

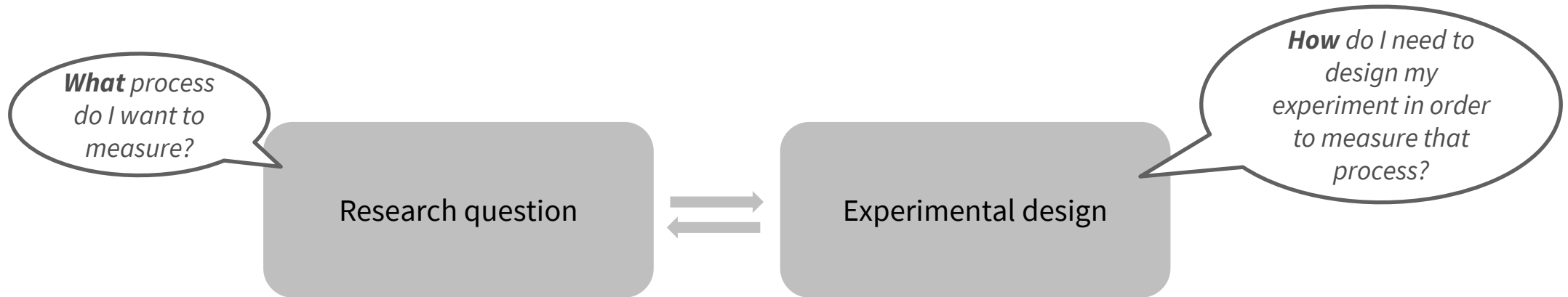
Experimental design

Carolin Moessnang, PhD
SRH Heidelberg University, Germany

With thanks to:

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

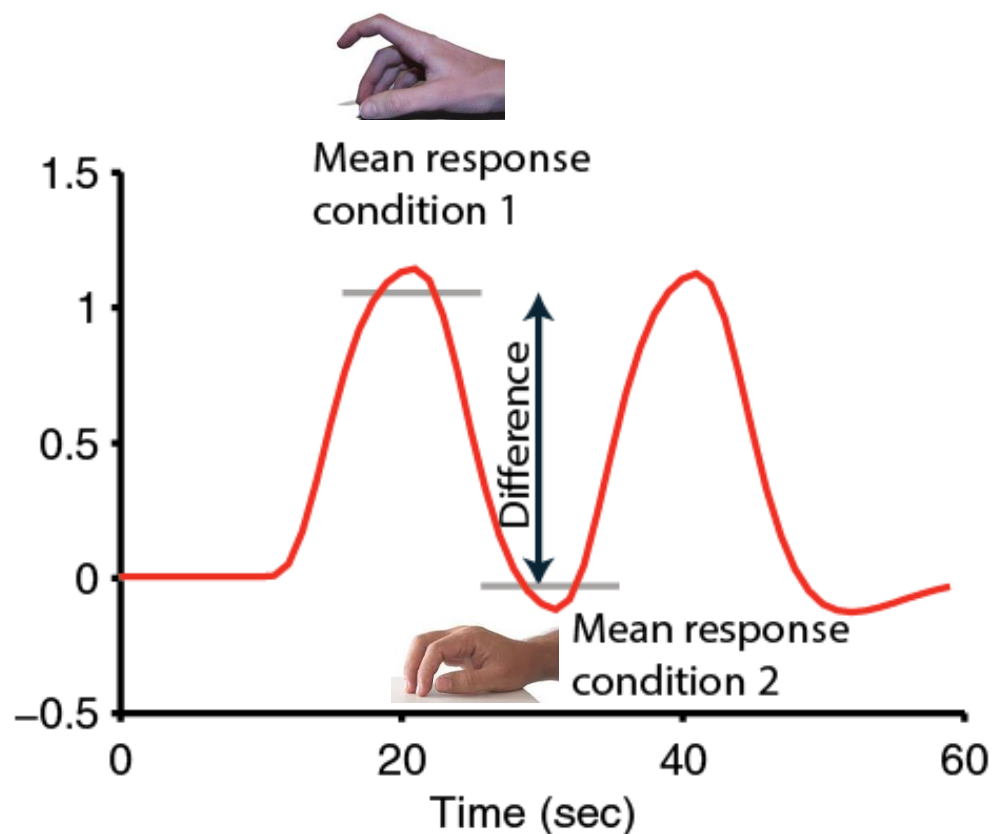
It all starts with a good design!



The fMRI researcher's challenge

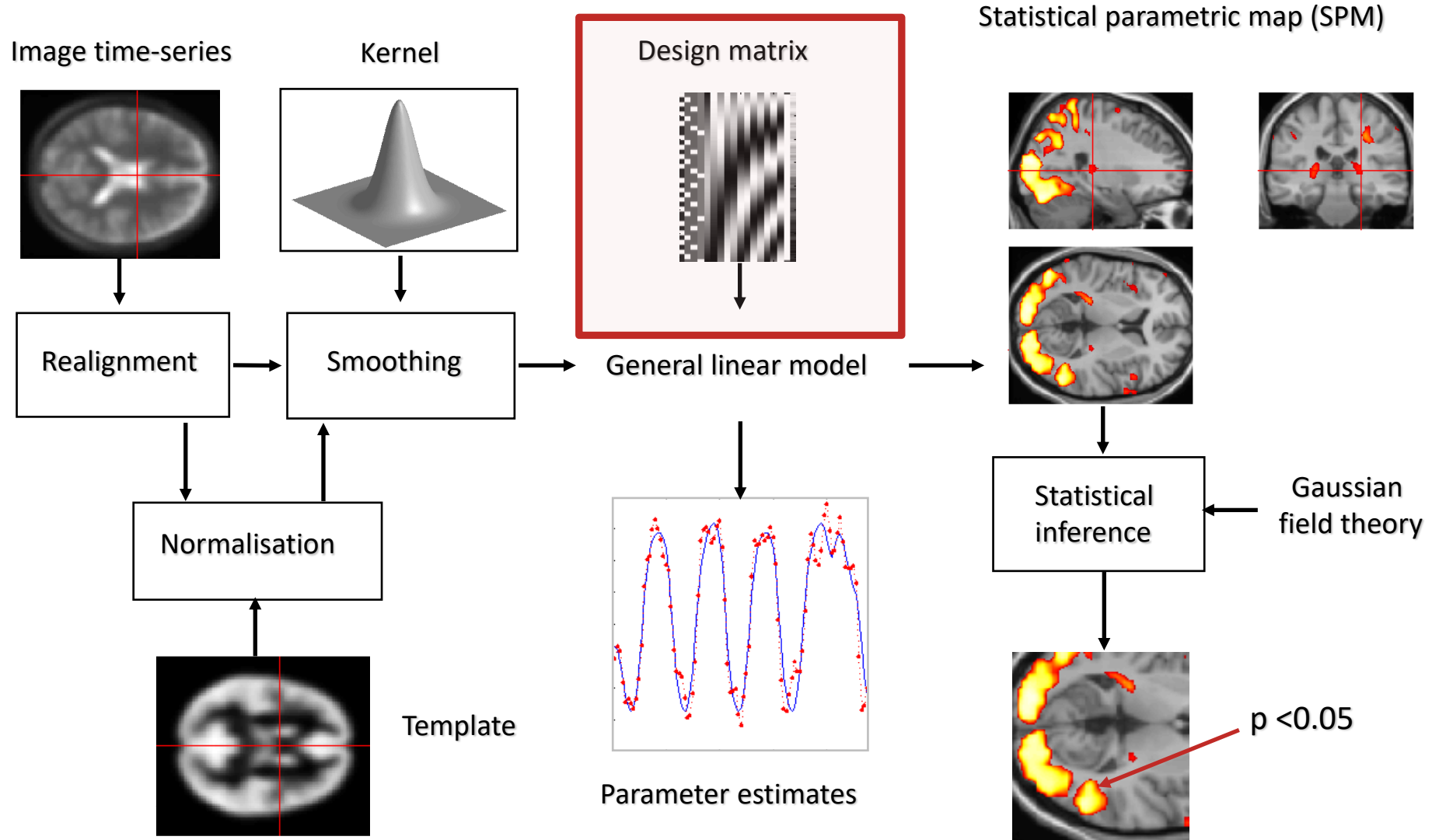
The BOLD signal does NOT provide you with an absolute measure of neural activity

Therefore, you need to compare activity across conditions



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

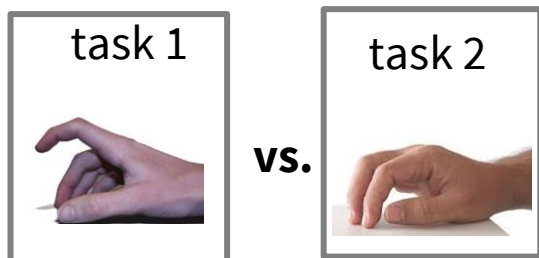
SPM processing hierarchy



The taxonomy of experimental designs

Categorical designs

What brain regions differentiate between the two tasks?

