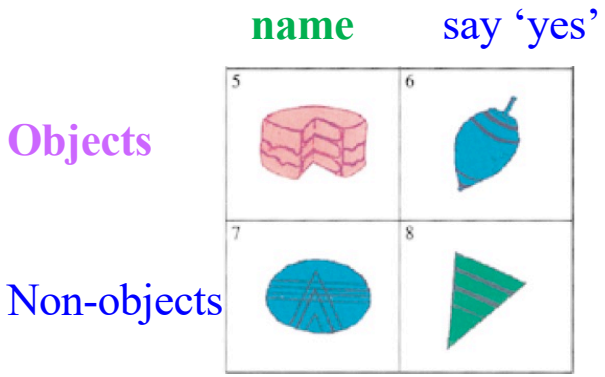
Factorial designs: Main effects and interaction

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

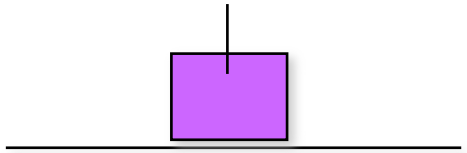


Main effect of task (naming): (ONAME + NNAME) – (OYES + NYES)

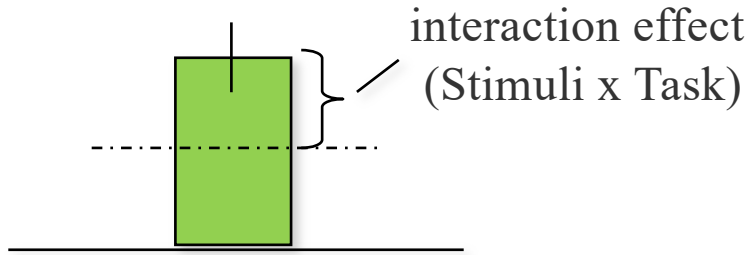
Main effect of stimuli (object): (**O**YES + **O**NAME) – (**N**YES + **N**NAME)

Interaction of task & stimuli: (**O**NAME + **N**YES) – (**O**YES + **N**NAME)

Can show a failure of pure insertion



'Say yes' (Object vs Non-objects)

