



# Experimental designs for functional neuroimaging

Lauri Nummenmaa

Turku PET Centre / TYKS

Twitter: @LNummenmaa

WWW: <http://emotion.utu.fi/>

# Lecture contents

- Basic problems in experimental design and model fitting
- Basic experimental designs
  - Boxcar design
  - Event-related design
  - Parametric designs
  - Analysing unconstrained conditions



A lateral view of a human brain, colored blue, with a world map overlay. The map shows continents in green and yellow, and oceans in blue. The text "Cerebral cartography with functional imaging" is overlaid on the brain.

# Cerebral cartography with functional imaging



# Magnetic resonance imaging (MRI)

- Based on the magnetic resonance of the hydrogen nuclei
- Measuring the behaviour of hydrogen nuclei in the strong magnetic field of the MRI device allows studying different tissues in vivo
- Adjusting imaging sequence allows highlighting different tissues or their different characteristics



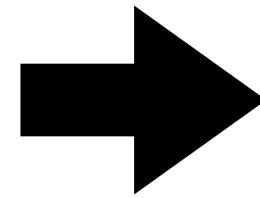


# Experiment: Linking stimulation model with measurements

## BACKGROUND LUMINOSITY



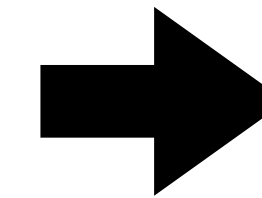
**Independent variable**  
Controlled by experimenter



## PUPIL DIAMETER



**Dependent variable**  
Researcher measures if changes in the independent variable cause changes in the dependent variable