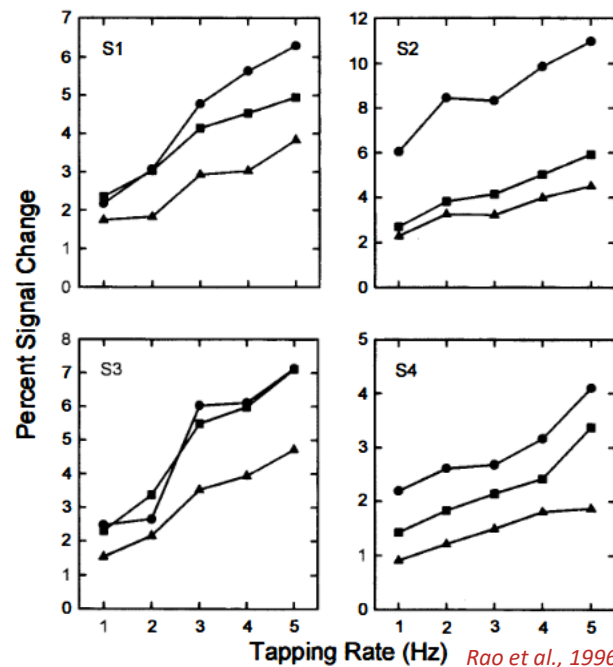


Turetsky et al., 2018

Isolation of activation in the “hand knob” area during finger tapping

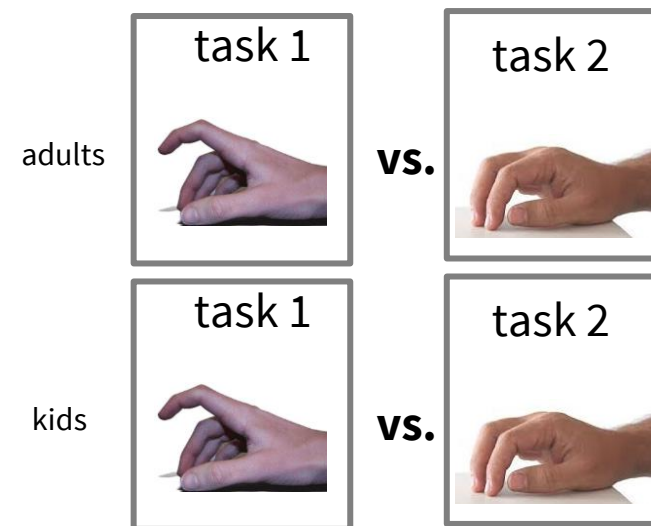
Parametric designs

What brain regions show a systematic relationship (correlation) with the “amount” of cognitive or sensorimotor processing?



Factorial designs

Is the effect of a task (relative to another task) on brain activation different between different contexts?



effect of age on finger tapping-induced brain activation

Turetsky et al., 2018

This session's outline

1. Categorical designs

- Subtraction
- Conjunction

The “baseline challenge”, pure insertion
Testing multiple hypotheses



A vs B

2. Parametric designs

- Linear and nonlinear
- Model-based regressors

Adaptation, cognitive dimensions
Polynomial expansions



AAAAAA

3. Factorial designs

- Categorical
- Parametric

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



A1	A2
B1	B2

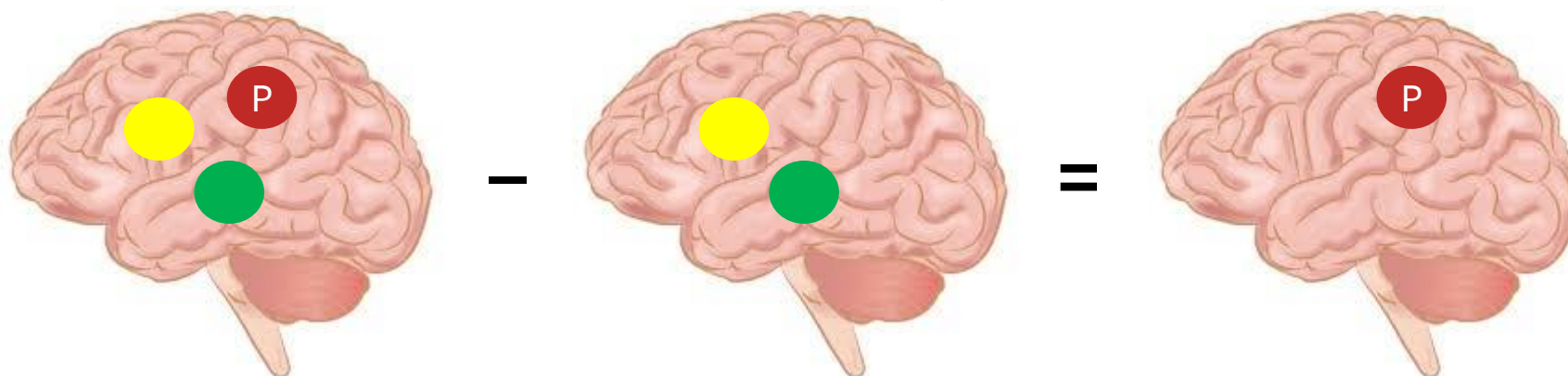
Cognitive subtraction (Friston et al., 1996)

Aim

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

Procedure

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

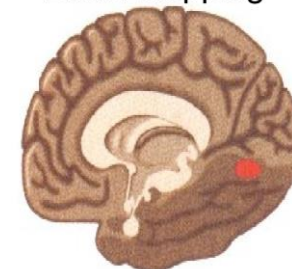


A nice example:



Colour > No colour
Luminance = Luminance
Contrast = Contrast
Shape = Shape

Brain mapping



Isolate functional area

Bishop, 2014

However...

Simple cognitive 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



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

Process P implicit in control task?
Difficulty matched?

Same stimulus, different tasks



Name the person! Name the gender!

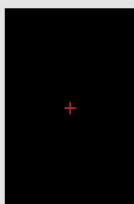
Process P cancelled out (highly specific
naming-related activity)?
Interaction of task and stimuli?

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



Name the person!

vs.



Name the gender!

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

The critical assumption of pure insertion

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



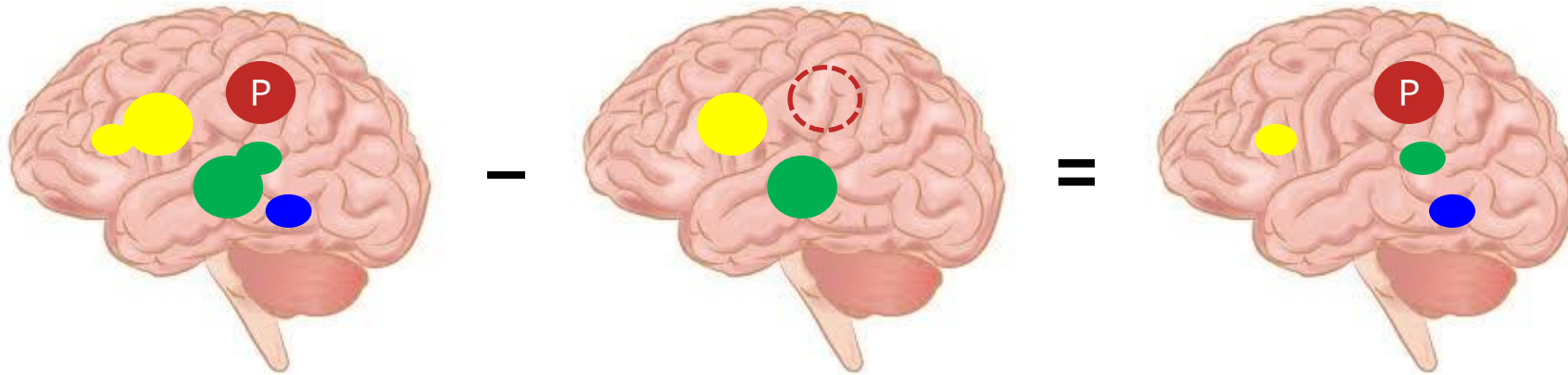
Pretty close to pure insertion...



...this one not...

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

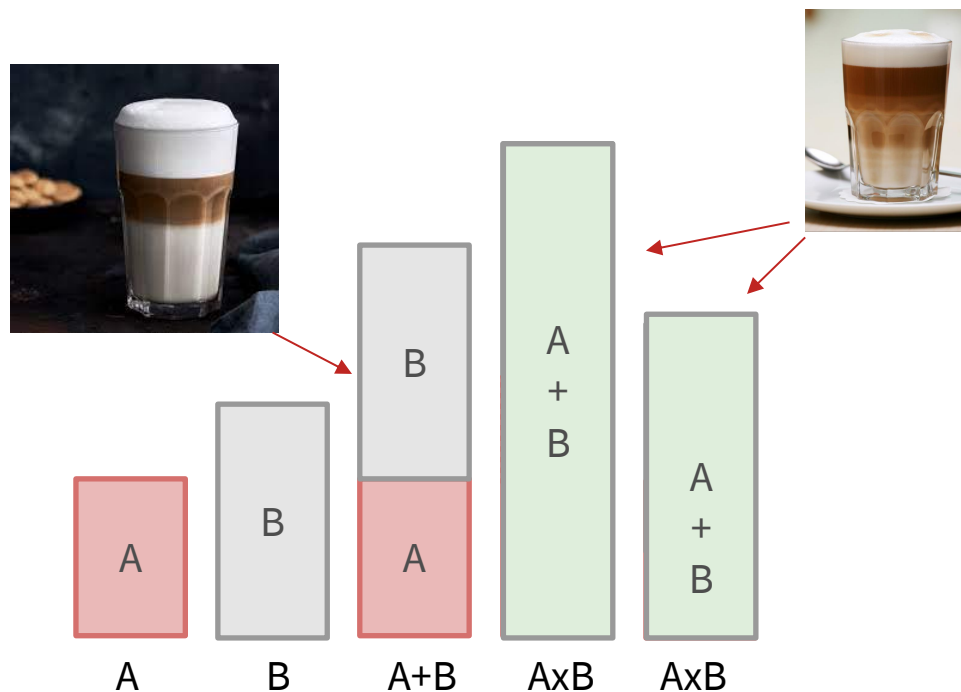
The critical assumption of pure insertion