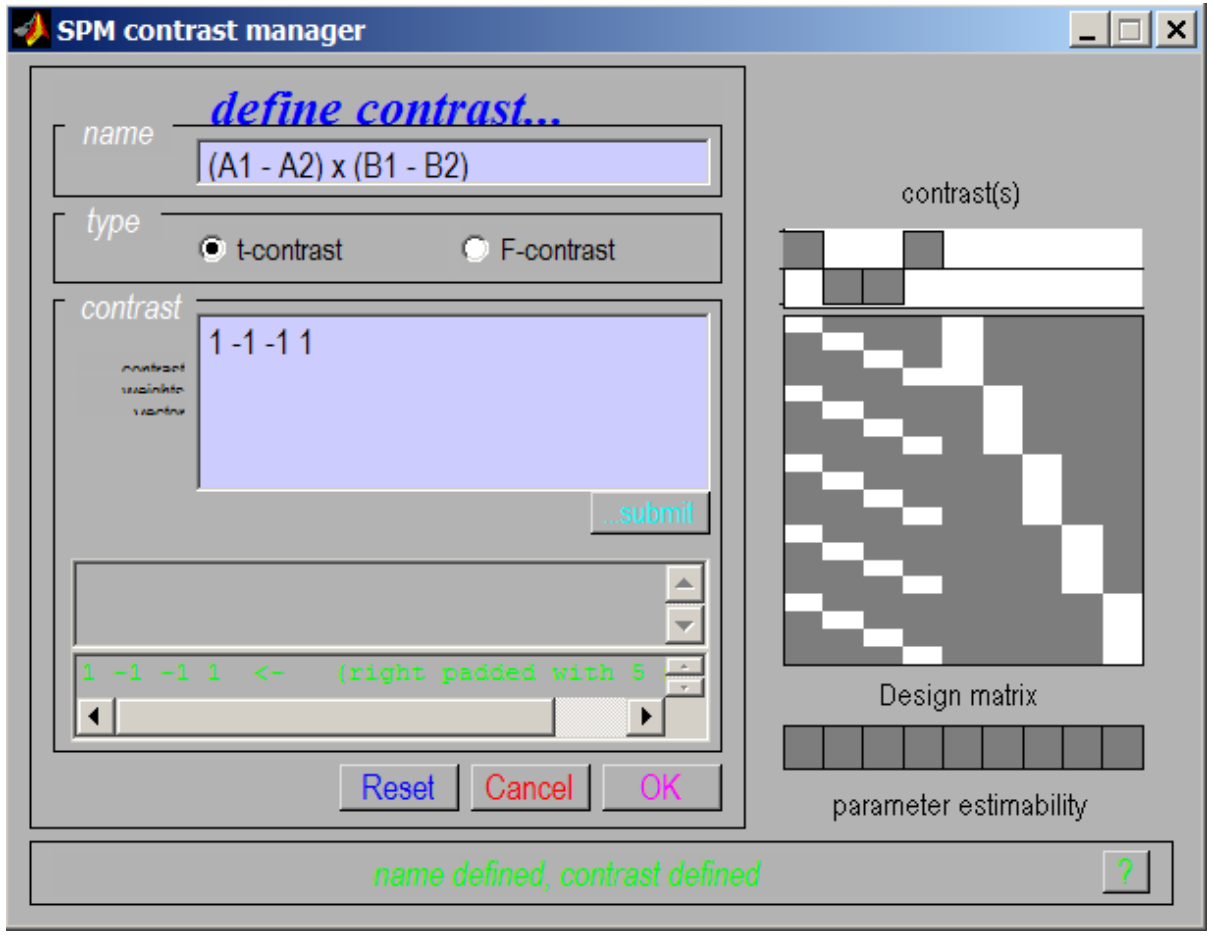


Phonological retrieval (Object vs Non-objects)

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.

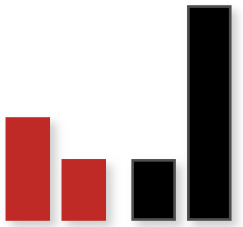
Friston et al., (1997)

Interaction in SPM



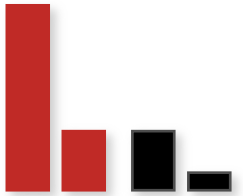
Interactions:

cross-over



and

simple

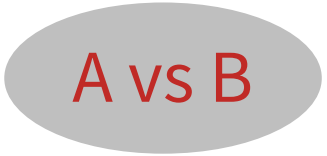


We can selectively inspect our data for one or the other by masking during inference

Overview

1. Categorical designs

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

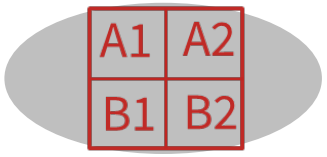


2. Parametric designs

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

3. Factorial designs

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

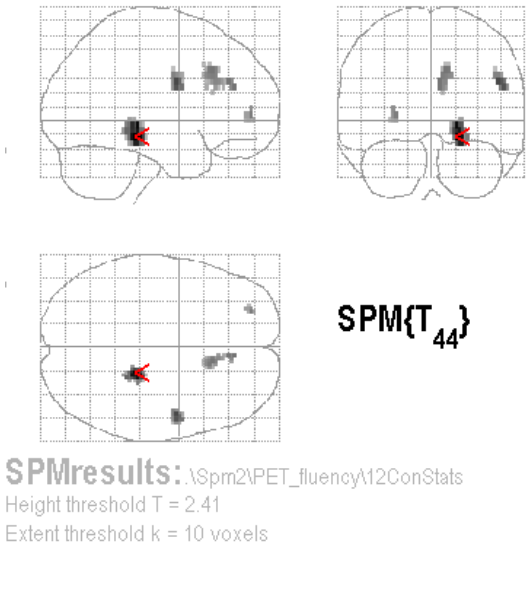


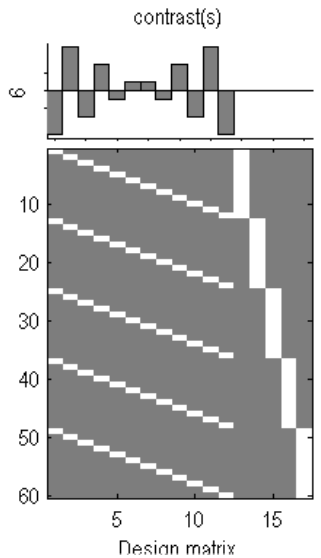
Linear Parametric Interaction

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"?)





