University of Zurich[UZH] | ETH Eidgenössische Technische Hochschule Zürich Swiss Federal Institute of Technology Zurich

Translational Neuromodeling Unit

Experimental design of fMRI studies

Zurich SPM Course 2016

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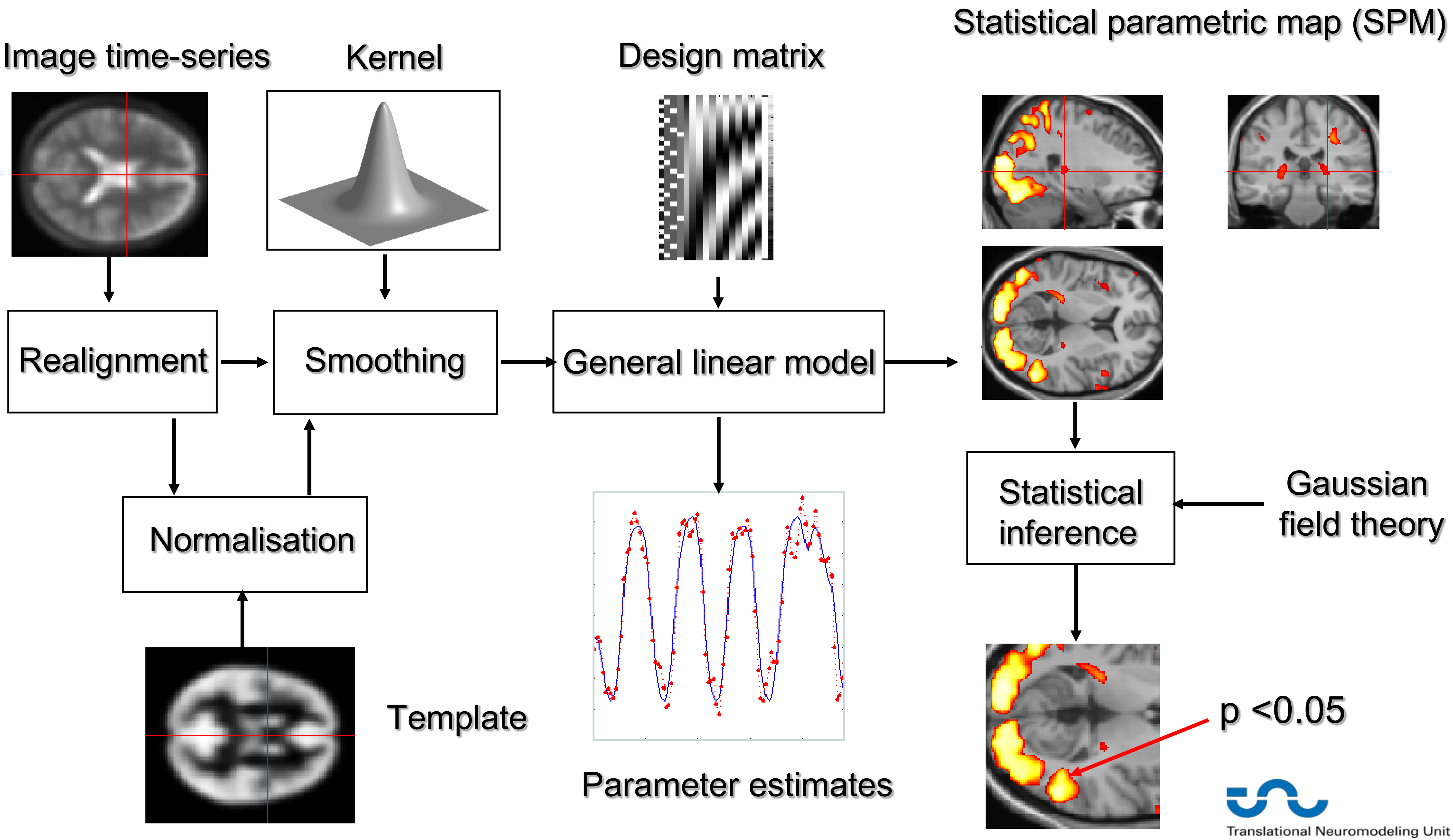
Klaas Enno Stephan,
FIL Methods group,
Christian Ruff

Overview of SPM



Overview of SPM

Research question:
Which neuronal structures support face recognition?

↓

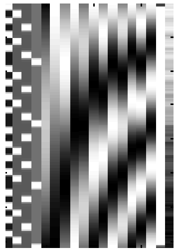
Hypothesis:
The fusiform gyrus is implicated in face recognition

↓

Experimental design

→

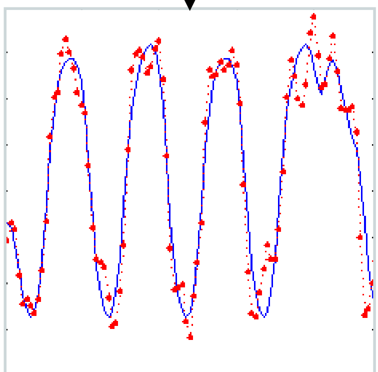
Design matrix



↓

General linear model

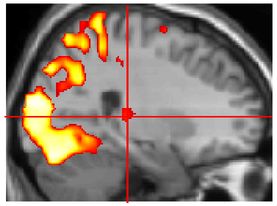
↓

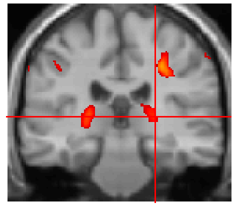


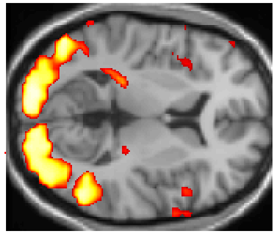
Parameter estimates

→

Statistical parametric map (SPM)





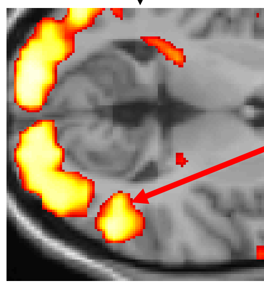


↓

Statistical inference

← Gaussian field theory

↓



$p < 0.05$

Translational Neuromodeling Unit

Overview

- 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

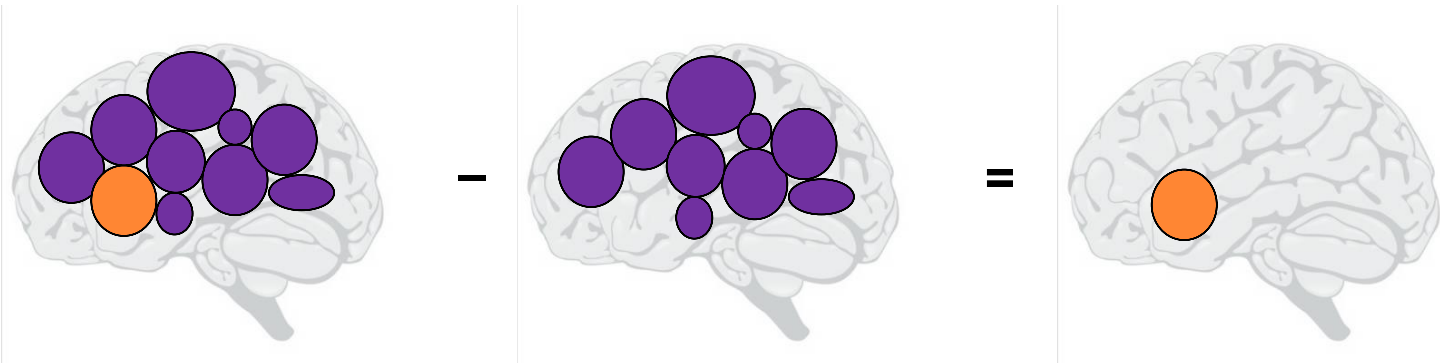
  - Psychophysiological Interactions

Cognitive subtraction

- **Aim:**
  - **Neuronal structures underlying a *single* process *P*?**

- **Procedure:**
  - **Contrast: [Task with *P*] – [control task without *P*] = *P***
  - **→ the critical assumption of „pure insertion“**

- **Example**: **[Task with *P*] – [task without *P*] = *P***



Cognitive subtraction

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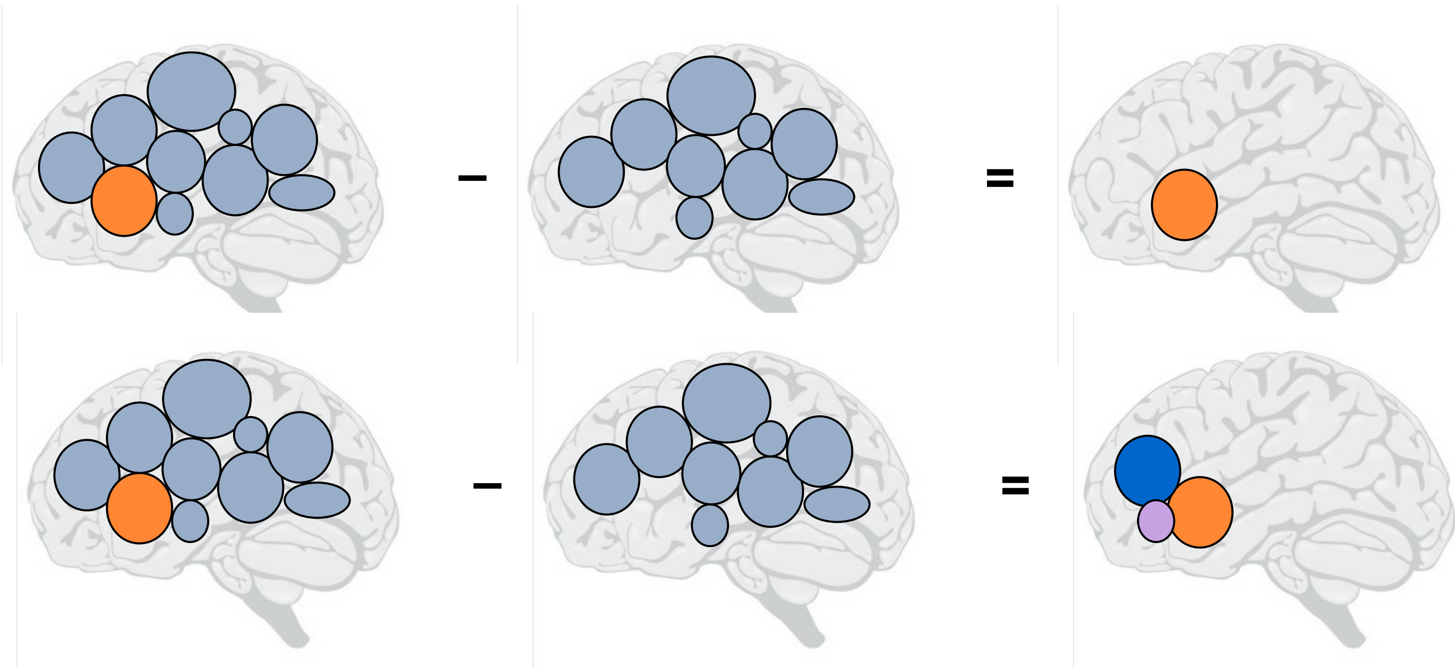


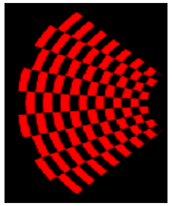
Translational Neuromodeling Unit

Cognitive subtraction: Baseline problems

Which neuronal structures support face recognition ?

- „Distant“ stimuli

-



➔ Several components differ!

- „Related“ stimuli

-

„Queen!“ „Aunt Jenny?“

➔ *P* implicit in control condition?

- Same stimuli, different task

-

Name Person! Name Gender!

➔ Interaction of task and stimuli (i.e. do task differences depend on stimuli chosen)?