## SIGNAL

Experiment-induced variations in pupil size

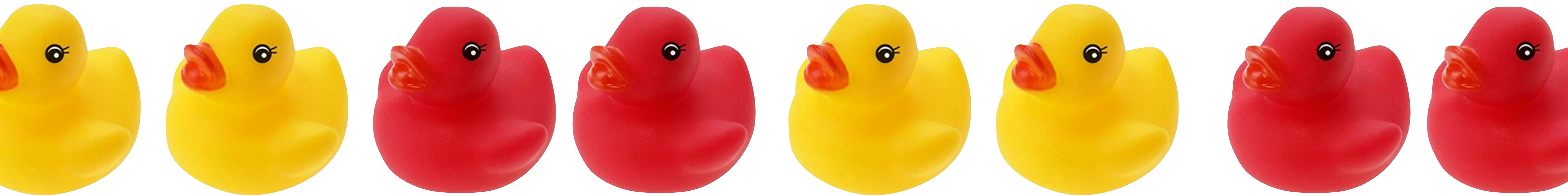
+

## NOISE

Errors in measurement, individual differences

**STATISTICS = SEPARATING NOISE FROM SIGNAL IN A PROBABILISTIC FASHION**

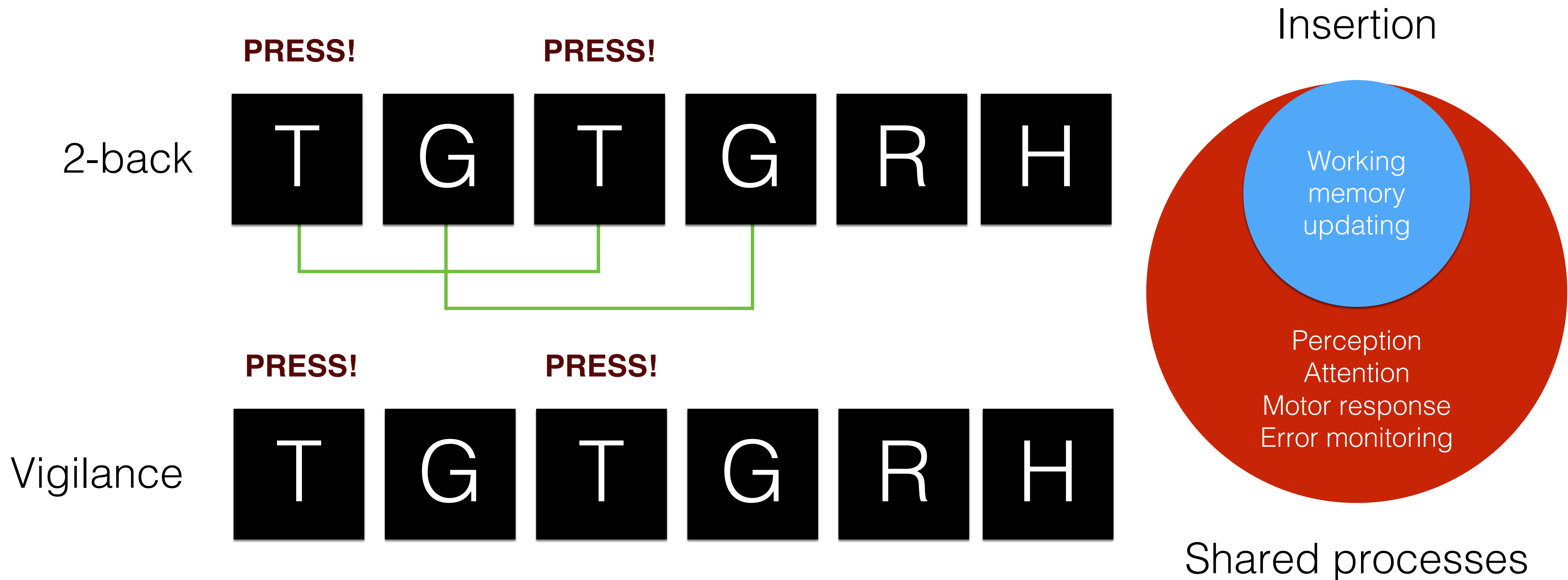
# Cognitive subtraction



Induce brain in states **A** and **B** and calculate the differential activation