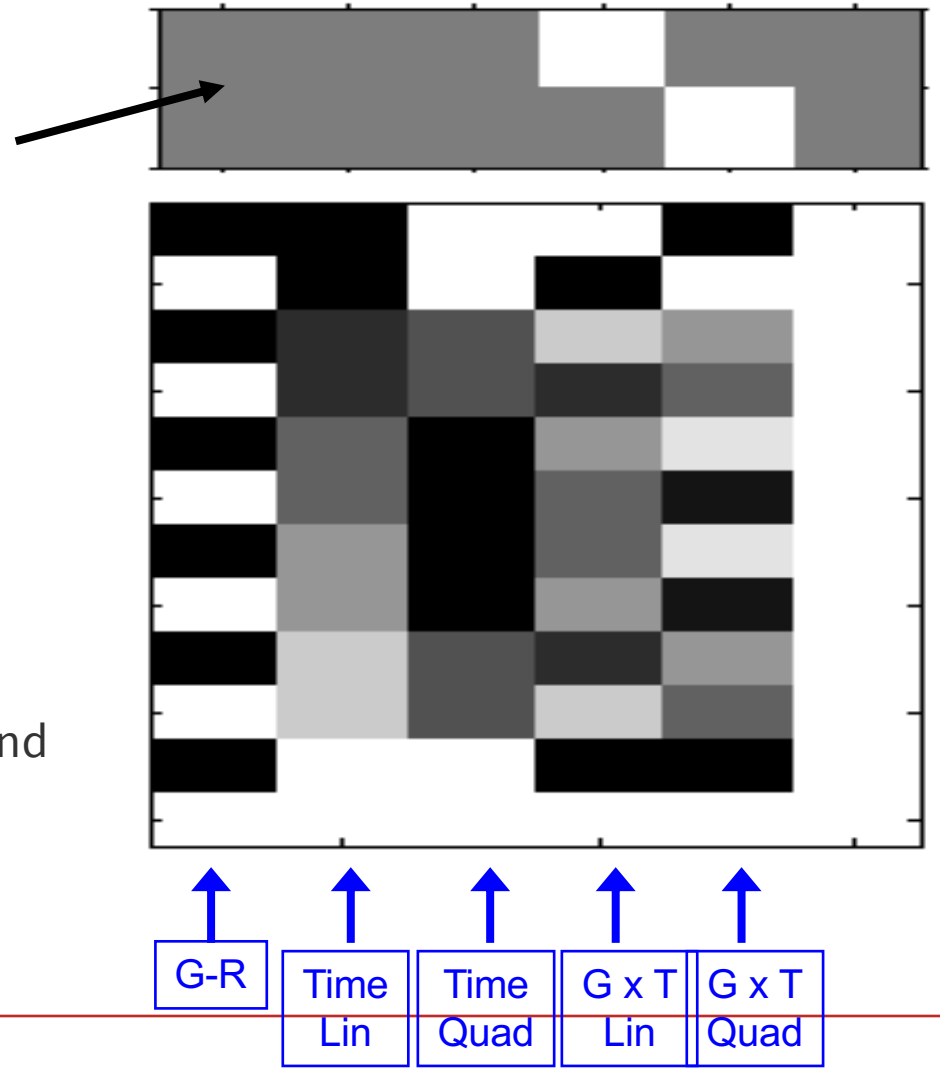
Contrast:

[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
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…

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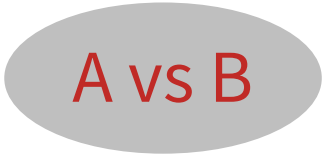

