University of Zurich UZH

ETH Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Translational Neuromodeling Unit

Methods & Models for fMRI Analysis 2018

Experimental design of fMRI studies

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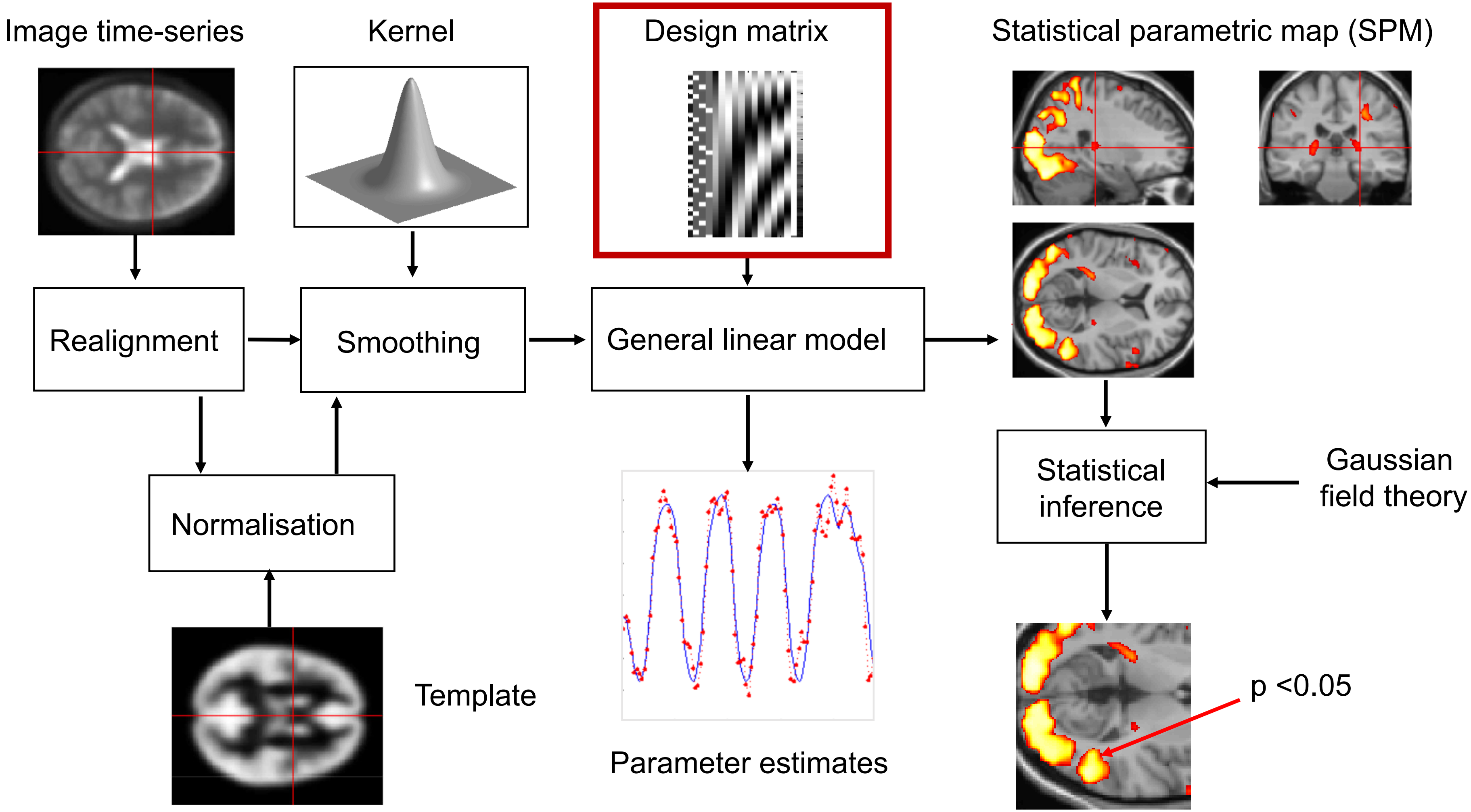
With many thanks for slides & images to:

Sara Tomiello,
Sandra Iglesias,
Klaas Enno Stephan,
FIL Methods group,
Christian Ruff

Overview of SPM



Overview of SPM

Research question:
Which neuronal structures support face recognition?

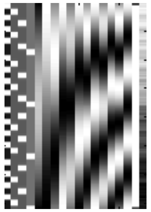
↓

Hypothesis:
The fusiform gyrus is implicated in face recognition

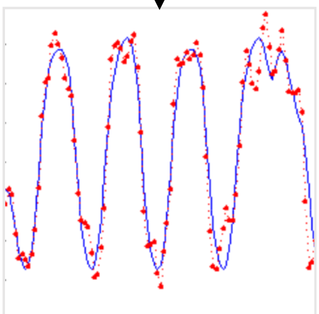
↓

Experimental design

Design matrix

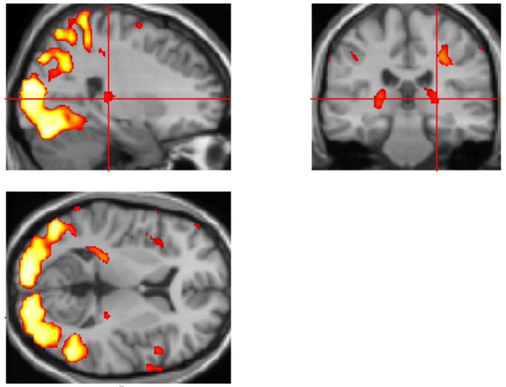


General linear model



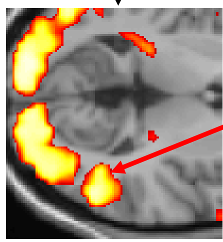
Parameter estimates

Statistical parametric map (SPM)



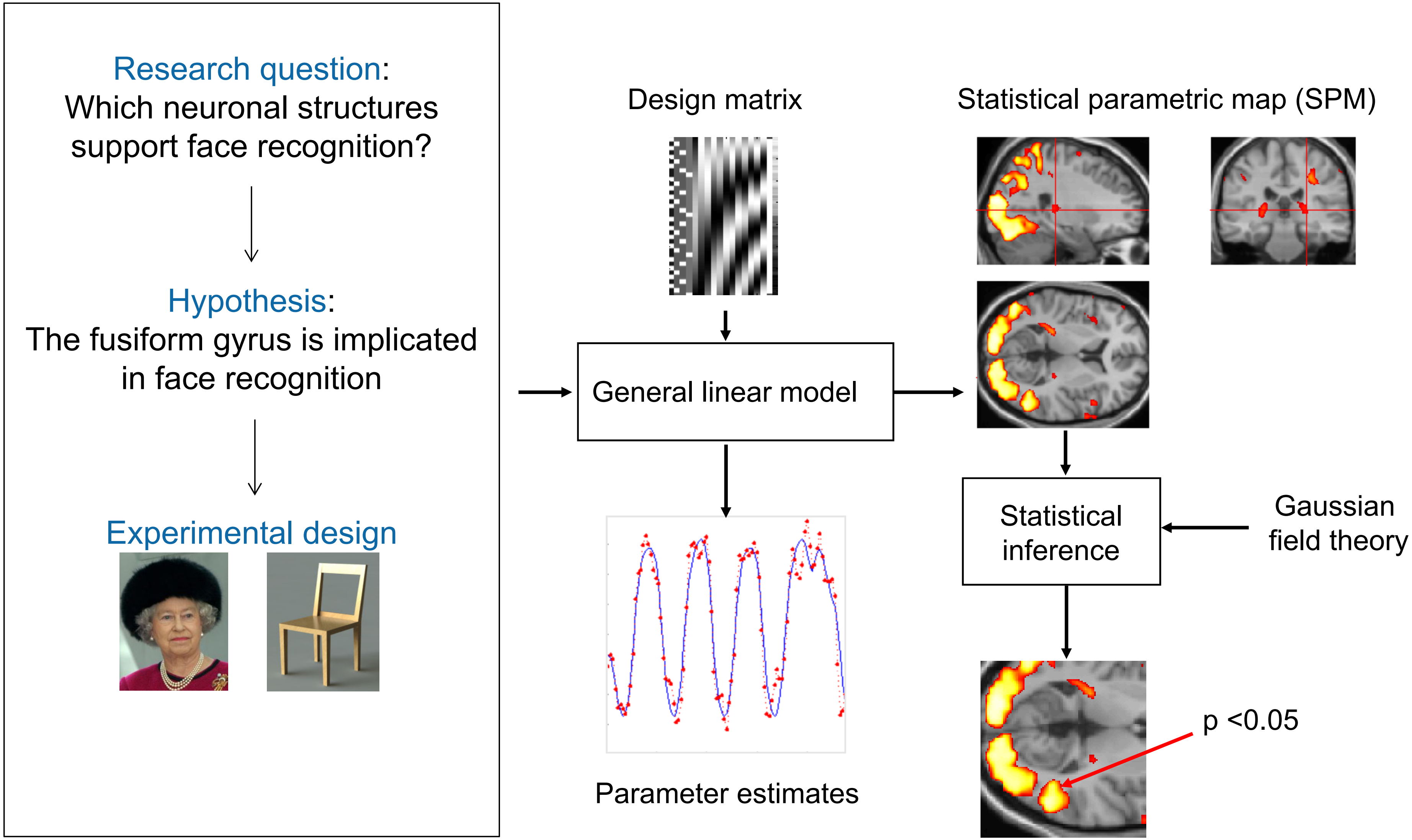
Statistical inference

Gaussian field theory



$p < 0.05$

Overview of SPM



Overview Experimental Designs

- Categorical designs

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

- Parametric designs

Linear	- Adaptation, cognitive dimensions
Nonlinear	- Polynomial expansions, neurometric functions

- Factorial designs

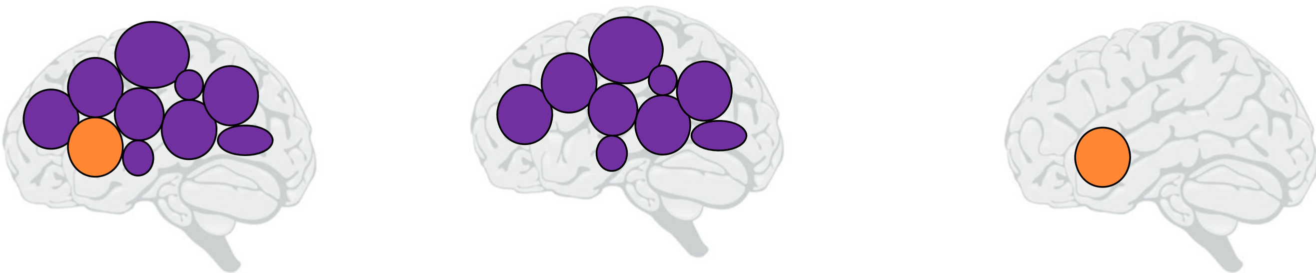
Categorical	- Interactions and pure insertion
Parametric	- Linear and nonlinear interactions
	- Psychophysiological interactions

Categorical Designs

Subtraction

- Aim: Find neuronal structures underlying a *single* process *P*
- Procedure: Under the critical assumption of „pure insertion“