**Problem:** assumption of pure insertion

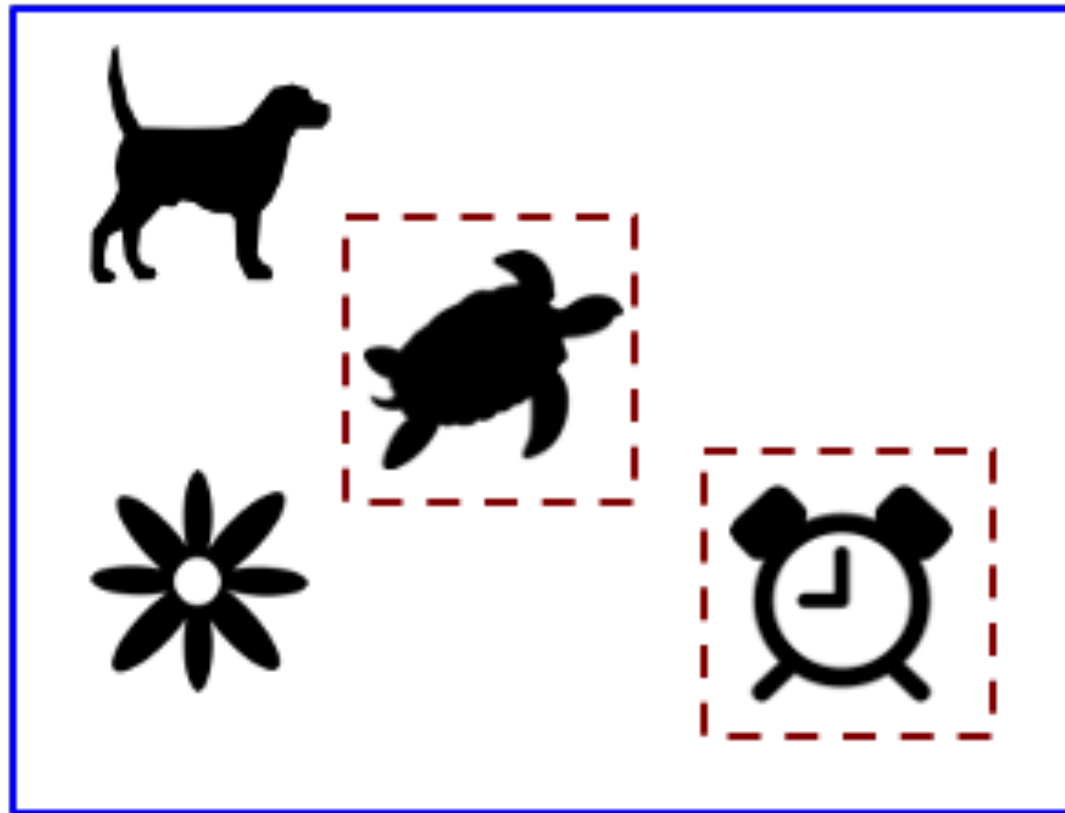




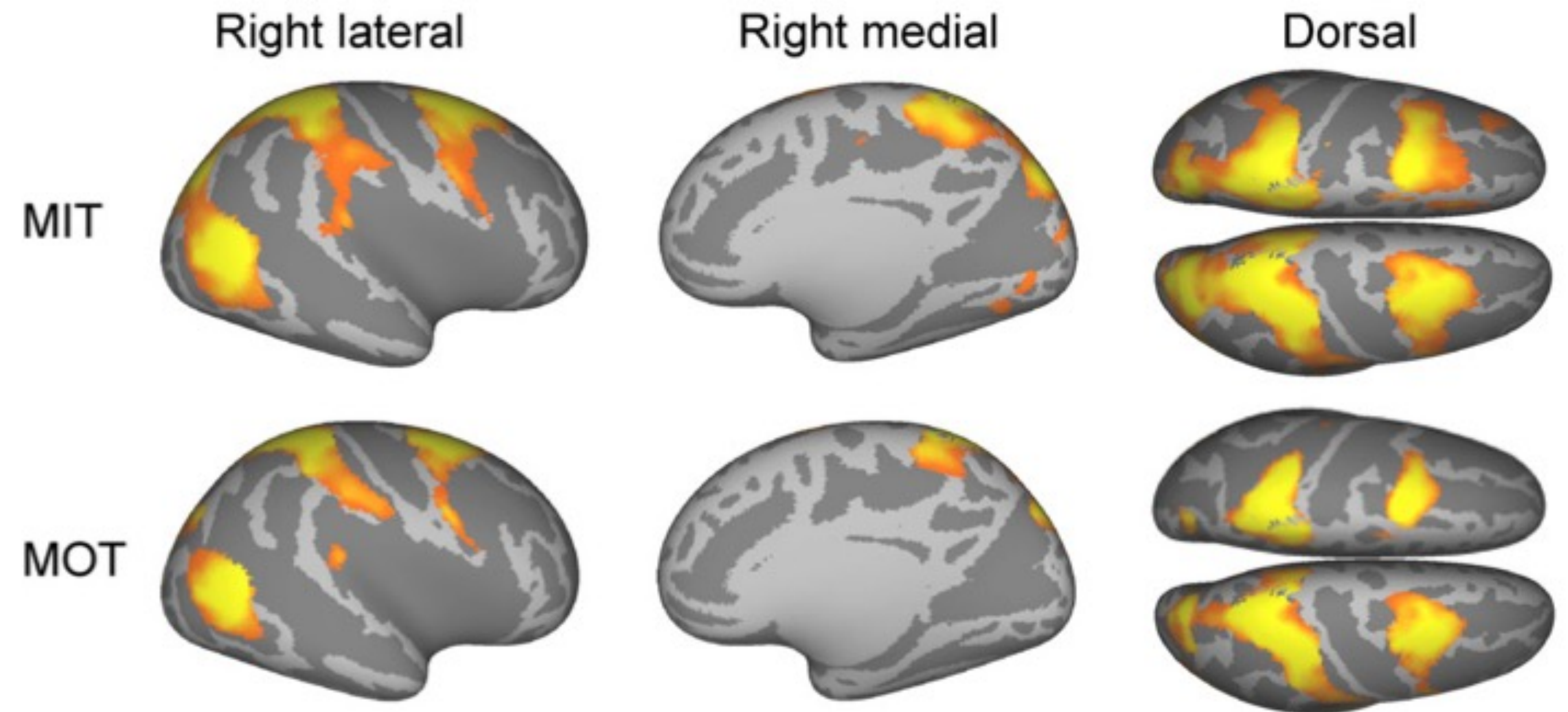
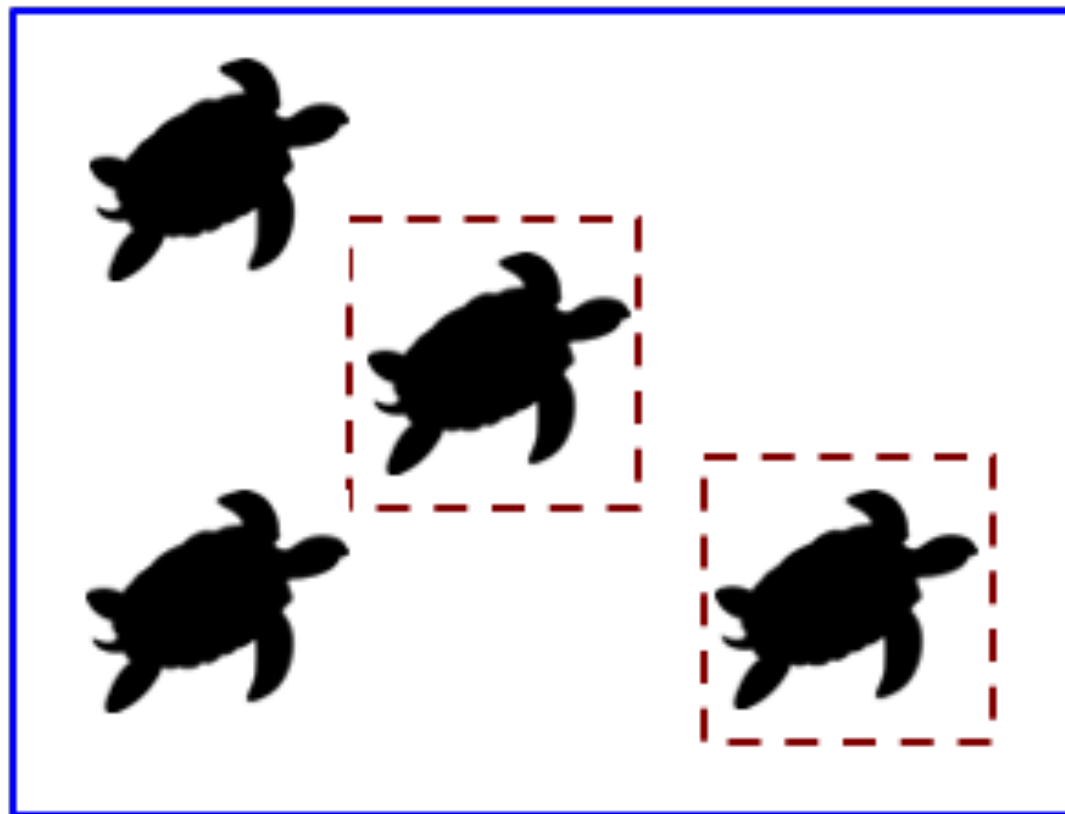
**Pure insertion:** assumption that inserting another component to the task does not affecting the remaining process

