



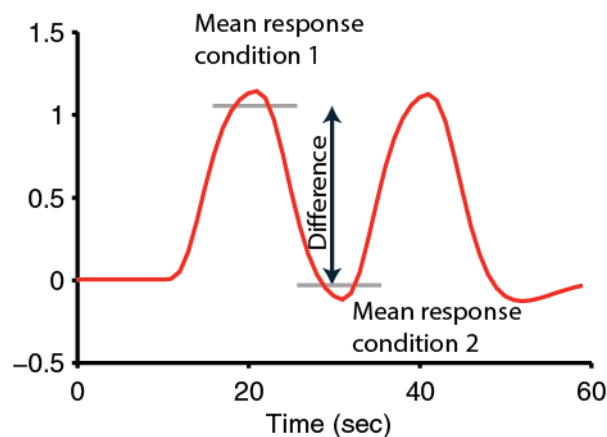
Experimental design

Mona Garvert

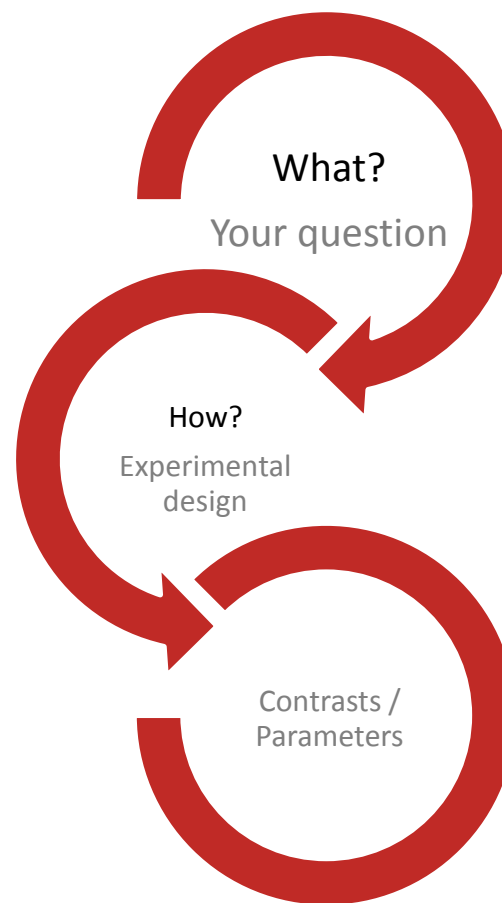
With thanks to:
Sara Bengtsson
Christian Ruff
Rik Henson

Goal

The BOLD signal does NOT provide you with an absolute measure of neural activity
Therefore, you need to compare activity across conditions (use contrasts).



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



Subtraction

Conjunction

Factorial

Parametric

Psycho-physiological Interaction (PPI)

fMRI adaptation

Simple subtraction

Aim: Isolation of a cognitive process

- Compare the neural signal for a task that activates the cognitive process of interest and a second task that controls for all but the process of interest

>> *The critical assumption of „**pure insertion**“*

Assume that adding components does not affect other processes

> **A good control task is critical!**



F.C. Donders, 1868

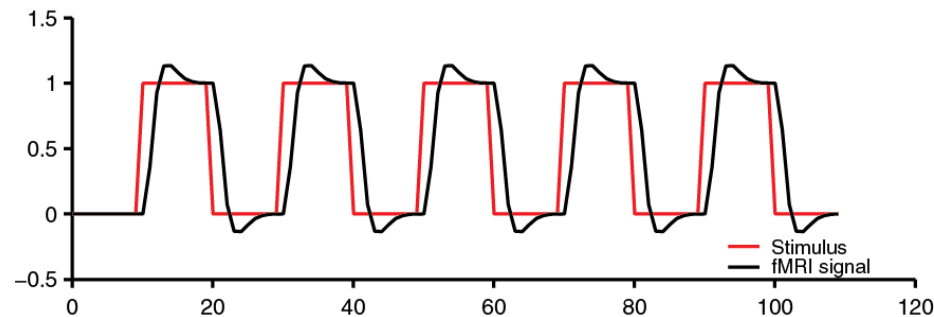
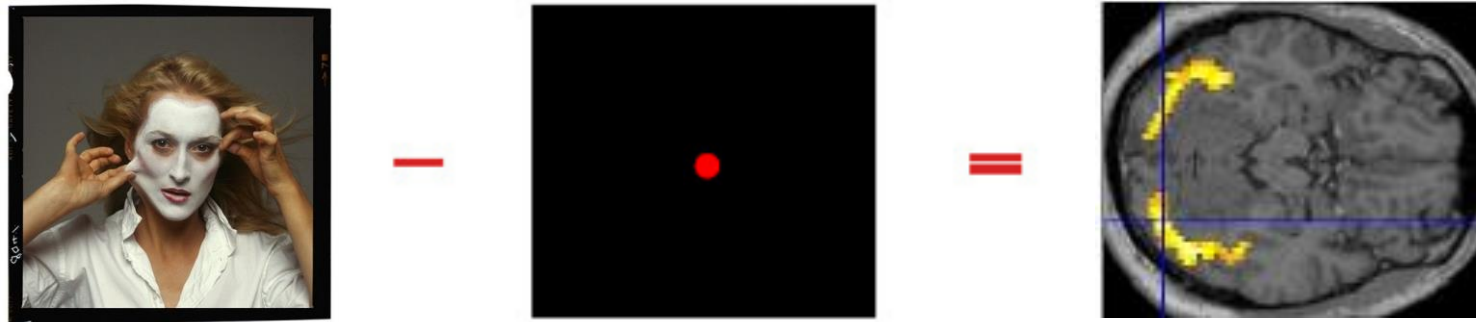
- Question: Which region is specialized for processing faces?



Simple subtraction

Aim: Isolation of a cognitive process

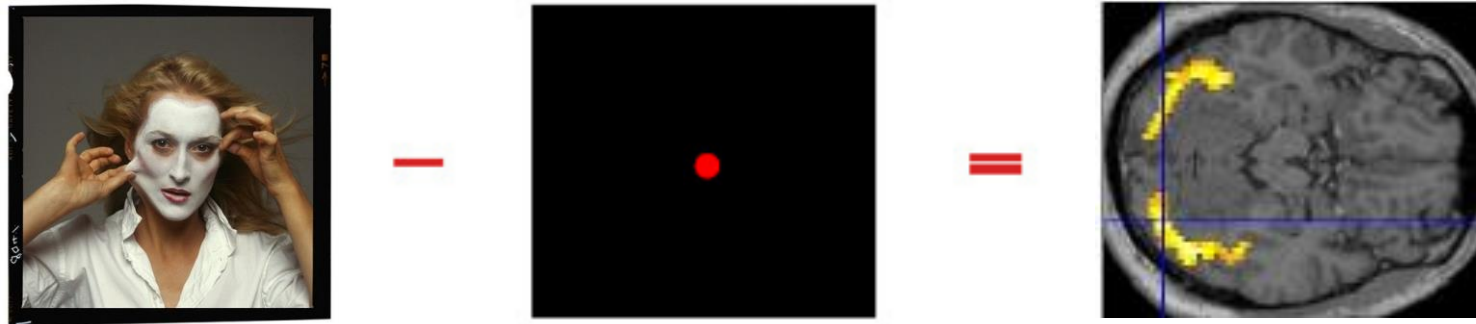
- Compare the neural signal for a task that activates the cognitive process of interest and a second task that controls for all but the process of interest



Simple subtraction

Aim: Isolation of a cognitive process

- Compare the neural signal for a task that activates the cognitive process of interest and a second task that controls for all but the process of interest



Not a great contrast

- Rest may not be truly rest
- Will give wide-spread activation. Hard to draw conclusions about specific cognitive processes
- Null events or long SOAs essential for estimation, which may result in an inefficient design.
- But can be useful to find define regions generally involved in the task

Choosing your baseline

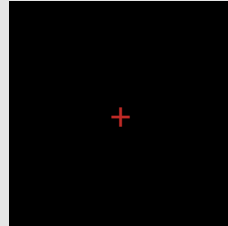
Problem: Difficulty of finding baseline tasks that activates all but the process of interest

Different stimuli and task



'Meryl Streep'

vs.



'I am so hungry...'

→ Several components differ!

Related stimuli



Name the person!

vs.



Name the gender!

→ P implicit in control task?

→ Difficulty matched?

Same stimulus, different tasks



Name the person!

vs.



Name the gender!