[task with ***P***] – [control task without ***P***] = ***P***

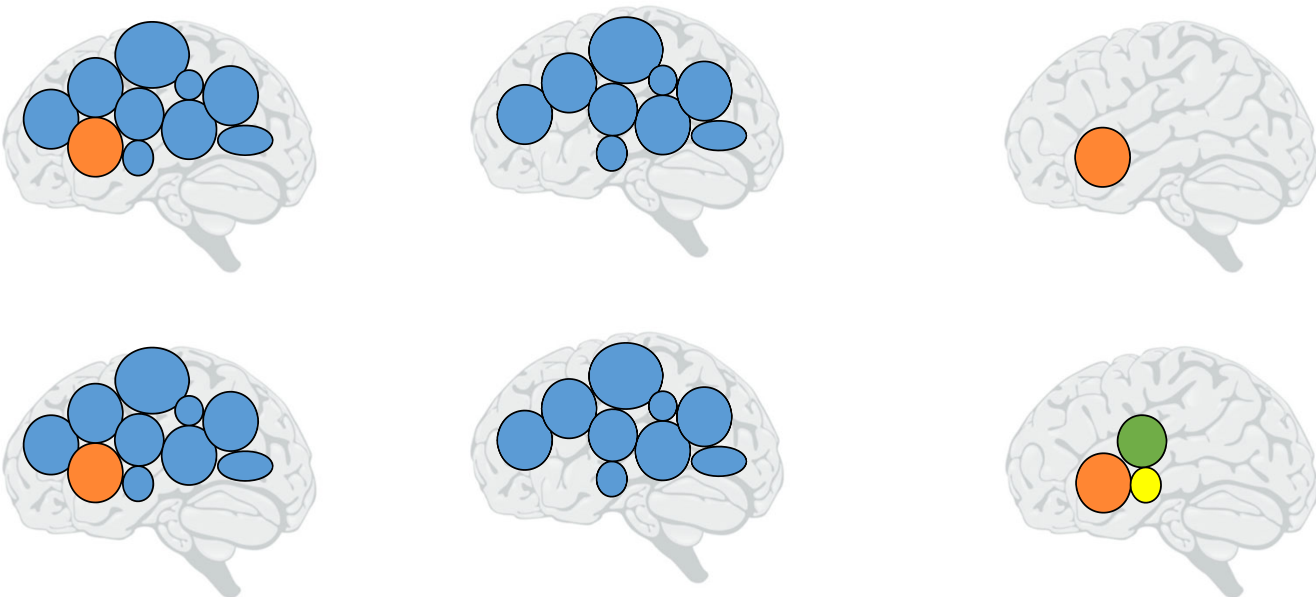


Categorical Designs

Subtraction

- Aim: Find neuronal structures underlying a *single* process *P*
- Procedure: Under the critical assumption of „pure insertion“

[task with ***P***] – [control task without ***P***] = ***P***



Categorical Designs

Subtraction, Example

Cognitive subtraction originated with reaction time experiments
(F. C. Donders).

Measure the time for a process to occur by comparing two reaction times, one which has the same components as the other + the process of interest.

Example:

T1: Hit a button when you see a light
T2: Hit a button when the light is green but not red
T3: Hit the left button when the light is green and the right button when the light is red

T2 – T1 = time to make discrimination between light color

T3 – T2 = time to make a decision

F.C. Donders 1868

Assumption of pure insertion:
You can insert a component process into a task without disrupting the other components.

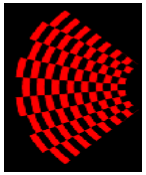
Categorical Designs

Subtraction: Baseline problem

Which neuronal structures support face recognition ?

- „Distant“ stimuli

\-



➔ Several components differ

- „Related“ stimuli

„Queen!“

\-

„Aunt Jenny?“

➔ Additional processes in control condition (?)

- Same stimuli, different task

Name Person!

\-

Name Gender!

➔ Interaction of task and stimuli (specificity for naming)

(i.e. do task differences depend on stimuli chosen (?))

Categorical Designs

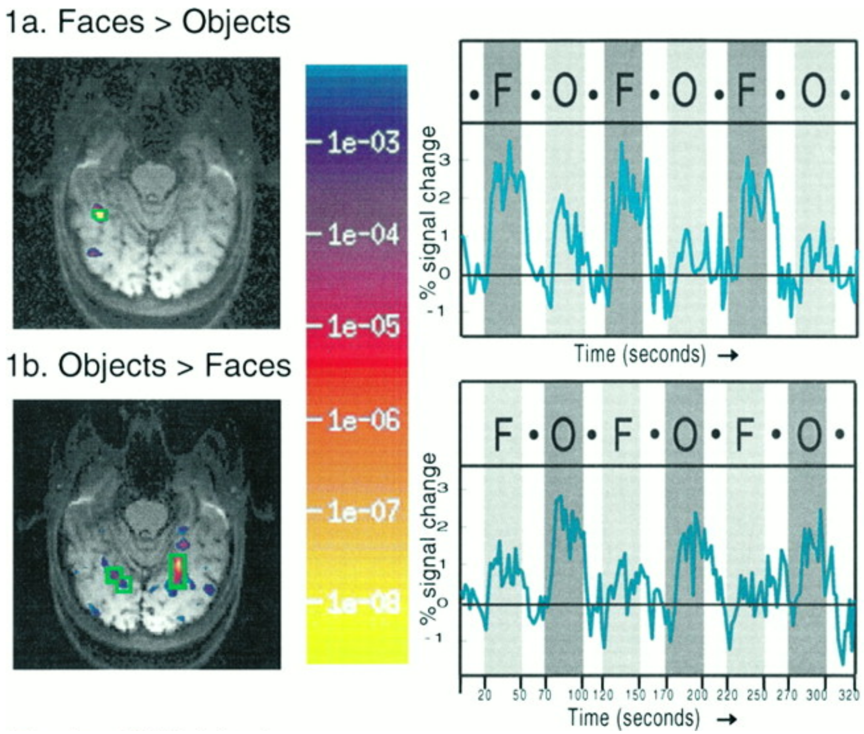
Subtraction, Example

Experimental design

Face viewing: F
Object viewing: O

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

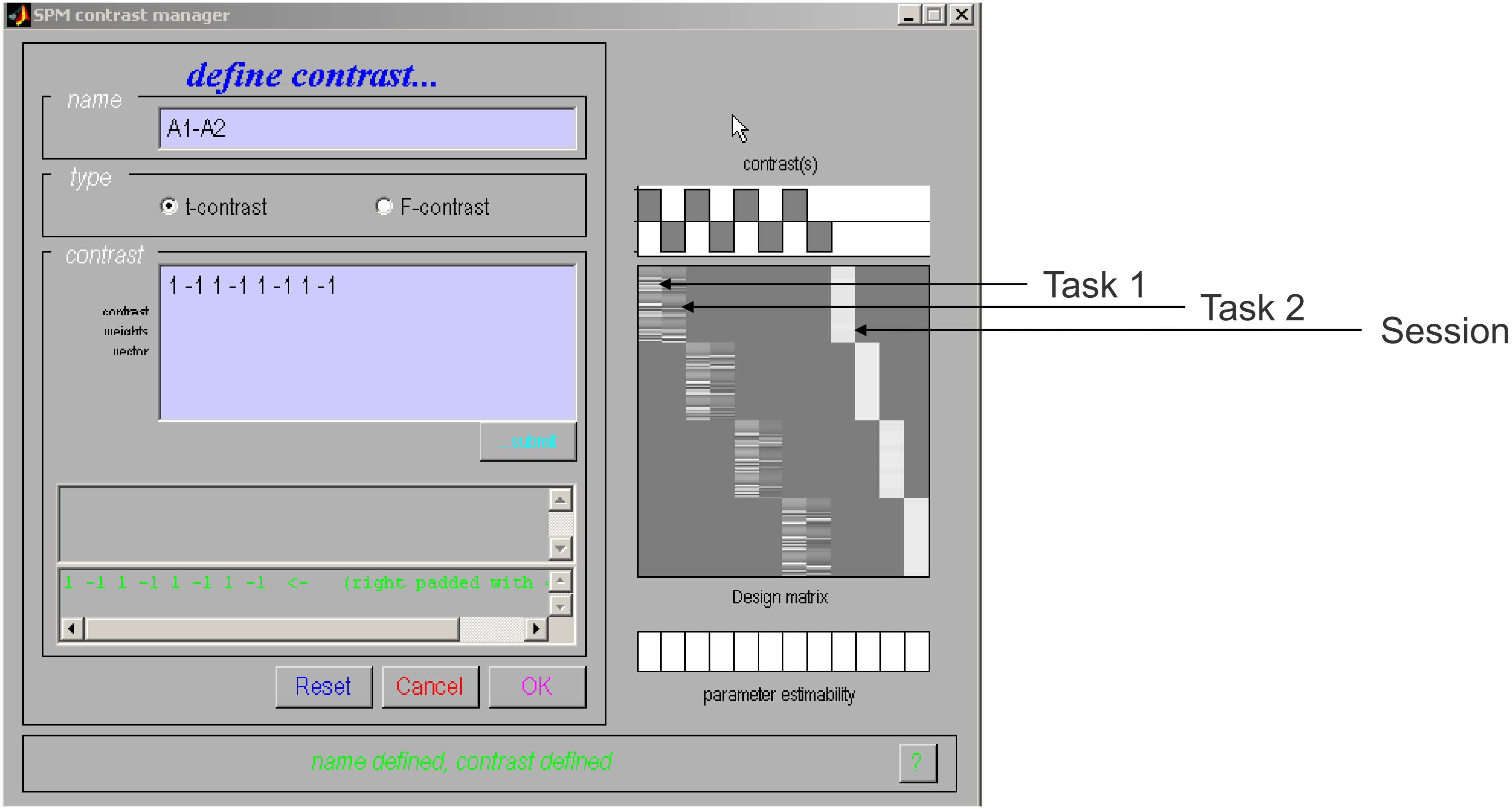
…under assumption of pure insertion



Kanwisher et al., 1997, J. Neurosci.

Categorical Designs

Subtraction, Example SPM



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Categorical Designs

Conjunction

- One way to minimize the baseline/pure insertion problem is to isolate the same process by two or more separate comparisons, and inspect the resulting simple effects for commonalities

- A test for such activation common to several independent contrasts is called “conjunction”

- Conjunctions can be conducted across a whole variety of different contexts:
  - tasks
  - stimuli
  - senses (vision, audition)
  - etc.

- Note: the contrasts entering a conjunction must be orthogonal

Categorical Designs

Conjunction, Example

Which neural structures support object recognition, independent of task (naming vs. viewing)?

Task (1/2)

Stimuli (A/B)		Viewing	Naming
	Colours	A1	A2
	Objects	B1	B2

Visual Processing: V
Object Recognition: R
Phonological Retrieval: P

Categorical Designs

Conjunction, Example

Which neural structures support object recognition, independent of task (naming vs. viewing)?