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

The problem of cognitive subtraction

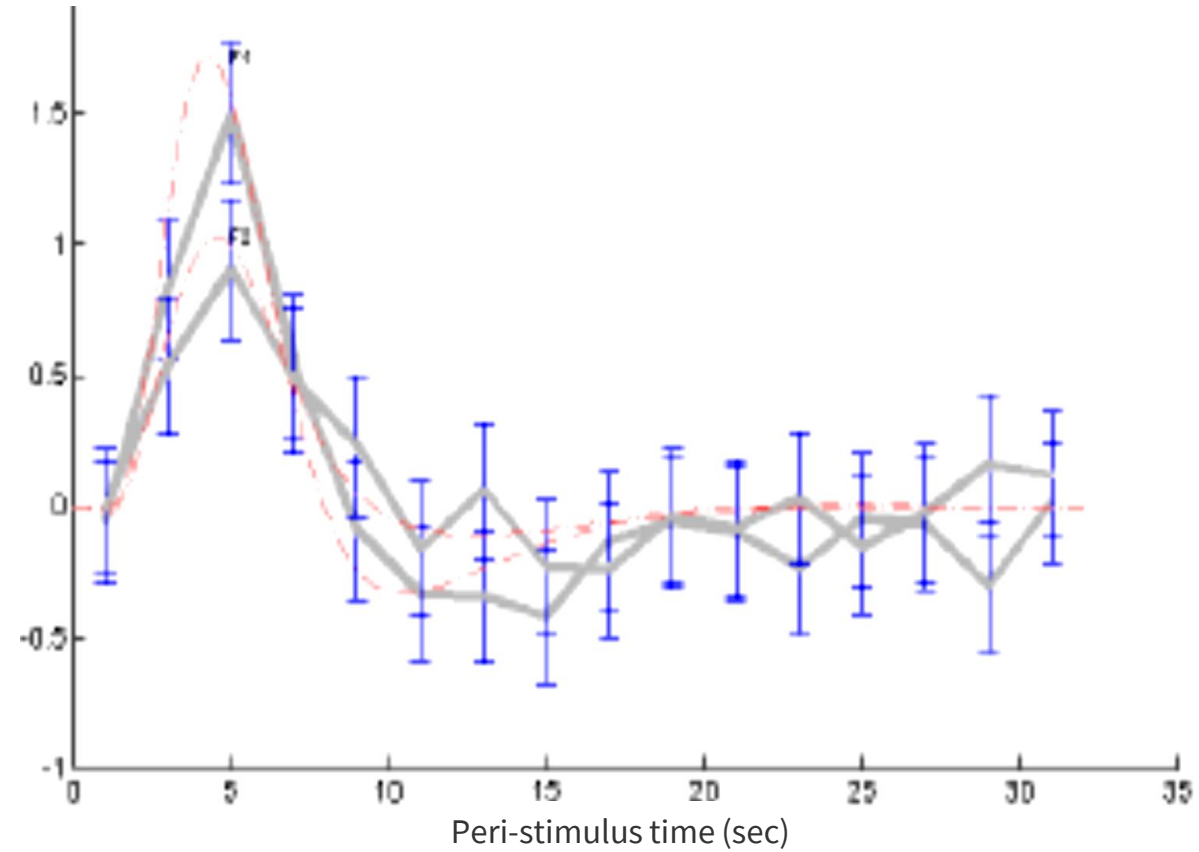
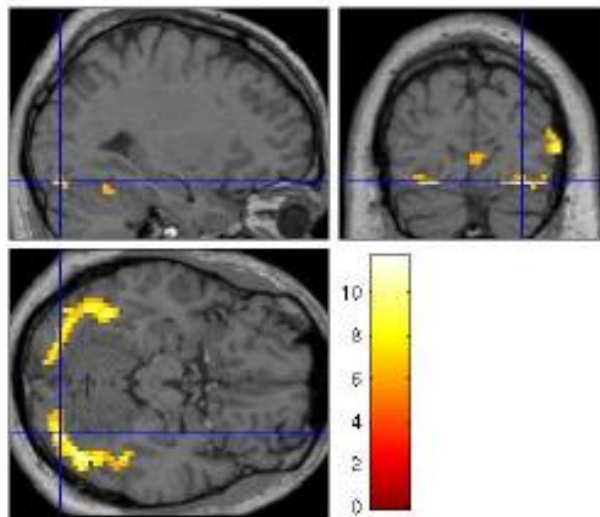
Subtraction depends on the assumption of “pure insertion” (an extra cognitive component can be inserted without affecting the pre-existing components)



[Friston et al. \(1996\)](#)

fMRI adaptation as an example of neural interaction

Face presentation: 1st time vs 2nd time



This session's outline

1. Categorical designs

- Subtraction
- **Conjunction**

The “baseline challenge”, pure insertion
Testing multiple hypotheses



A vs B

A gray oval containing the text 'A vs B' in red.

2. Parametric designs

- Linear and nonlinear
- Model-based regressors

Adaptation, cognitive dimensions
Polynomial expansions



A A A A A A A

A gray oval containing the text 'A A A A A A A' in red.

3. Factorial designs

- Categorical
- Parametric

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

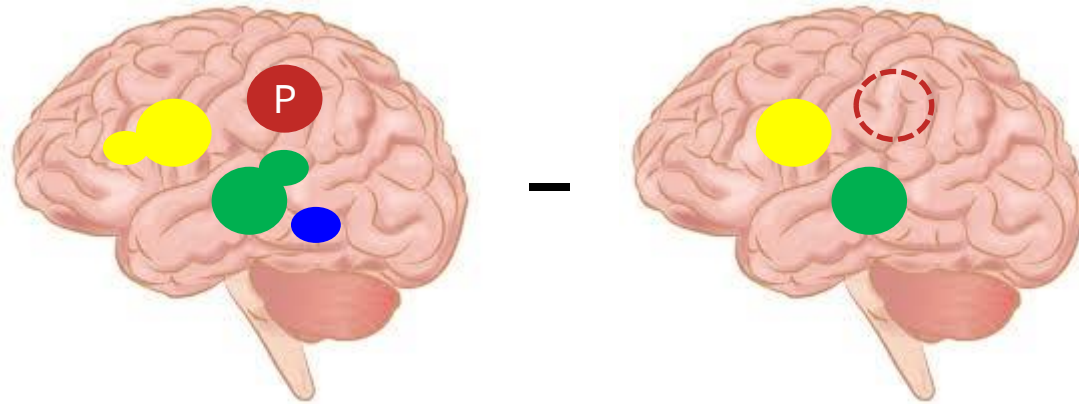


A1	A2
B1	B2

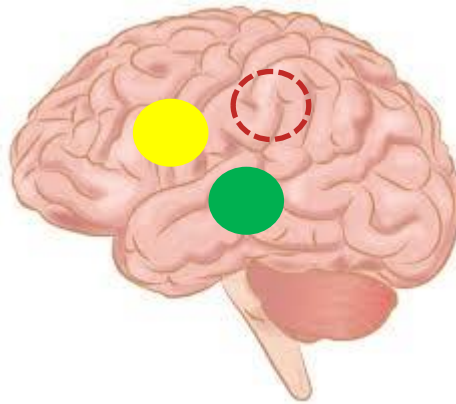
A gray oval containing a 2x2 grid of red text: A1, A2, B1, B2.

Tackling the baseline problem

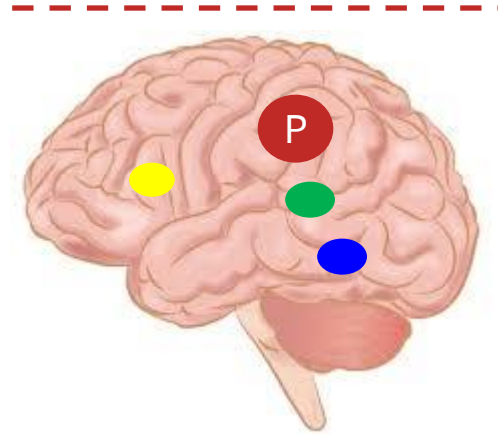
Contrast 1: condition A – condition B



–

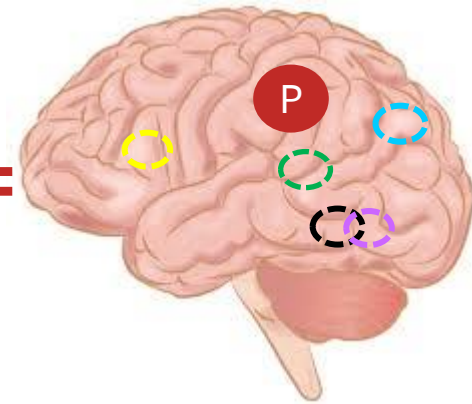


=

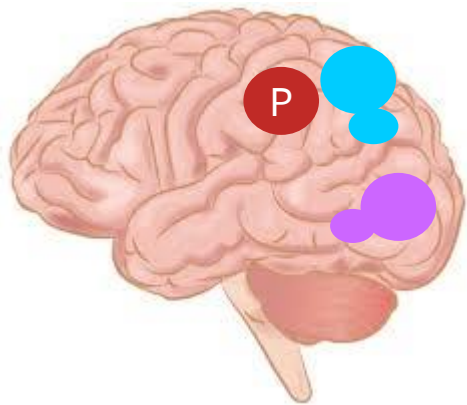


and

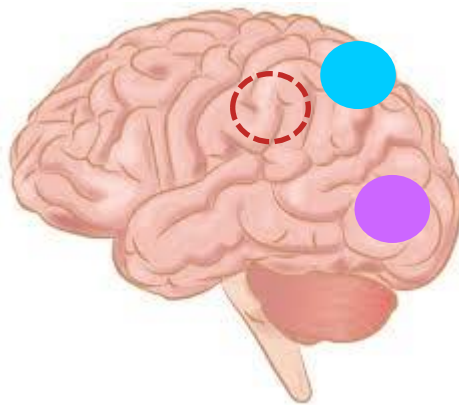
+



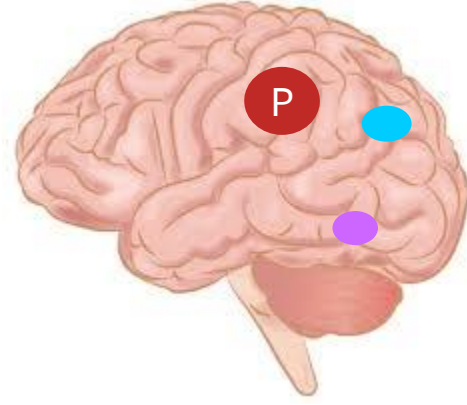
Contrast 2: condition C – condition D



–



=



Conjunction

Addresses the “baseline challenge” 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