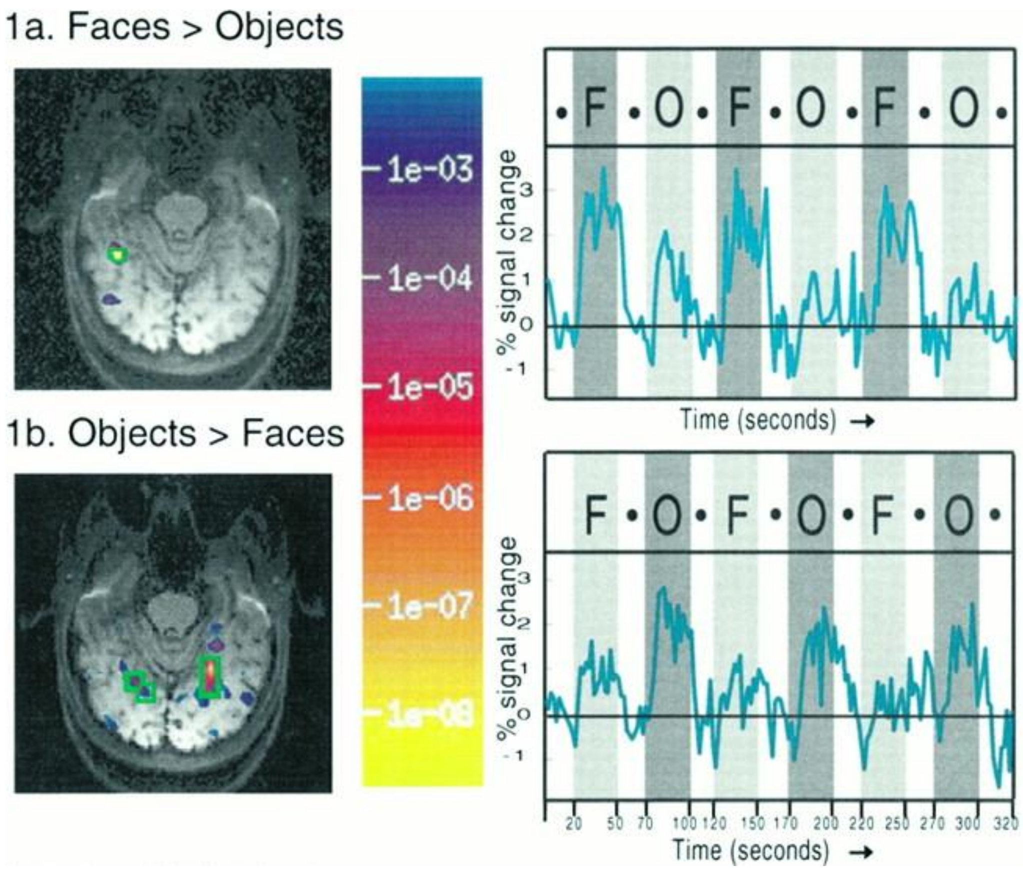
A categorical analysis

Experimental design

Face viewing F
Object viewing O

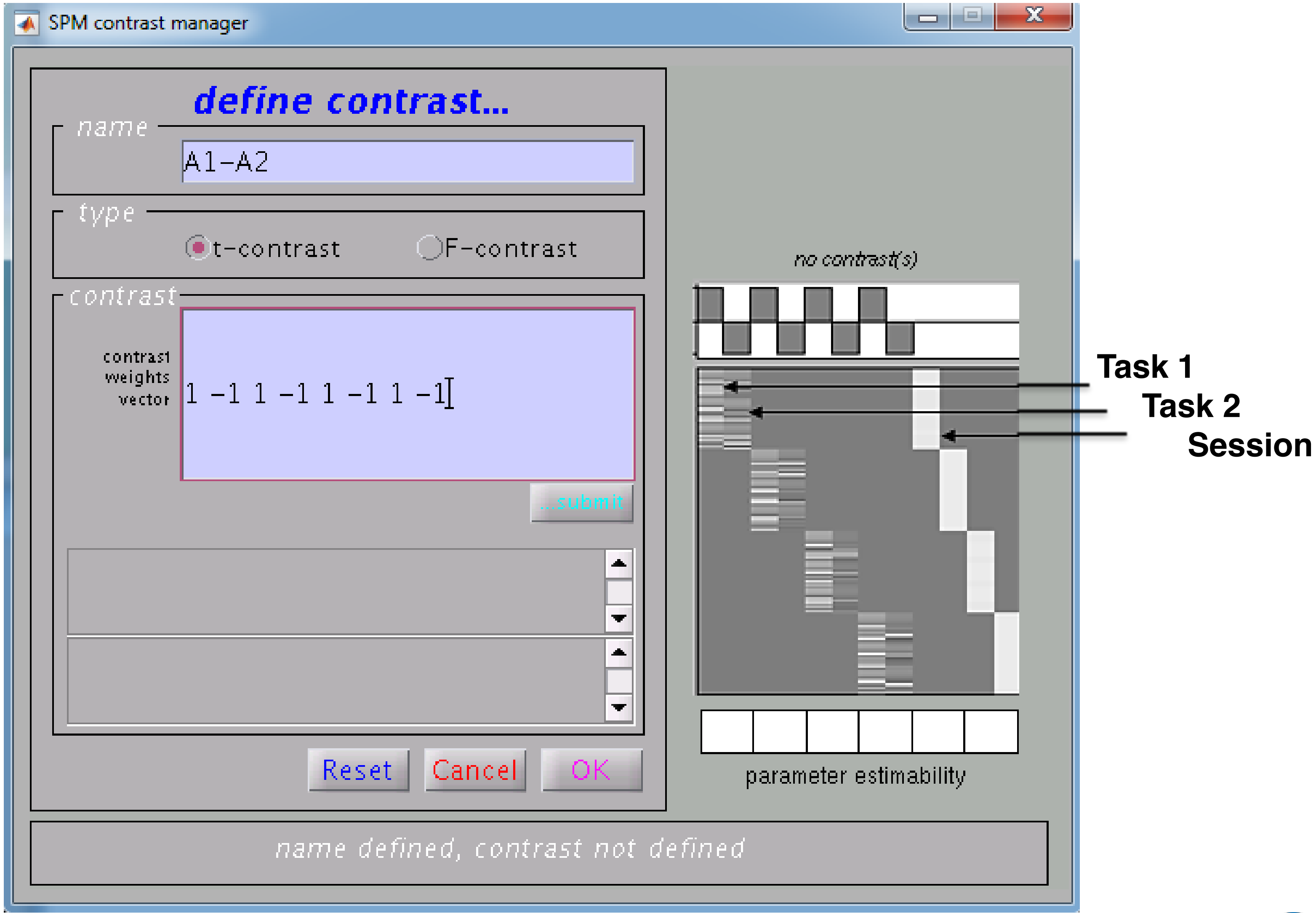
F - O = Face recognition
O - F = Object recognition

…under assumption of **pure insertion**



Kanwisher N et al. J. Neurosci. 1997;

Categorical design



Translational Neuromodeling Unit

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  Parametric - Linear and nonlinear interactions

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Conjunctions

- 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 (this is ensured automatically by SPM)

Conjunctions

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

Conjunctions

Task (1/2)

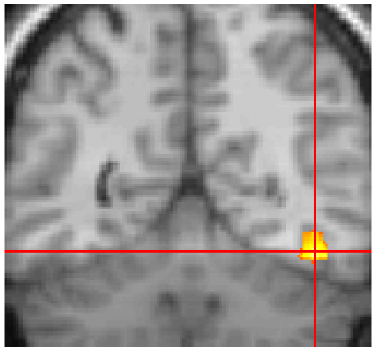
Stimuli (A/B)		Viewing	Naming
	Colours	A1 Visual Processing V	A2 Visual Processing V Phonological Retrieval P
	Objects	B1 Visual Processing V Object Recognition R	B2 Visual Processing V Phonological Retrieval P Object Recognition R

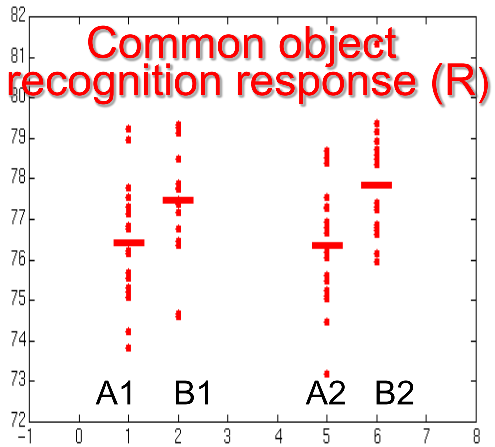
Which neural structures support object recognition?

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

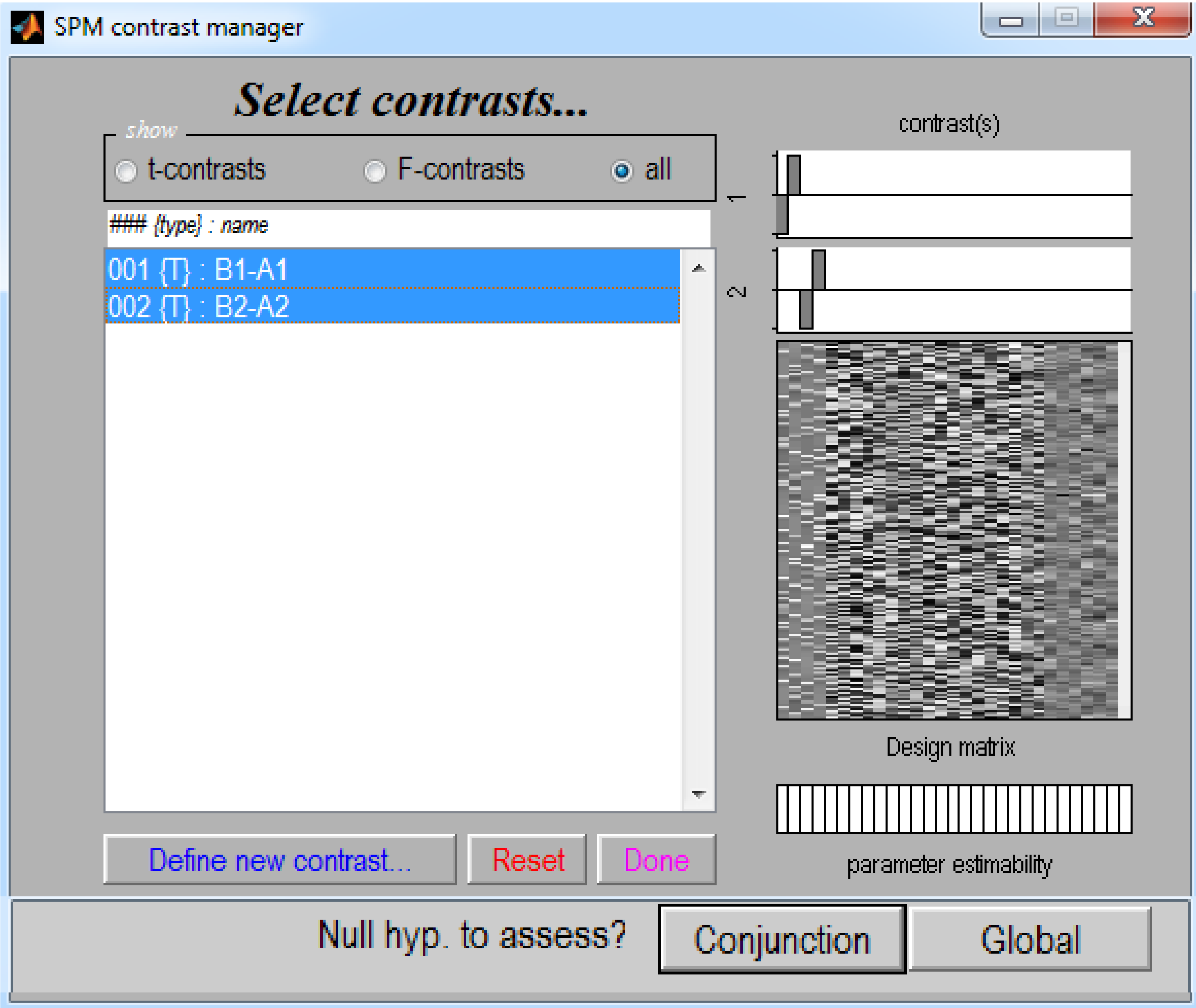
[V,R - V] & [P,V,R - P,V] = R & R = R

Price et al. 1997





Conjunctions



Translational Neuromodeling Unit

Two types 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?"

➔ **Null hypothesis:** No contrast is significant: **k = 0**

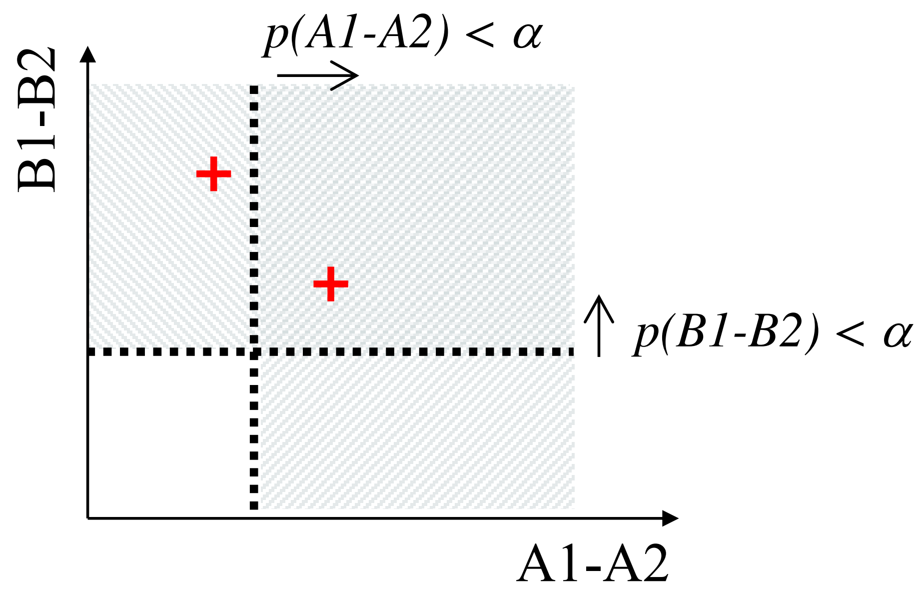
➔ does not correspond to a logical AND !

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

➔ "Which voxels show, for each specified contrast, significant effects?"

➔ **Null hypothesis:** Not all contrasts are significant: **k < n**

➔ corresponds to a logical AND



Friston et al. (2005). *Neuroimage,* 25:661-667.