### A) Multiple Identity Tracking (MIT)

4 s

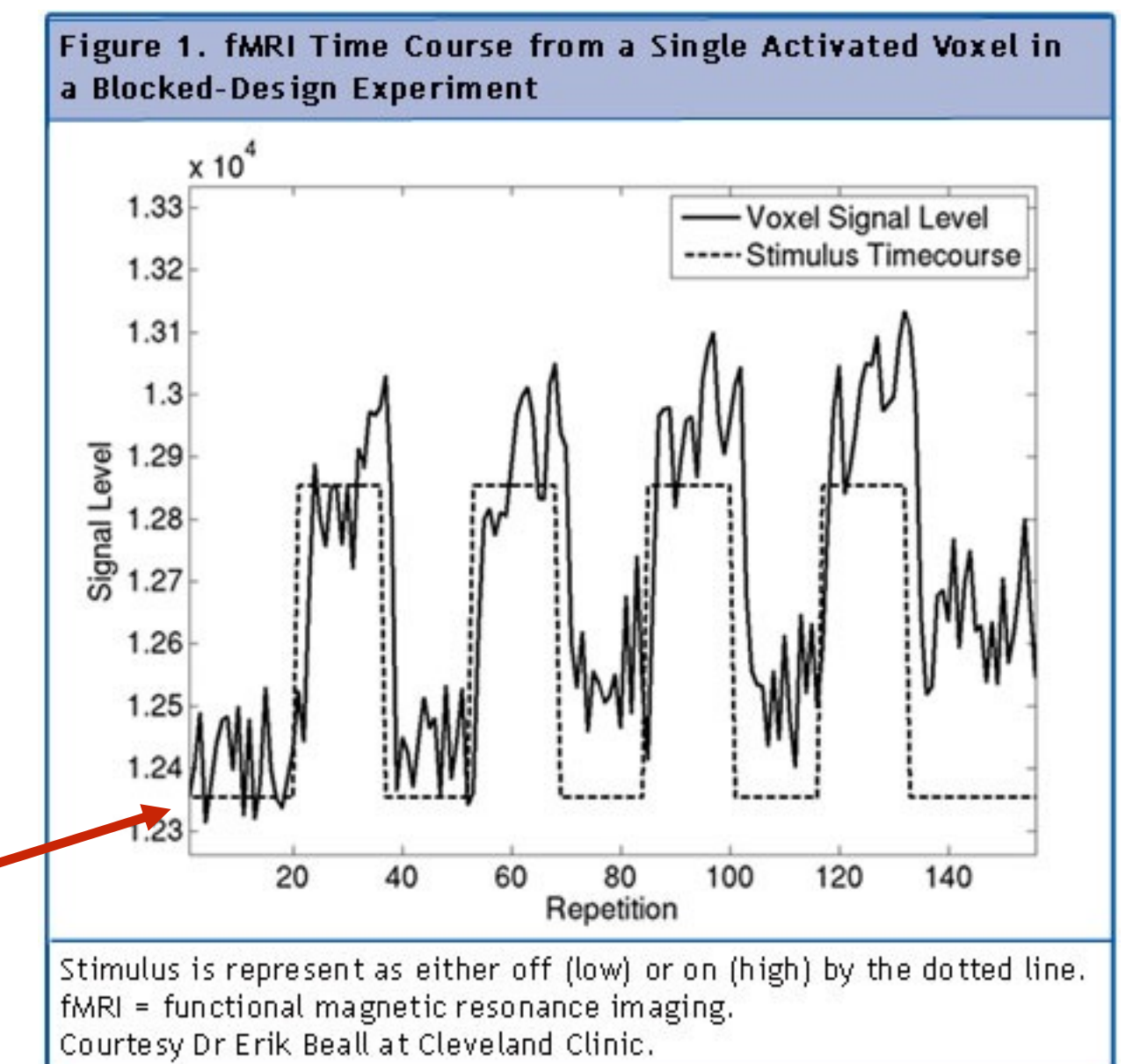
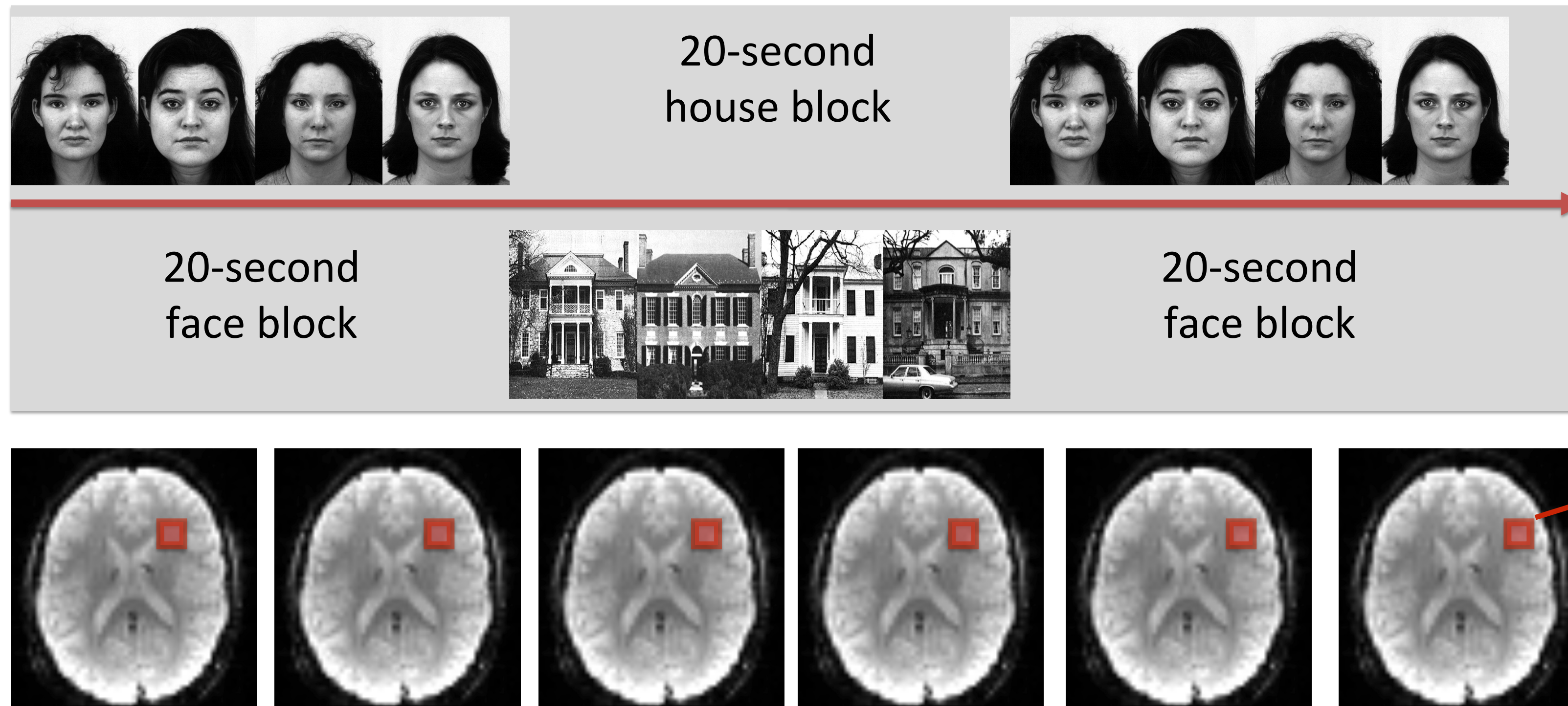