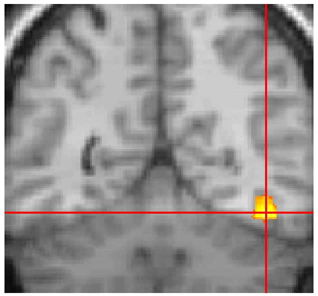
Task (1/2)

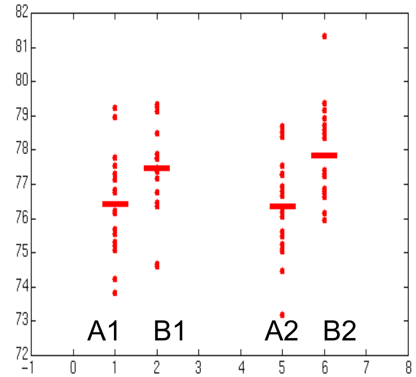
Stimuli (A/B)	Viewing	Naming
Colours	**A1** Visual Processing V	**A2** Visual Processing V Phonological Retrieval P
Objects	**B1** Visual Processing V Object Recognition R	**B2** Visual Processing V Phonological Retrieval P Object Recognition R

(Object - Colour viewing) [B1 - A1]
&
(Object - Colour naming) [B2 – A2]

[V,R - V] & [P,V,R - P,V] = R & R = R

Common object recognition response (R)

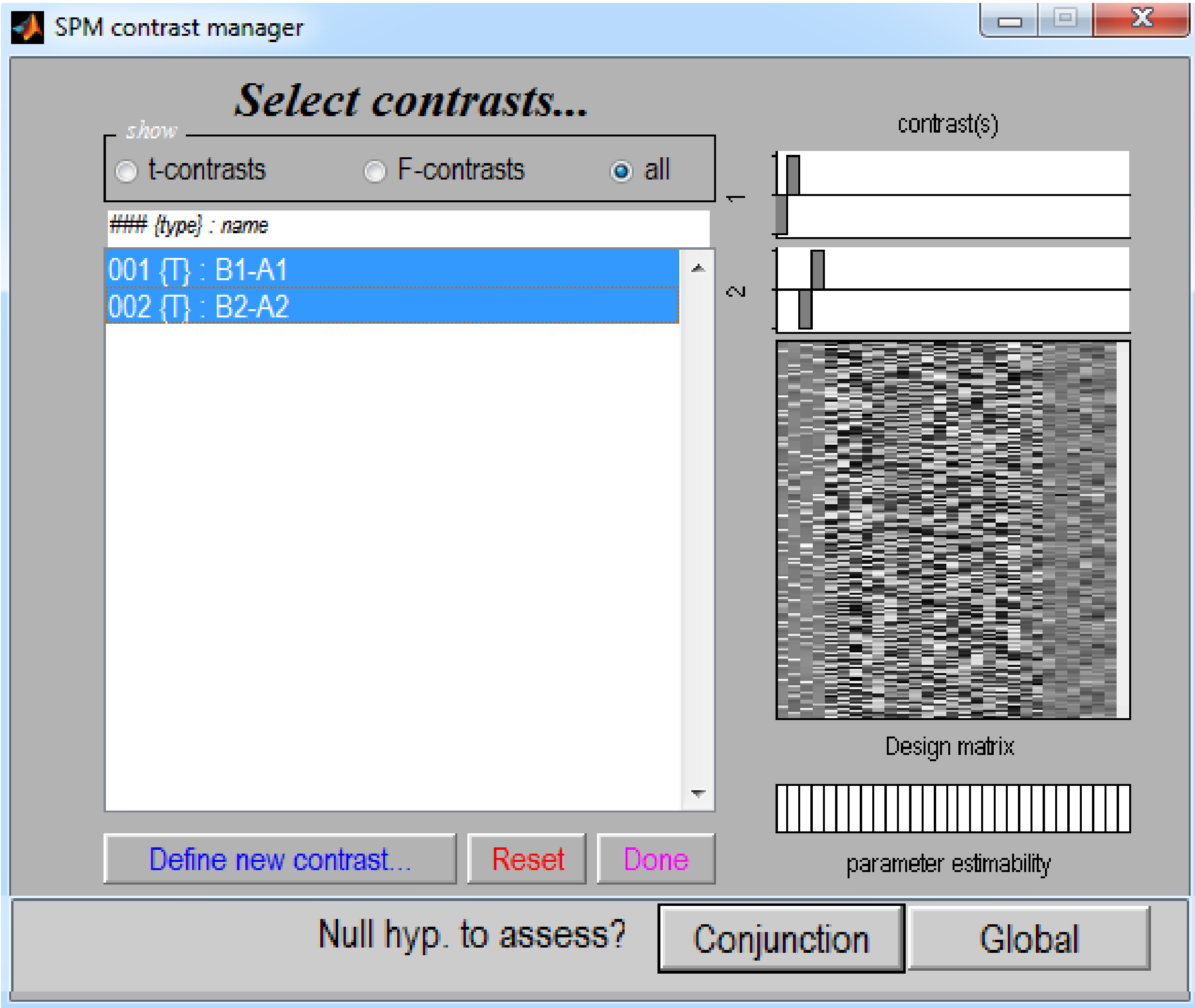




Price et al. 1997, NeuroImage

Categorical Designs

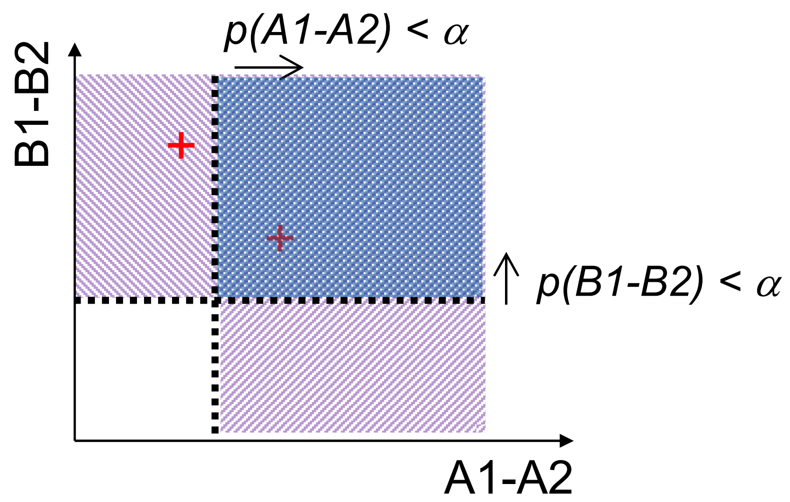
Conjunction, Example SPM



Categorical Designs

Types of Conjunctions

- Test of global null hypothesis:
  Significant set of consistent effect
  - ➔ "Which voxels show effects of similar direction (but not necessarily individual significance) across contrasts?"
  - ➔ H1: k > 0
  - ➔ H0: No contrast is significant: k = 0
  - ➔ Does **not** correspond to a logical AND !
- Test of conjunction null hypothesis:
  Set of consistently significant effects
  - ➔ "Which voxels show, for each specified contrast, significant effects?"
  - ➔ H1: k = n
  - ➔ H0: Not all contrasts are significant: k < n
  - ➔ Corresponds to a logical AND



k = effects
n = contrasts

Friston et al., 2005, NeuroImage
Nichols et al., 2005, NeuroImage

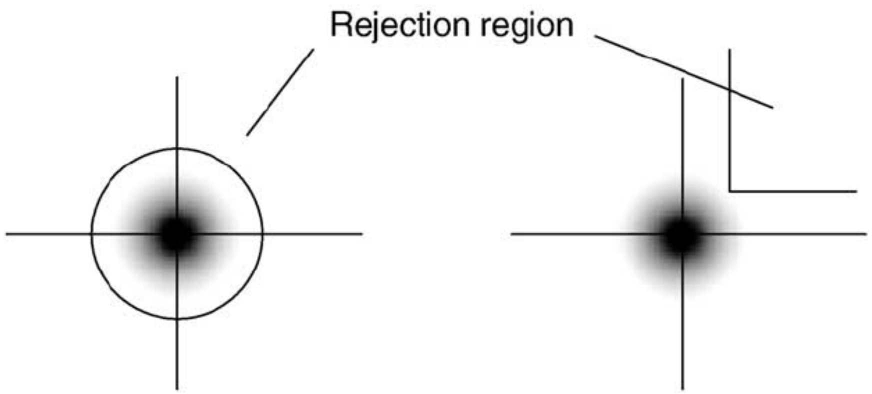
Categorical Designs

Conjuction, Global Null Hypothesis

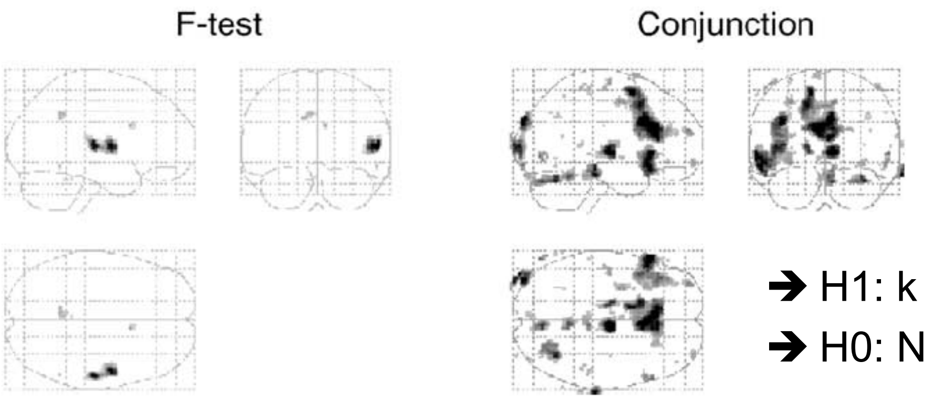
- Based on the "minimum t statistic":
  - imagine a voxel where contrast A gives t=1 and contrast B gives t=1.4
  - neither t-value is significant alone, but the fact that both values are larger than zero suggests that there may be a real effect
- Test: compare the observed minimum t value to the null distribution of minimal t-values for a given set of contrasts
  - assuming independence between the tests, one can find uncorrected and corrected thresholds for a minimum of two or more t-values (Worsley & Friston, Stat. Probab. Lett., 2000, 47 (2), 135–140)
  - this means the contrasts have to be orthogonal!