→ Specific naming-related activity

Categorical responses

SPM

The image shows the 'SPM contrast manager' dialog box. The title bar reads 'SPM contrast manager'. The main window is titled 'define contrast...'. It contains the following fields and controls:

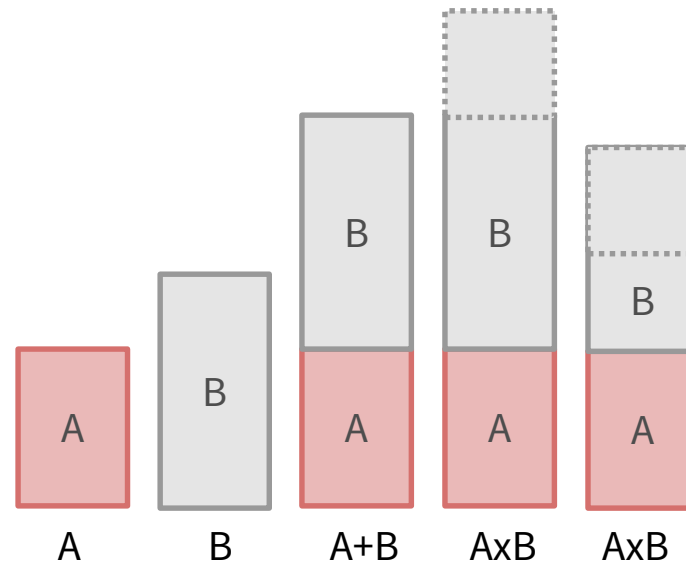
- name:** A1-A2
- type:** t-contrast, F-contrast
- contrast weights vector:** 1 -1 1 -1 1 -1 1 -1
- Design matrix:** A large matrix visualization with a mouse cursor pointing to a specific cell. Three red arrows point to the first three rows of the matrix, labeled 'Task 1', 'Task 2', and 'Session'.
- parameter estimability:** A row of 12 empty boxes.
- Buttons:** Reset, Cancel, OK, and a help button (?) at the bottom right.
- Status bar:** name defined, contrast defined

The contrast weights vector is displayed in a text area and also in a scrollable list at the bottom of the dialog. The design matrix is a large grid of cells, with the first three rows highlighted by red arrows and labels: Task 1, Task 2, and Session.

Subtraction

Problems:

- Difficulty of finding baseline tasks that activate all but the process of interest
- 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)

Subtraction

Conjunction

Factorial

Parametric

Psycho-physiological Interaction (PPI)

fMRI adaptation

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	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

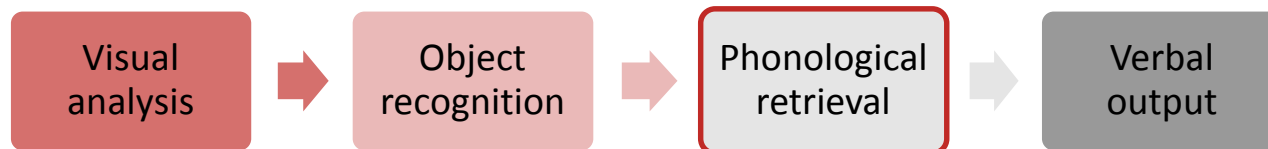
only the component of interest is common to all task pairs

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

Note: The contrasts entering a conjunction have to be **independent**

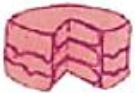



Conjunction analysis

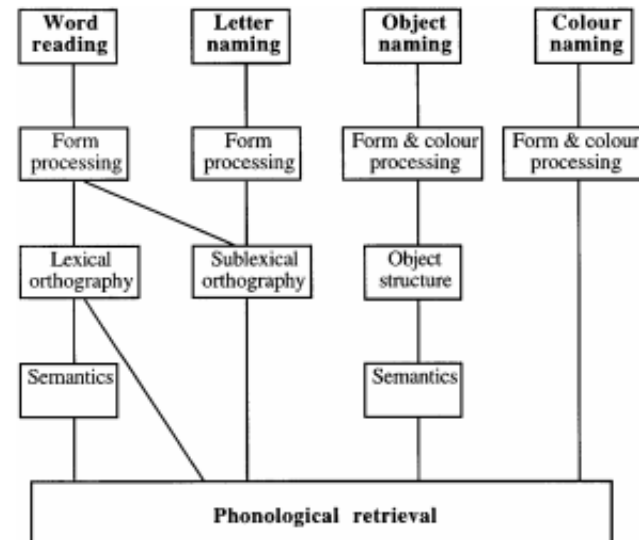
Which neural structures support **phonological retrieval**, independent of item?



Conjunction analysis

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

	Name (A)	Say "YES" (C)
Words:	1 badge	2 ᐃᐃᐃᐃᐃ
Letters:	3 r	4 n
Objects:	5 	6 
Colours:	7 	8 

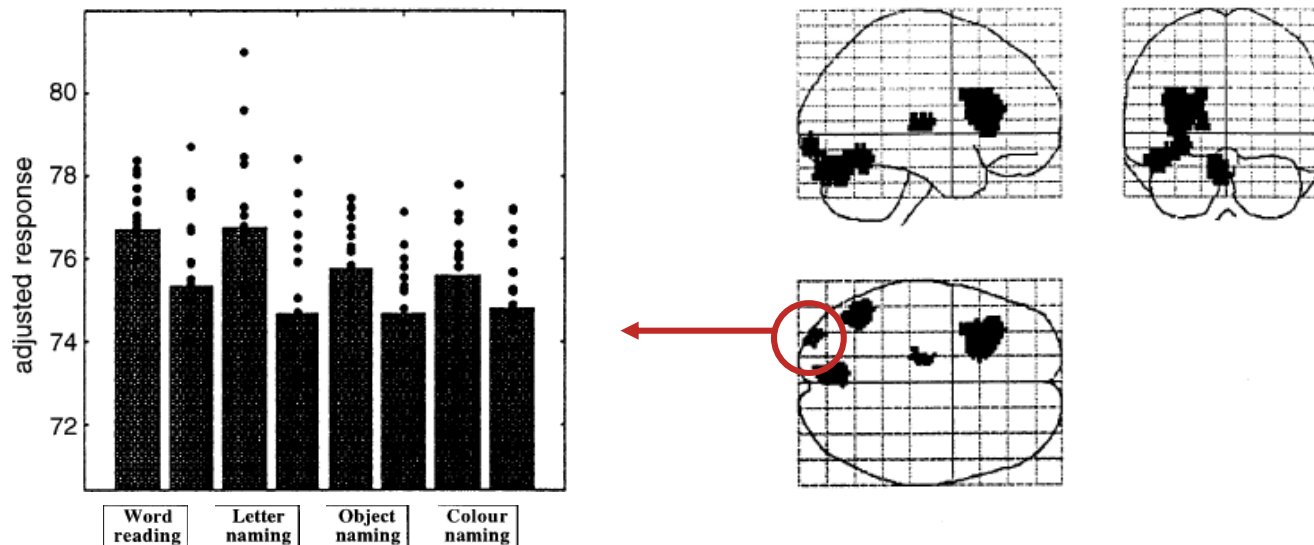


Phonological retrieval is the only cognitive component common to all task pair differences

Conjunction analysis

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

Overlap of 4 subtractions



Areas are identified in which task-pair effects are **jointly significant** and are **not significantly different**

Price & Friston (1996)

Conjunction analysis

SPM

The image shows the SPM contrast manager window titled "Select contrasts...". It features three radio buttons for contrast types: "t-contrasts" (selected), "F-contrasts", and "all". Below these is a list of contrasts with columns for ID, type, and name. The selected contrasts are:

###	{type}	name
018	{T}	A1-A2
019	{T}	B1-B2
020	{T}	C1-C2
021	{T}	D1-D2

At the bottom of the list are buttons for "Define new contrast...", "Reset", and "Done". To the right, a "contrast(s)" plot shows a staircase pattern of gray bars. Below it is a "Design matrix" heatmap with an arrow pointing to a specific cell labeled "1 task/session". At the bottom right is a "parameter estimability" bar chart.

Selected 4 contrasts for conjunction, press "Done" when finished.