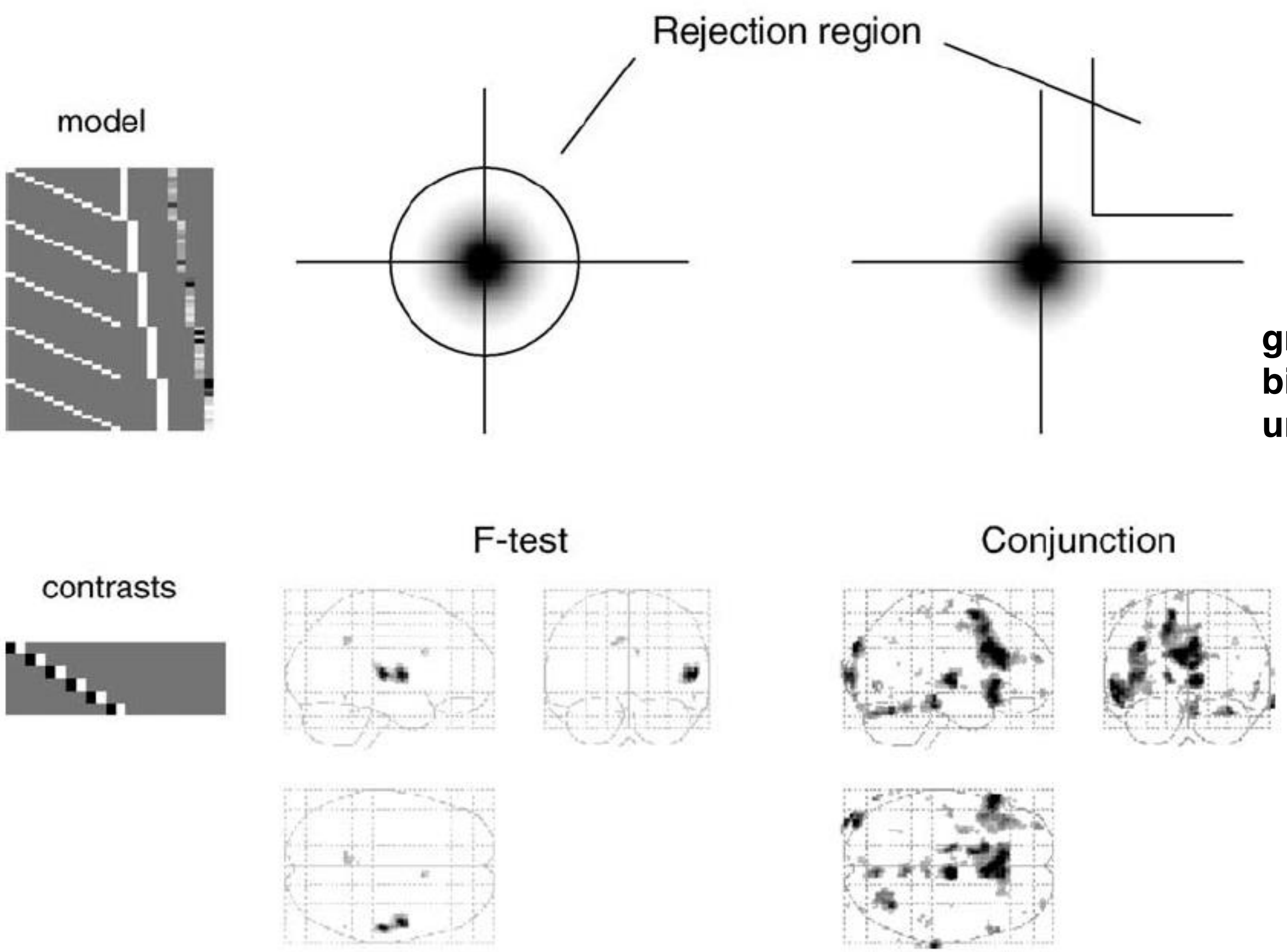
Nichols et al. (2005). *Neuroimage,* 25:653-660.

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 and Friston, 2000)
  - this means the contrasts have to be orthogonal!

Worsley &Friston (2000) Stat. Probab. Lett. 47 (2), 135–140

F-test vs. conjunction based on global null



grey area:
bivariate t-distriution
under global null hypothesis

➔ **Null hypothesis:** No contrast is significant: **k = 0**

Friston et al. 2005, *Neuroimage*, 25:661-667.

Overview

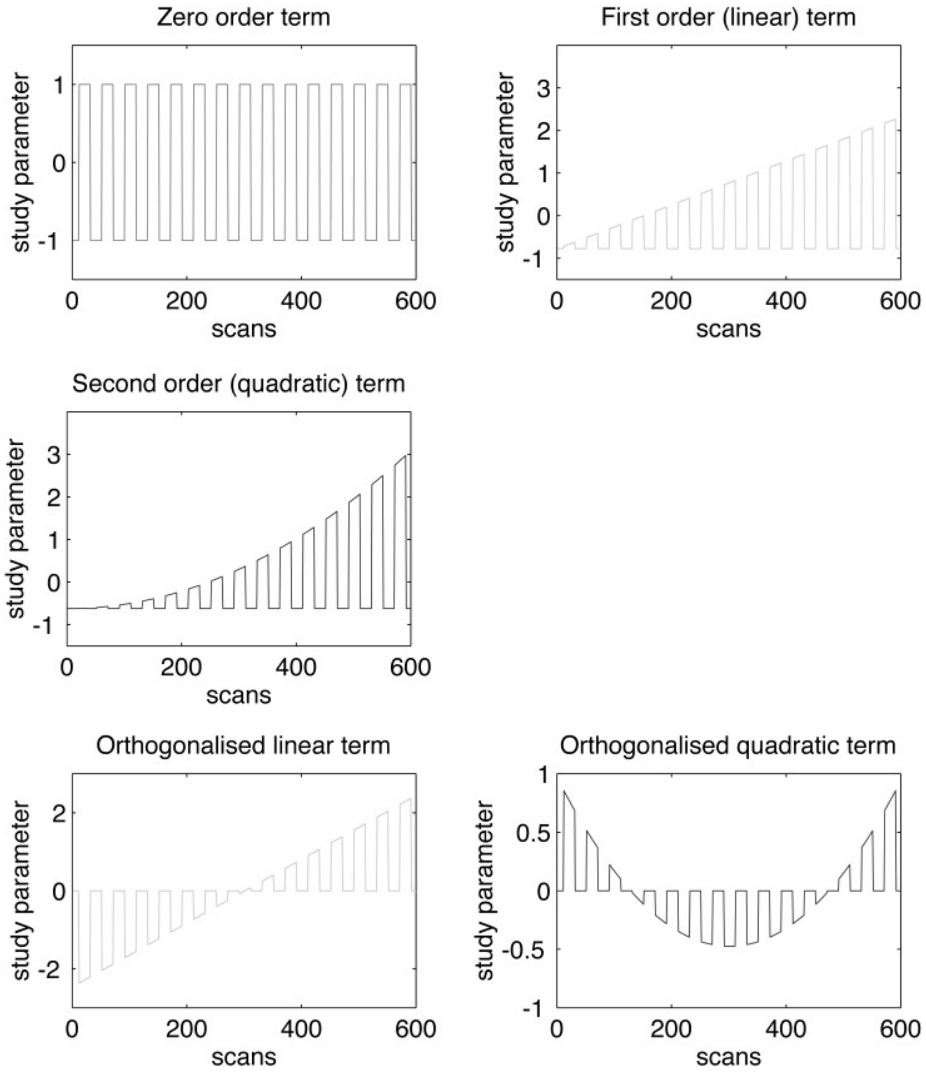
- Categorical designs
  - Subtraction - Pure insertion, evoked / differential responses
  - Conjunction - Testing multiple hypotheses
- **Parametric designs**
  - Linear - Adaptation, cognitive dimensions
  - Nonlinear - Polynomial expansions, neurometric functions
- Factorial designs
  - Categorical - Interactions and pure insertion
  - Parametric - Linear and nonlinear interactions
    - Psychophysiological Interactions

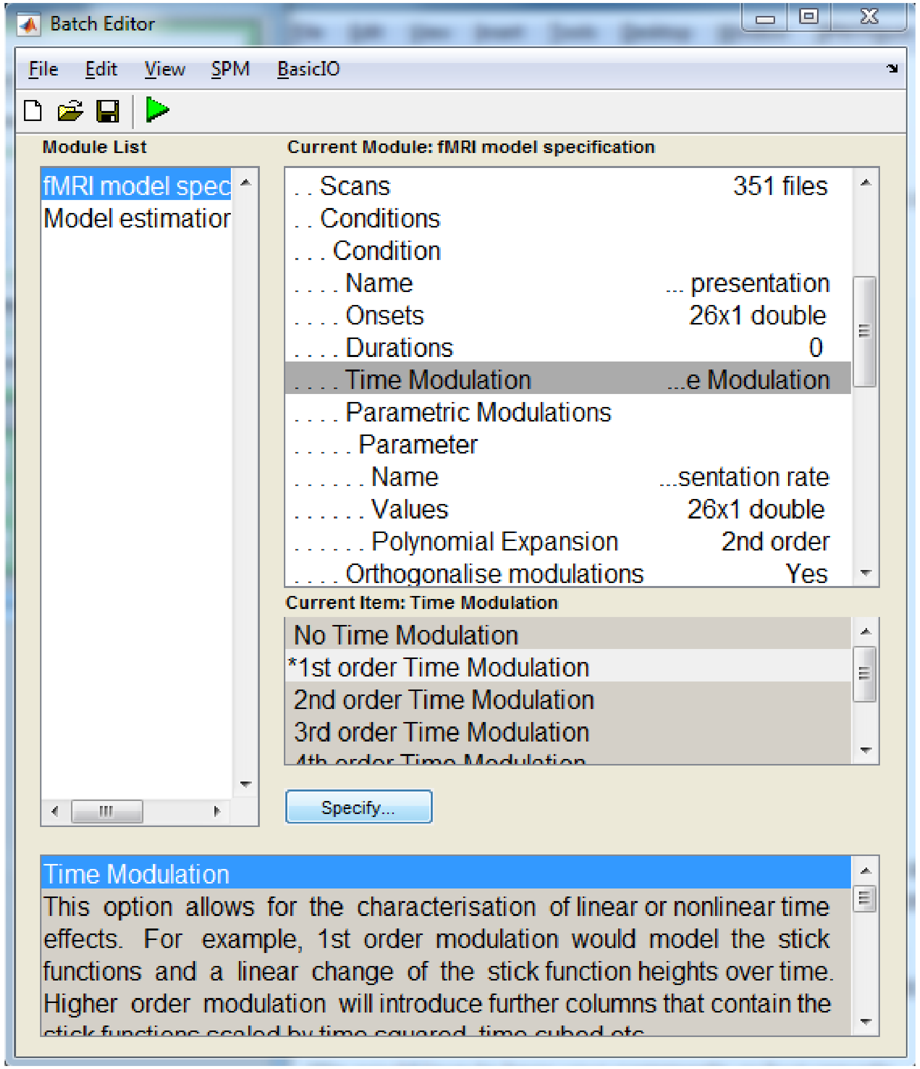
Parametric designs

- 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)

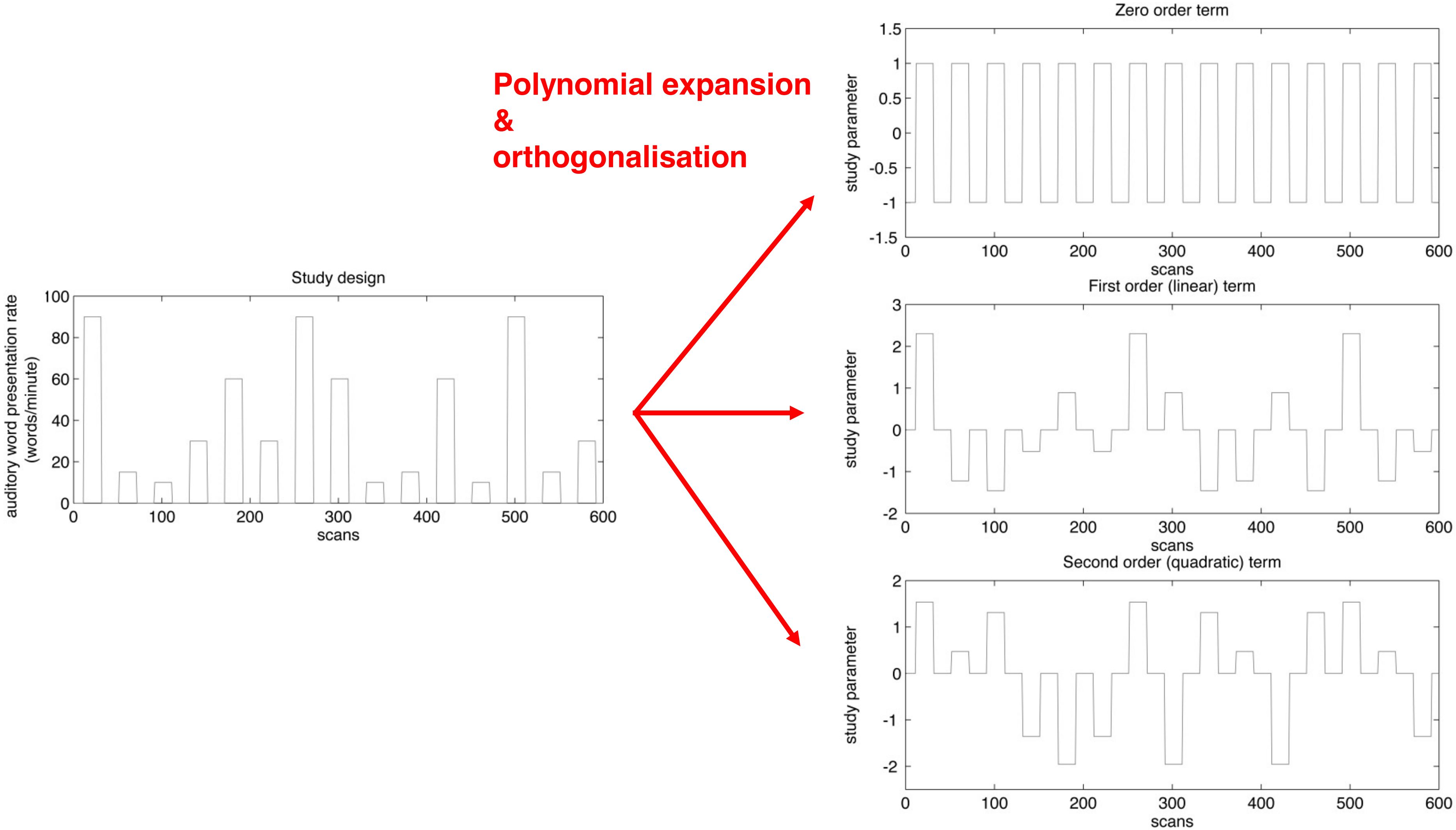
Parametric modulation of regressors by time