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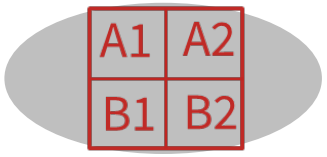
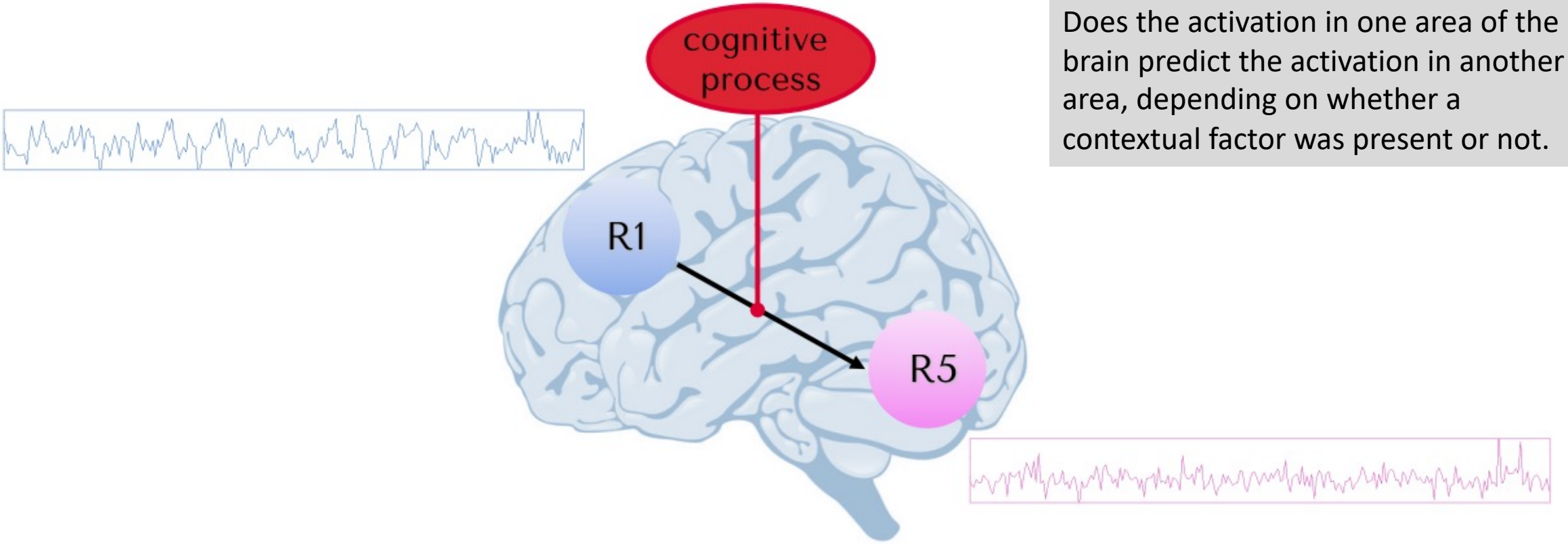


Psycho-physiological Interaction (PPI)