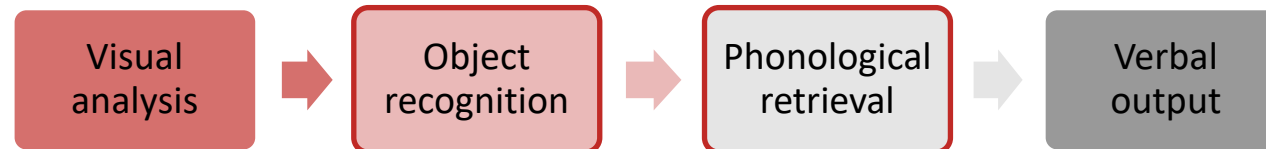
		Task Pair I		Task Pair II	
		A	B	A	B
Process	1				
	2				
	3				
	4 (PI)				
	5				

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

Conjunction isolates the context-invariant activation associated with a specific cognitive process!

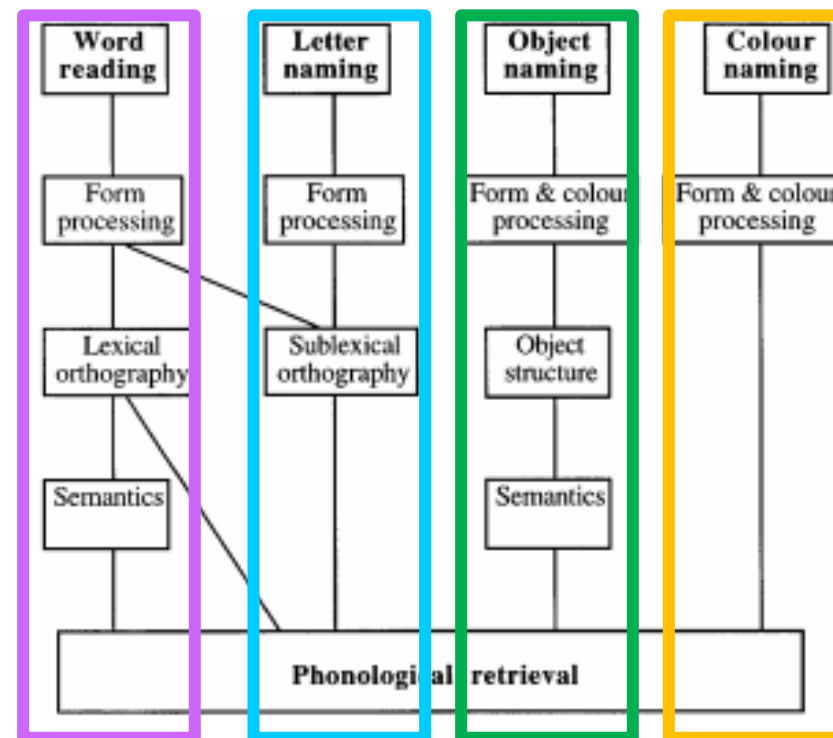
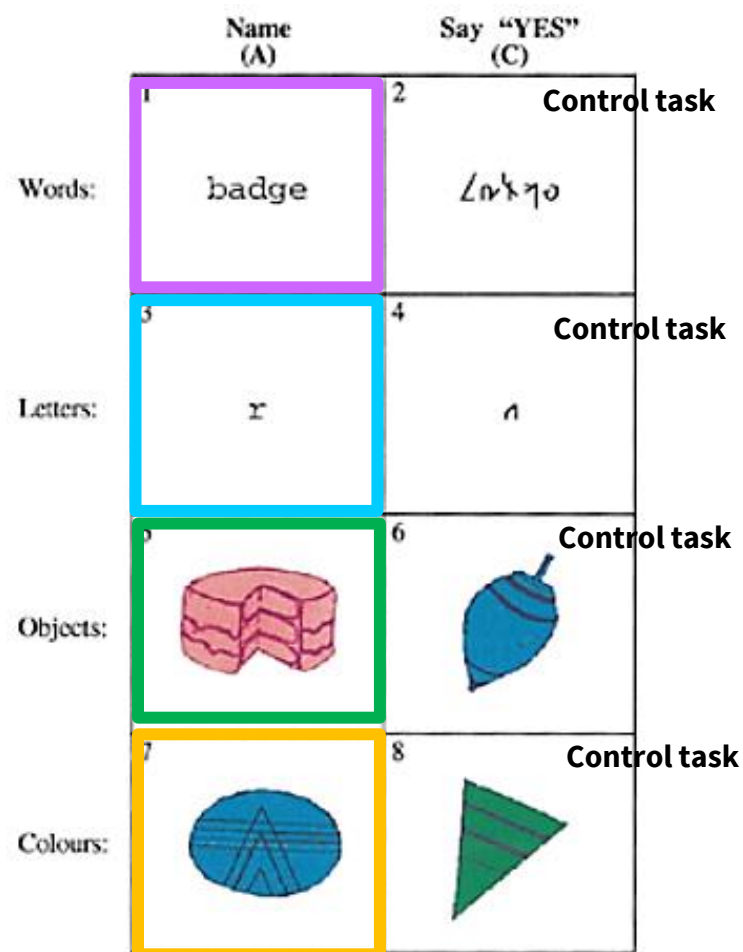
An example...

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



Conjunction analysis

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



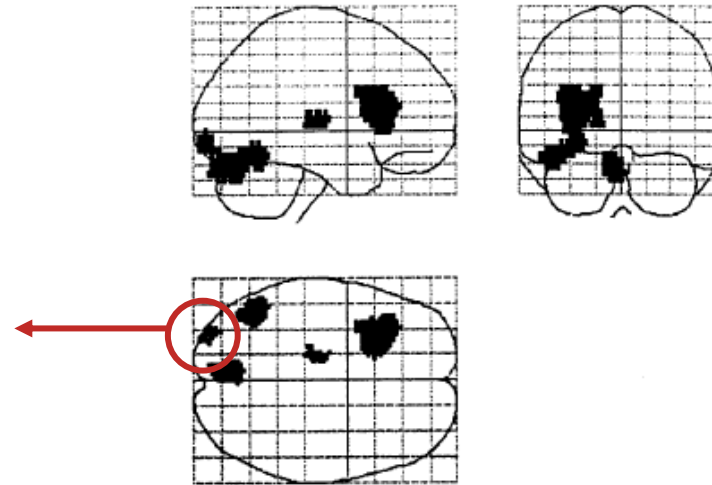
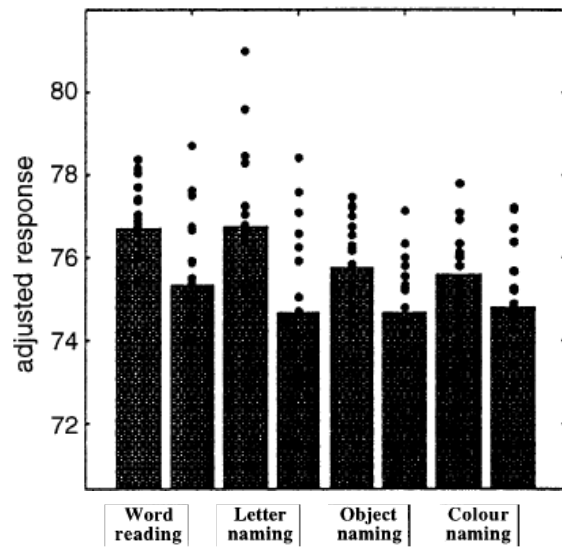
Phonological retrieval is the only cognitive component common to all task pair differences.

Price & Friston (1996)

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)

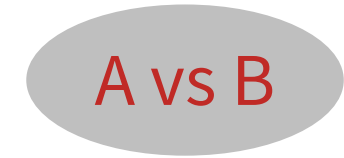
→ Associated with process of interest (phonological retrieval)

Overview

1. Categorical designs

- Subtraction
- Conjunction

Pure insertion, evoked / differential responses
Testing multiple hypotheses



2. Parametric designs

- Linear and nonlinear
- Model-based regressors

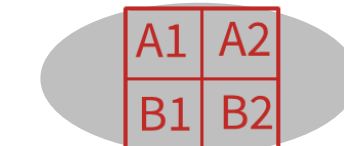
Adaptation, cognitive dimensions
Polynomial expansions



3. Factorial designs

- Categorical
- Parametric

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



Parametric designs

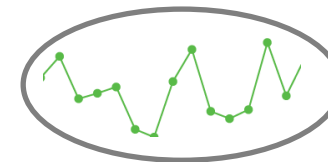
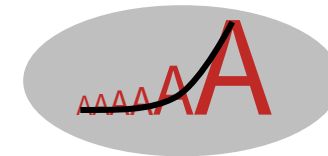
Does activity vary systematically with a continuously varying parameter?