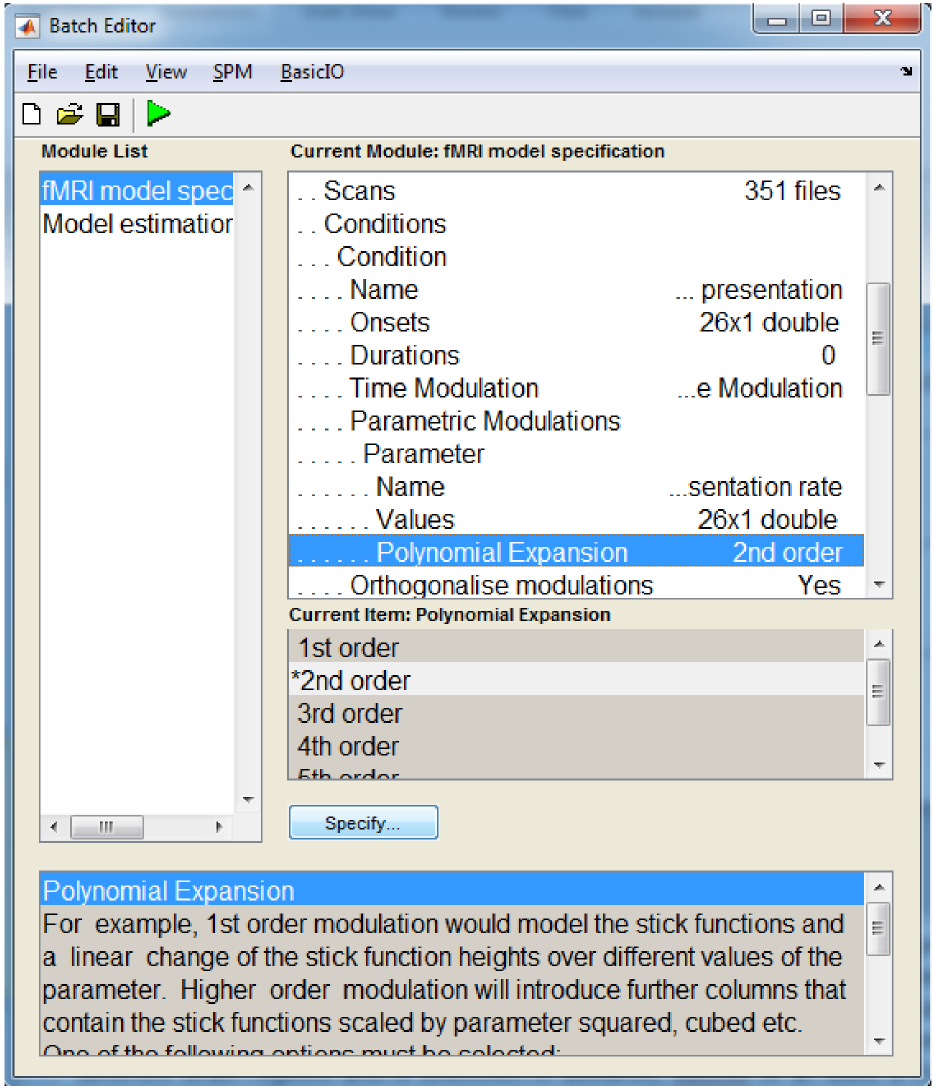
Büchel et al. 1998, *NeuroImage* 8:140-148

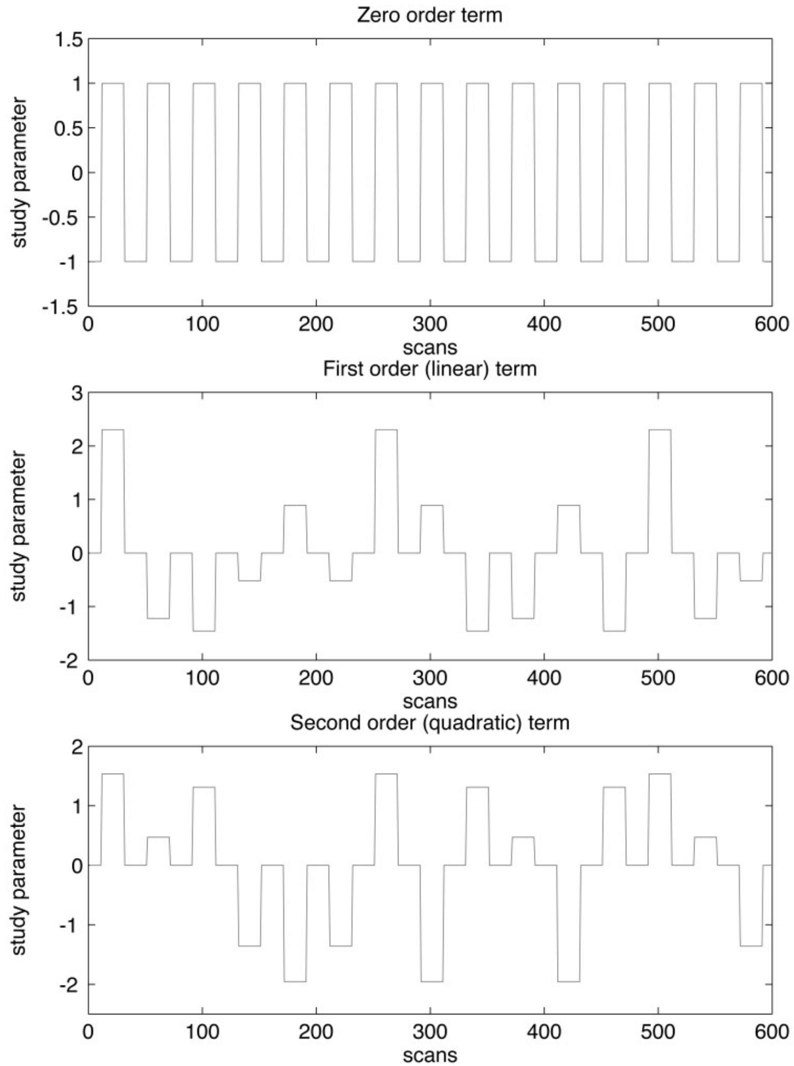
“User-specified” parametric modulation of regressors



Büchel et al. 1998, *NeuroImage* 8:140-148

"User-specified" parametric modulation of regressors





Büchel et al. 1998, *NeuroImage* 8:140-148

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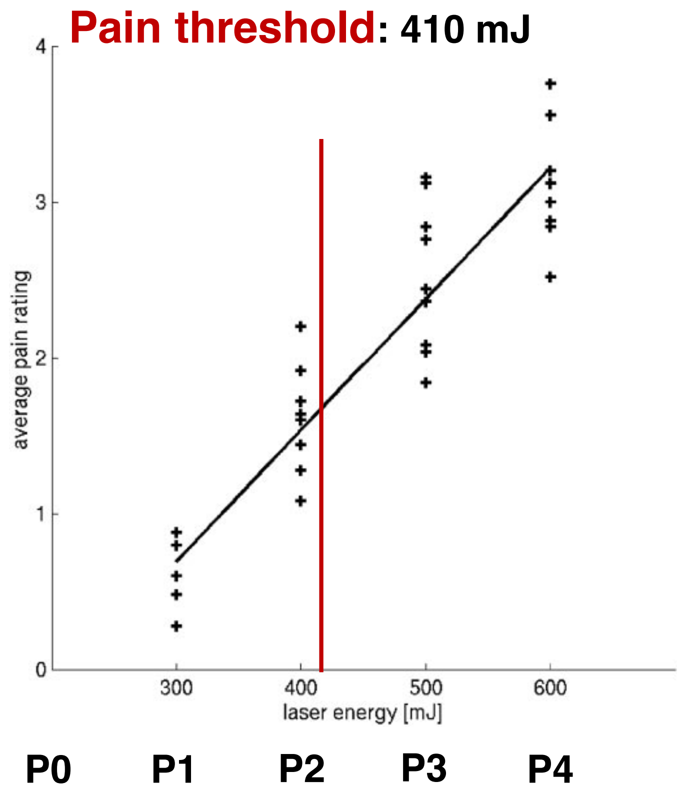
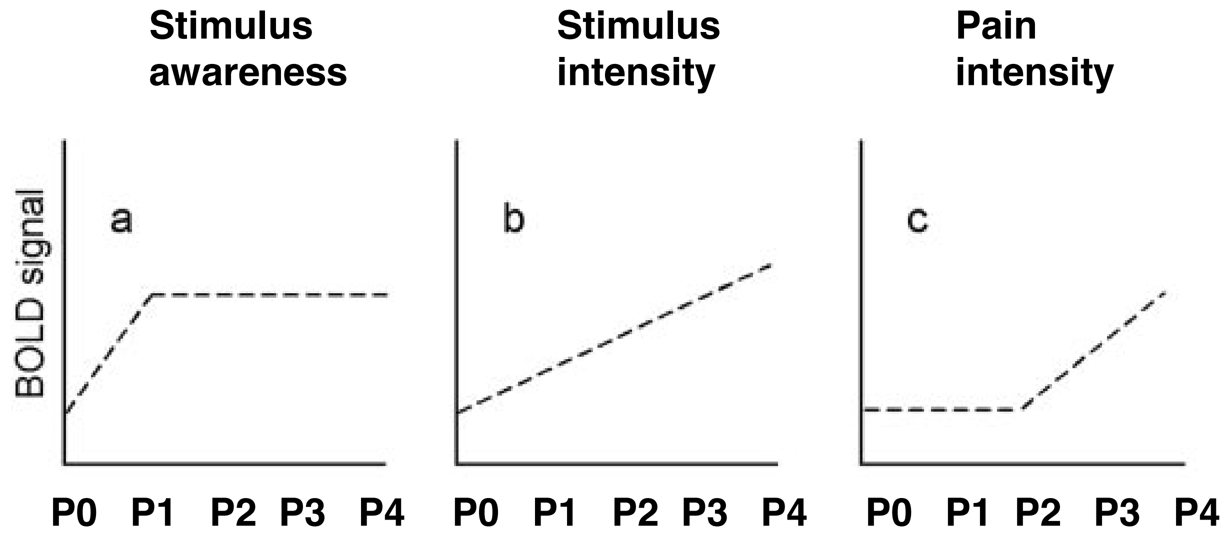
Investigating neurometric functions

(= relation between a stimulus property and the neuronal response)

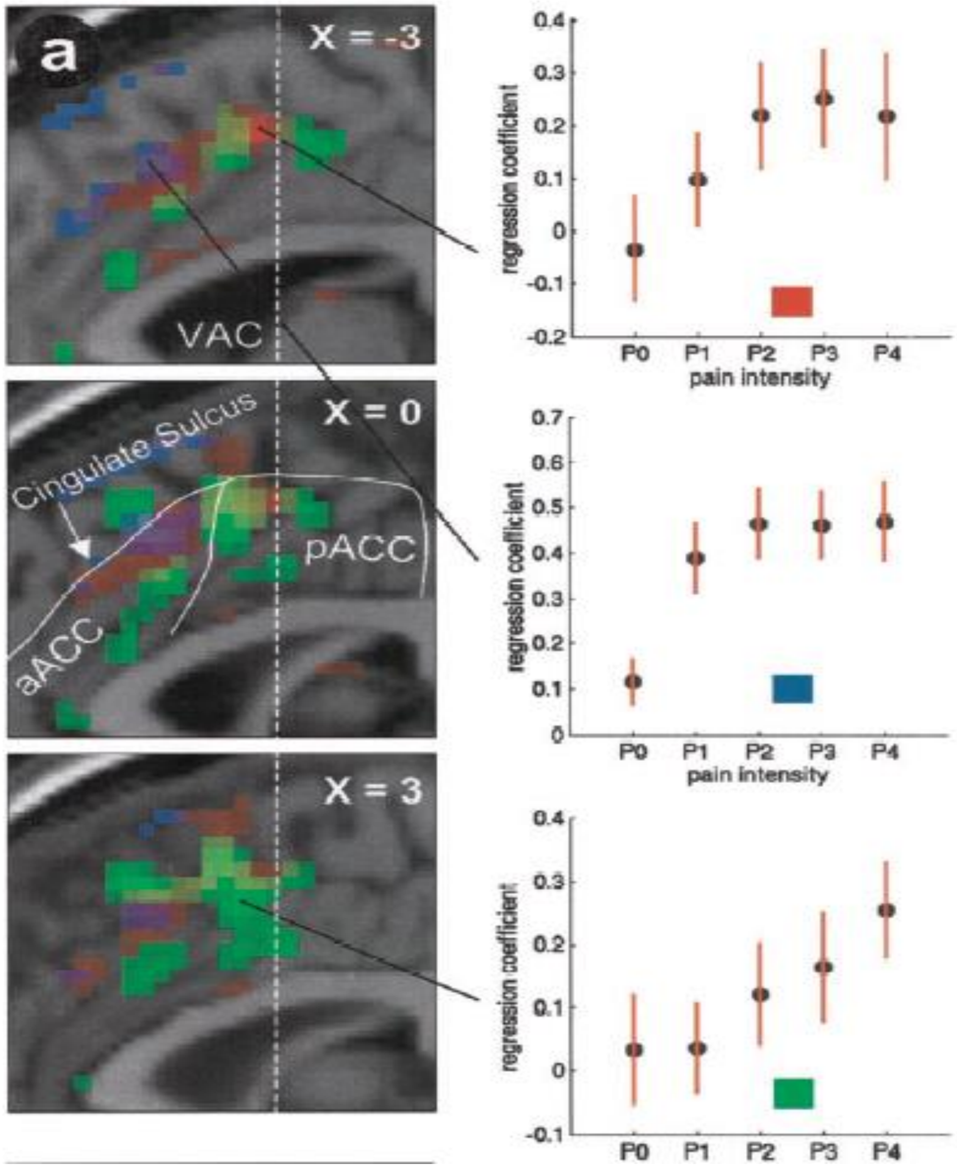


P0-P4: Variation of intensity of a laser stimulus applied to the right hand (0, 300, 400, 500, and 600 mJ)