Categorical Designs

F-test vs. Conjunction based on global null



grey area:
bivariate t-distriution
under global null hypothesis



➔ H1: k > 0
➔ H0: No contrast is significant: k = 0

Friston et al., 2005, NeuroImage

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  Linear - Adaptation, cognitive dimensions

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  Categorical - Interactions and pure insertion

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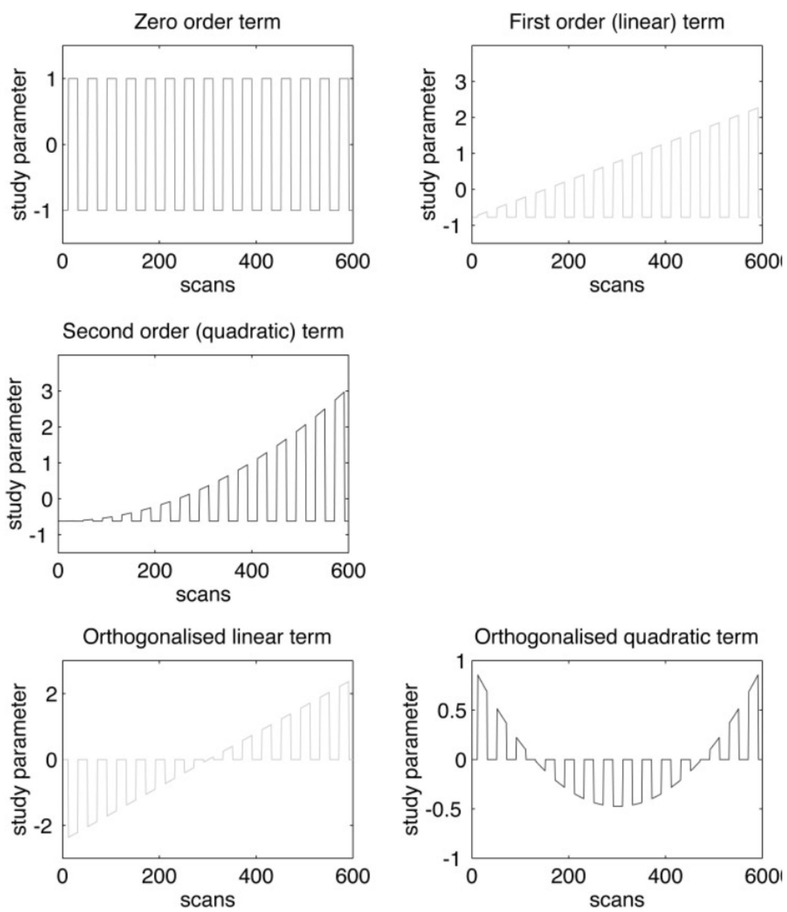
Parametric Designs

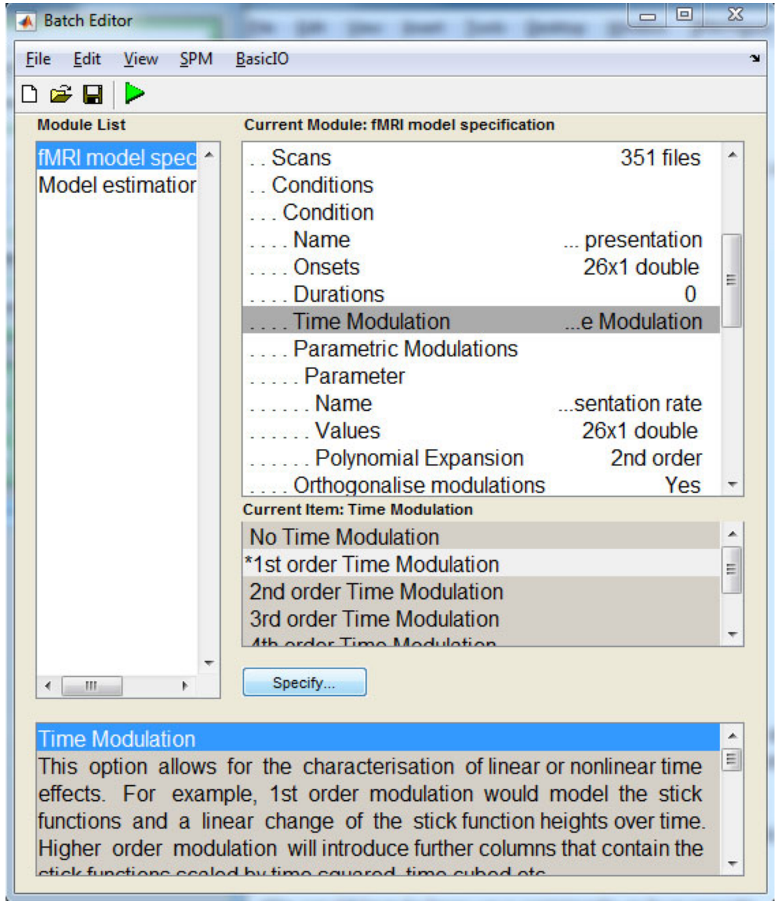
- Parametric designs approach the baseline problem by:
  - varying the stimulus-parameter of interest on a continuum, in multiple (n>2) steps...
  - ... and relating measured BOLD signal to this parameter

- Possible tests for such relations are manifold:
  - Linear
  - Nonlinear: Quadratic/cubic/etc. (polynomial expansion)
  - Model-based (e.g. predictions from learning models)