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 :

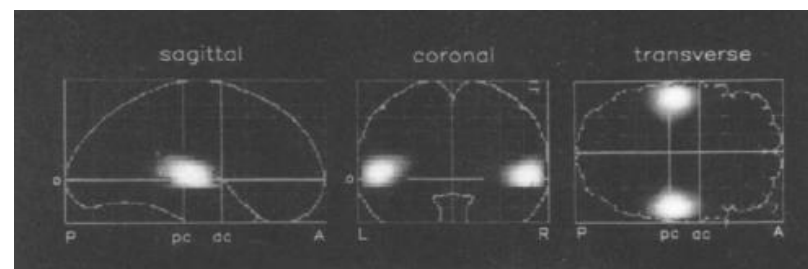
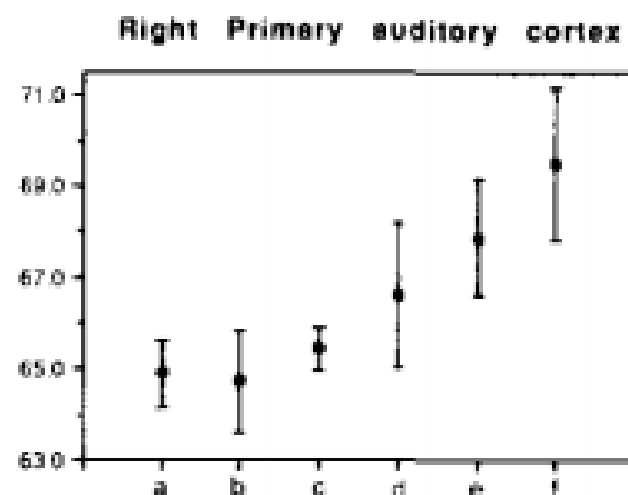
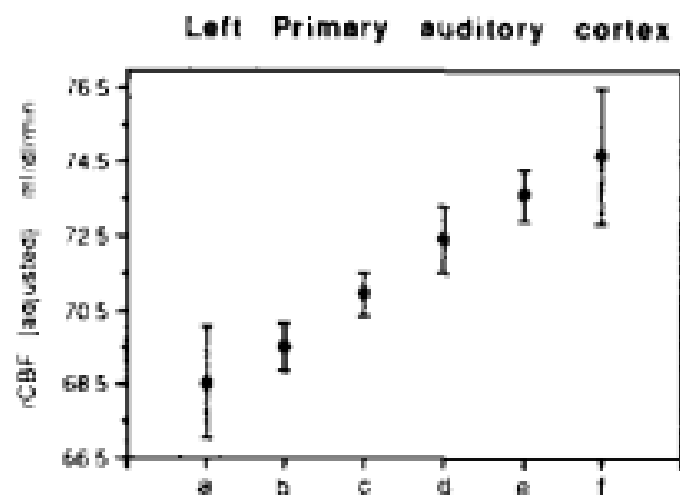
- Linear
- Nonlinear: Quadratic/cubic/etc.
- „Data-driven“ (e.g., neurometric functions, computational modelling)

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



Parametric designs

- 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)

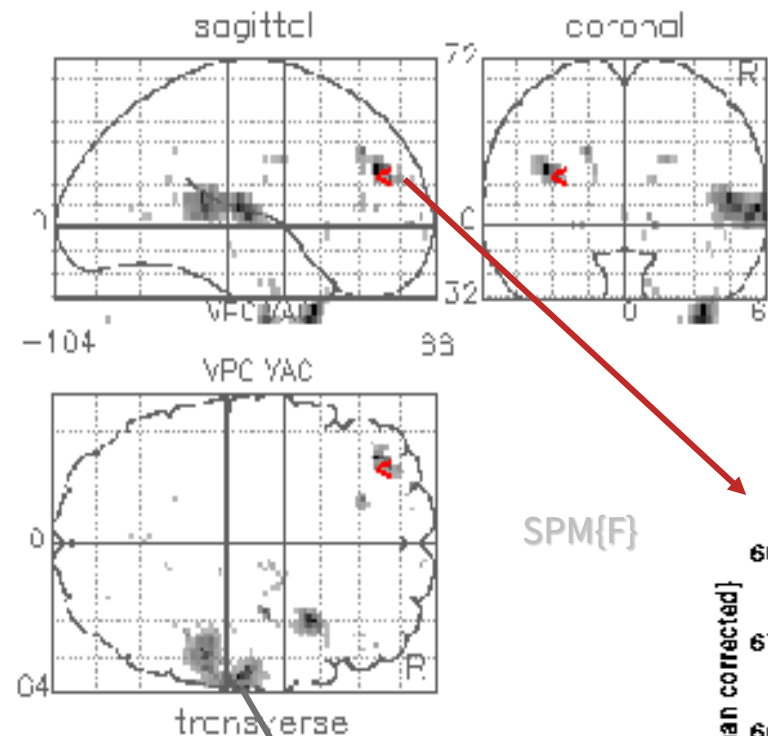
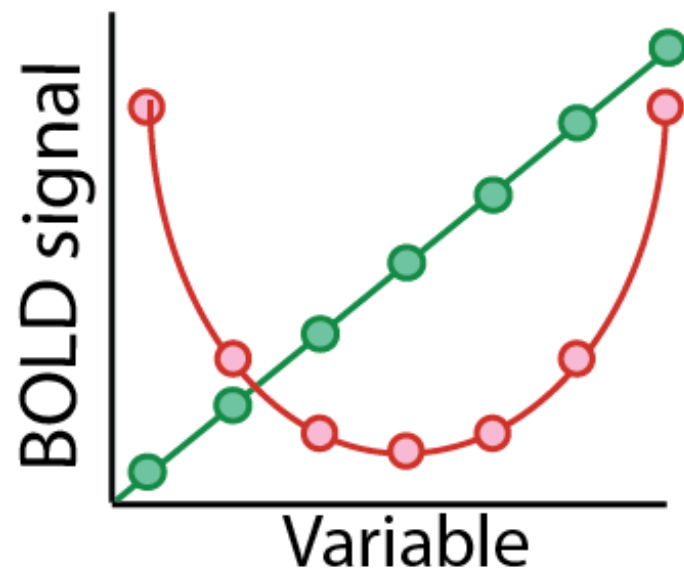
Non-linear parametric designs

Polynomial expansion:

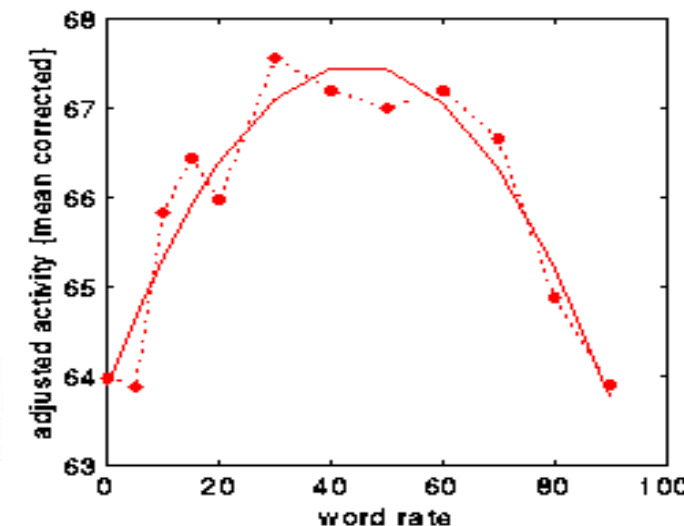
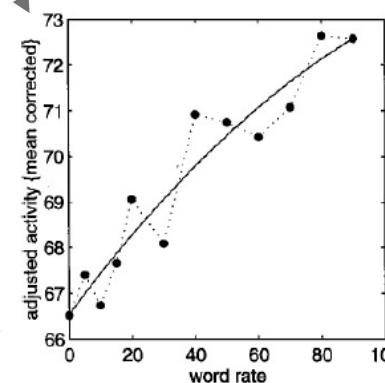
$$f(x) = b_1 x + b_2 x^2 +$$

...up to $(N-1)^{\text{th}}$ order for N levels

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



F-contrast [1 0] on linear parametric regressor
F-contrast [0 1] on quadratic parametric regressor