Subtraction

Conjunction

Factorial

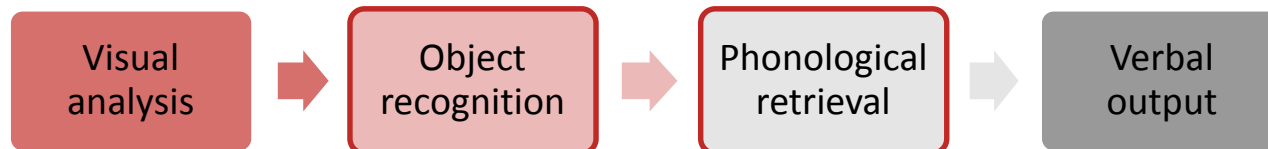
Parametric

Psycho-physiological Interaction (PPI)

fMRI adaptation

Factorial design

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

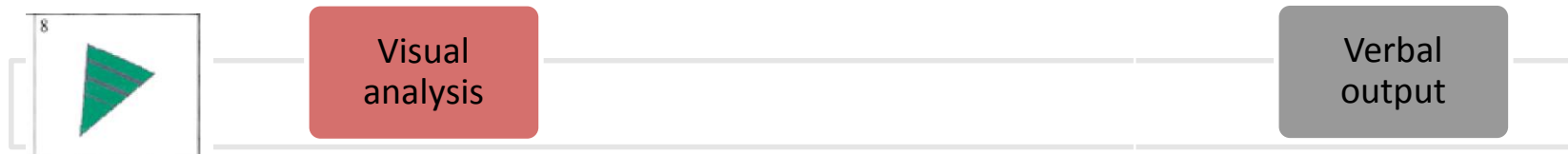


Factorial design

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

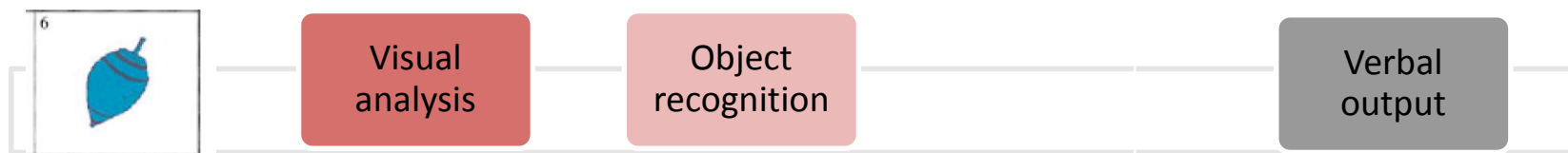
A

Say 'yes' when you see an abstract image



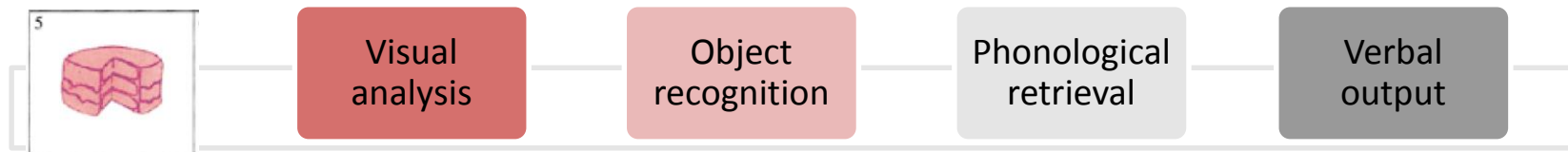
B

Say 'yes' when you see an object



C

Name the object




Factorial design

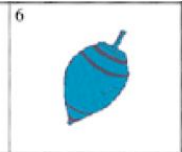
Is the inferotemporal cortex sensitive to both object recognition and phonological retrieval of object names?

Friston et al., (1997)

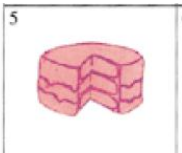
A Say 'yes' when you see an abstract image



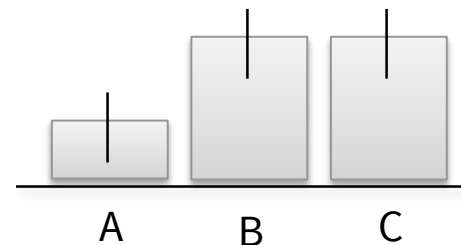
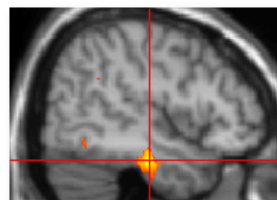
B Say 'yes' when you see an object



C Name the object



Results in inferotemporal cortex:



B > **A** Object recognition

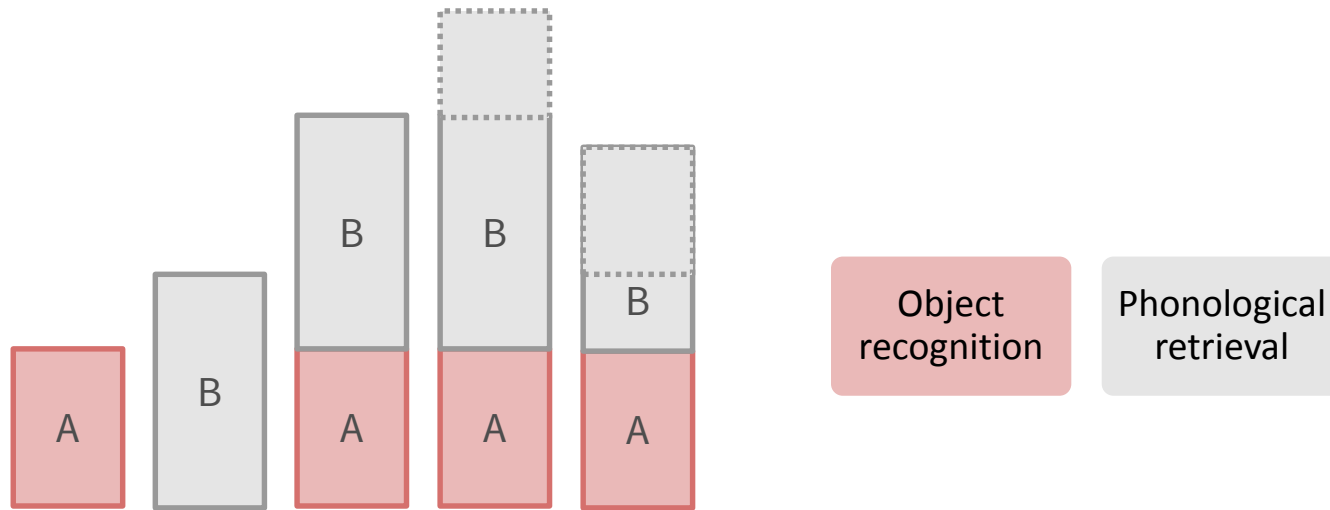
C = **B** IT not involved in phonological retrieval?!

Problem:

We assumed that IT response to object recognition is context independent

Interactions

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






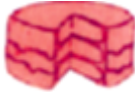
Vary A and B independently!

Main effects

Factorial design

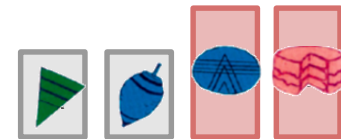
Is the task the sum of its component processes, or does A modulate B?

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

	No phonological retrieval	Phonological retrieval
No object recognition	A 	C 
Object recognition	B 	D 

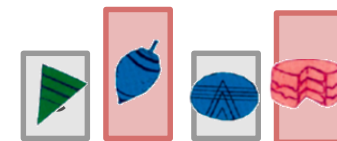
Main effect, phonological retrieval:

$$(C + D) > (A + B)$$



Main effect, object recognition:

$$(B + D) > (A + C)$$



Main effects

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

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

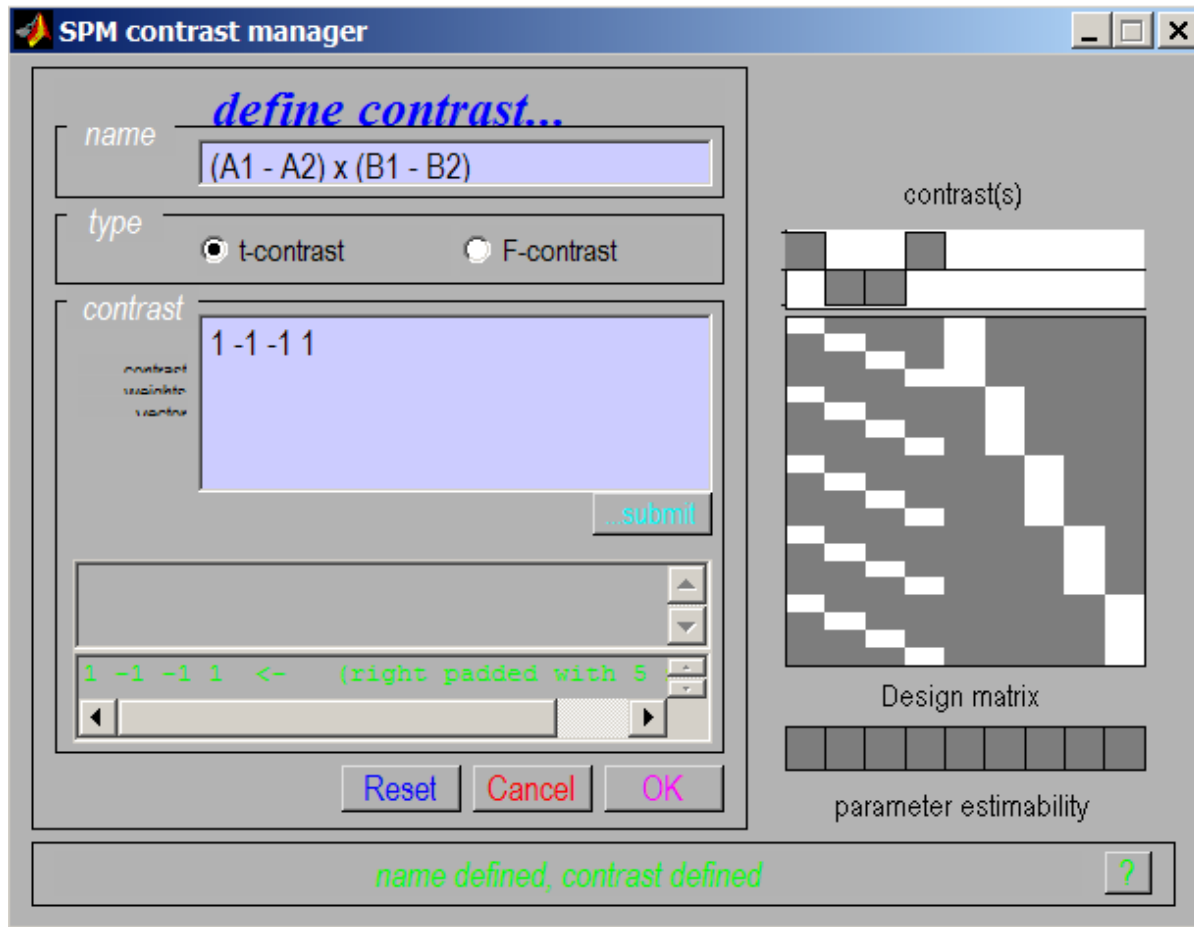
	No phonological retrieval	Phonological retrieval
No object recognition	A	C
Object recognition	B	D

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.

Interaction:

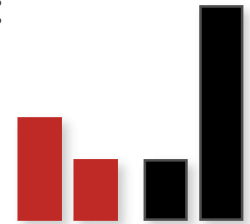
$$(D - C) > (B - A)$$

Interaction in SPM



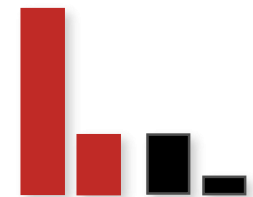
Interactions:

cross-over



and

simple



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

Subtraction

Conjunction

Factorial

Parametric

Psycho-physiological Interaction (PPI)

fMRI adaptation

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 :

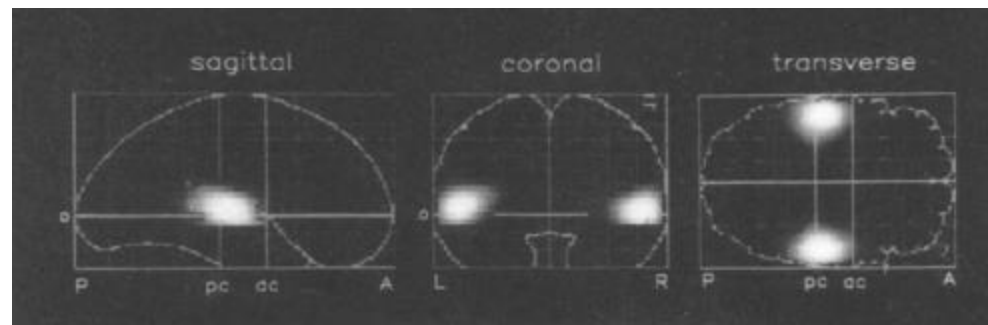
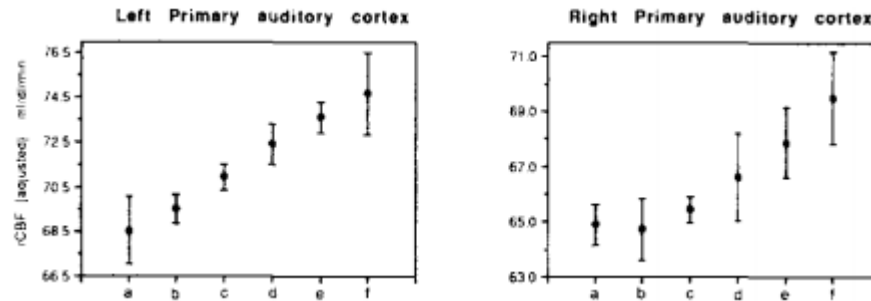
- Linear
- Nonlinear: Quadratic/cubic/etc.
- „Data-driven“ (e.g., neurometric functions, computational modelling)

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

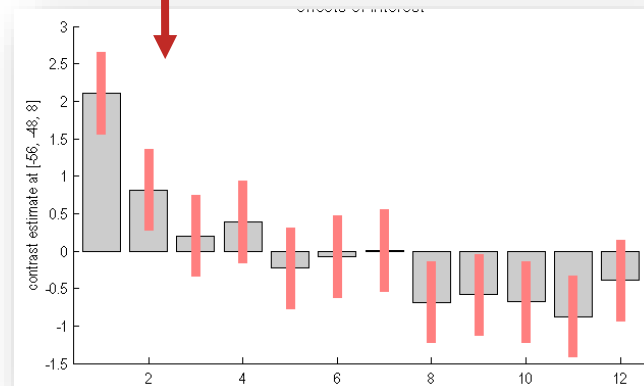
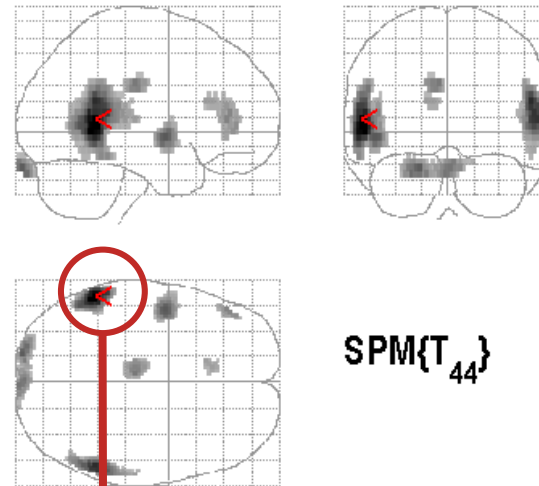
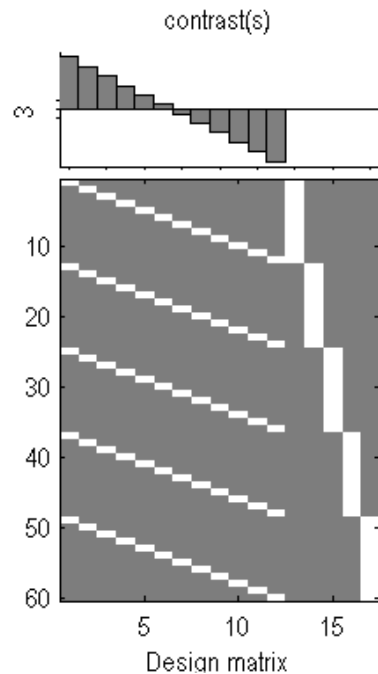