Parametric Designs

Parametric modulation of regressors by time

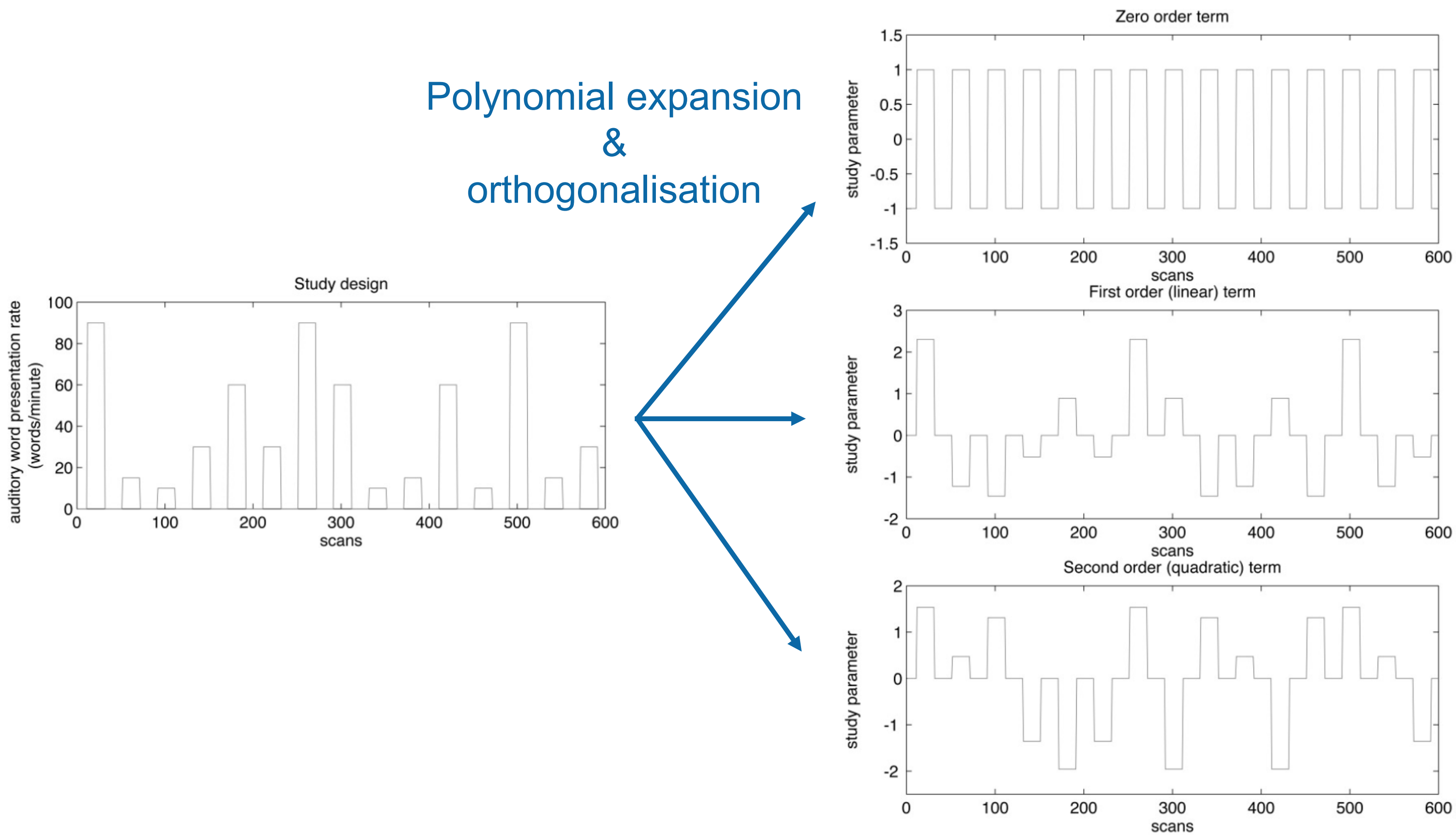




Büchel et al., 1998, NeuroImage

Parametric Designs

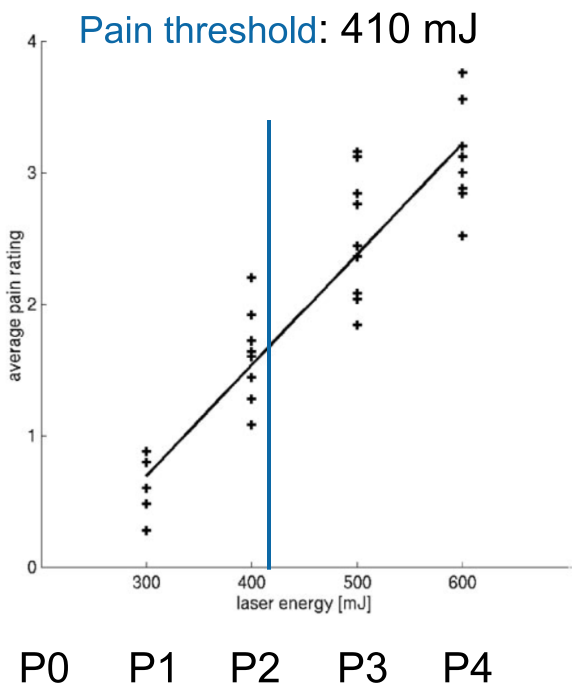
Parametric modulation of regressors



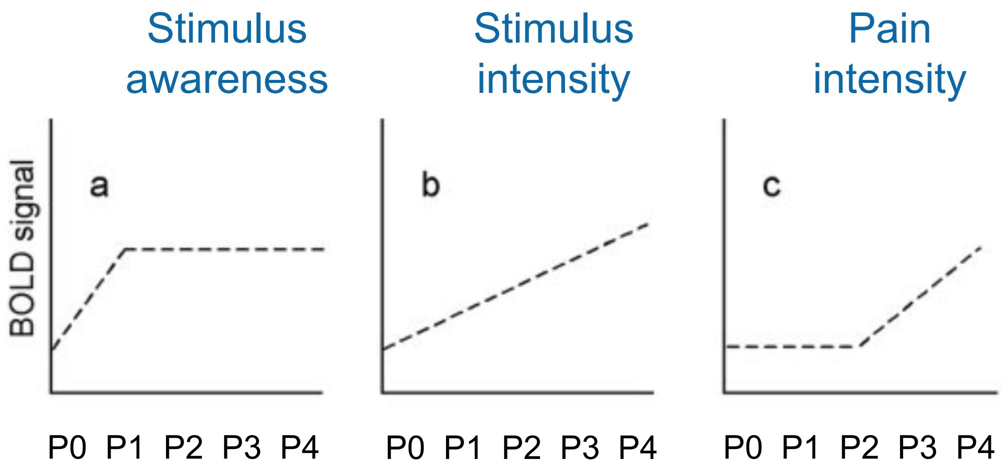
Büchel et al., 1998, NeuroImage

Parametric Designs

Investigating neurometric functions



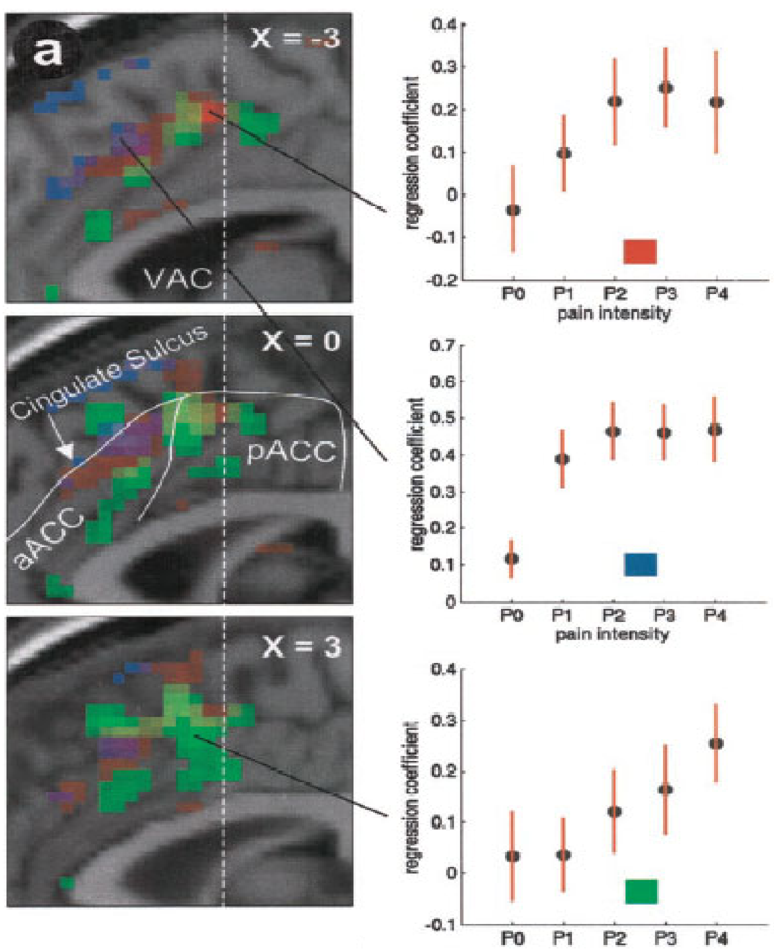
P0-P4: Variation of intensity of a laser stimulus applied to the right hand (0, 300, 400, 500, and 600 mJ)



Büchel et al., 2002, JNeurosci

Parametric Designs

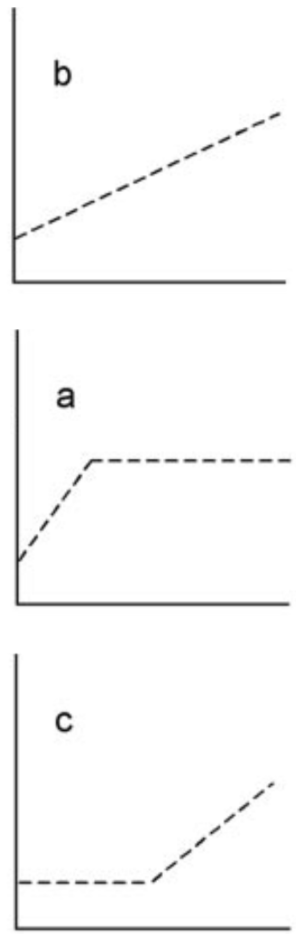
Investigating neurometric functions



→ Stimulus intensity
dorsal pACC

→ Stimulus awareness
cingulate sulcus aACC

→ Pain intensity
ventral pACC



Büchel et al., 2002, J Neurosci

Parametric Designs

Model-based regressors

- General idea:
  generate predictions from a computational model, e.g. of learning or decision-making

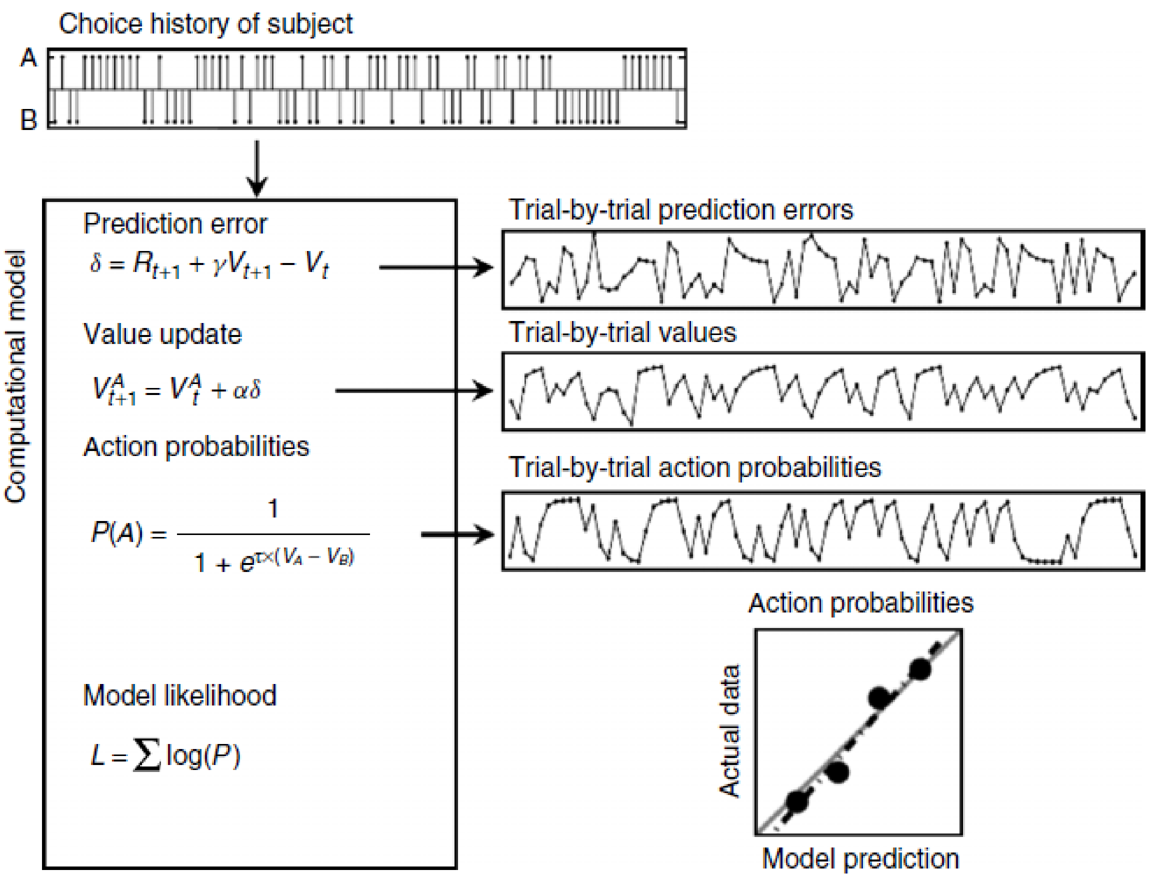
- Commonly used models:
  - Rescorla-Wagner learning model
  - Temporal difference (TD) learning model
  - Bayesian models

- Predictions used to define regressors

- Inclusion of these regressors in a GLM and testing for significant correlations with voxel-wise BOLD responses

Parametric Designs

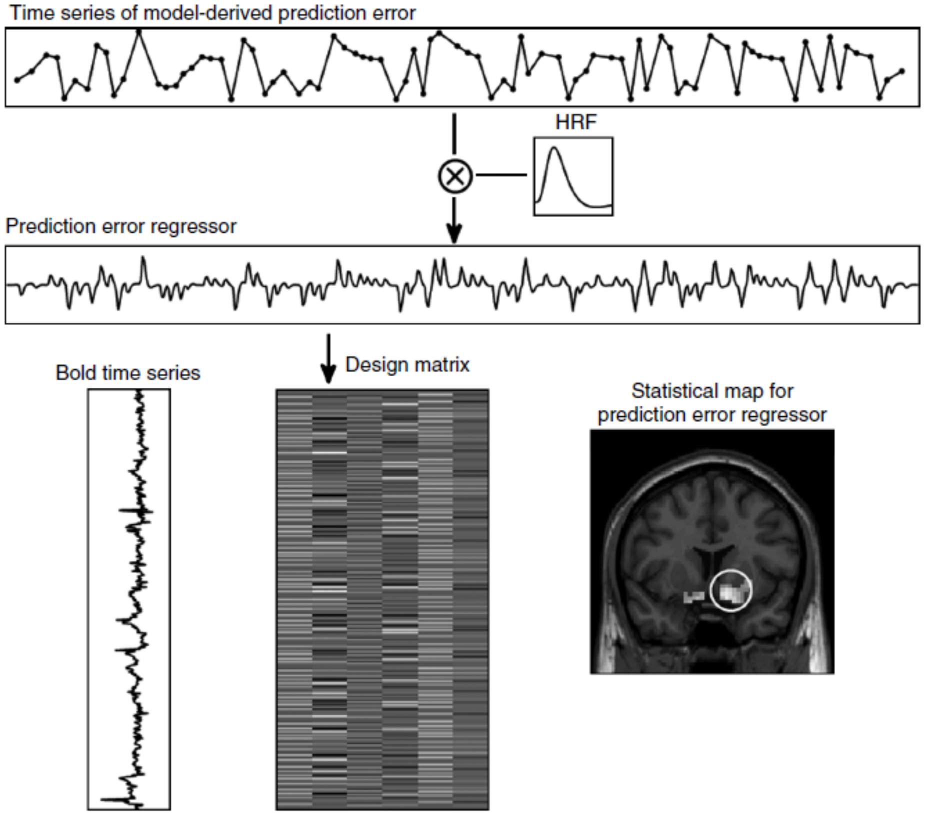
Model-based fMRI analysis, Example



Gläscher & O'Doherty, 2010, WIREs Cogn. Sci.

Parametric Designs

Model-based fMRI analysis, Example

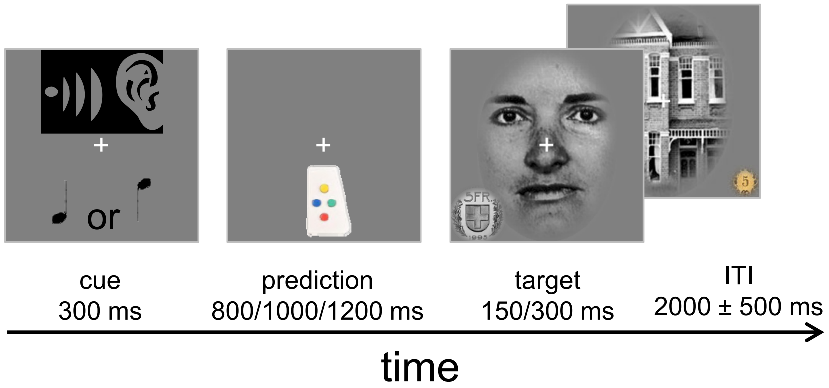


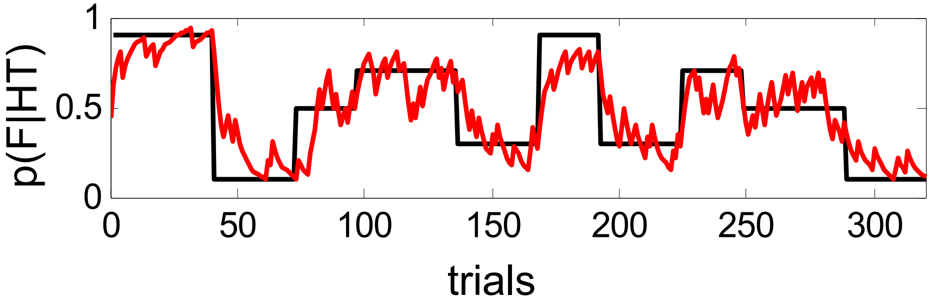
Gläscher & O‘Doherty, 2010, WIREs Cogn. Sci.