This session's outline

1. Categorical designs

- Subtraction
- Conjunction

The “baseline challenge”, pure insertion
Testing multiple hypotheses



A vs B

2. Parametric designs

- Linear and nonlinear
- **Model-based regressors**

Adaptation, cognitive dimensions
Polynomial expansions




AAAAAA

3. Factorial designs

- Categorical
- Parametric

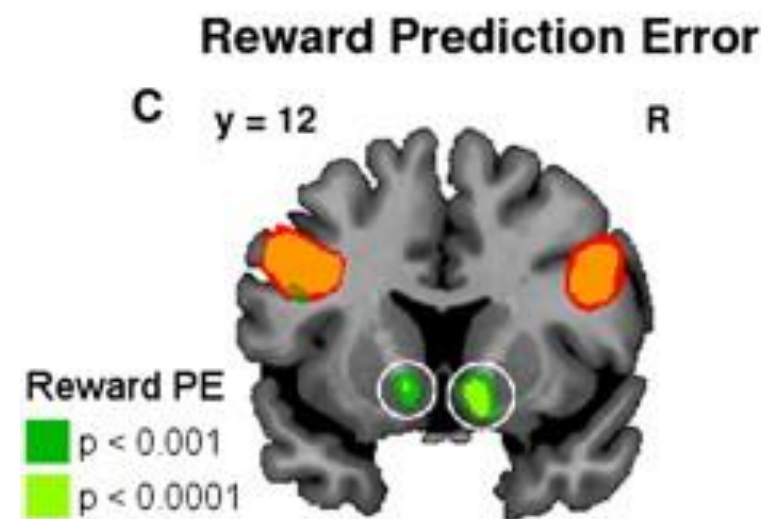
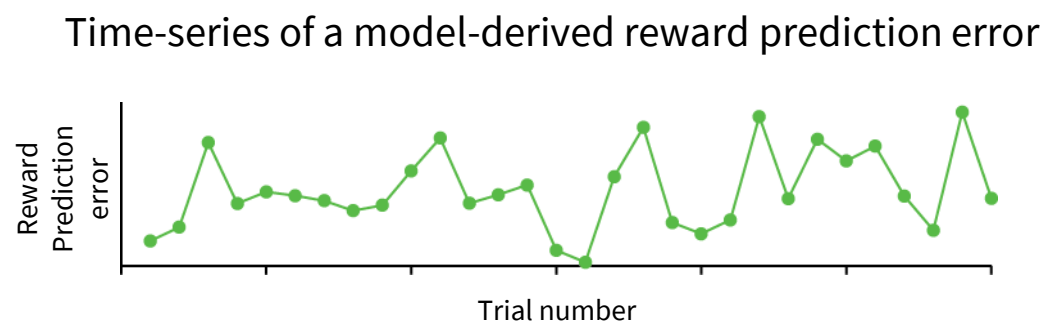
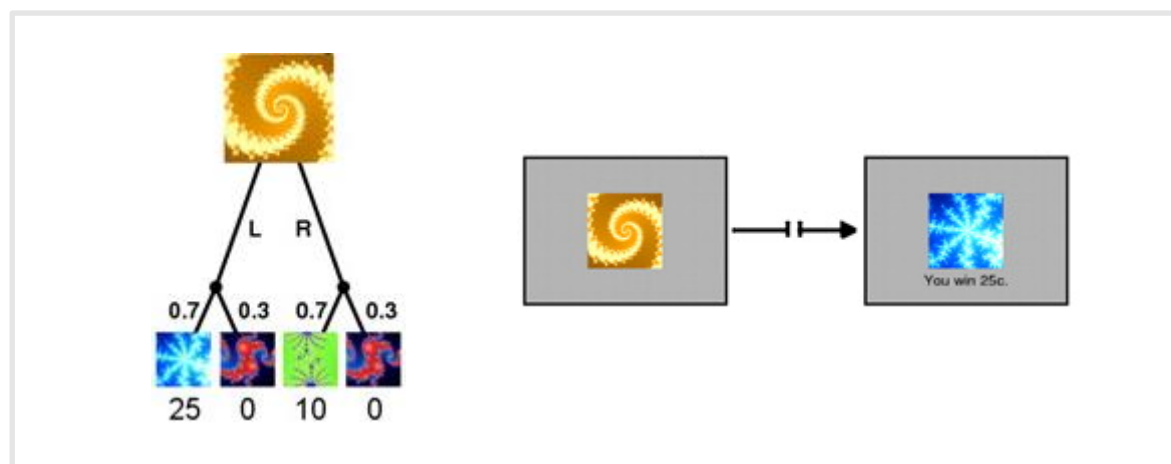
Interactions and pure insertion
Linear and nonlinear interactions
Psychophysiological Interactions (PPI)



A1	A2
B1	B2

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 \(2010\)](#) [Gläscher et al. \(2010\)](#)

This session's outline

1. Categorical designs

- Subtraction
- Conjunction

The “baseline challenge”, pure insertion
Testing multiple hypotheses



A vs B

2. Parametric designs

- Linear and nonlinear
- Model-based regressors

Adaptation, cognitive dimensions
Polynomial expansions




AAAAAA

3. Factorial designs

- **Categorical**
- Parametric

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



A1	A2
B1	B2

Factorial design

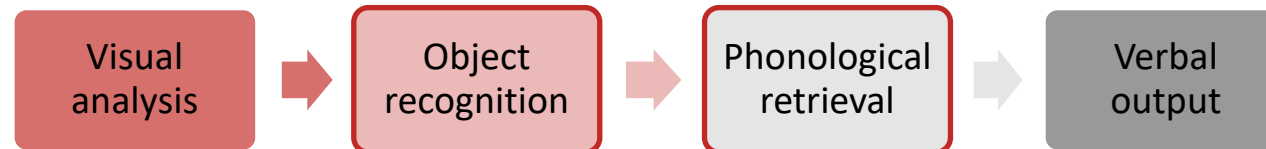
		Factor A	
		A	a
Factor B	B	A B	a B
	b	A b	a b

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?

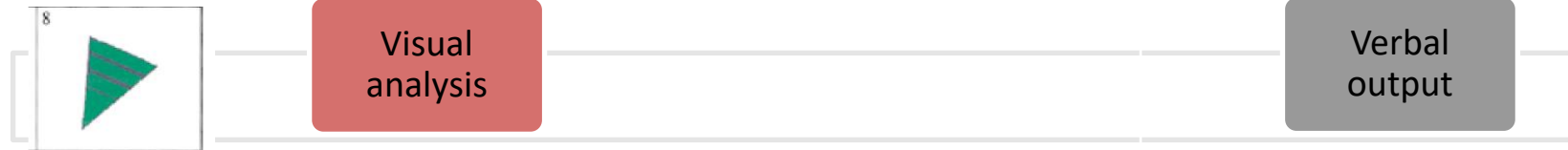


Factorial design

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

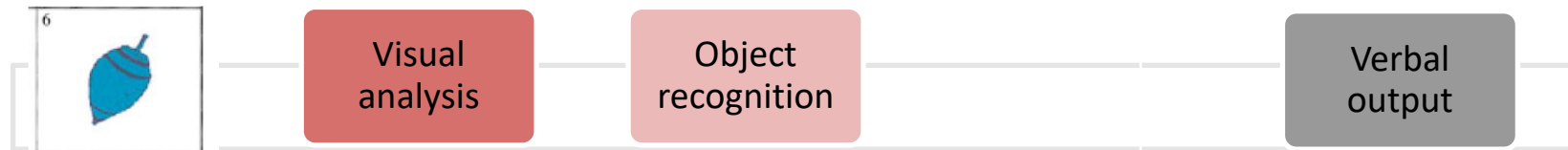
A

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



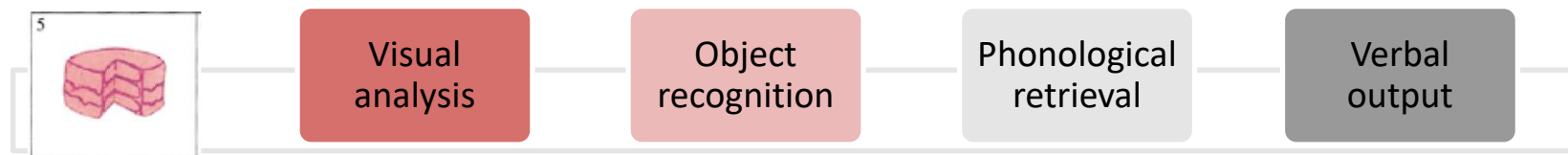
B

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



C

Name the object



Factorial design

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

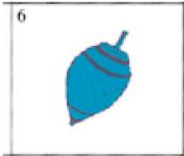
A

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



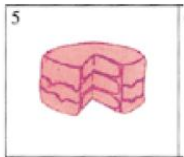
B

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



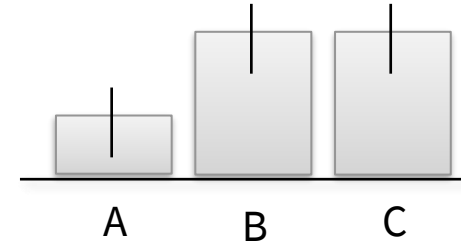
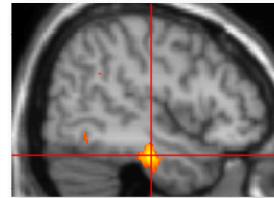
C

Name the object



Friston et al., (1997)

Results in inferotemporal cortex:

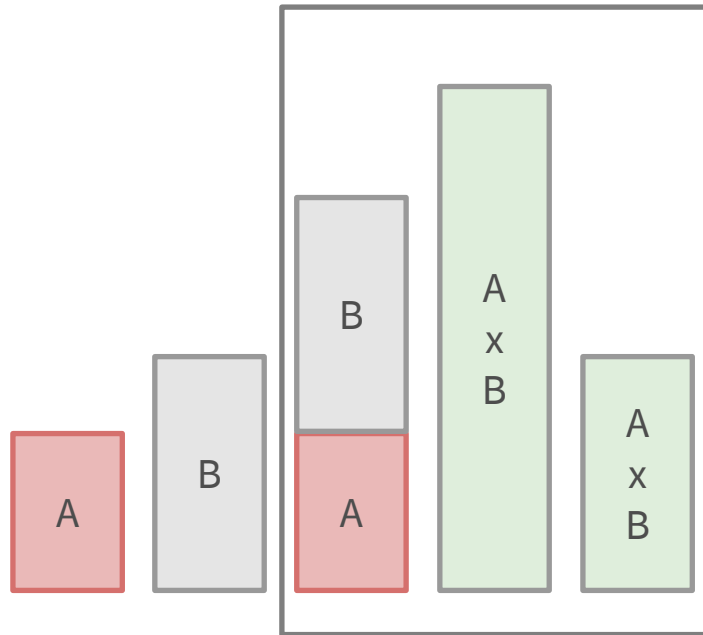


$B > A$ Object recognition

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

Addressing interactions in factorial designs

Is the resulting activation equivalent to the sum of its component processes, or does A modulate B?