### B) Multiple Object Tracking (MOT)





# Typical fMRI experiment

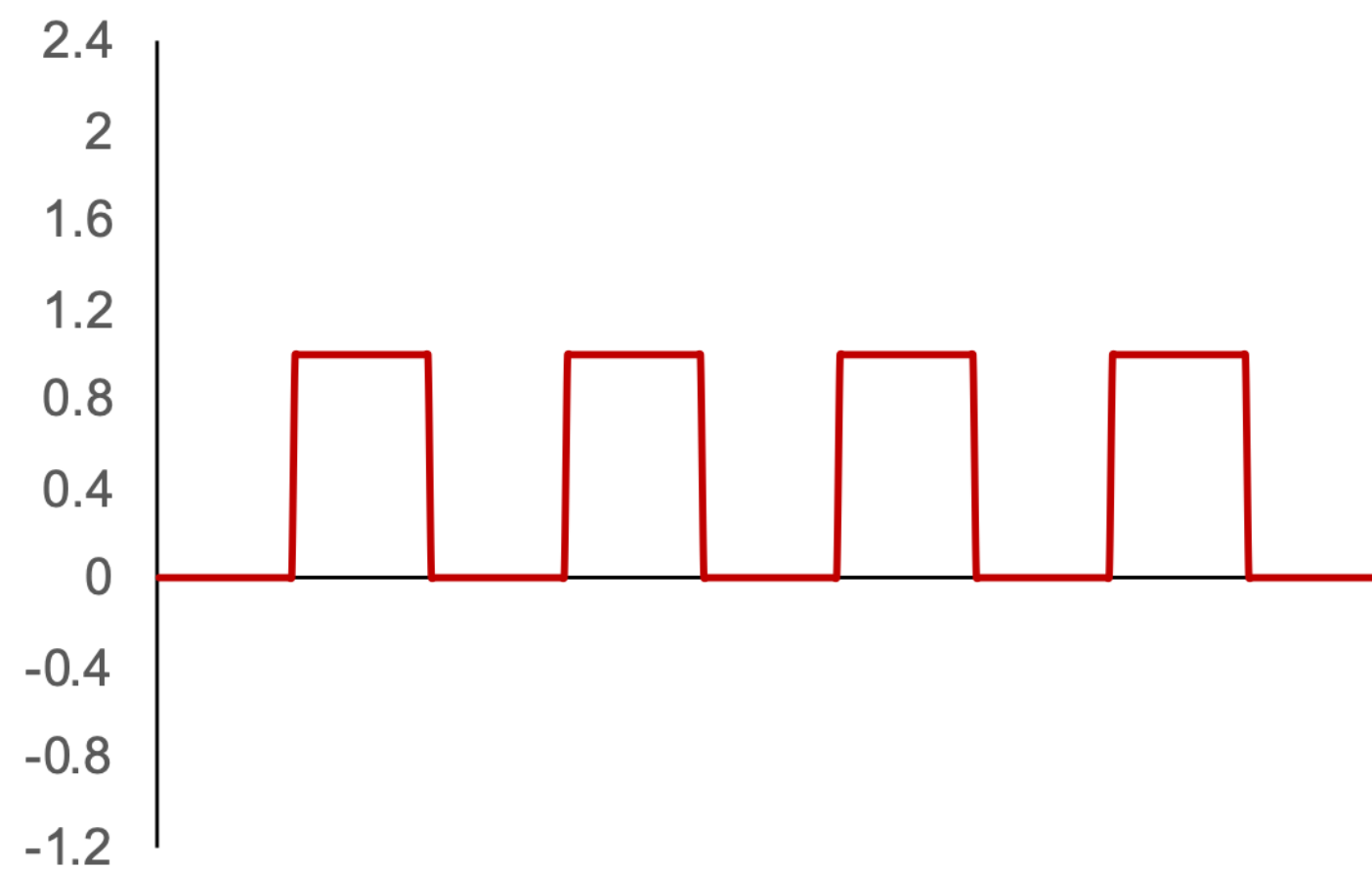


Acquiring one 3D functional volume takes about 1.5 seconds

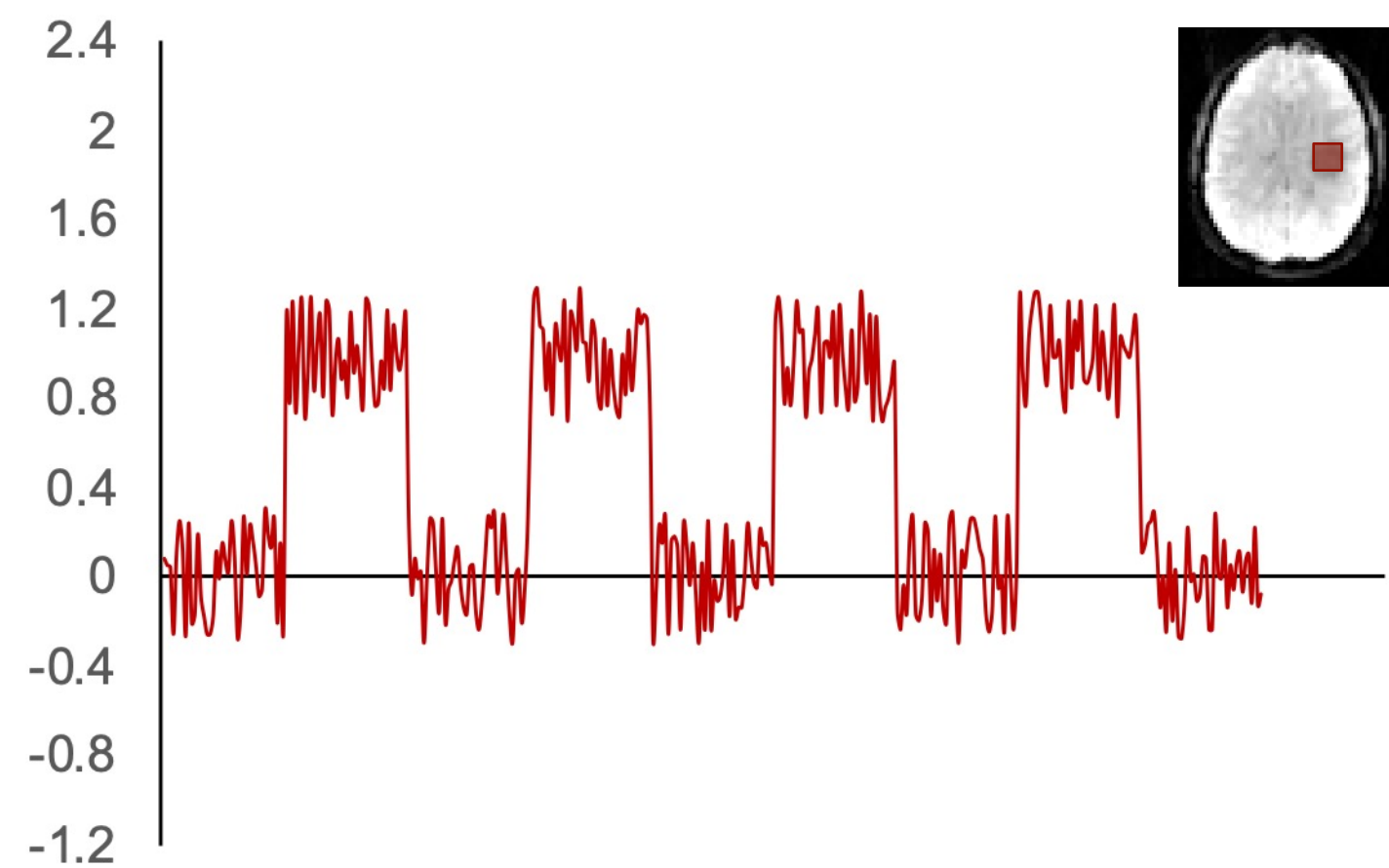
We can distinguish events  $\sim 100\text{ms}$  apart, yet their actual timing can be resolved with about 2-s accuracy

# Fitting the model to the data

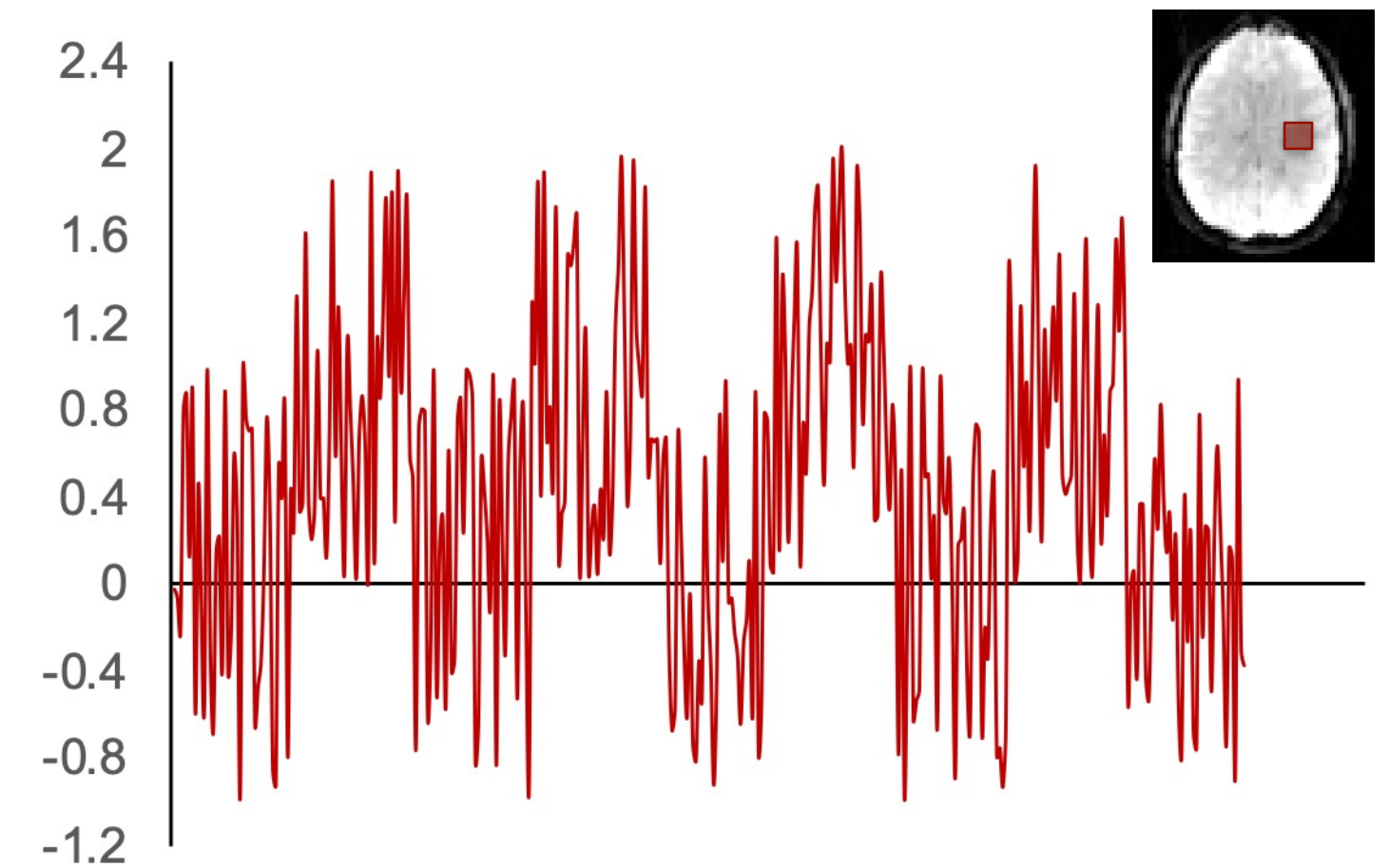
Stimulation model (boxcar)