Price et al. 1992

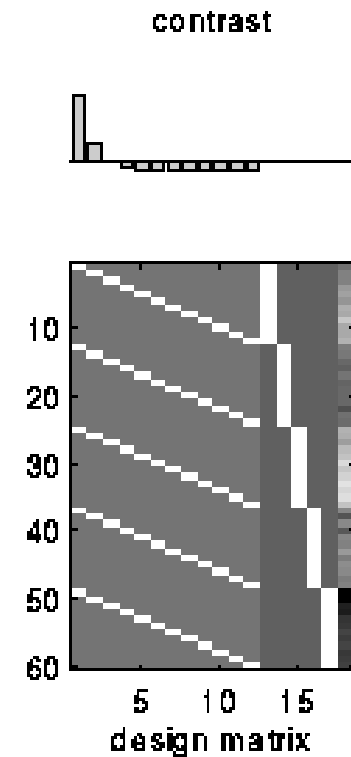
A linear parametric contrast

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

Linear effect of time

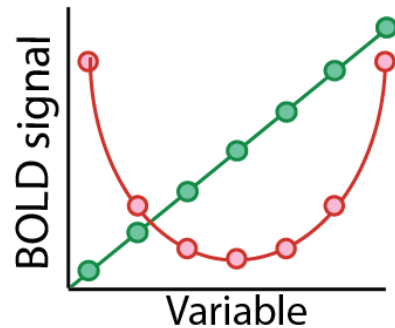


Non-linear effect of time



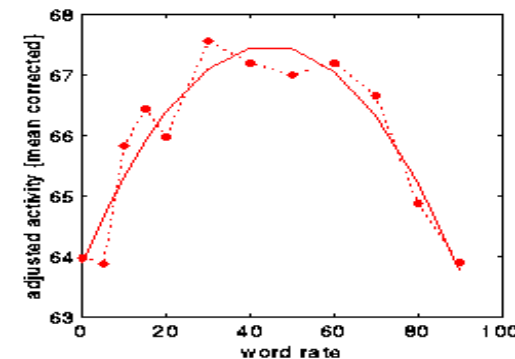
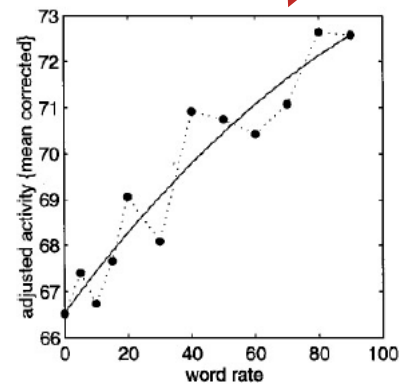
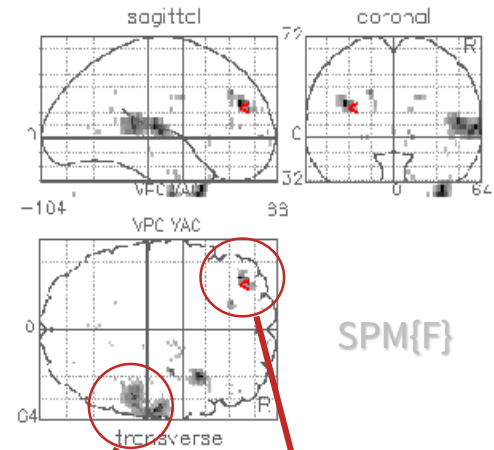
A non-linear parametric design matrix

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

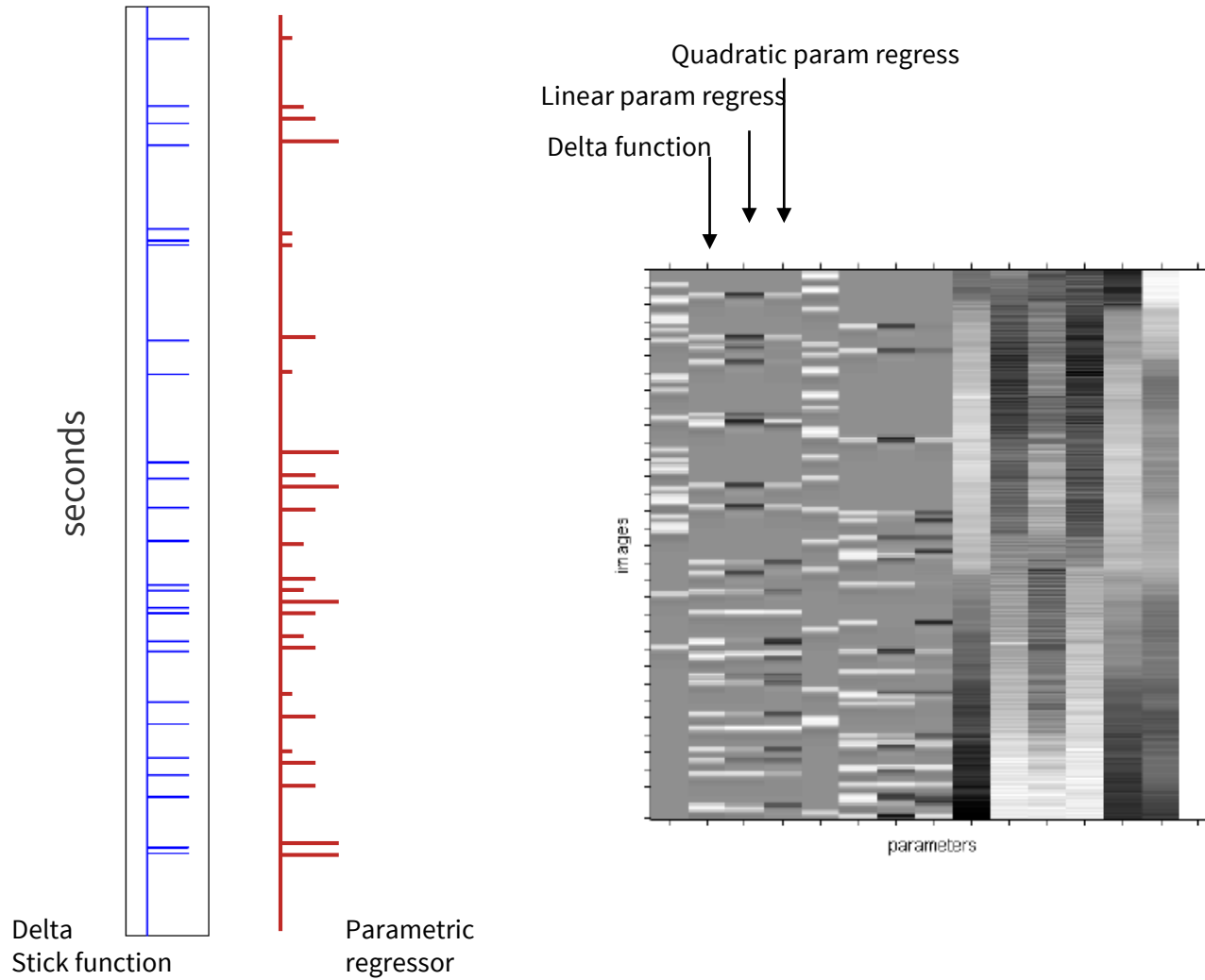


Büchel et al., (1996)

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



Parametric modulation

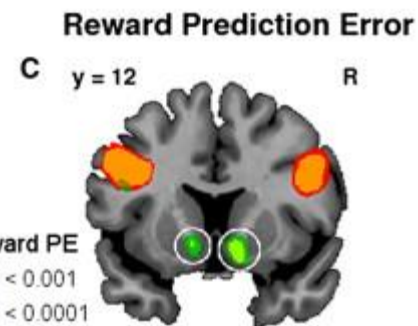
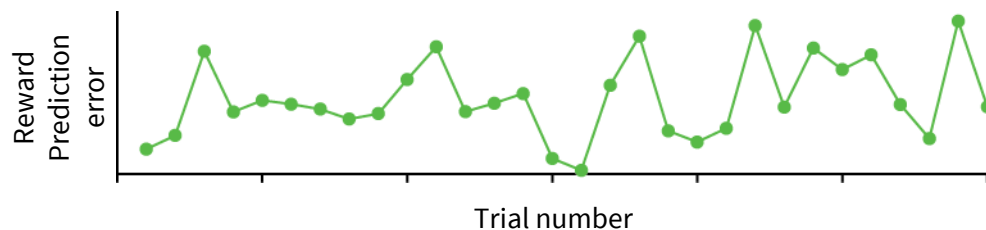


Parametric design: Model-based regressors

- 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



Subtraction

Conjunction

Factorial

Parametric

Psycho-physiological Interaction (PPI)