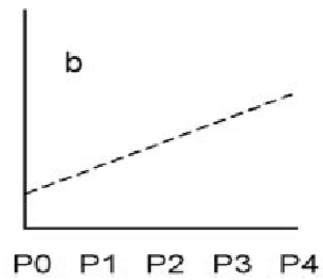


Büchel et al. 2002, *J. Neurosci*. 22:970-976

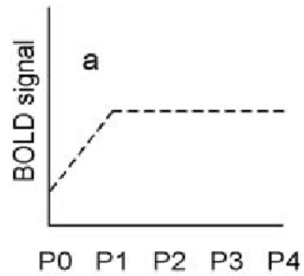
Neurometric functions



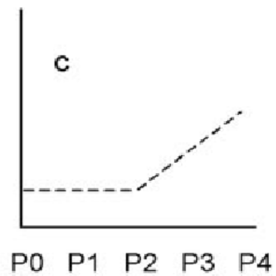
→ Stimulus intensity
dorsal pACC



→ Stimulus awareness
dorsal ACC



→ Pain intensity
ventral pACC



Büchel et al. 2002, *J. Neurosci*. 22:970-976

Model-based regressors

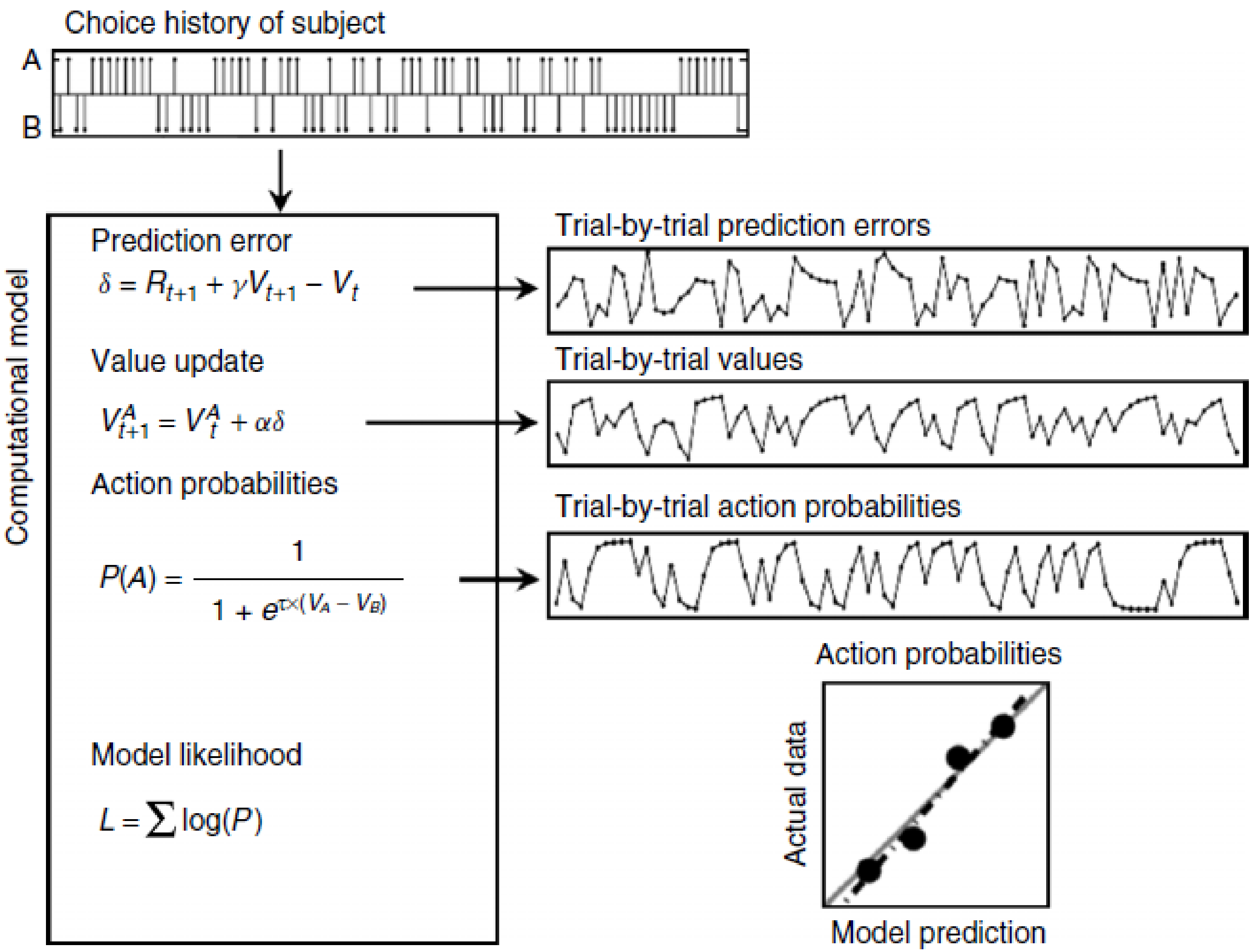
- general idea:
  generate predictions from a computational model, e.g. of learning or decision-making

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

- use these predictions to define regressors

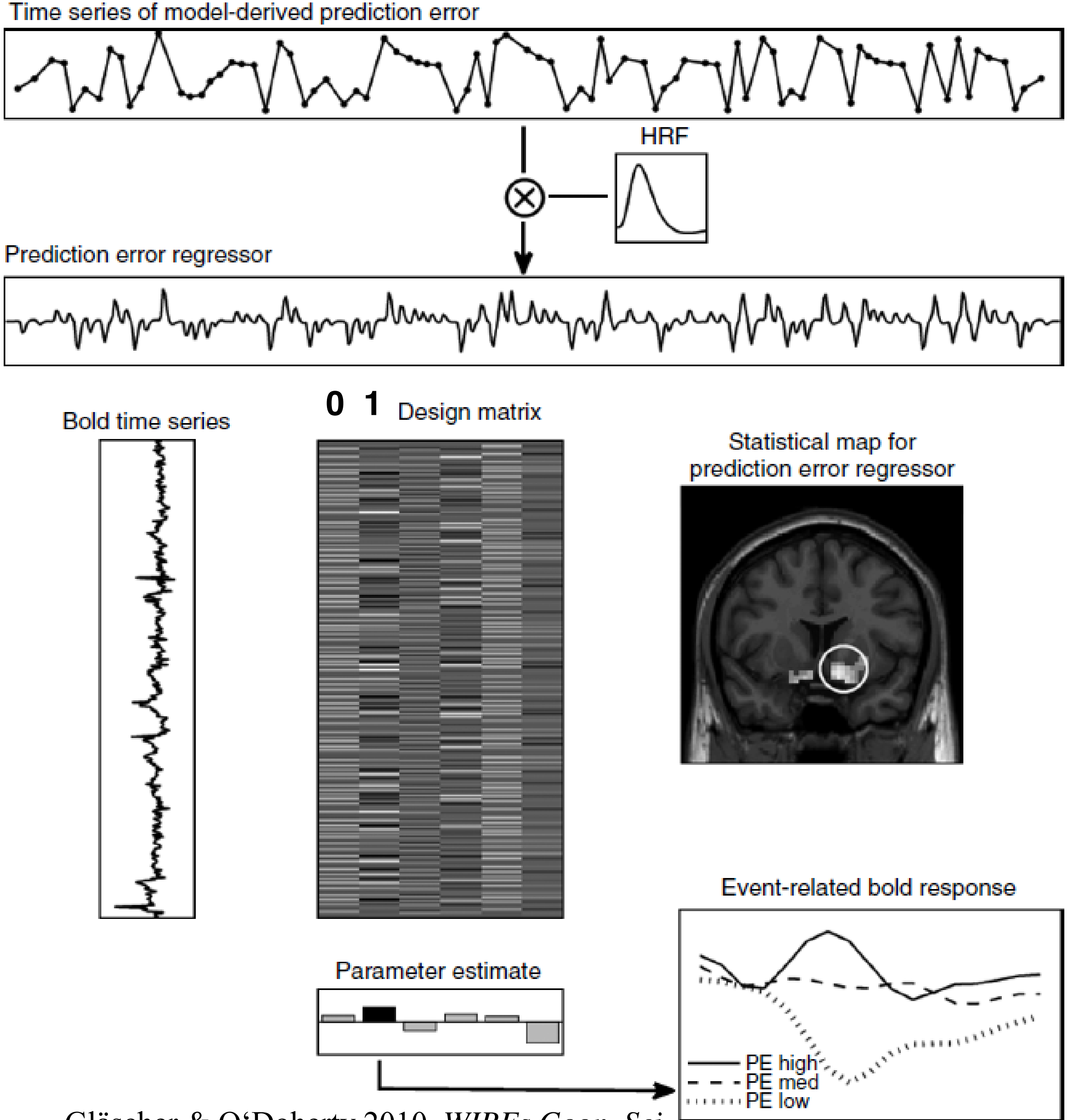
- include these regressors in a GLM and test for significant correlations with voxel-wise BOLD responses

Model-based fMRI analysis



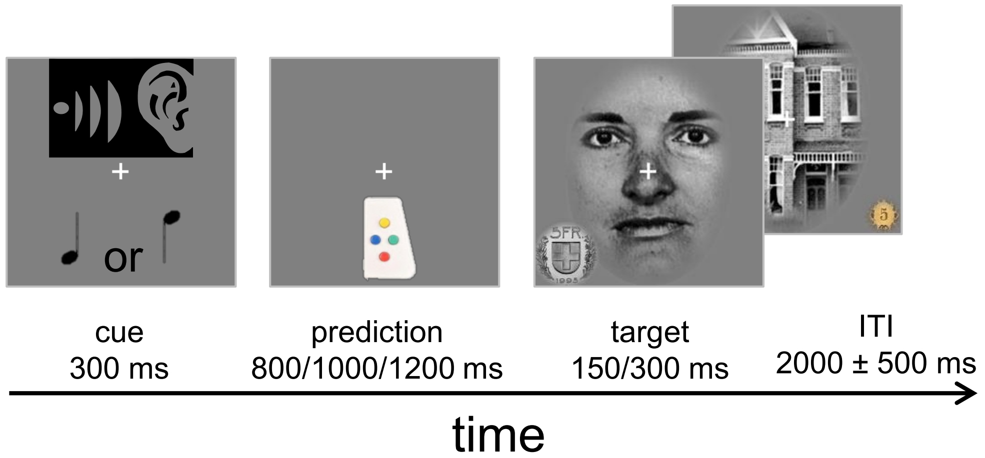
Gläscher & O'Doherty 2010, *WIREs Cogn. Sci.*