Parametric Designs

Model-based fMRI analysis, Example

Hierarchical prediction errors
about sensory outcome and its probability





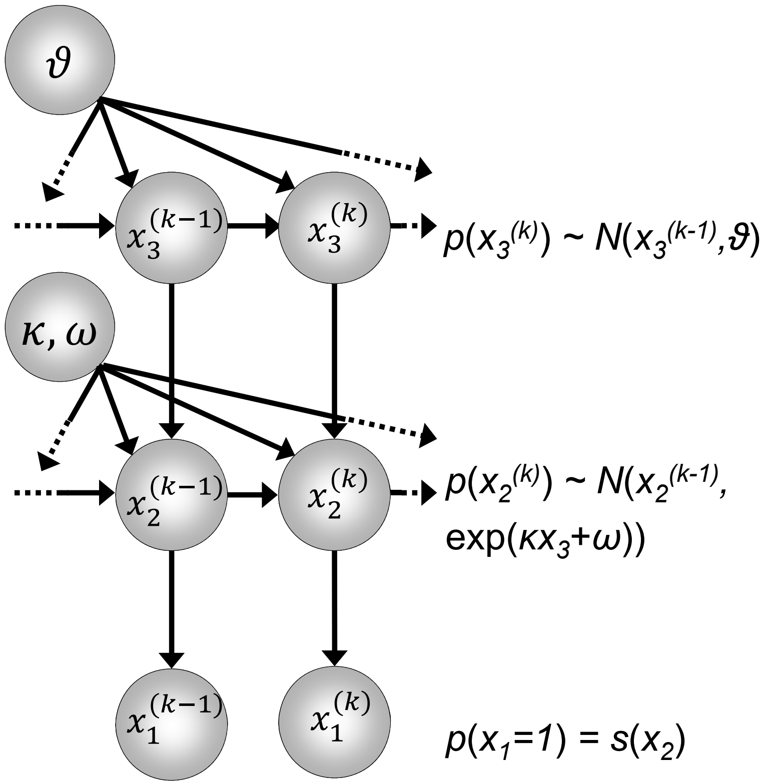
Iglesias et al., 2013, Neuron

Parametric Designs

Model-based fMRI analysis, Example

The Hierarchical Gaussian Filter (HGF)

$$\Delta\mu_i \propto \frac{\hat{\pi}_{i-1}}{\pi_i} PE_{i-1}$$



$$\varepsilon_3 \propto \sigma_3^{(k)} \delta_2^{(k)}$$

$$\varepsilon_2 = \sigma_2^{(k)} \delta_1^{(k)}$$

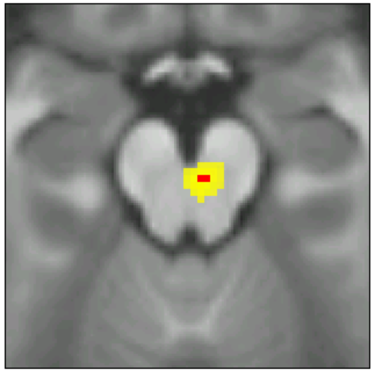
Mathys et al., 2011, Front Hum Neurosci.

Parametric Designs

Model-based fMRI analysis, Example

Hierarchical prediction errors
about sensory outcome and its probability

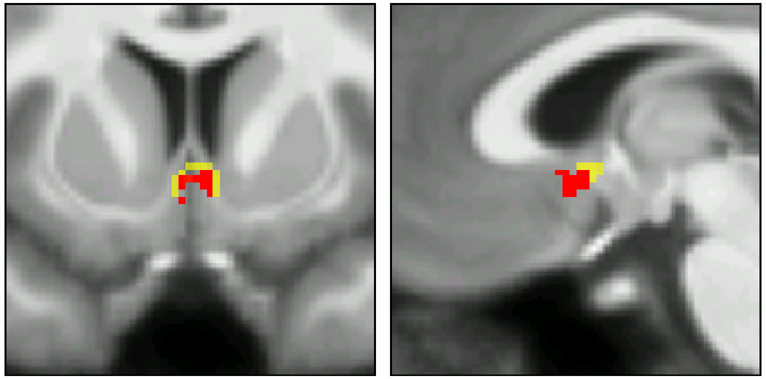
ε_2 in midbrain (N=45)



$$\varepsilon_2 = \sigma_2^{(k)} \delta_1^{(k)}$$

p<0.05, whole brain FWE corrected
p<0.05, SVC FWE corrected

ε_3 in basal forebrain (N=45)



$$\varepsilon_3 \propto \sigma_3^{(k)} \delta_2^{(k)}$$

p<0.05, SVC FWE corrected
p<0.001, uncorrected

Iglesias et al., 2013, Neuron

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Factorial Designs

Main effects and Interactions

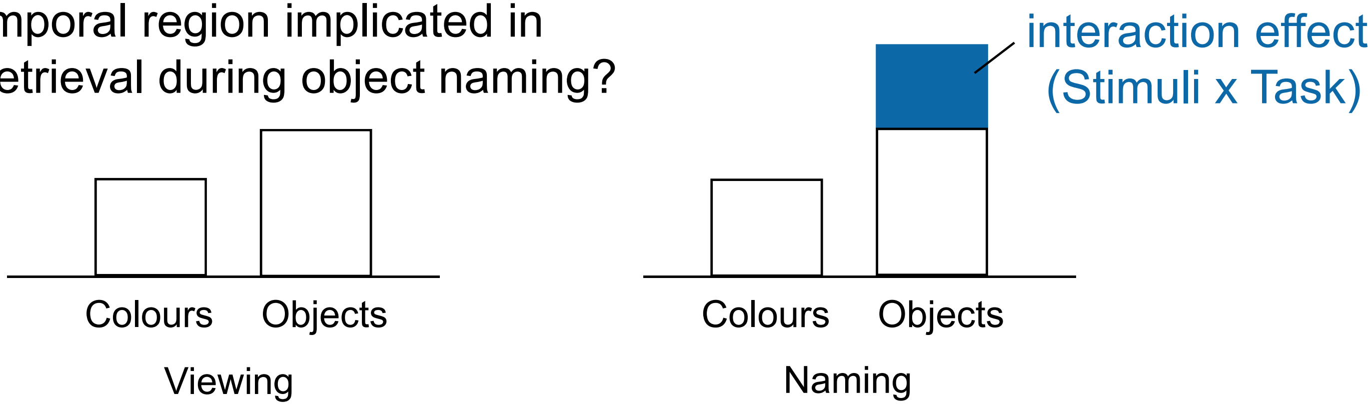
Task (1/2)

Stimuli (A/B)		Viewing	Naming
	Colours	A1	A2
	Objects	B1	B2

- **Main effect of task**: (A1 + B1) – (A2 + B2)
- **Main effect of stimuli**: (A1 + A2) – (B1 + B2)
- **Interaction of task and stimuli**:
  Can show a failure of pure insertion

  (A1 – B1) – (A2 – B2)

Is the inferotemporal region implicated in phonological retrieval during object naming?



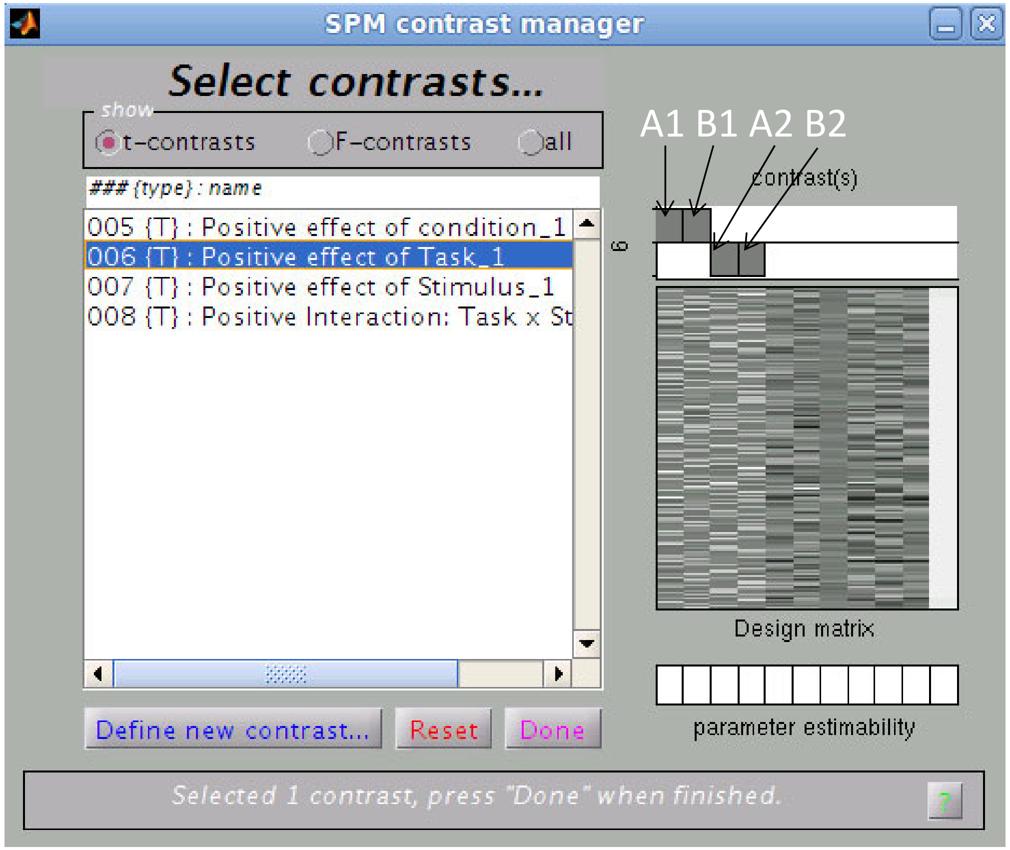
Factorial Designs

Main effect, Example SPM

Task (1/2)

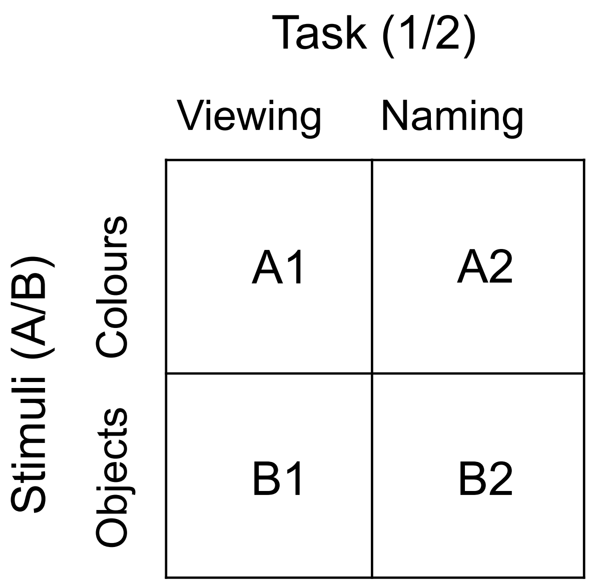
Stimuli (A/B)		Viewing	Naming
	Colours	A1	A2
	Objects	B1	B2

Main effect of task:
(A1 + B1) – (A2 + B2)