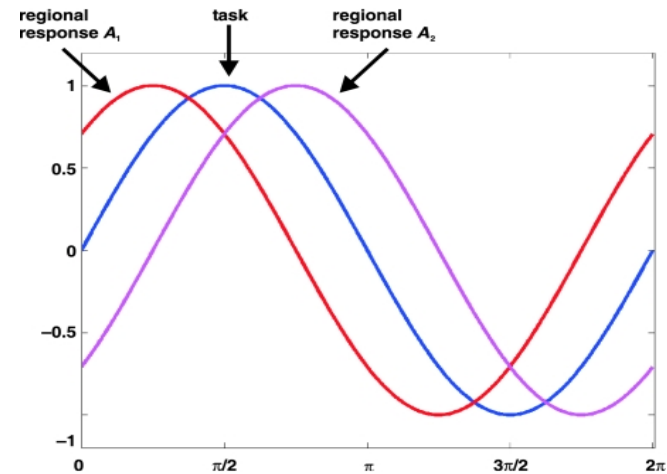
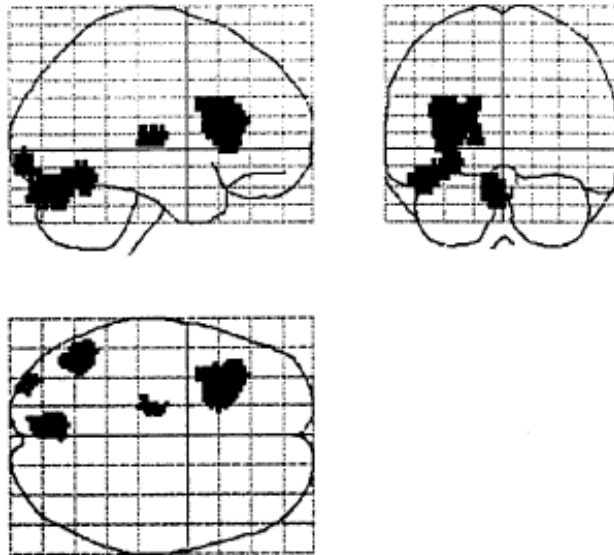
fMRI adaptation

Psycho-physiological Interaction (PPI)

Functional connectivity measure

Can activity in a part of the brain be predicted by an interaction between task and activity in another part of the brain?

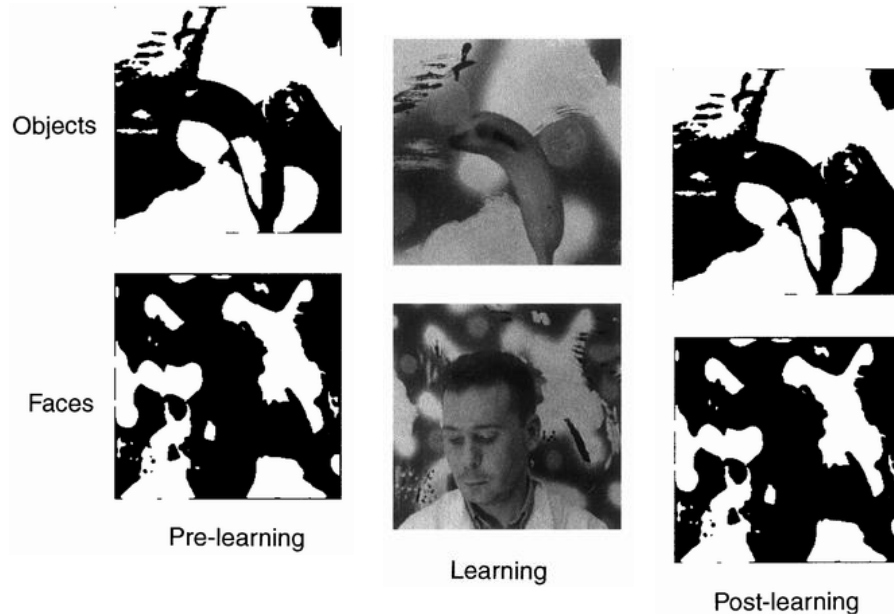
If two areas interact they will display synchronous activity



Stephan, 2004

Psycho-physiological Interaction (PPI)

Factorial design

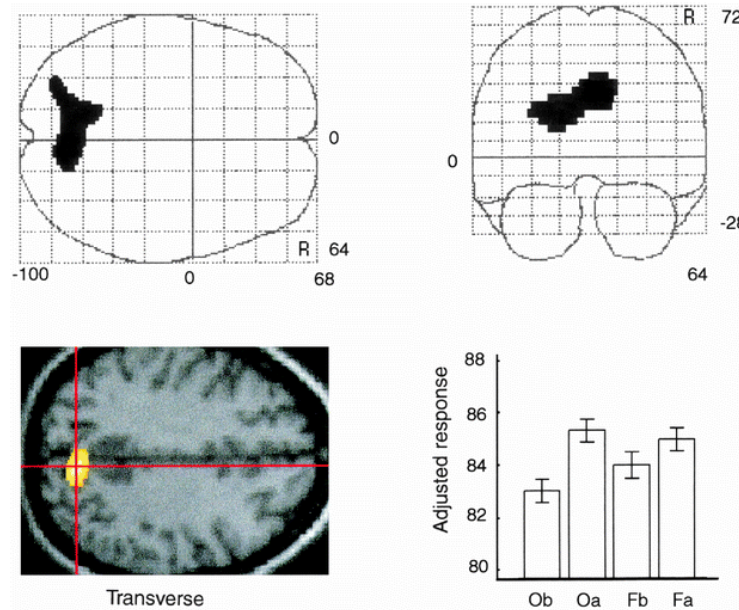


Learning

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

Psycho-physiological Interaction (PPI)

Main effect of learning



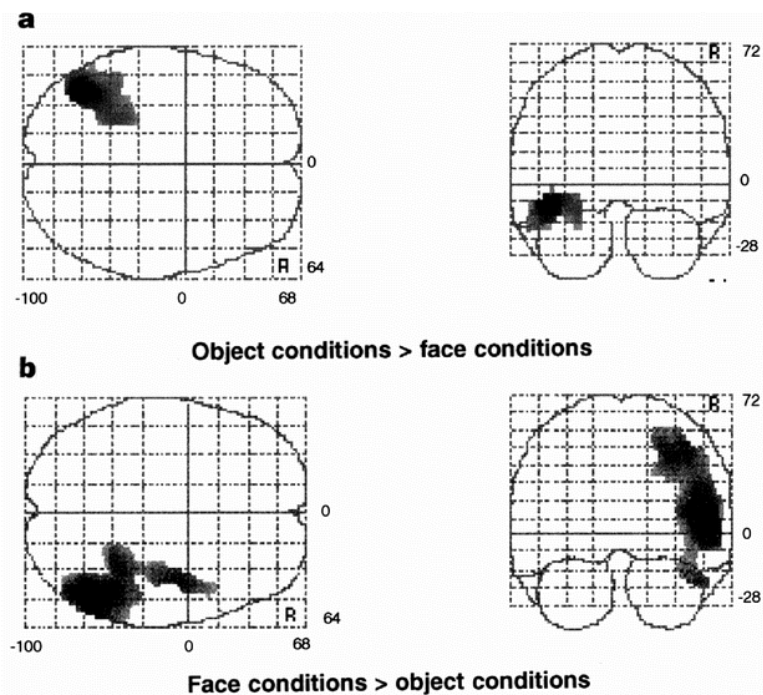
Learning

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

Dolan et al., 1997

Psycho-physiological Interaction (PPI)

Main effect of stimulus



Learning

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

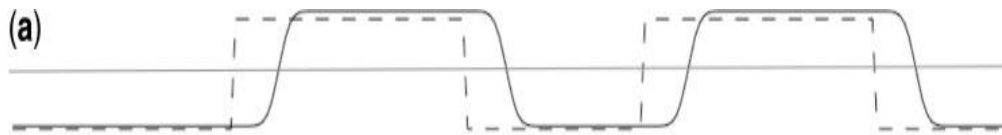
Does learning involve functional connectivity between parietal cortex and stimuli specific areas?