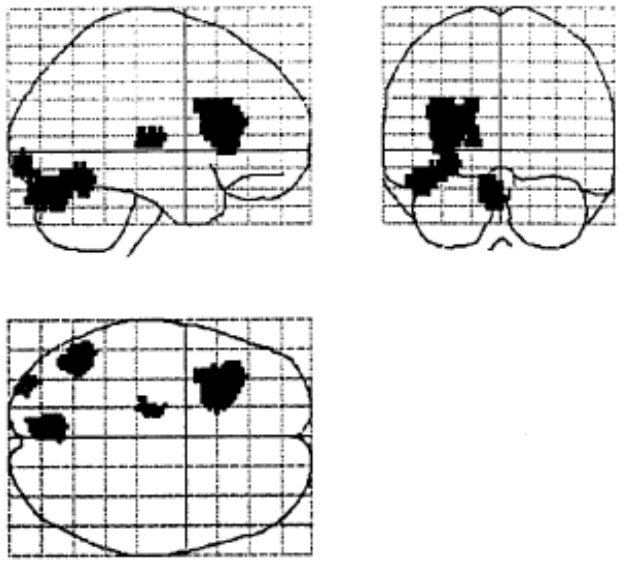


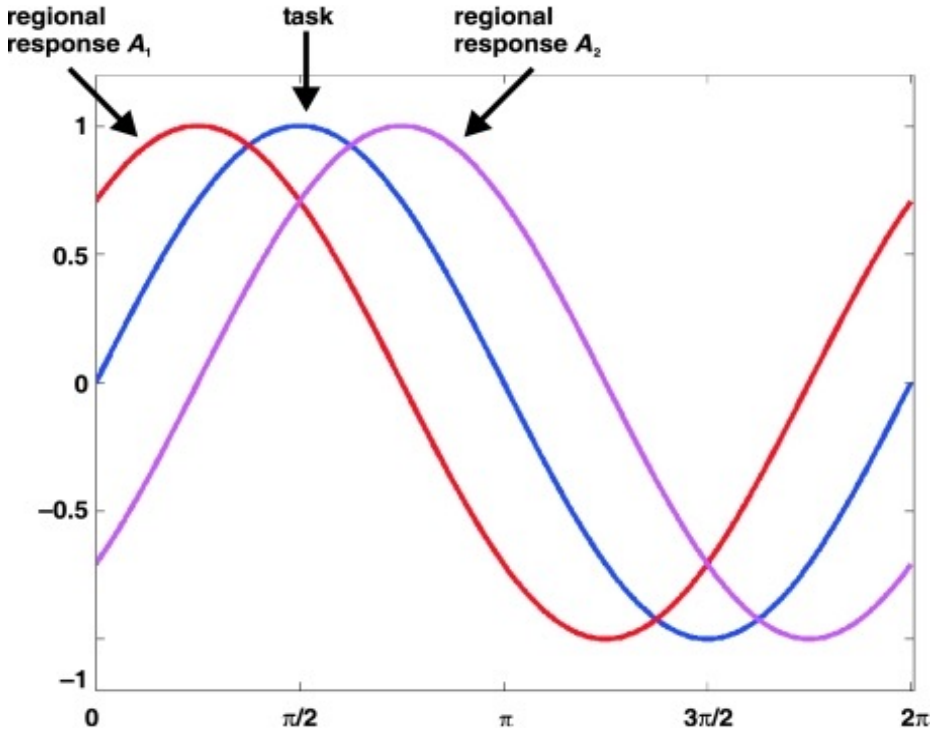
Question:

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)

- Functional connectivity measure
- Can activity in one part of the brain be predicted by an interaction between task and activity in another part of the brain?
- If two areas interact, they will display synchronous activity

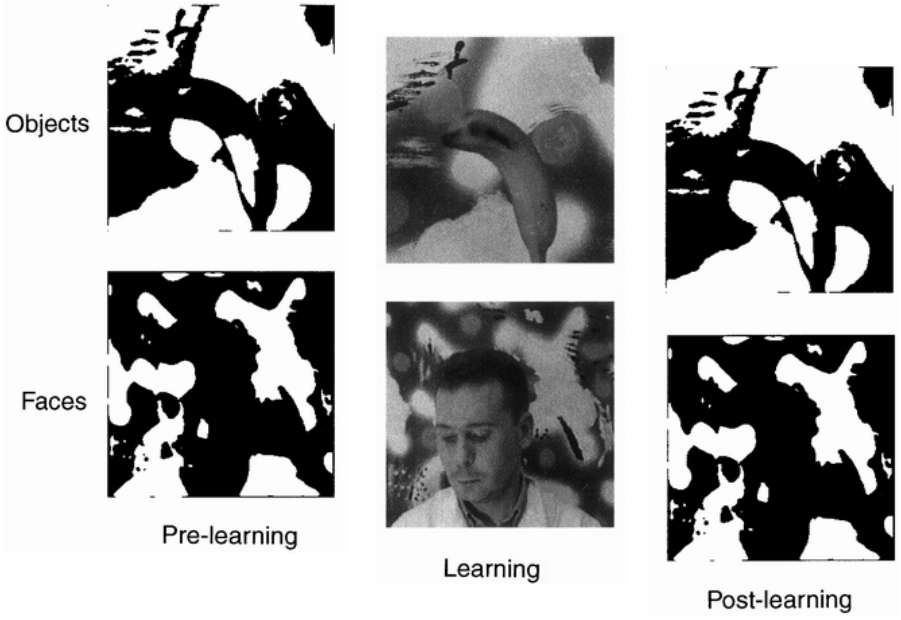




Stephan, 2004

Psycho-physiological Interaction (PPI)