Clean data

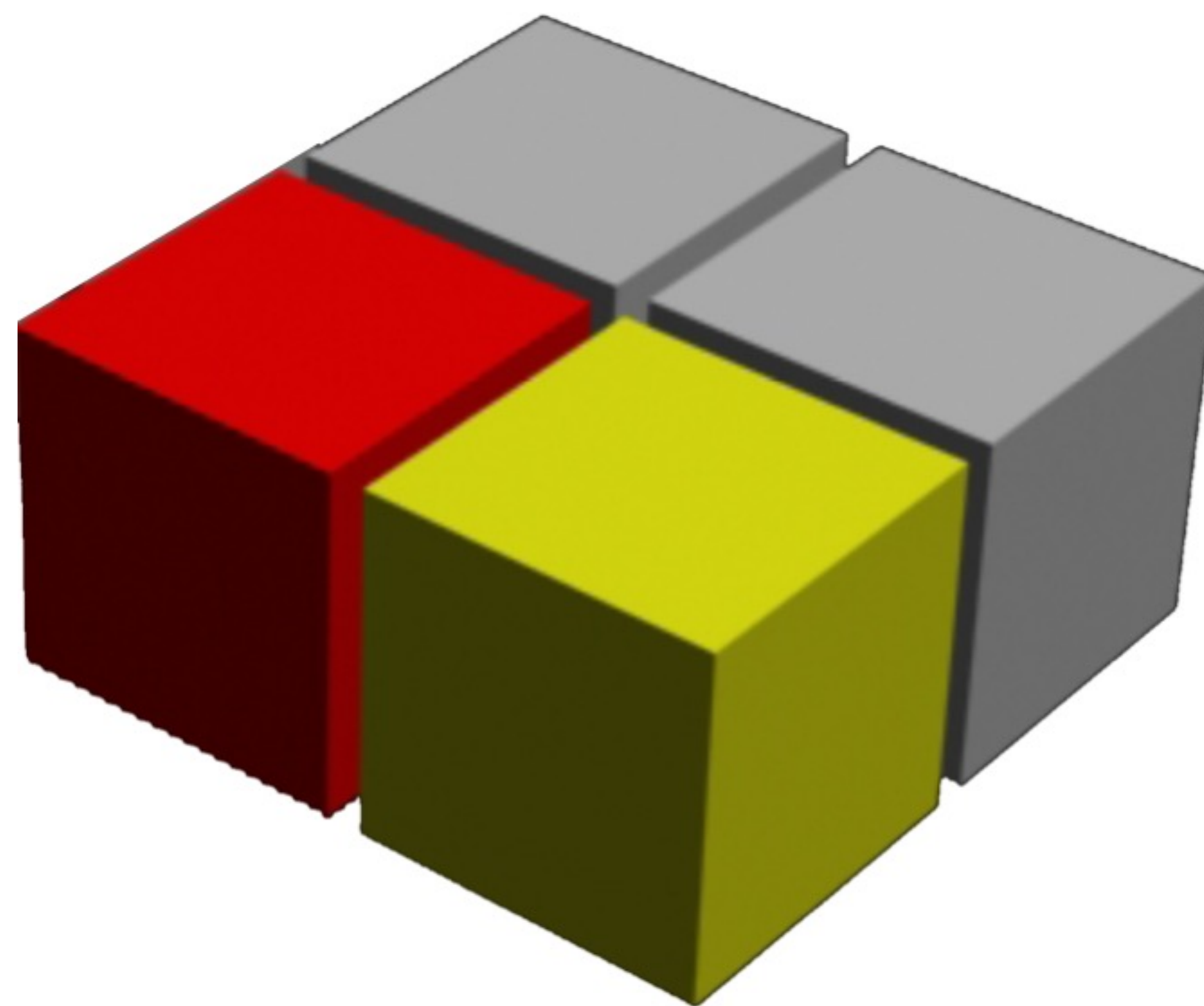
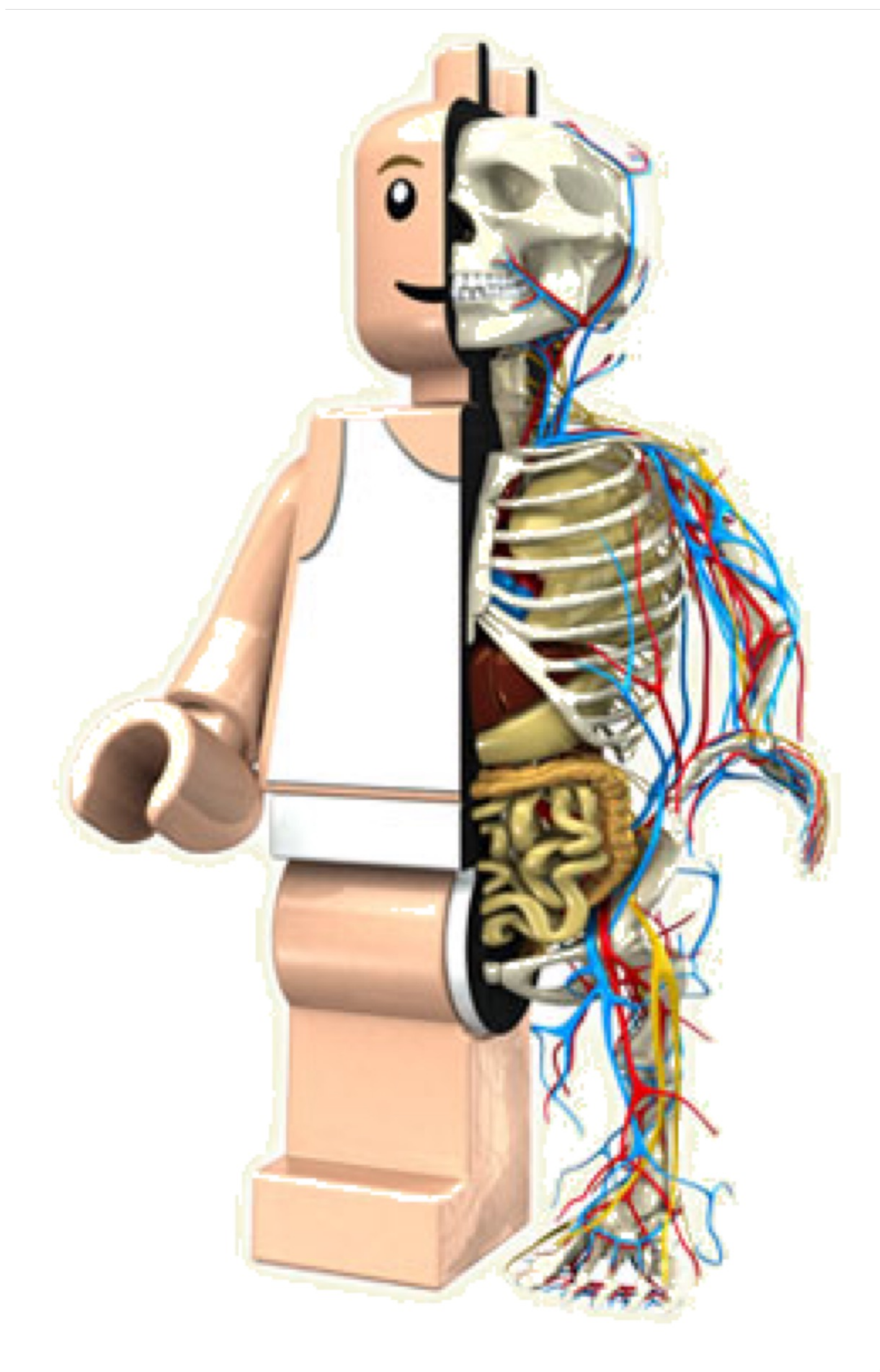