Phonological
retrieval

Object
recognition

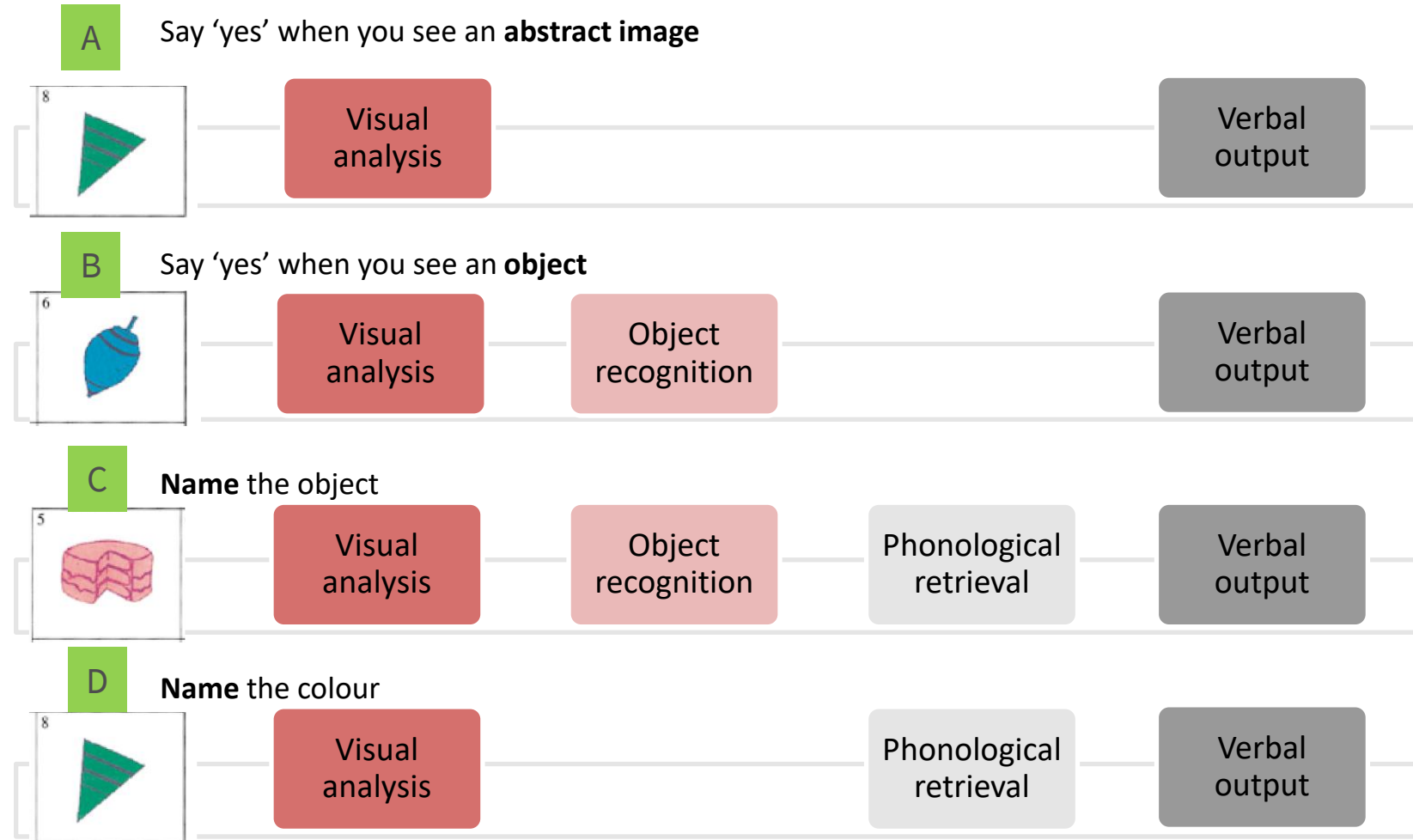
Let's test the interaction explicitly!

How?

→ Vary A and B independently!

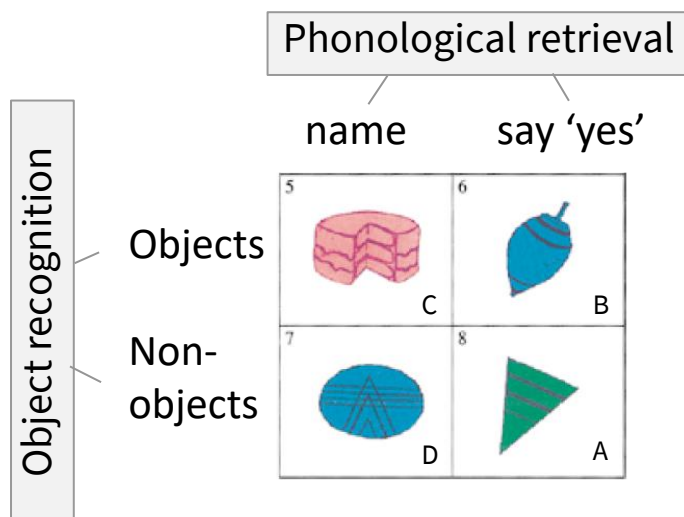
Factorial design

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



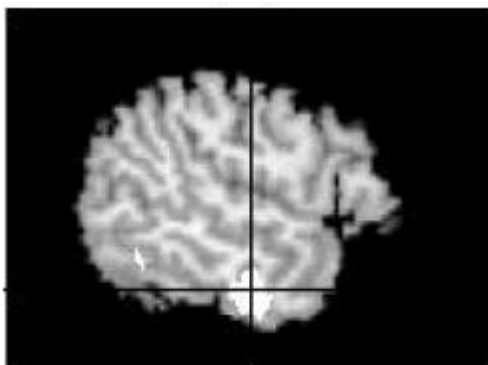
Phonological retrieval
in the **absence** of
object recognition

Factorial designs: Main effects and interaction

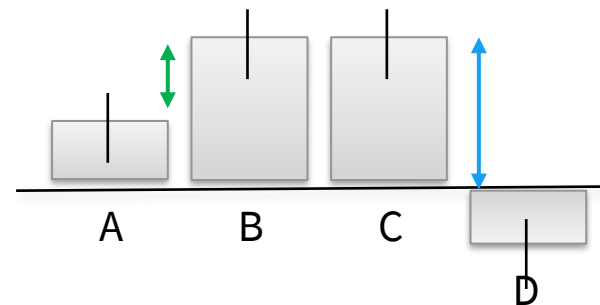
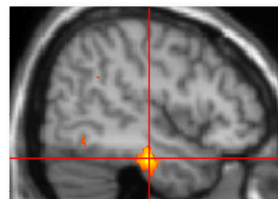


2x2 factorial design

Interaction effect



Results in inferotemporal cortex:



B > A

Object recognition in the *absence* of phonological retrieval

C > D

Object recognition in the *presence* of phonological retrieval

Pure insertion: The activation to object recognition should be identical!

This is not true!

→ The inferotemporal cortex shows a *stronger differentiation* between object and non-object *in the context of phonological retrieval*!