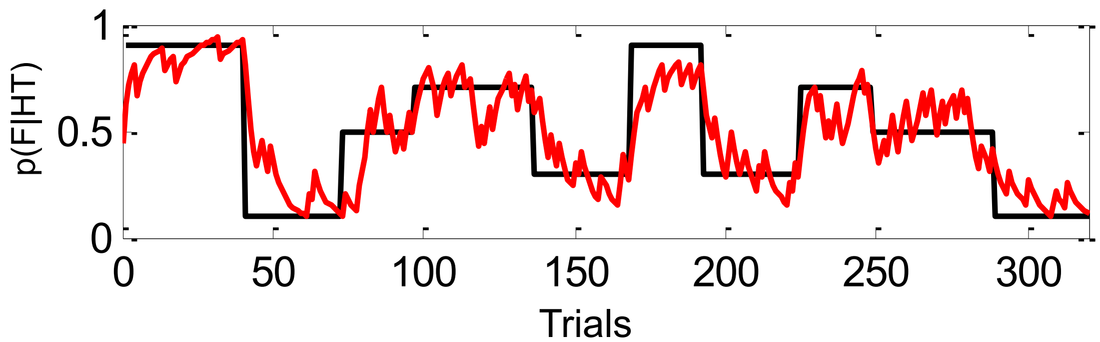
Model-based fMRI analysis



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

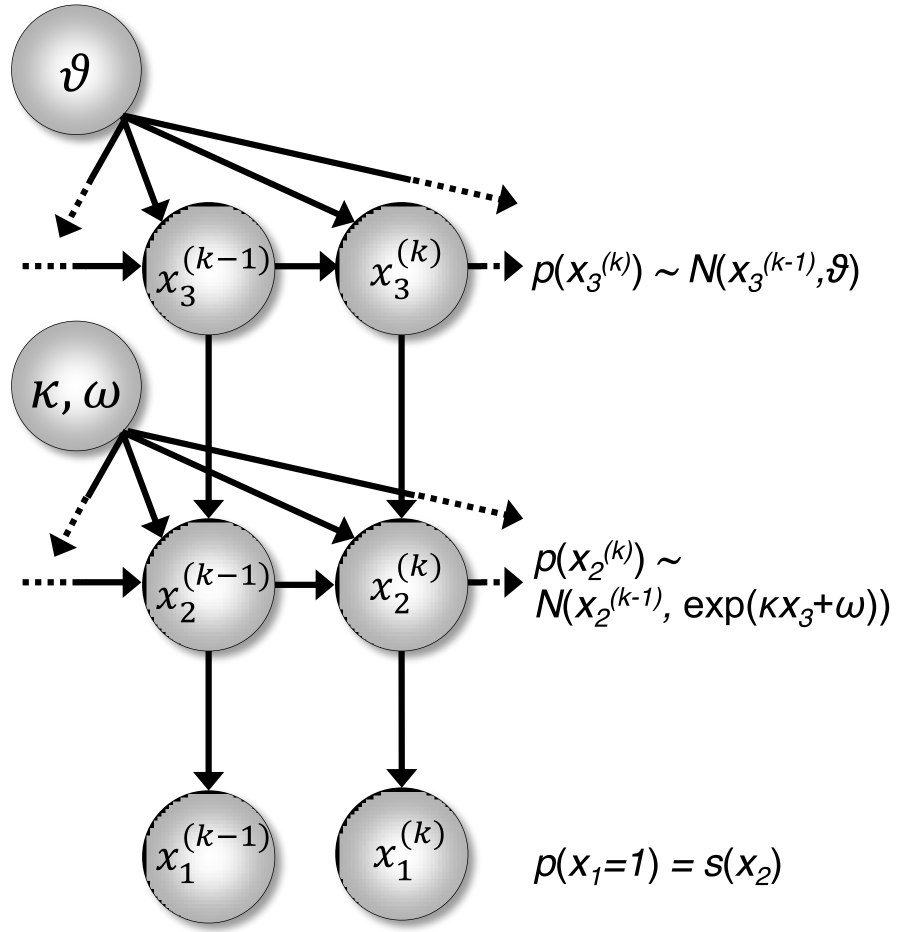
Hierarchical prediction errors about sensory outcome and its probability





Iglesias et al. 2013, *Neuron*

The Hierarchical Gaussian Filter (HGF)



Mathys et al. 2011, *Front. Hum. Neurosci.*

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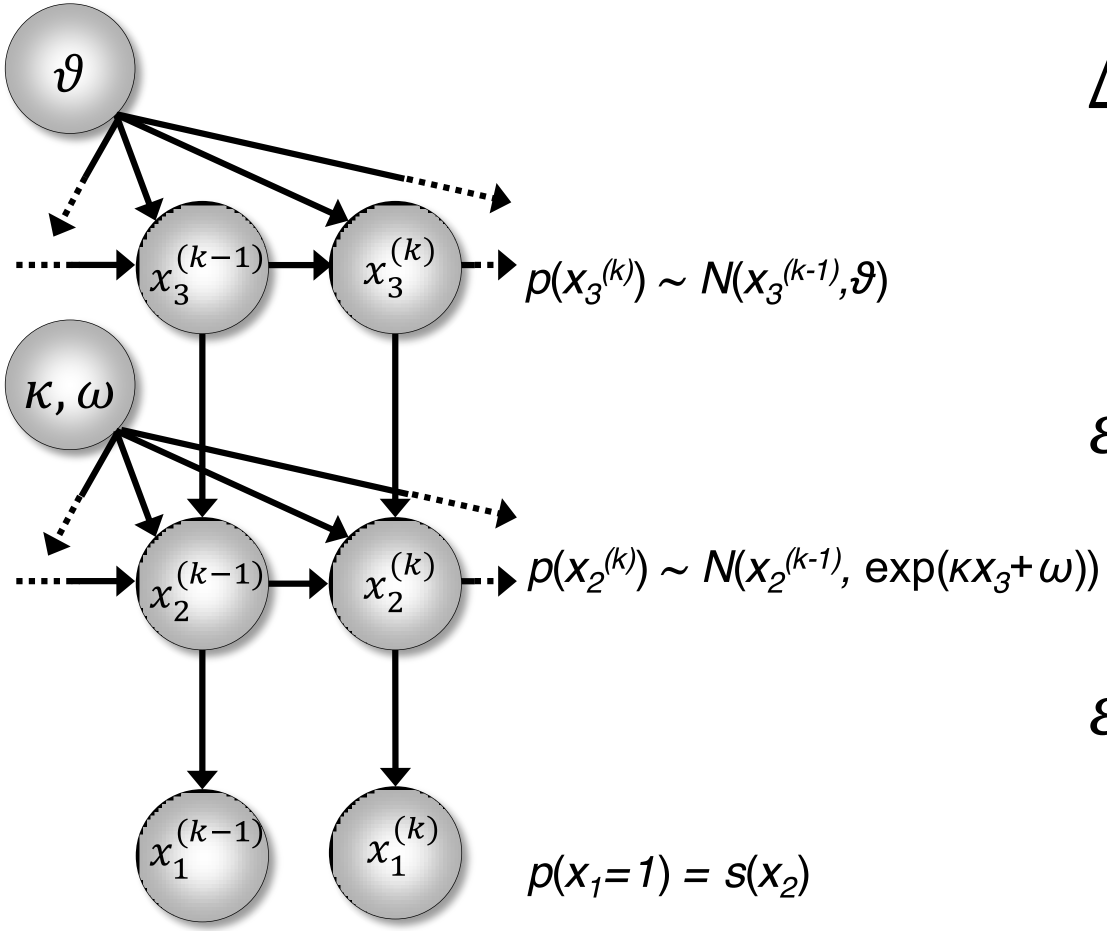


$$\Delta\mu_i \propto \frac{\hat{\pi}_{i-1}}{\pi_i} PE_{i-1}$$

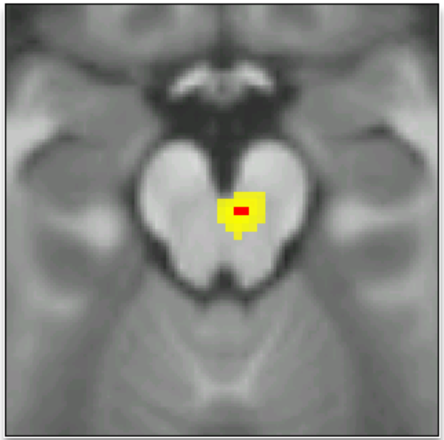
$$\varepsilon_3 \propto \sigma_3^{(k)} \delta_2^{(k)}$$

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

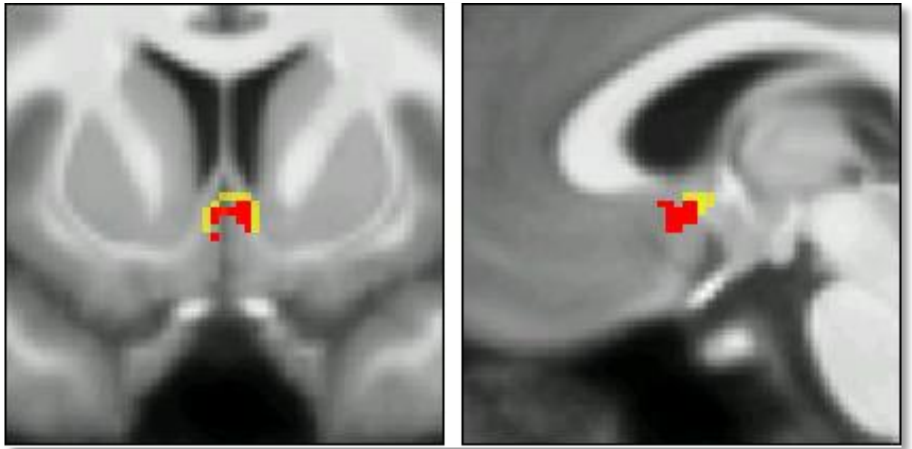
Mathys et al. 2011, *Front Hum Neurosci.*

Sensory prediction errors

ε_2 in midbrain (N=45)



ε_3 in basal forebrain (N=45)



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

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

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

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

Iglesias et al. 2013, *Neuron*

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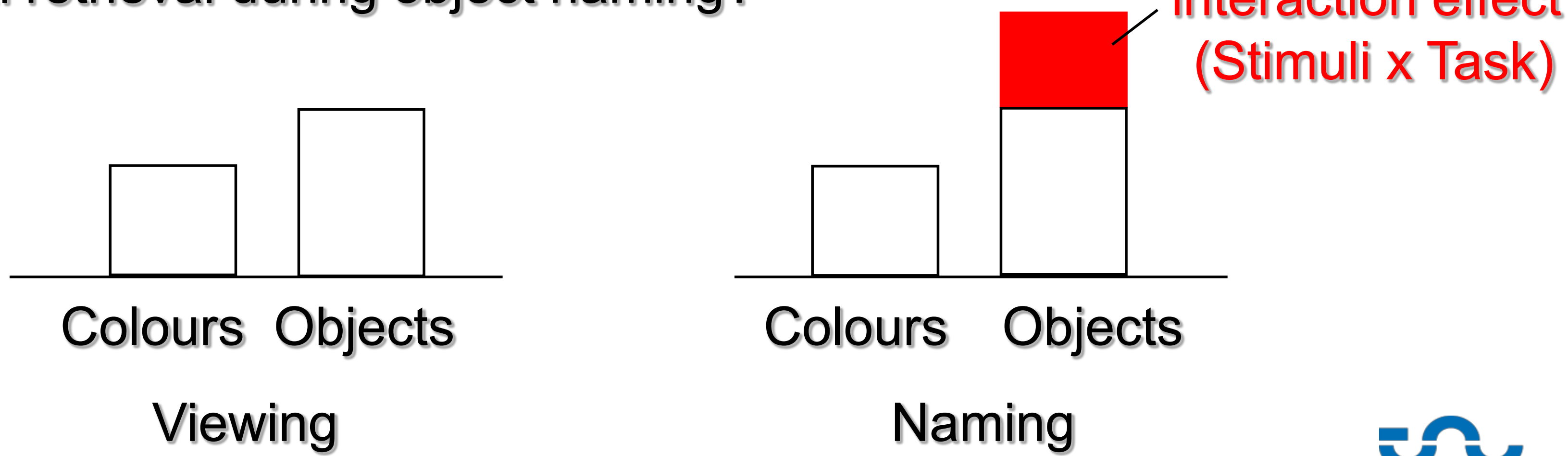
Main effects and interactions

Stimuli (A/B)	Task (1/2): Viewing	Task (1/2): 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?