Noisy data



**Basic idea:** model how well the stimulation model predicts BOLD time course at each voxel

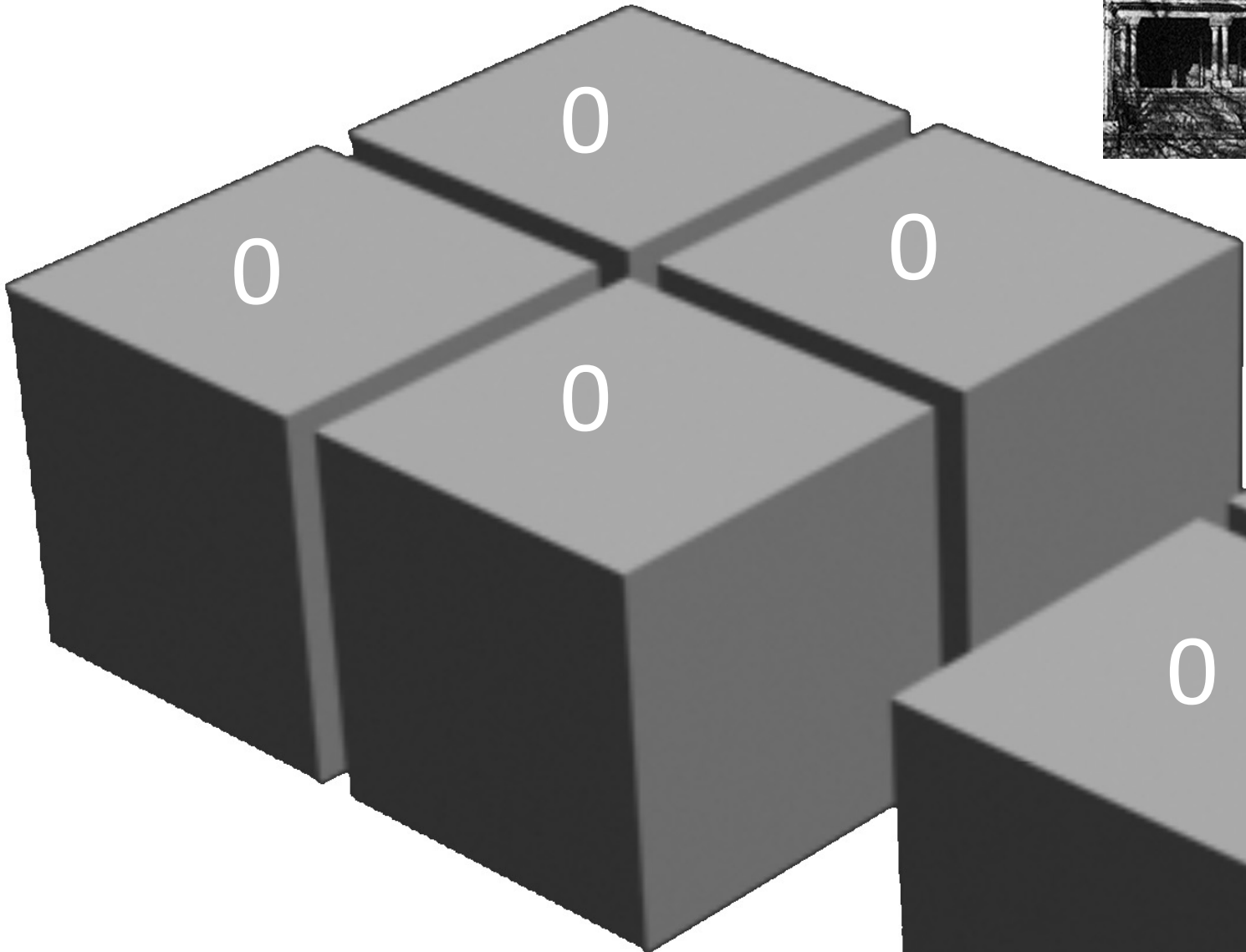