Factorial design



Learning

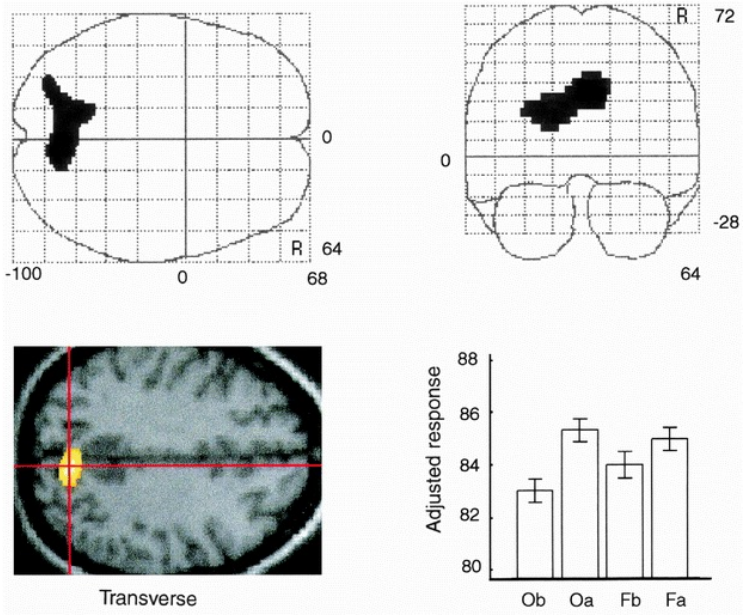
Stimuli

Objects before (Ob)	Objects after (Oa)
Faces before (Fb)	Faces after (Fa)

Dolan et al., 1997

Psycho-physiological Interaction (PPI)

Main effect of learning



Learning

Stimuli		
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Dolan et al., 1997

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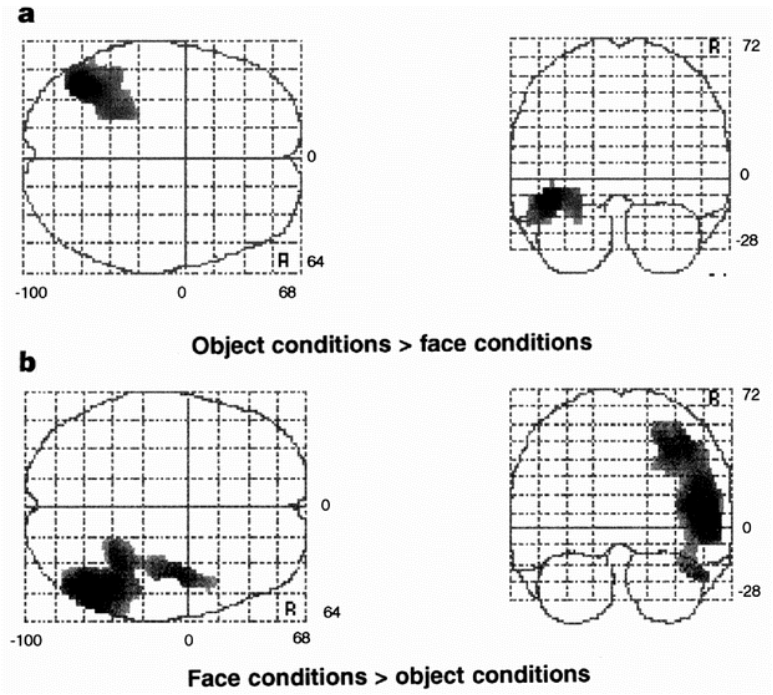
Main effect of stimulus



Learning

Stimuli

Objects before (Ob)	Objects after (Oa)
Faces before (Fb)	Faces after (Fa)

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

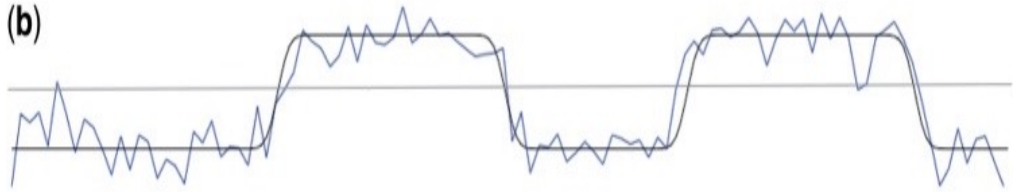
Dolan et al., 1997

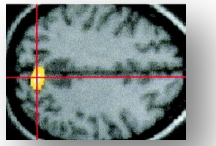
Psycho-physiological Interaction (PPI)

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

Main effect of task (Faces - objects)

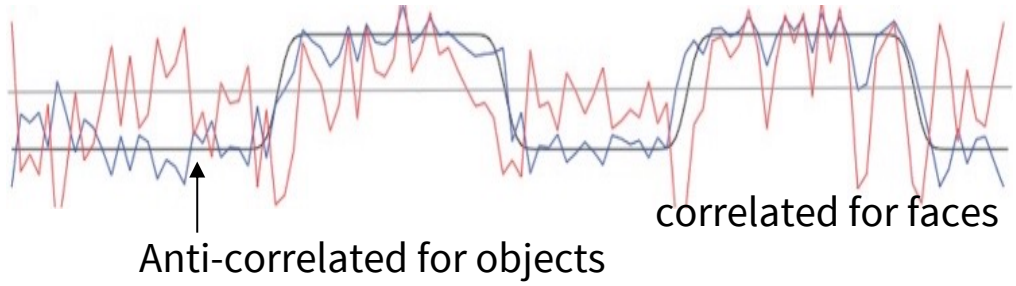
Activity in parietal cortex (main effect learning)