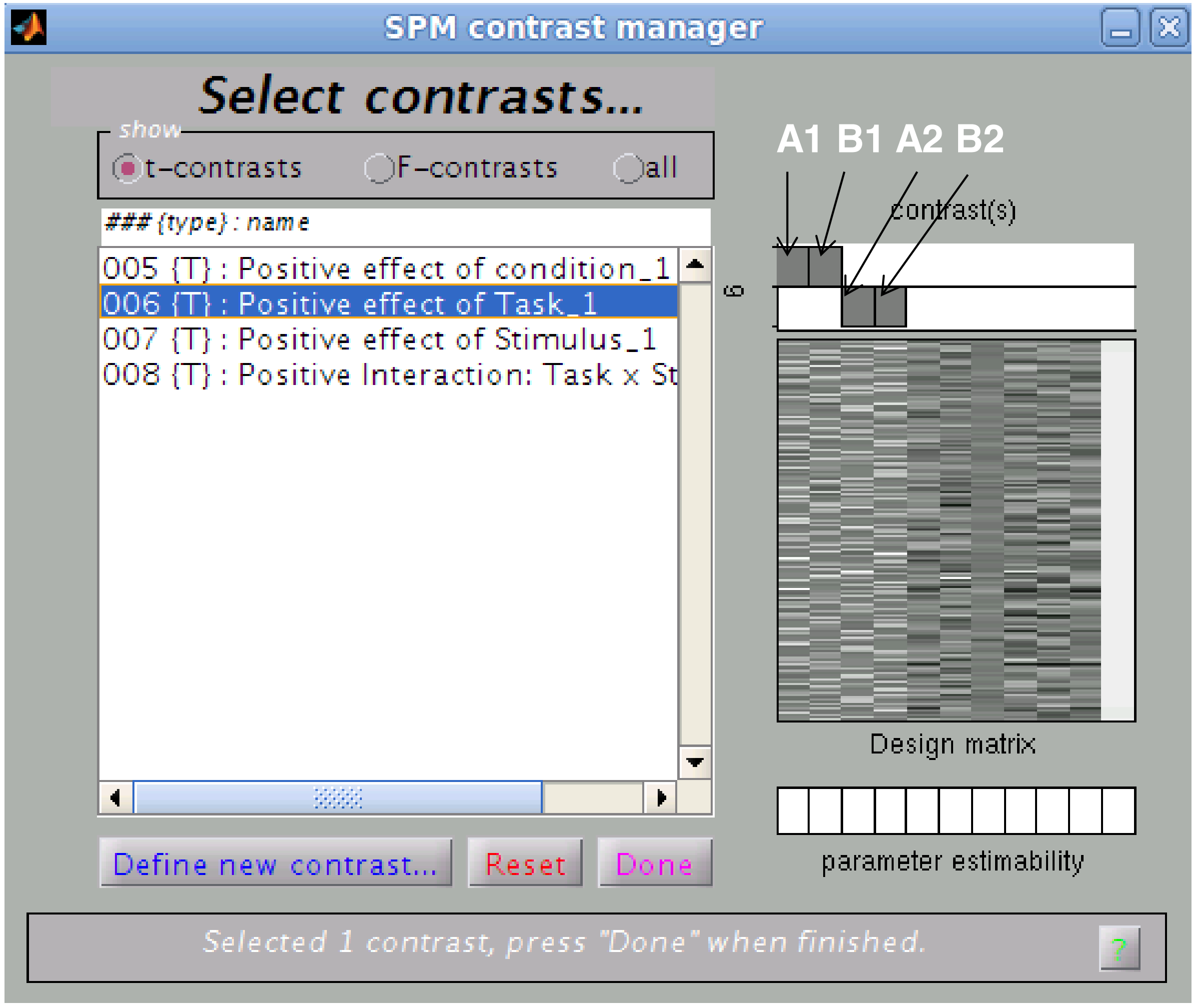


Translational Neuromodeling Unit

Factorial design

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

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

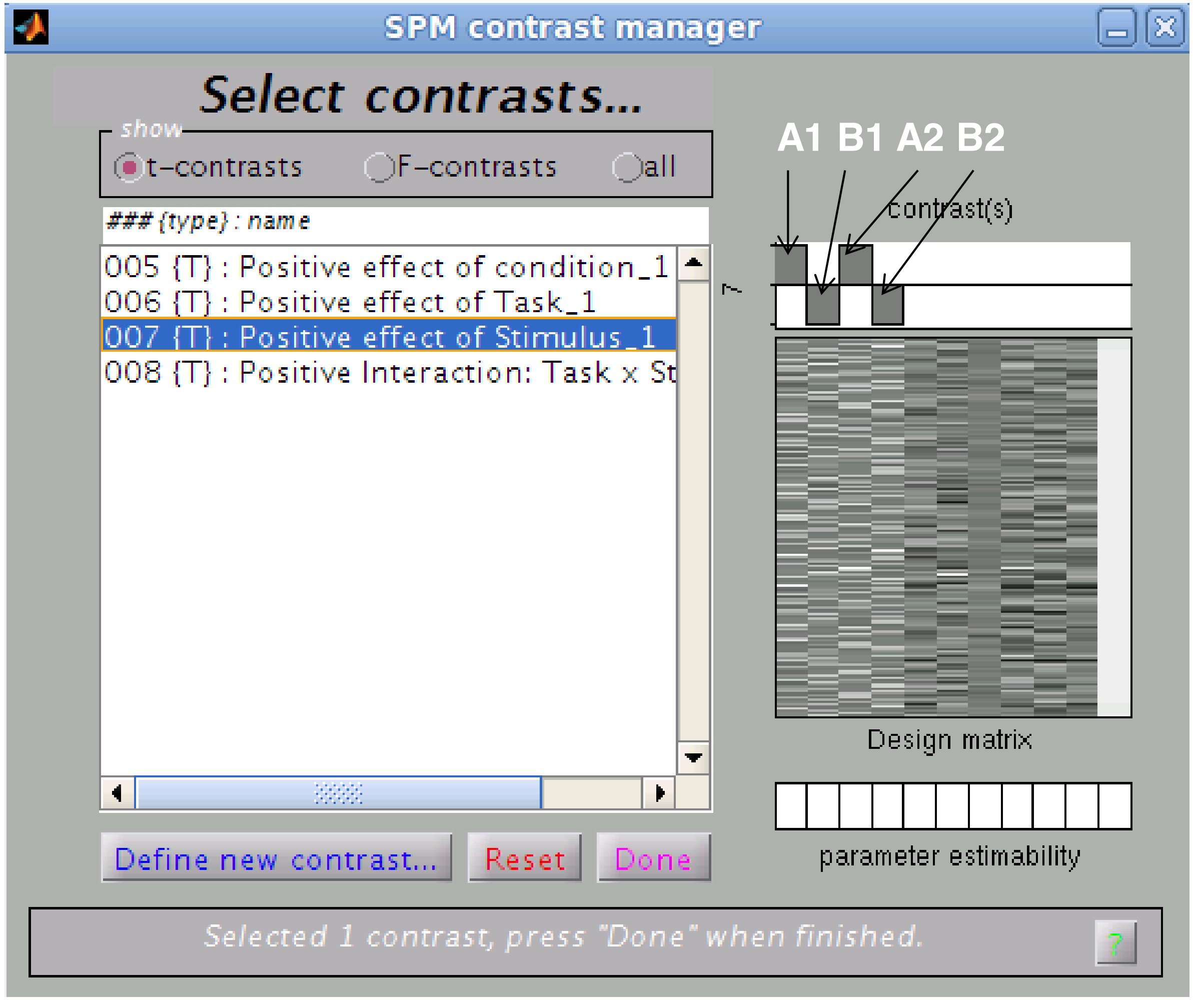


Factorial design

Task (1/2)

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

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



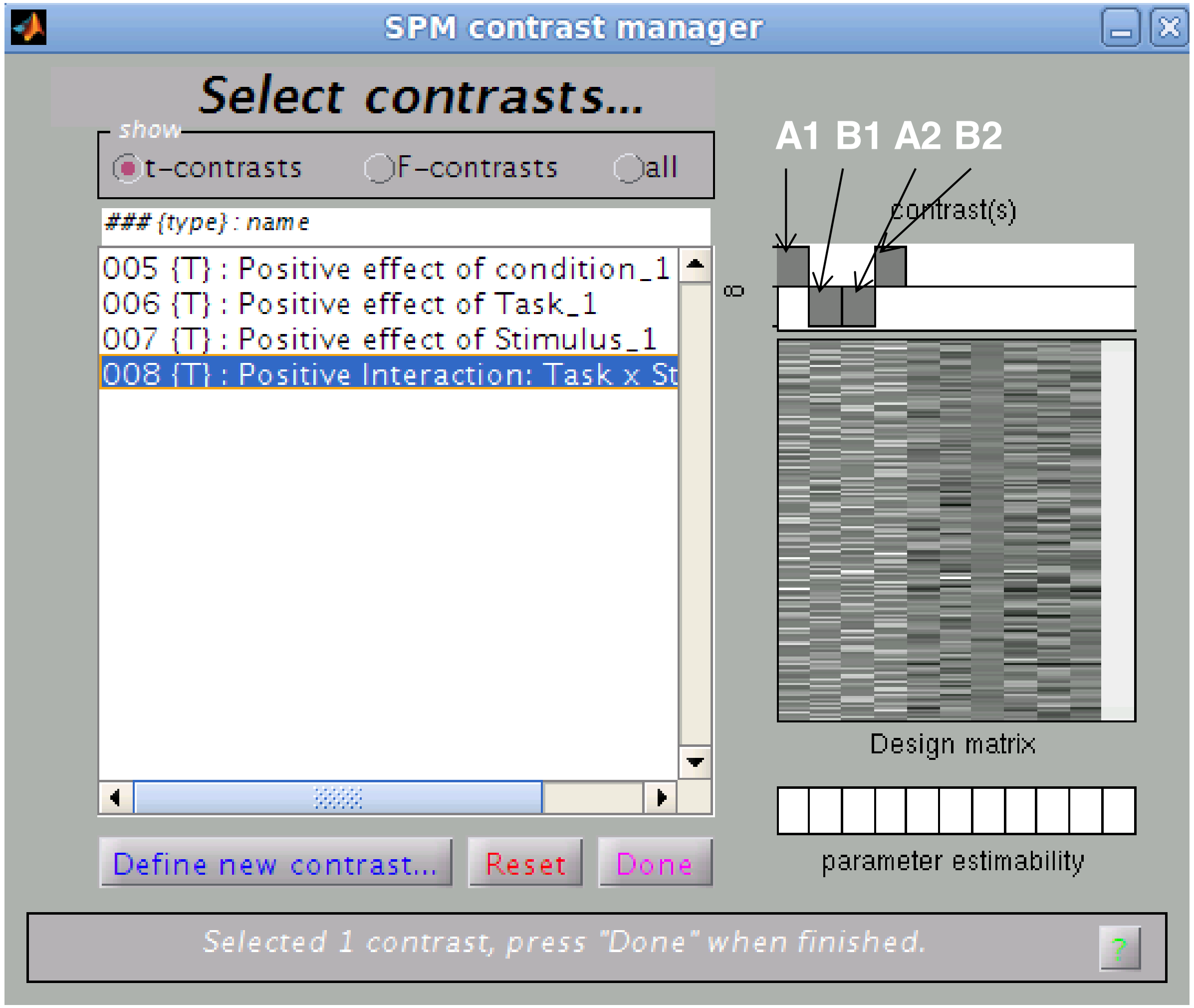
Factorial design

Task (1/2)

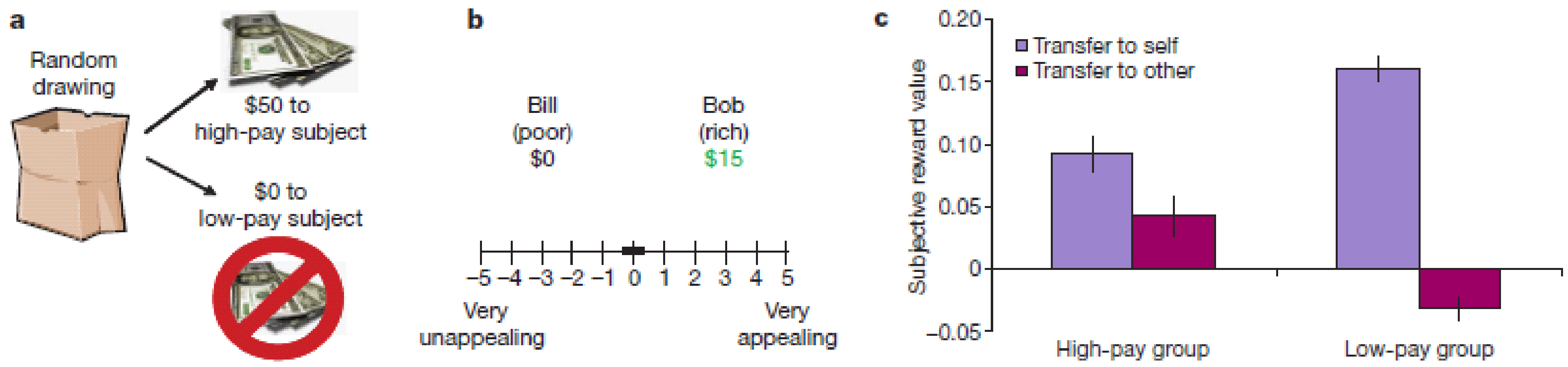
Stimuli (A/B)	Viewing	Naming
Colours	A1	A2
Objects	B1	B2

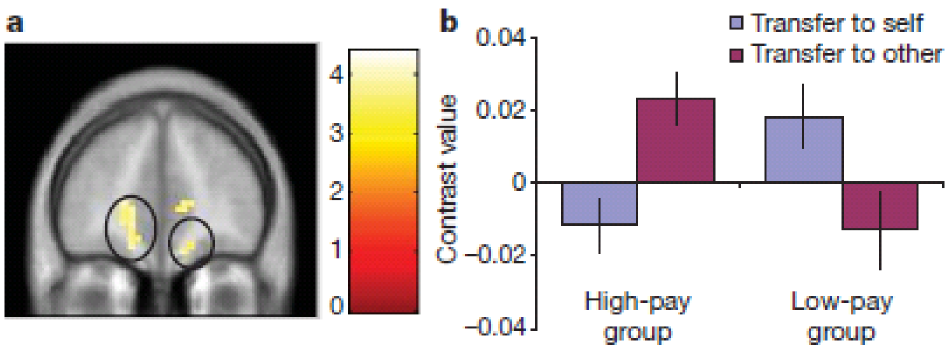
Interaction of task and stimuli:

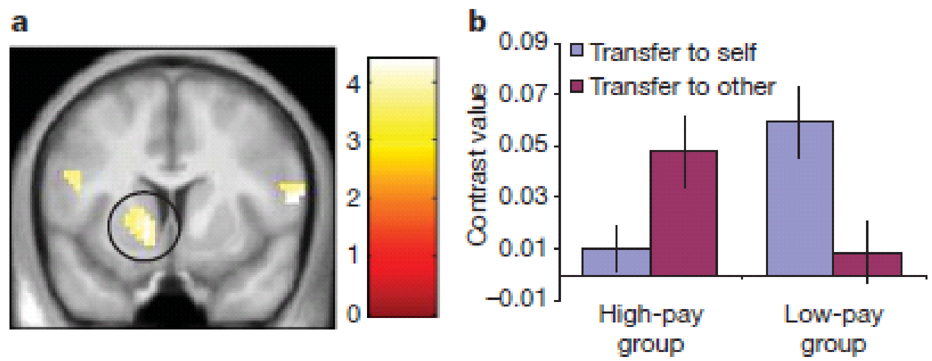
(A1 – B1) – (A2 – B2)