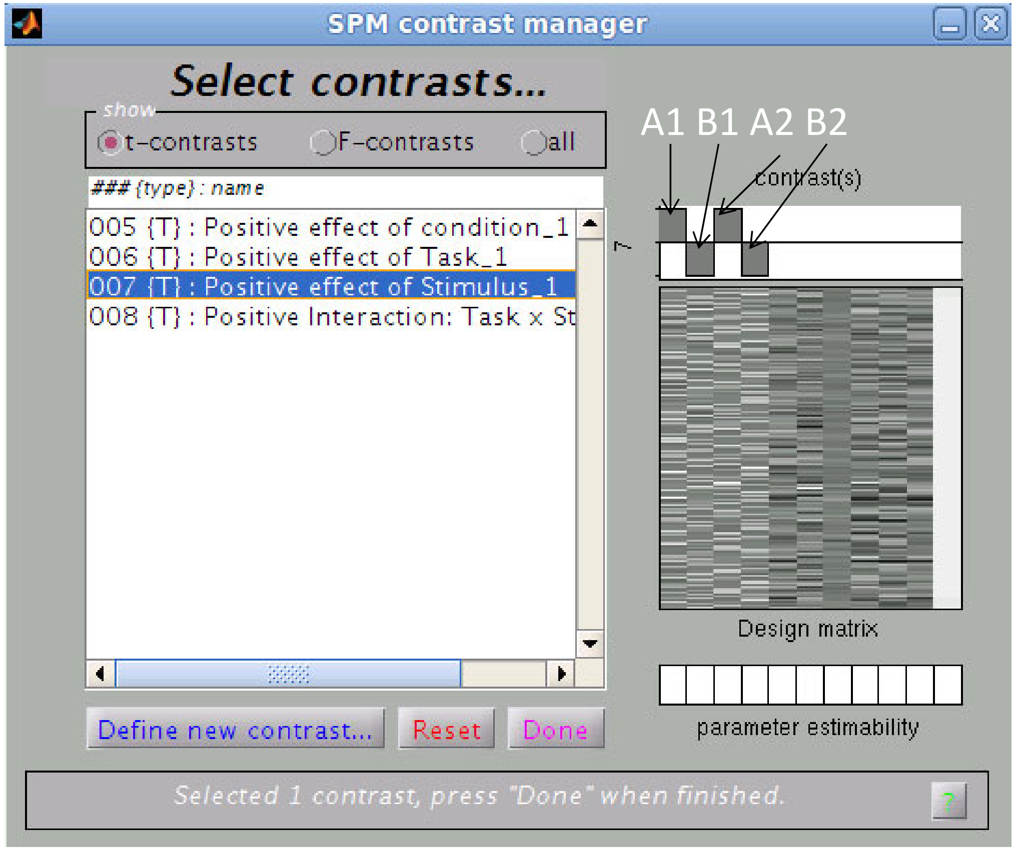


Factorial Designs

Main effect, Example SPM



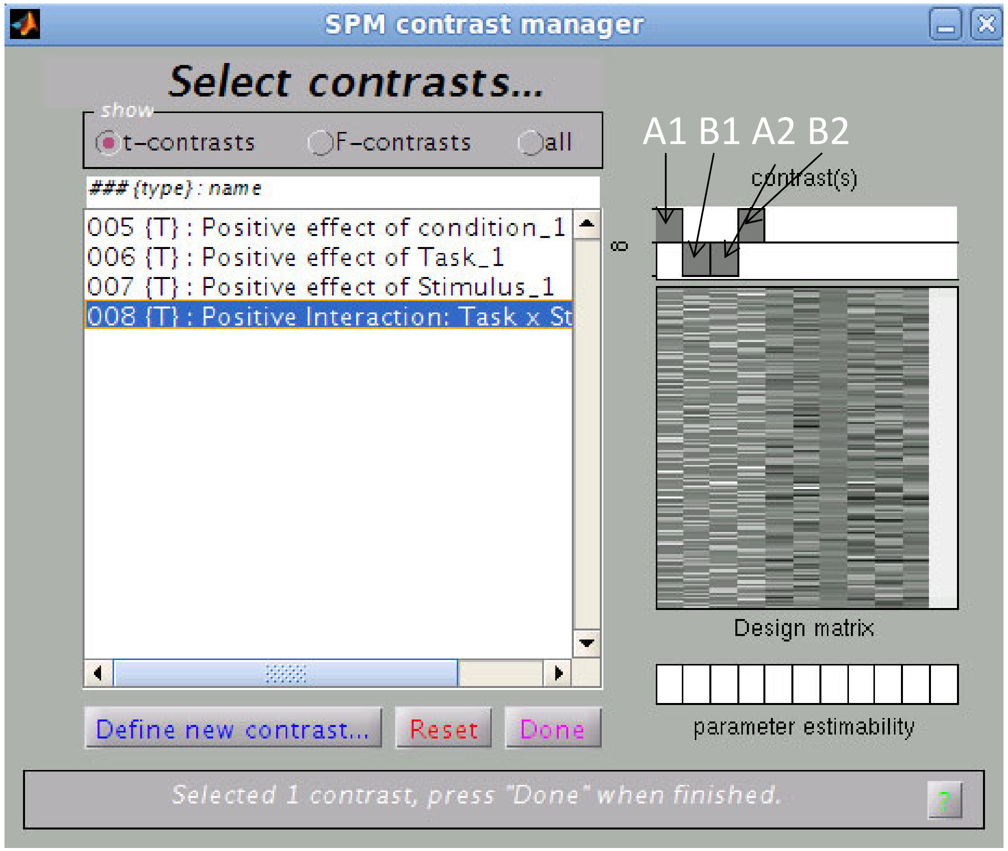
Main effect of stimuli:
(A1 + A2) – (B1 + B2)



Factorial Designs

Interaction, Example SPM

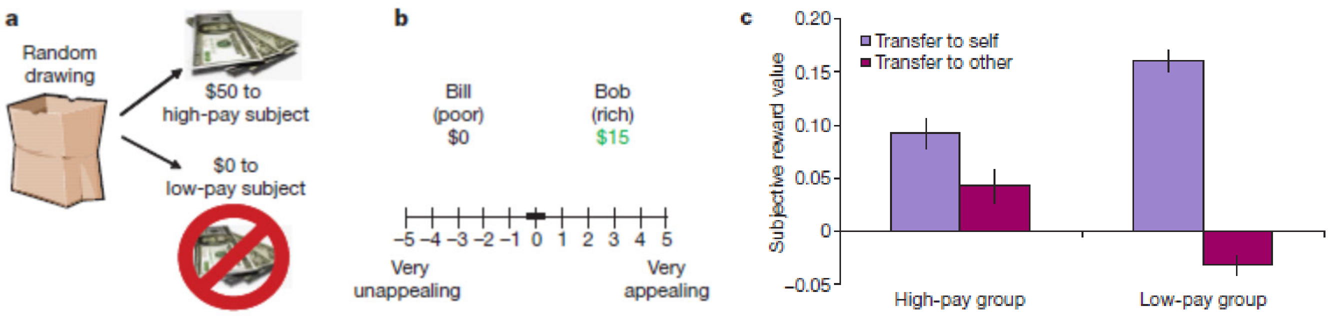
Stimuli (A/B)	Task (1/2): Viewing	Task (1/2): Naming
Colours	A1	A2
Objects	B1	B2

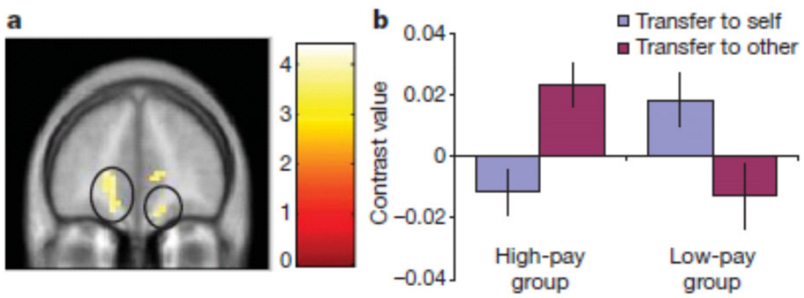


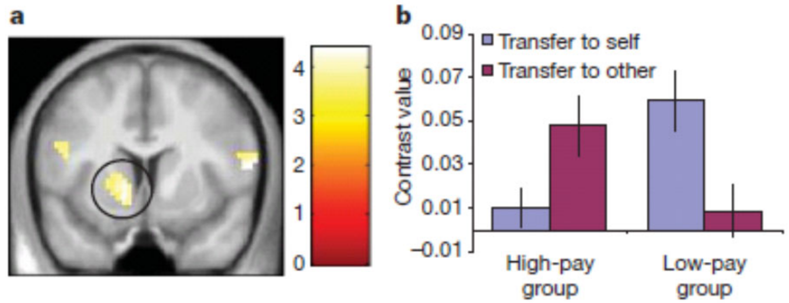
Interaction of task and stimuli:
(A1 – B1) – (A2 – B2)

Factorial Designs

Example







Tricomi et al., 2010, Nature

Factorial Designs

Psycho-Physiological Interactions (PPIs)

Task factor

Stimulus factor		Task A	Task B
	Stim 1	T_A/S_1	T_B/S_1
	Stim 2	T_A/S_2	T_B/S_2

GLM of a 2x2 factorial design:

$$
\begin{aligned}
y = \; & (T_A - T_B)\,\beta_1 && \leftarrow \text{main effect of task} \\
& + (S_1 - S_2)\,\beta_2 && \leftarrow \text{main effect of stim. type} \\
& + (T_A - T_B)(S_1 - S_2)\,\beta_3 && \text{interaction} \\
& + e
\end{aligned}
$$

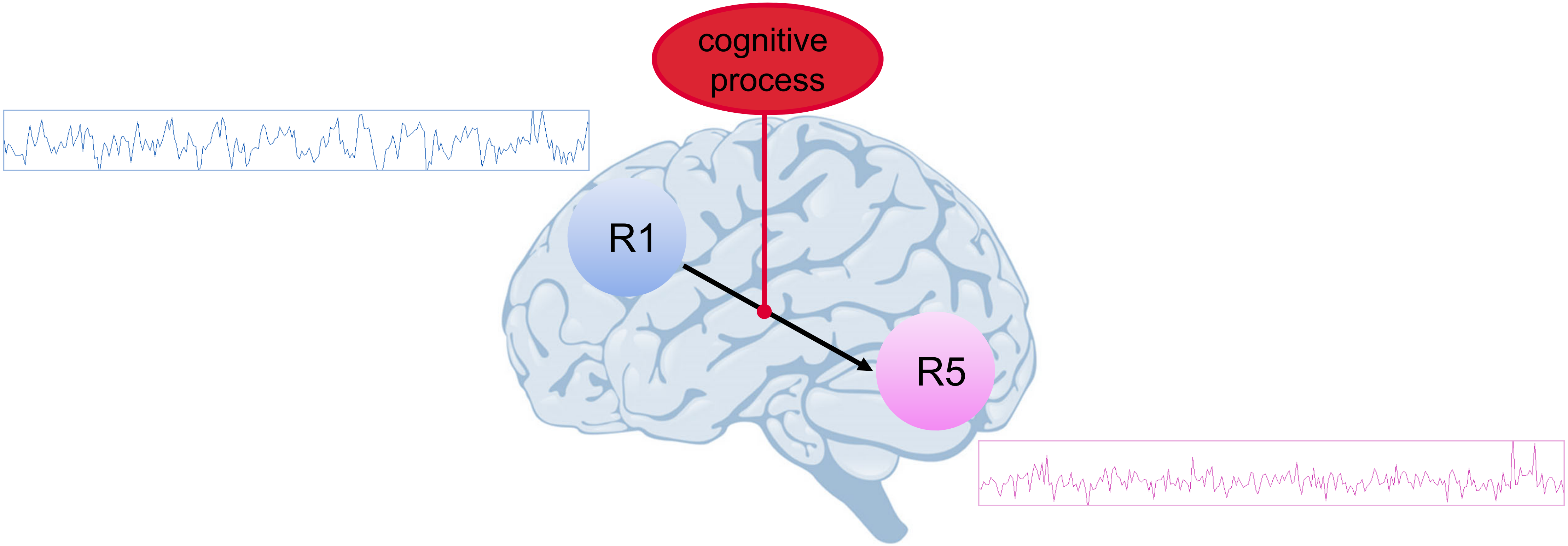
We can replace one main effect in the GLM by the time series of an area that shows this main effect.