Dolan et al., 1997

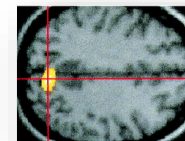
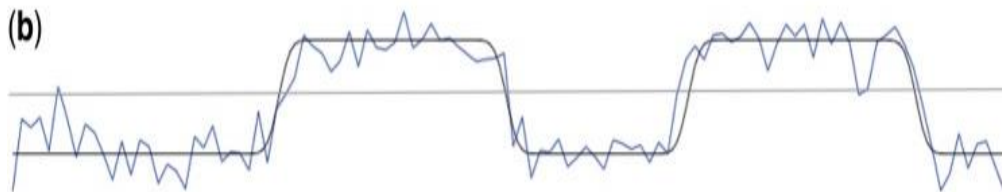
Psycho-physiological Interaction (PPI)

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

Main effect of task (Faces - objects)

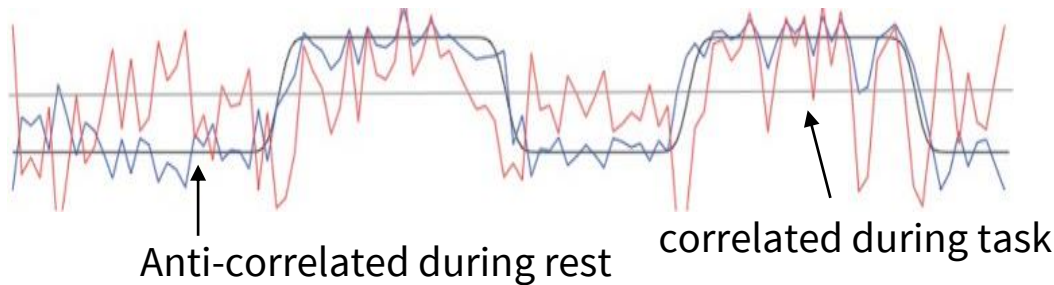


Activity in parietal cortex



Seed region

PPI regressor = HRF convolved task x seed ROI regressors



Whole brain

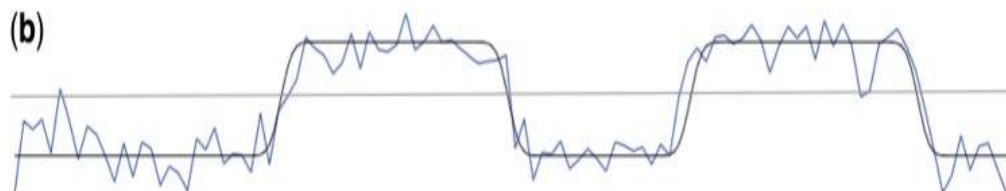
Psycho-physiological Interaction (PPI)

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

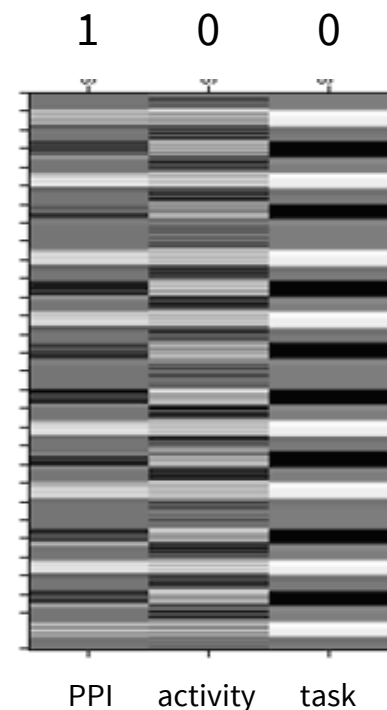
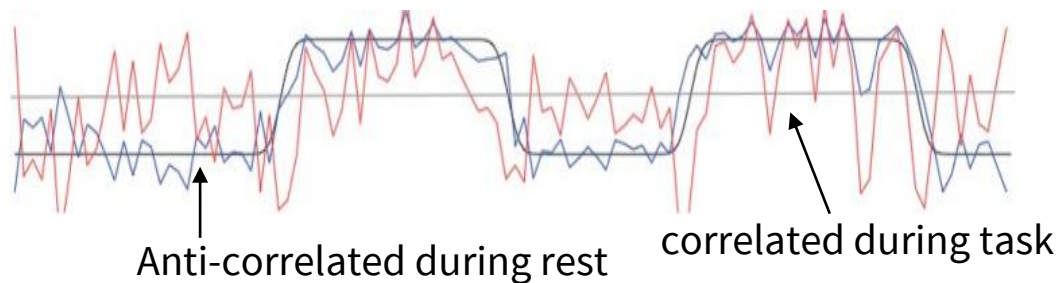
Main effect of task (Faces - Objects)



Activity in parietal cortex



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)

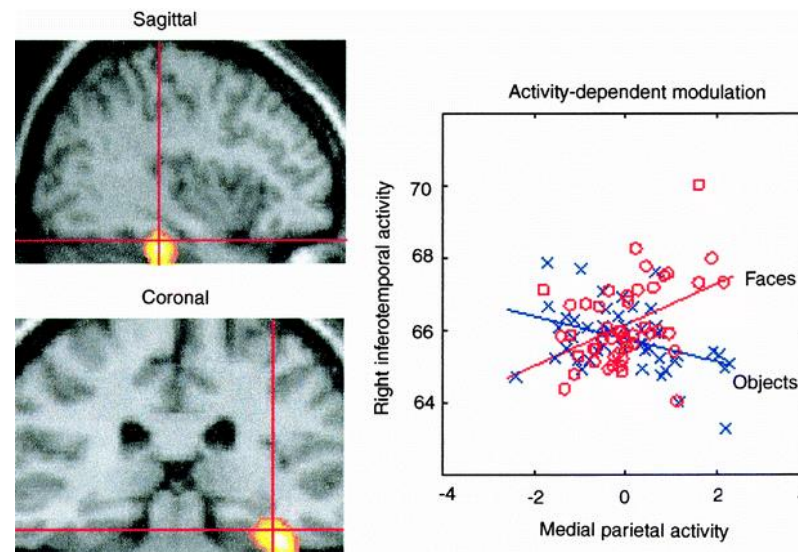
Learning

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

Orthogonal contrasts reduce correlation between PPI vector and the regressors of no interest

Psycho-physiological Interaction (PPI)

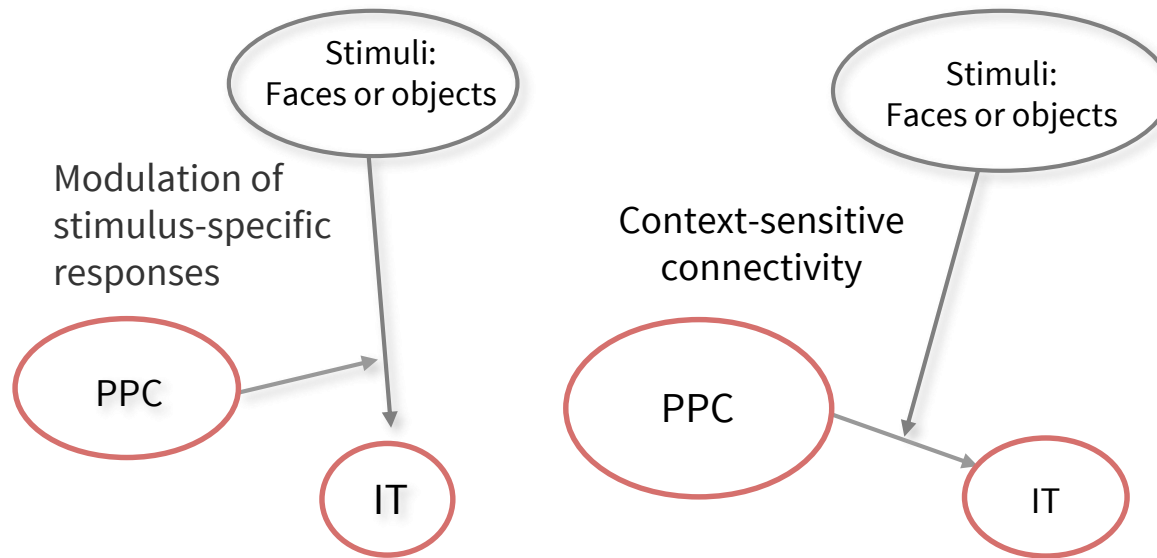
ITC can differentiate between faces and objects **only if parietal activity is high**



The right fusiform region responds to faces (relative to objects) when, and only when, parietal activity is high

Psycho-physiological interactions (PPI)