This session's outline

1. Categorical designs

- Subtraction
- Conjunction

The “baseline challenge”, pure insertion
Testing multiple hypotheses



A vs B

2. Parametric designs

- Linear and nonlinear
- Model-based regressors

Adaptation, cognitive dimensions
Polynomial expansions



AAAAAA

3. Factorial designs

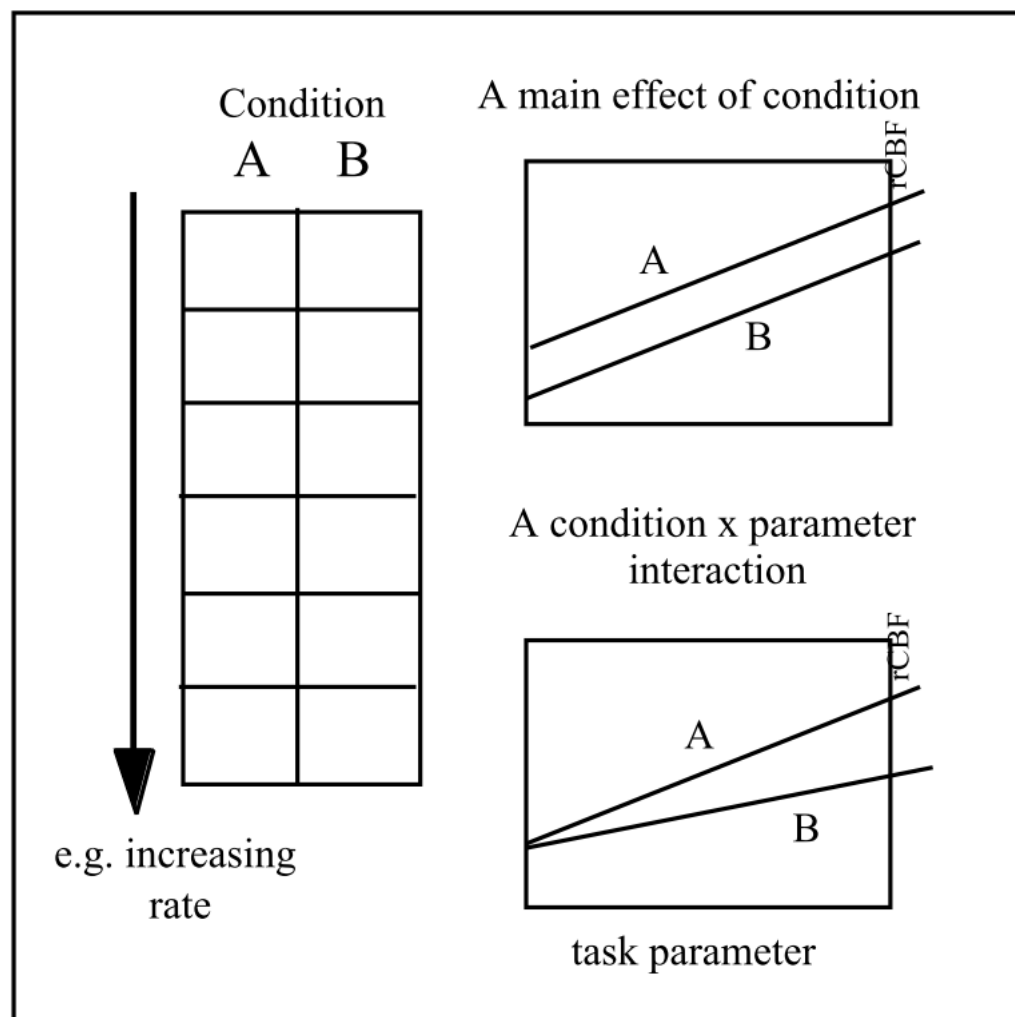
- Categorical
- **Parametric**

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

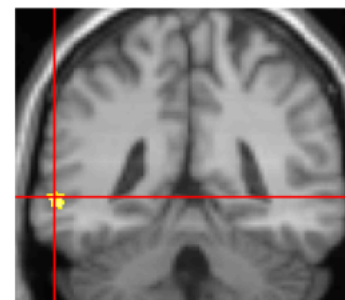


A1	A2
B1	B2

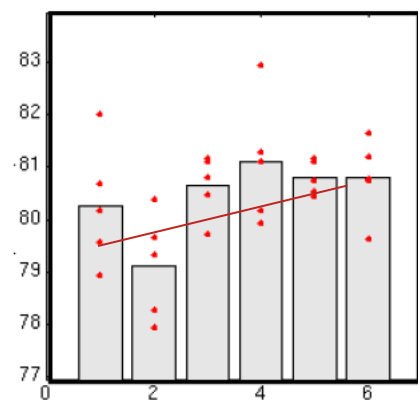
Linear Parametric Interaction



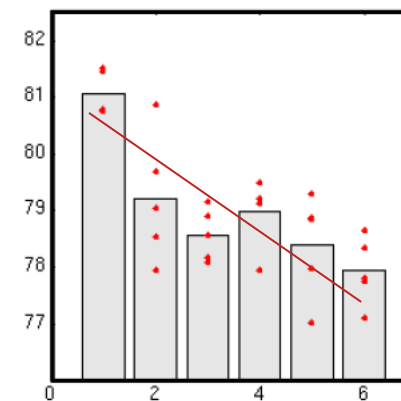
Responses in the right posterior superior temporal region



to increasing rate of word production



whilst repeating words



and producing new ones

This session's outline

1. Categorical designs

- Subtraction
- Conjunction

The “baseline challenge”, pure insertion
Testing multiple hypotheses



A vs B

2. Parametric designs

- Linear and nonlinear
- Model-based regressors

Adaptation, cognitive dimensions
Polynomial expansions



AAAAAA

3. Factorial designs

- Categorical
- Parametric

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

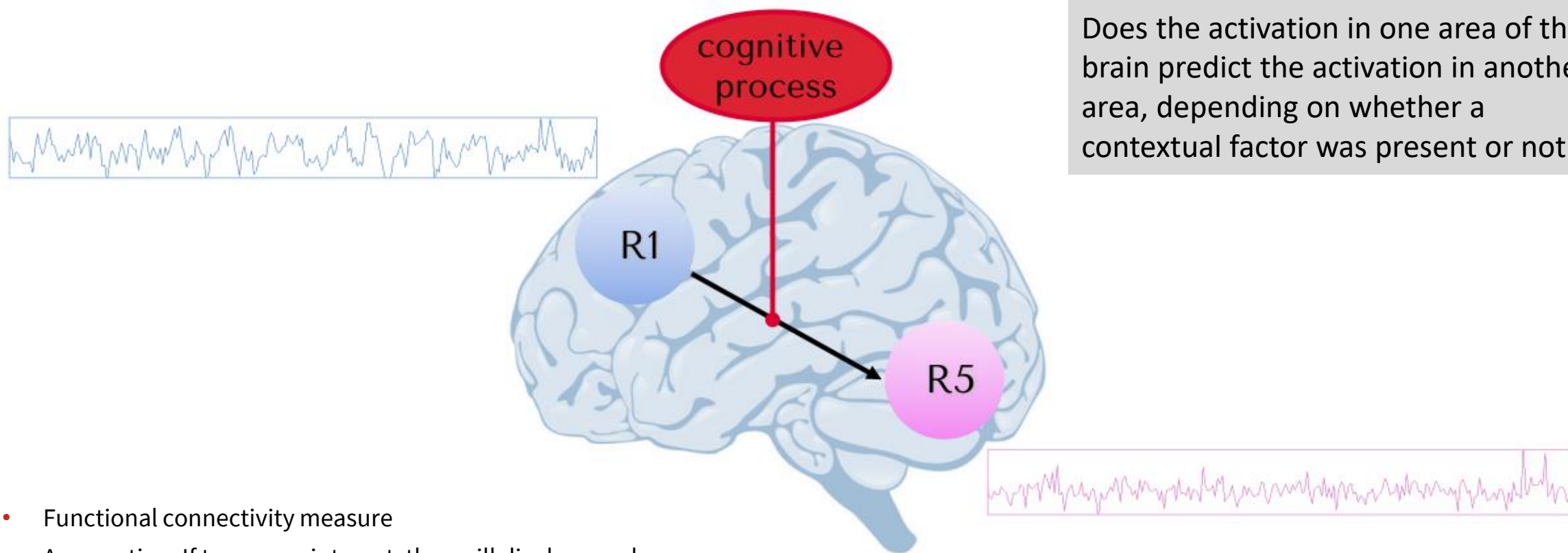


A1	A2
B1	B2

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.



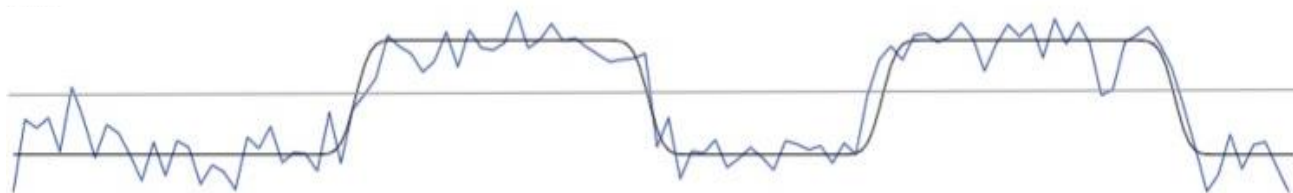
- Functional connectivity measure
- Assumption: If two areas interact, they will display synchronous activity

Psycho-physiological Interaction (PPI)

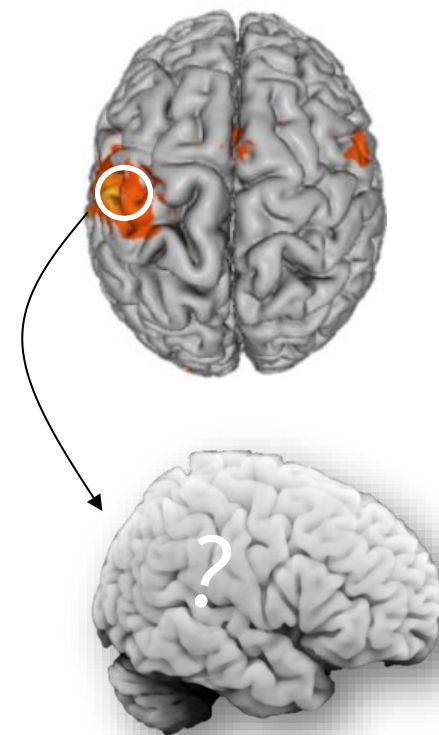
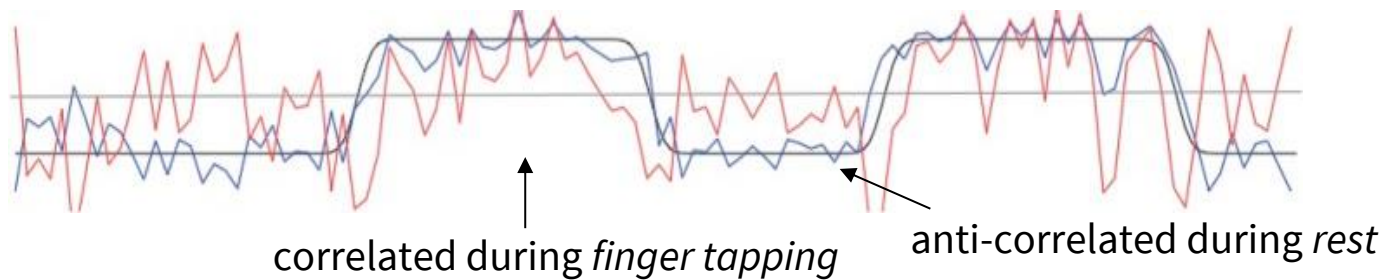
Task regressor (e.g. *finger tapping - rest*)



BOLD time series extracted from seed region (e.g. motor cortex)



PPI regressor = task regressor x seed ROI regressors



This session's outline

1. Categorical designs

- Subtraction
- Conjunction

The “baseline challenge”, pure insertion
Testing multiple hypotheses



A vs B

2. Parametric designs

- Linear and nonlinear
- Model-based regressors

Adaptation, cognitive dimensions
Polynomial expansions



AAAAAA

3. Factorial designs

- Categorical
- Parametric

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



A1	A2
B1	B2