E.g. let's replace the main effect of stimulus type by the time series of area V1.

$$
\begin{aligned}
y = \; & (T_A - T_B)\,\beta_1 && \leftarrow \text{main effect of task} \\
& + V1\,\beta_2 && \leftarrow \text{V1 time series} \approx \text{main effect of stim. type} \\
& + (T_A - T_B)\,V1\,\beta_3 && \text{PPI} \\
& + e
\end{aligned}
$$

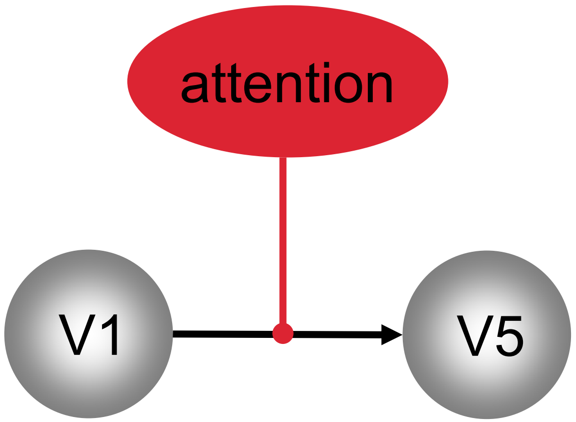
Factorial Designs

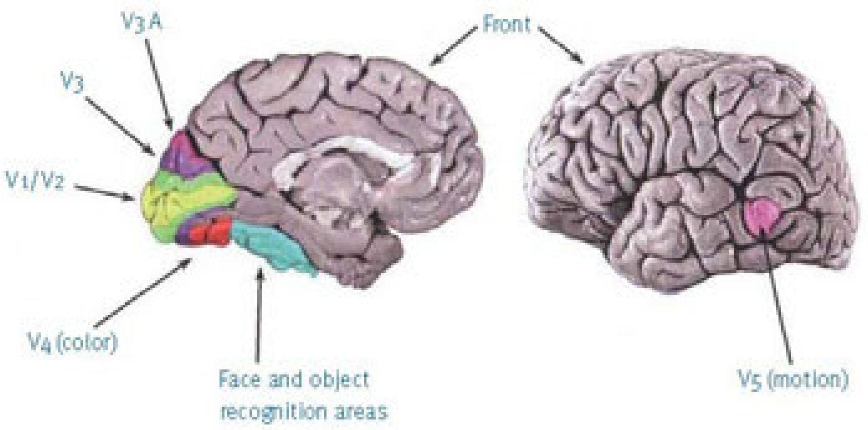
Psycho-Physiological Interactions (PPIs)

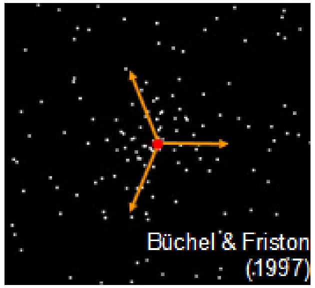


Factorial Designs

PPI, Example





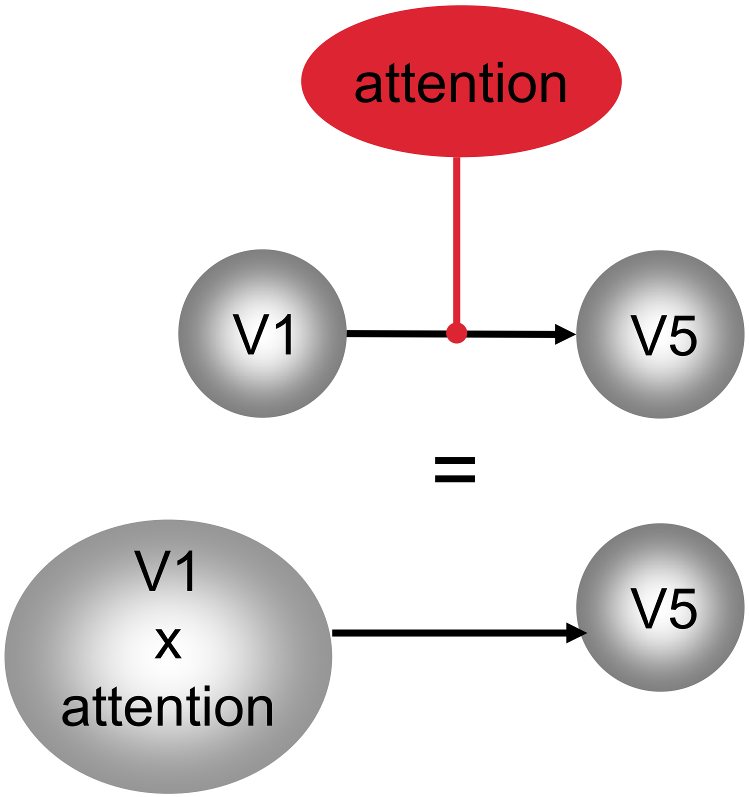


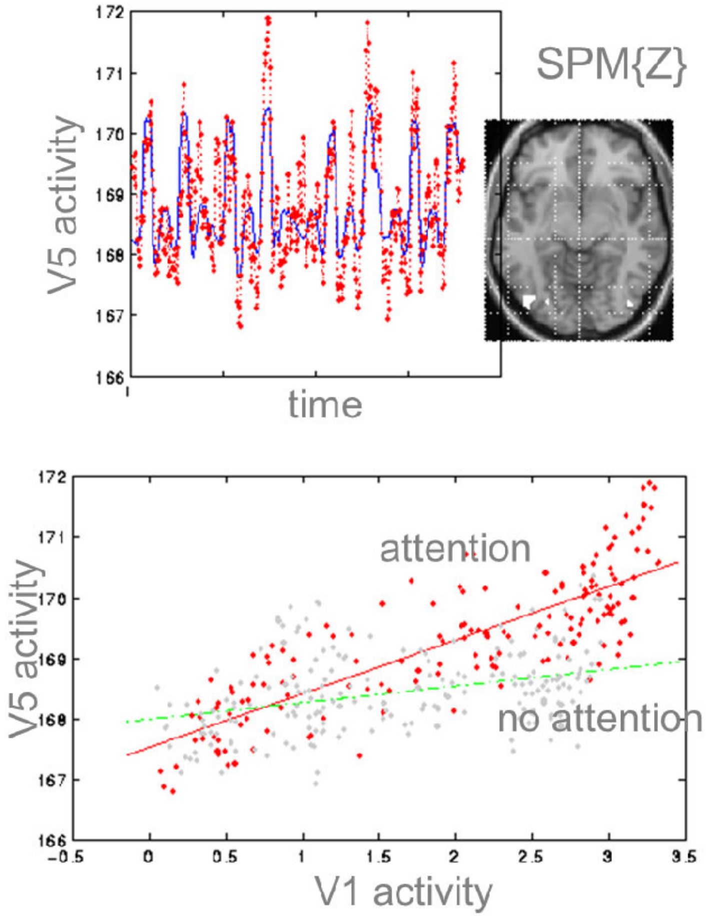
Radially moving dots

Conditions:
- Stationary
- Motion and attention ("detect changes")
- Motion without attention

Factorial Designs

PPI, Example





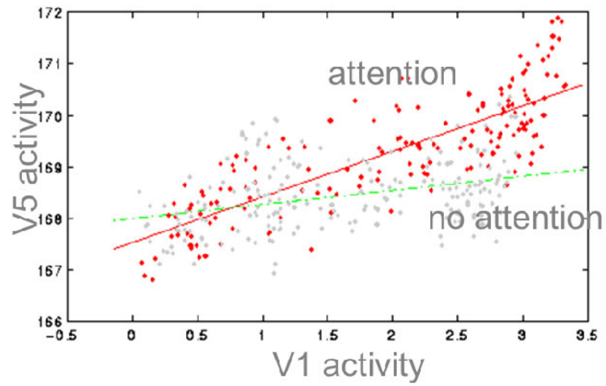
Friston et al. 1997, NeuroImage

Büchel & Friston, 1997, Cereb. Cortex

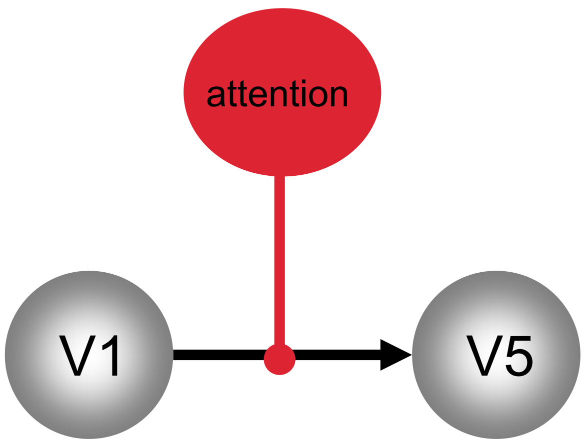
Factorial Designs

PPI, Example

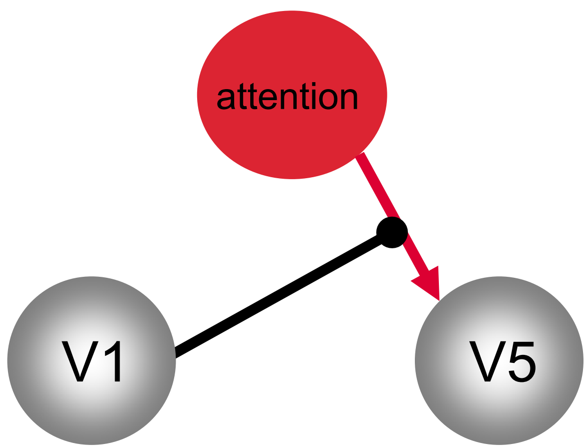
$$
\begin{aligned}
y = \ & (T_A - T_B)\,\beta_1 \\
& + V1\,\beta_2 \\
& + (T_A - T_B)\,V1\,\beta_3 \\
& + e
\end{aligned}
$$



Two possible interpretations of the PPI term



Modulation of V1 → V5 **by attention**



Modulation of attention → V5 **by V1**

Questions?

- Categorical designs

    Subtraction - Pure insertion, evoked / differential responses

    Conjunction - Testing multiple hypotheses

- Parametric designs

    Linear - Adaptation, cognitive dimensions

    Nonlinear - Polynomial expansions, neurometric functions

- Factorial designs

    Categorical - Interactions and pure insertion

    Parametric - Linear and nonlinear interactions

    - Psychophysiological interactions