Example: evidence for inequality-aversion







Tricomi et al. 2010, *Nature*

Psycho-physiological interactions (PPI)

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:

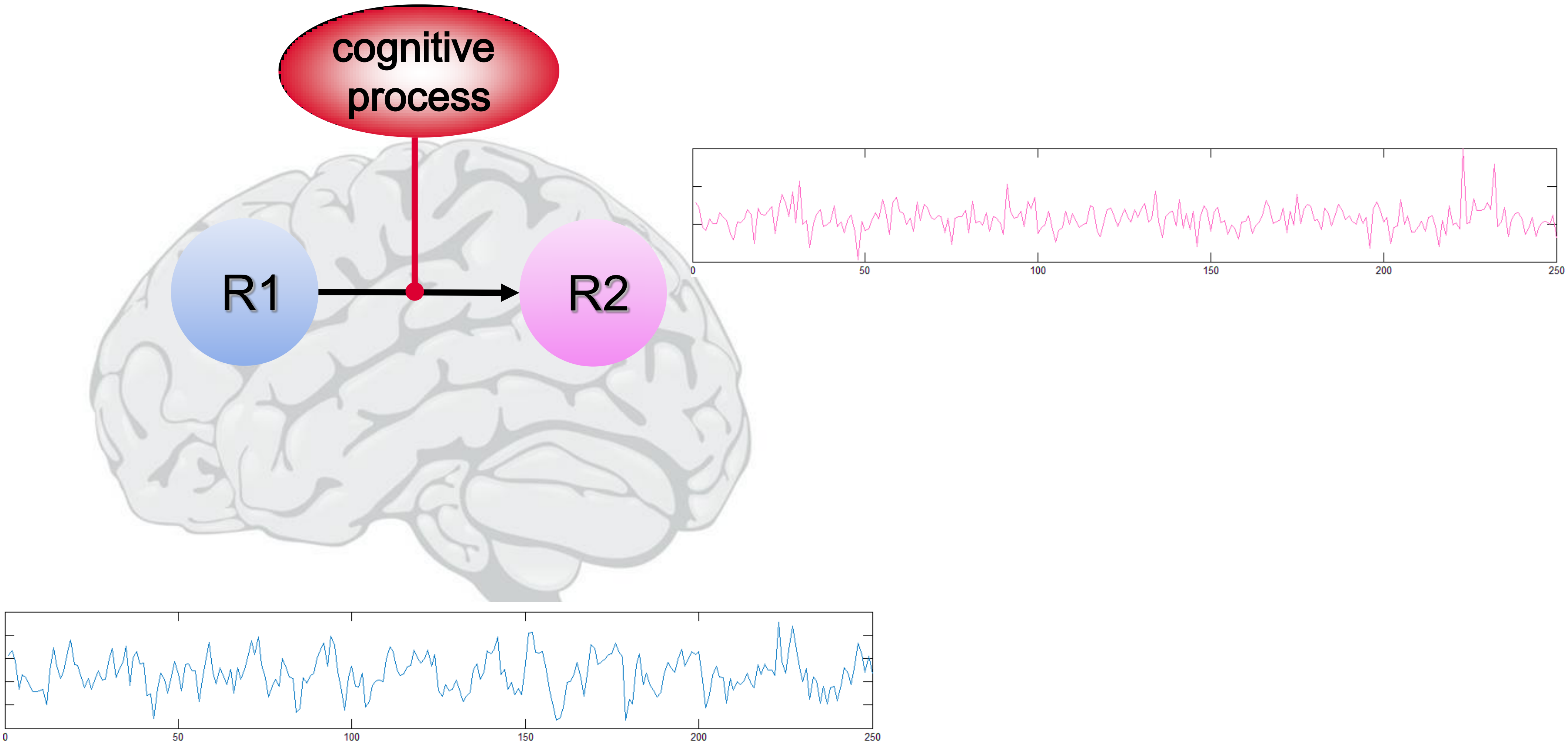
$$y = (T_A - T_B)\beta_1 \quad \text{main effect of task}$$
$$+ (S_1 - S_2)\beta_2 \quad \text{main effect of stim. type}$$
$$+ (T_A - T_B)(S_1 - S_2)\beta_3 \quad \text{interaction}$$
$$+ e$$

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:

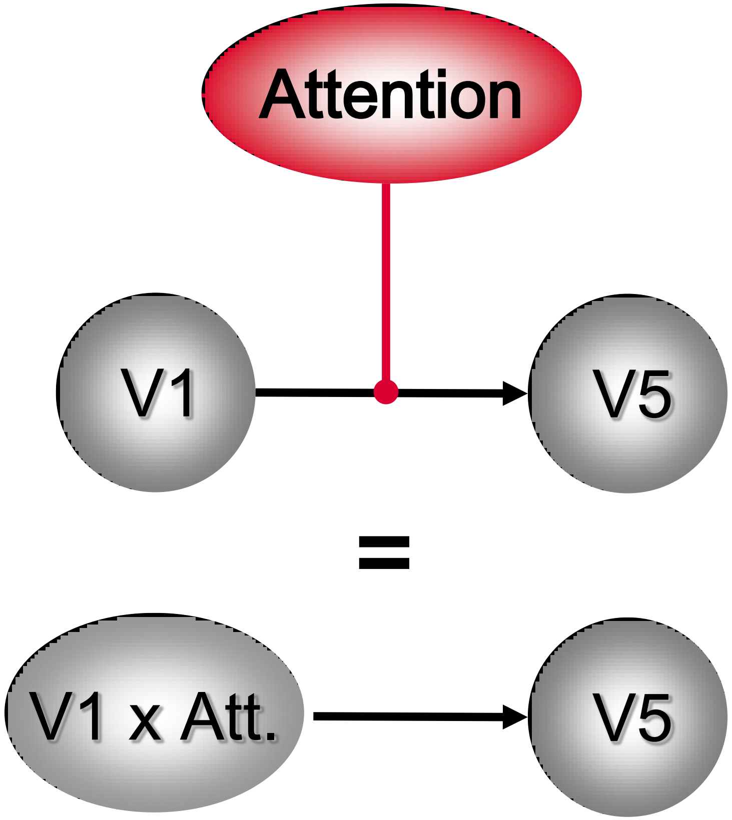
$$y = (T_A - T_B)\beta_1 \quad \text{main effect of task}$$
$$+ V1\beta_2 \quad \text{V1 time series} \approx \text{main effect of stim. type}$$
$$+ (T_A - T_B)V1\beta_3 \quad \text{psycho-physiological interaction}$$
$$+ e$$

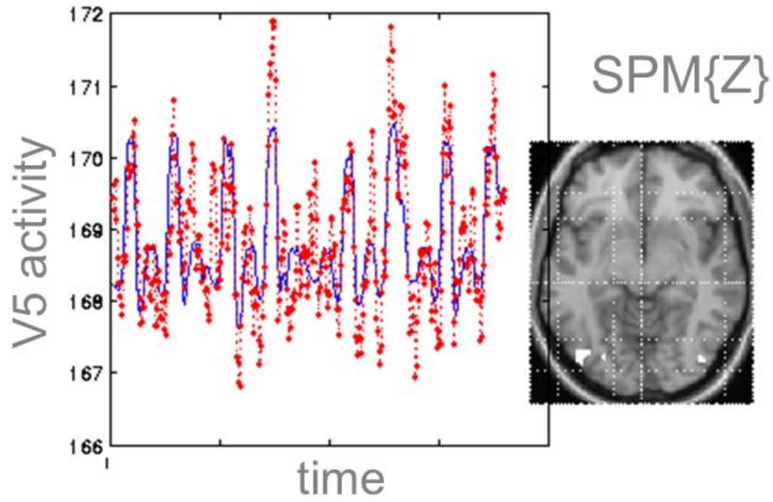
Psycho-physiological interactions (PPI)

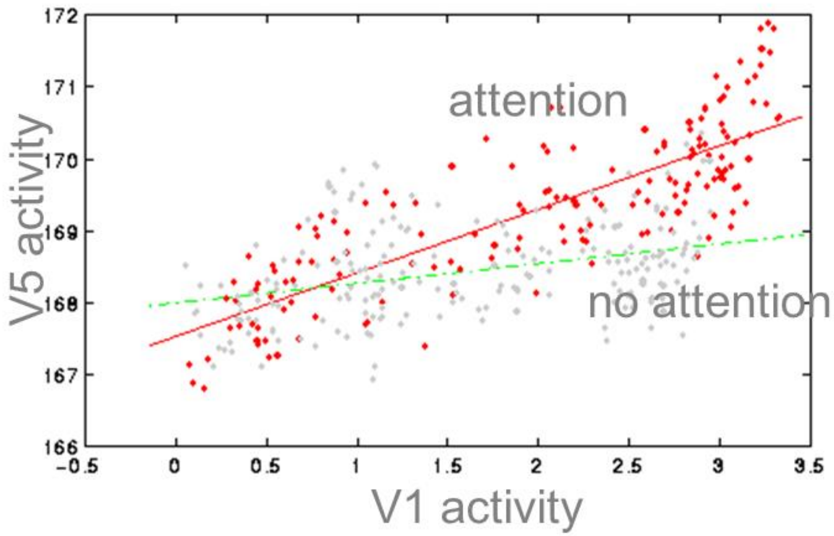


Translational Neuromodeling Unit

PPI example: attentional modulation of V1→V5





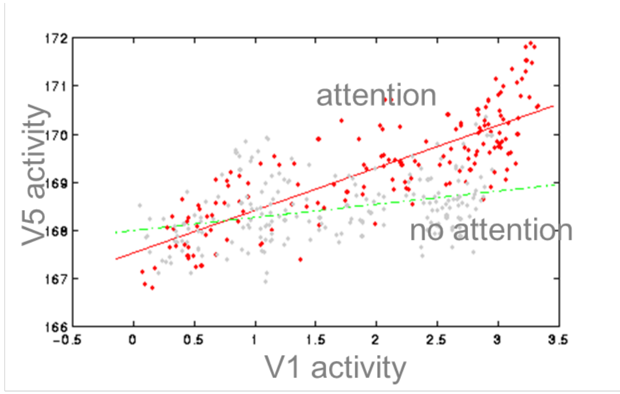


Friston et al. 1997, *NeuroImage* 6:218-229
Büchel & Friston 1997, *Cereb. Cortex* 7:768-778

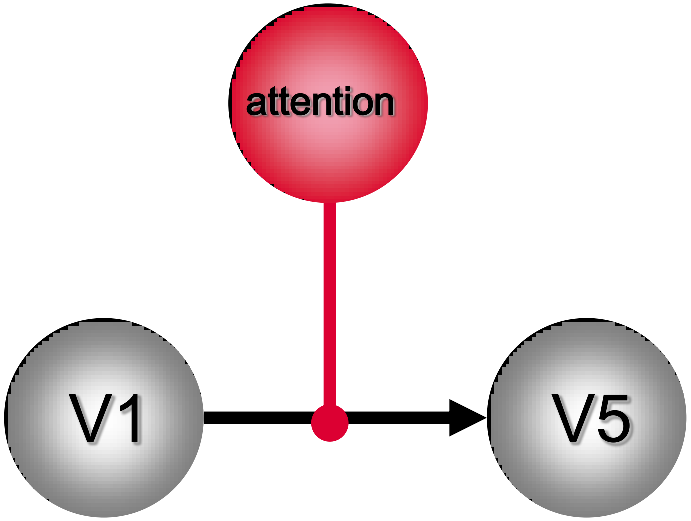
Translational Neuromodeling Unit

PPI: interpretation

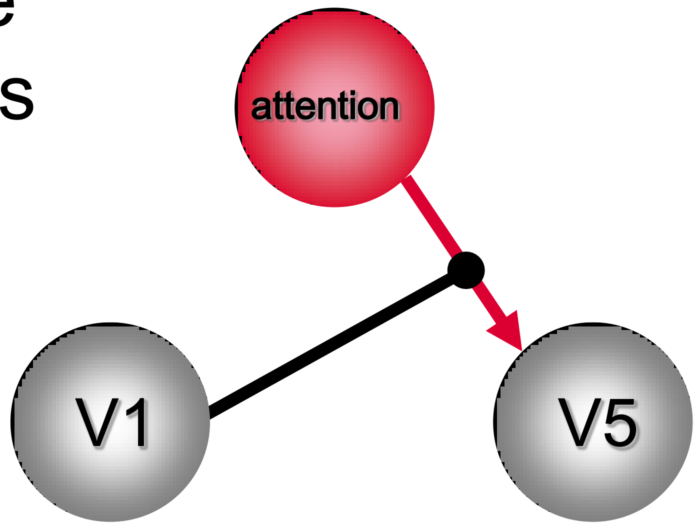
$$y = (T_A - T_B)\beta_1 + V1\beta_2 + (T_A - T_B)V1\beta_3 + e$$



Two possible interpretations of the PPI term:



Modulation of V1→V5 by attention



Modulation of the impact of attention on V5 by V1.

Overview

- 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

Thank you