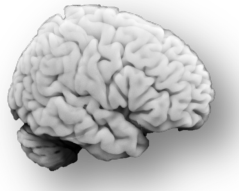




Seed region

PPI regressor = HRF convolved task x seed ROI regressors





Whole brain

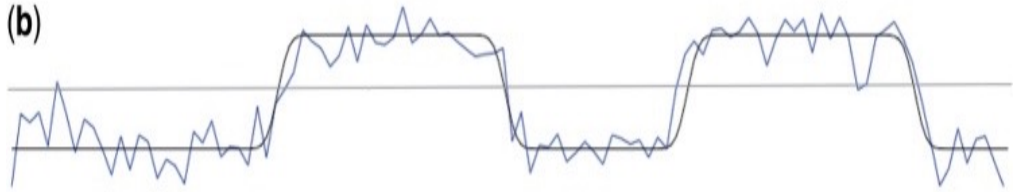
O'Reilly (2012)

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 of learning)



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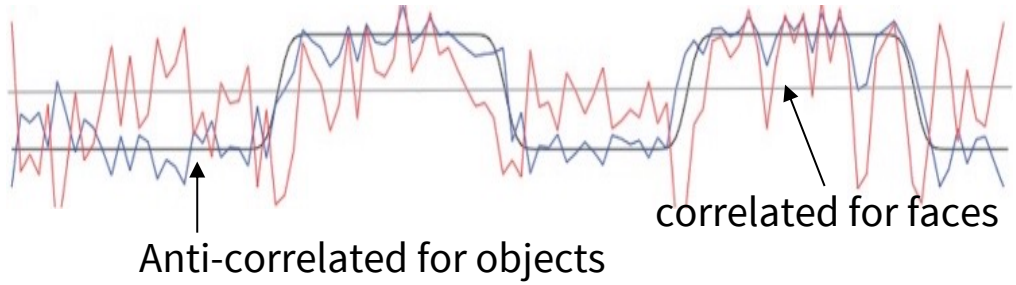
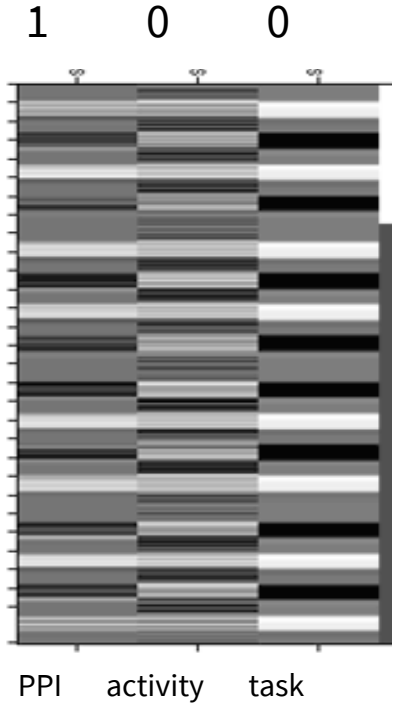