Interpretation



Experimental designs



Subtraction

Conjunction

Factorial

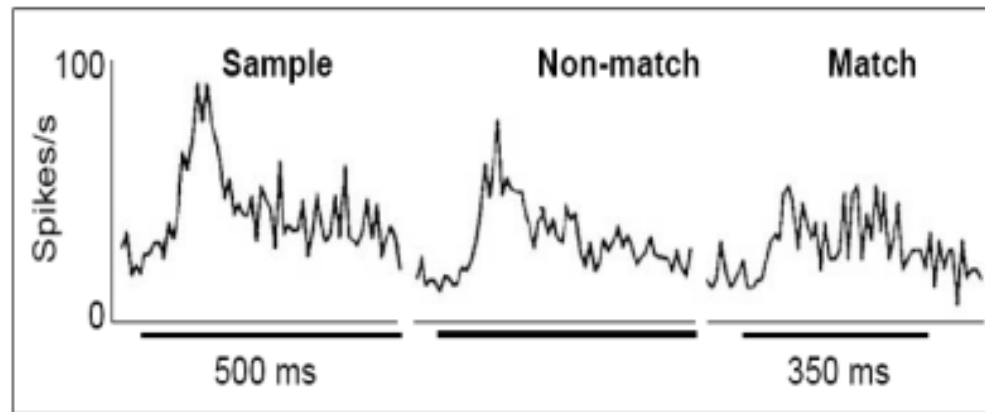
Parametric

Psycho-physiological Interaction (PPI)

fMRI adaptation

Repetition suppression

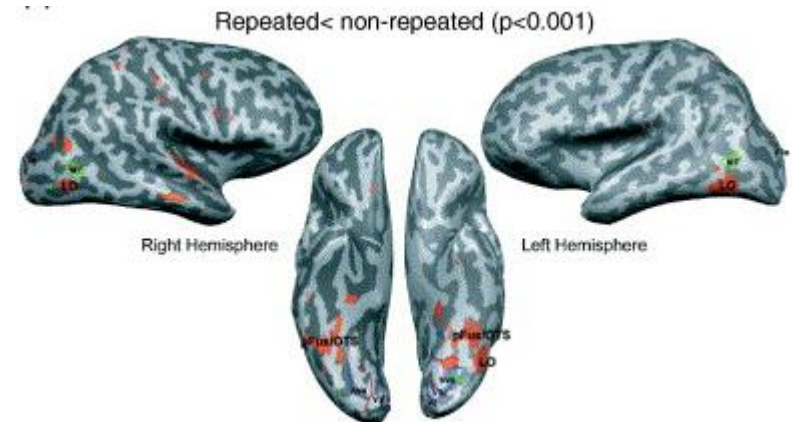
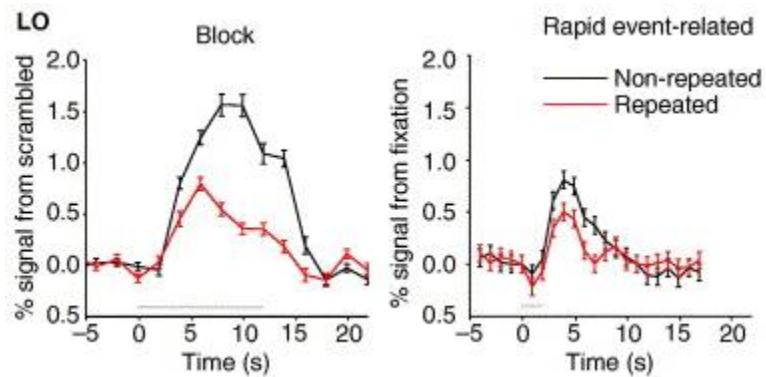
Neurons in inferotemporal cortex display a diminished response if a stimulus is repeated



Li et al. (1993),
Grill-Spector (2006)

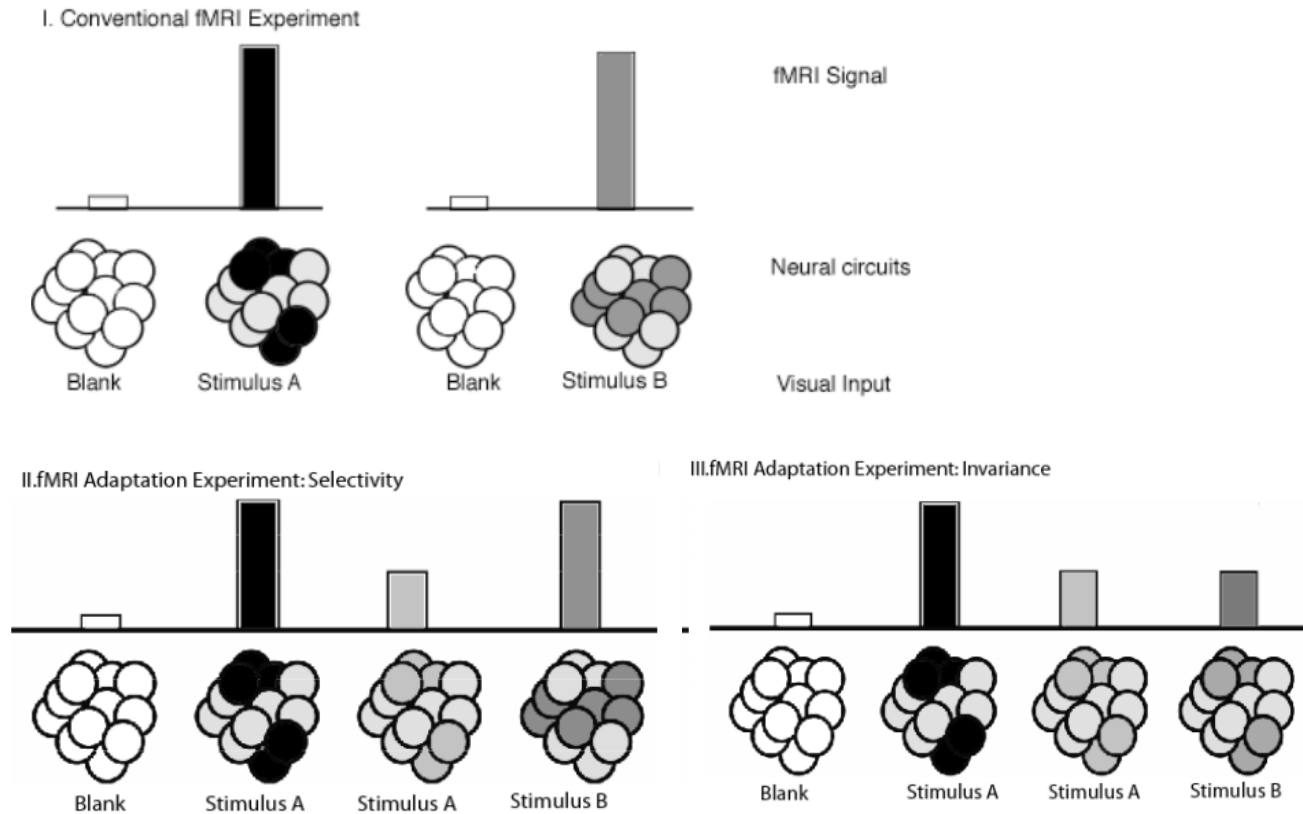
fMRI adaptation

Object-repetition effects measured with fMRI



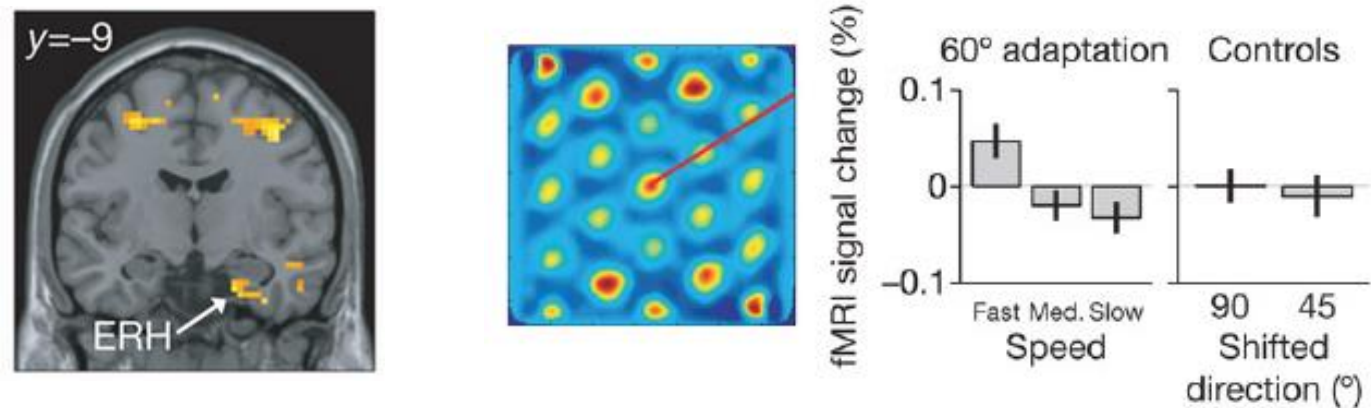
Grill-Spector et al. (2006)

Conventional fMRI vs fMRI adaptation



Kourtzi & Grill-Spector (2005)

fMRI adaptation as a tool for measuring grid cells in human entorhinal cortex



Doeller et al. (2010)



Questions?