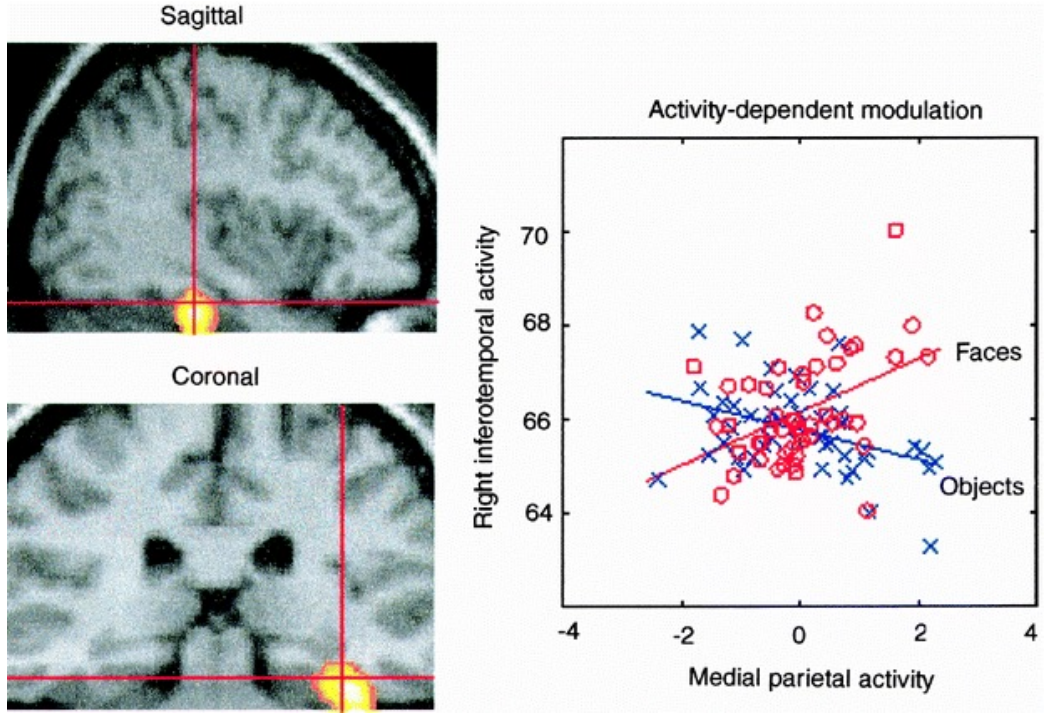


The interaction term should account for variance over and above what is accounted for by the main effect of task and physiological correlation

O'Reilly (2012)

Psycho-physiological Interaction (PPI)

Coupling between ITC and parietal cortex depends on the stimulus



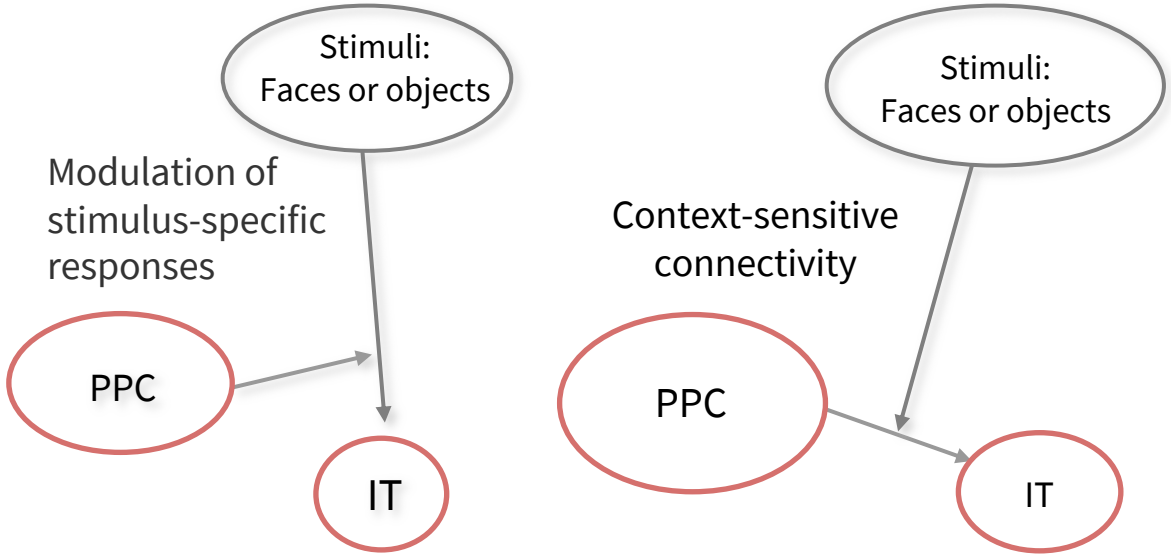
Coupling between the temporal face area and the medial parietal cortex when, and only when, faces were perceived

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)



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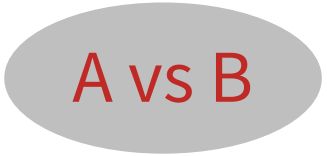

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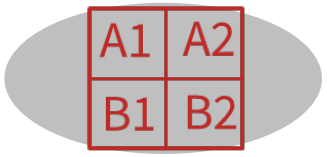

Questions?