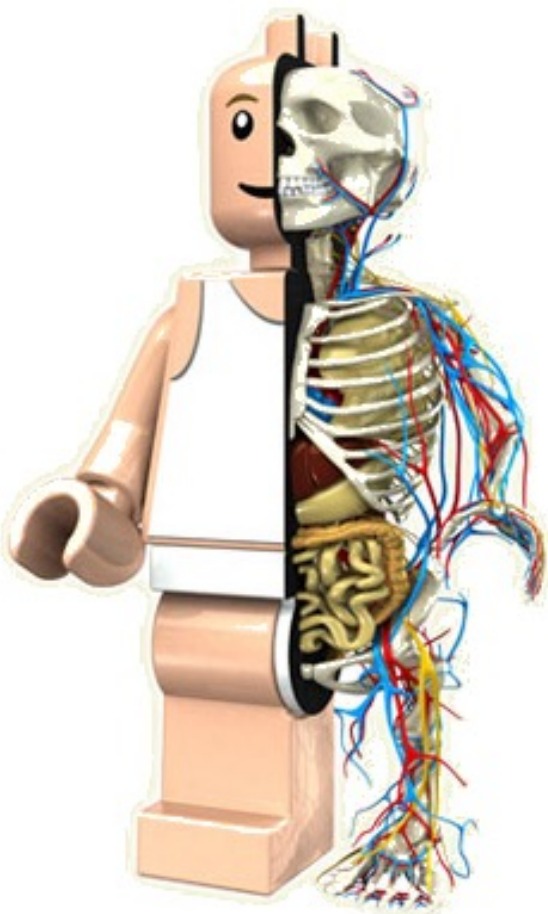
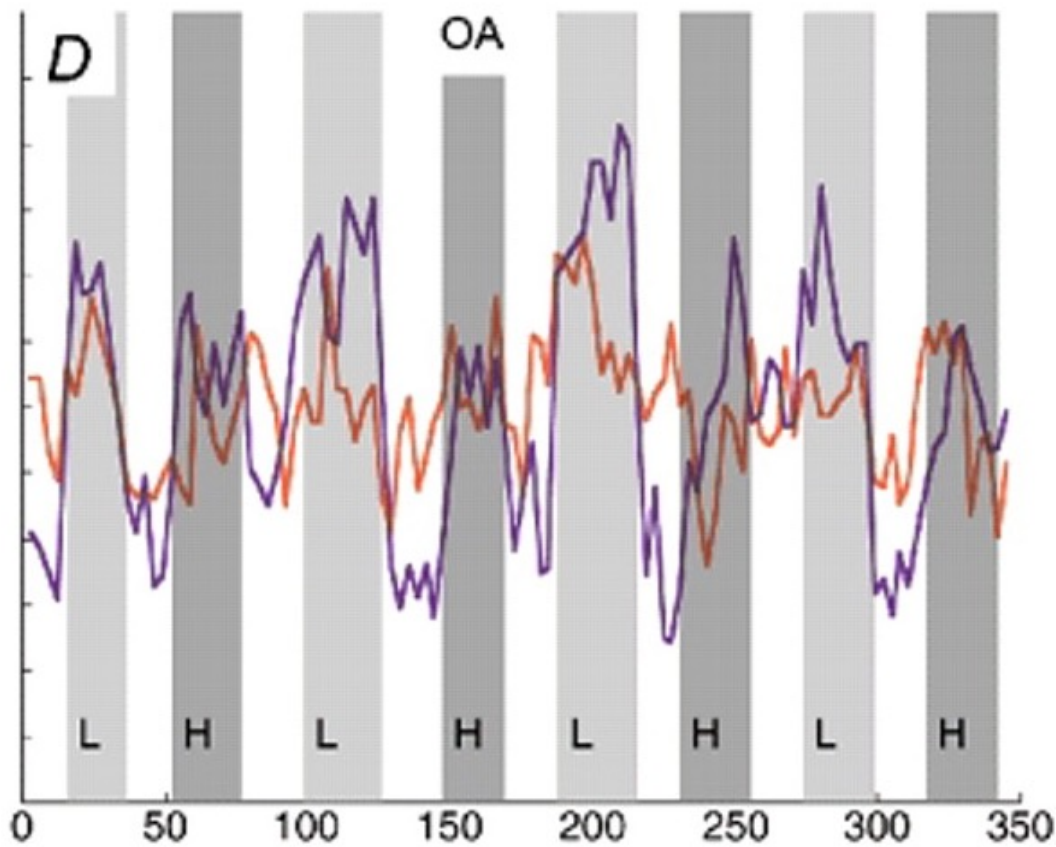
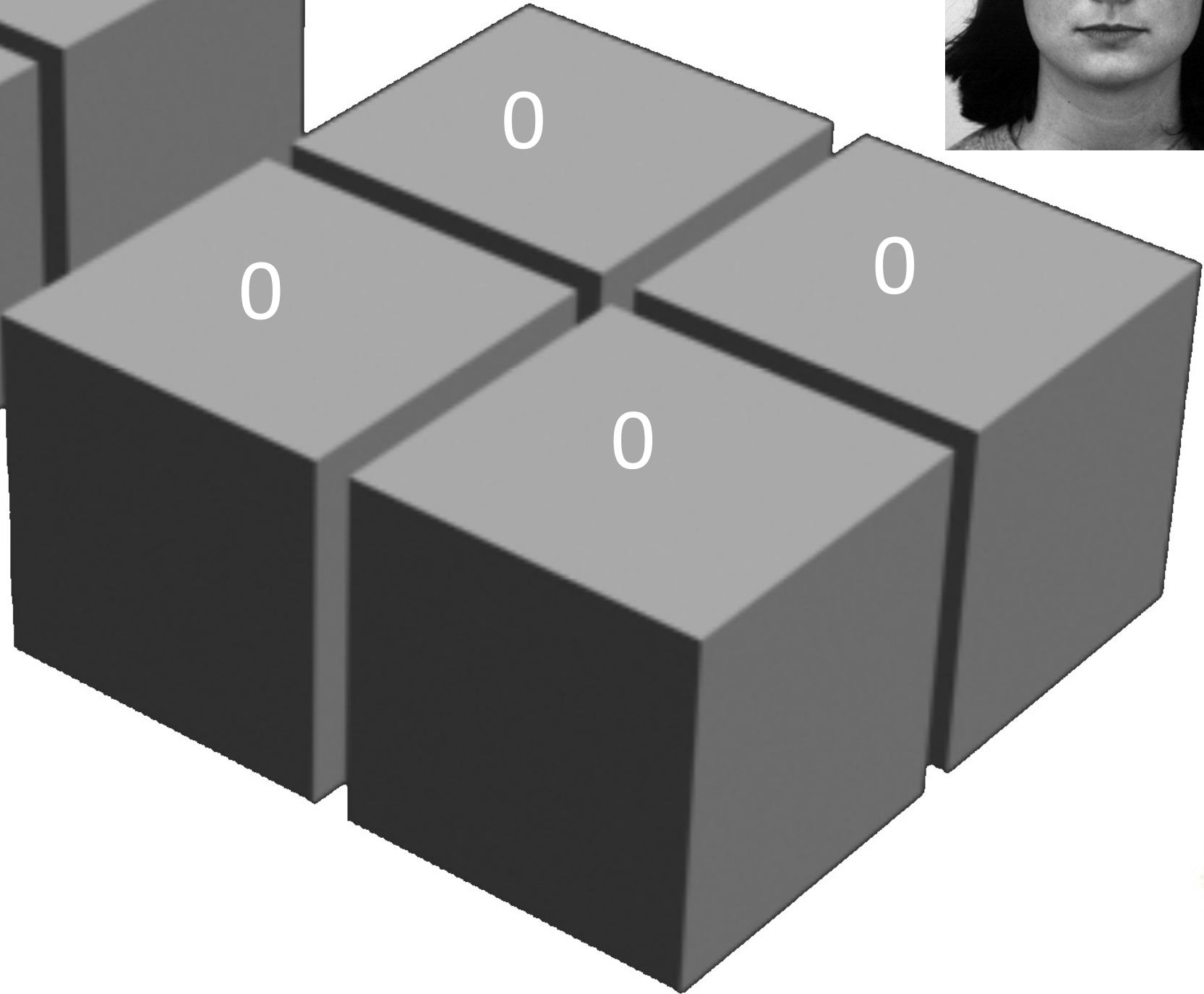


# First level model with LEGO brains

HOUSES

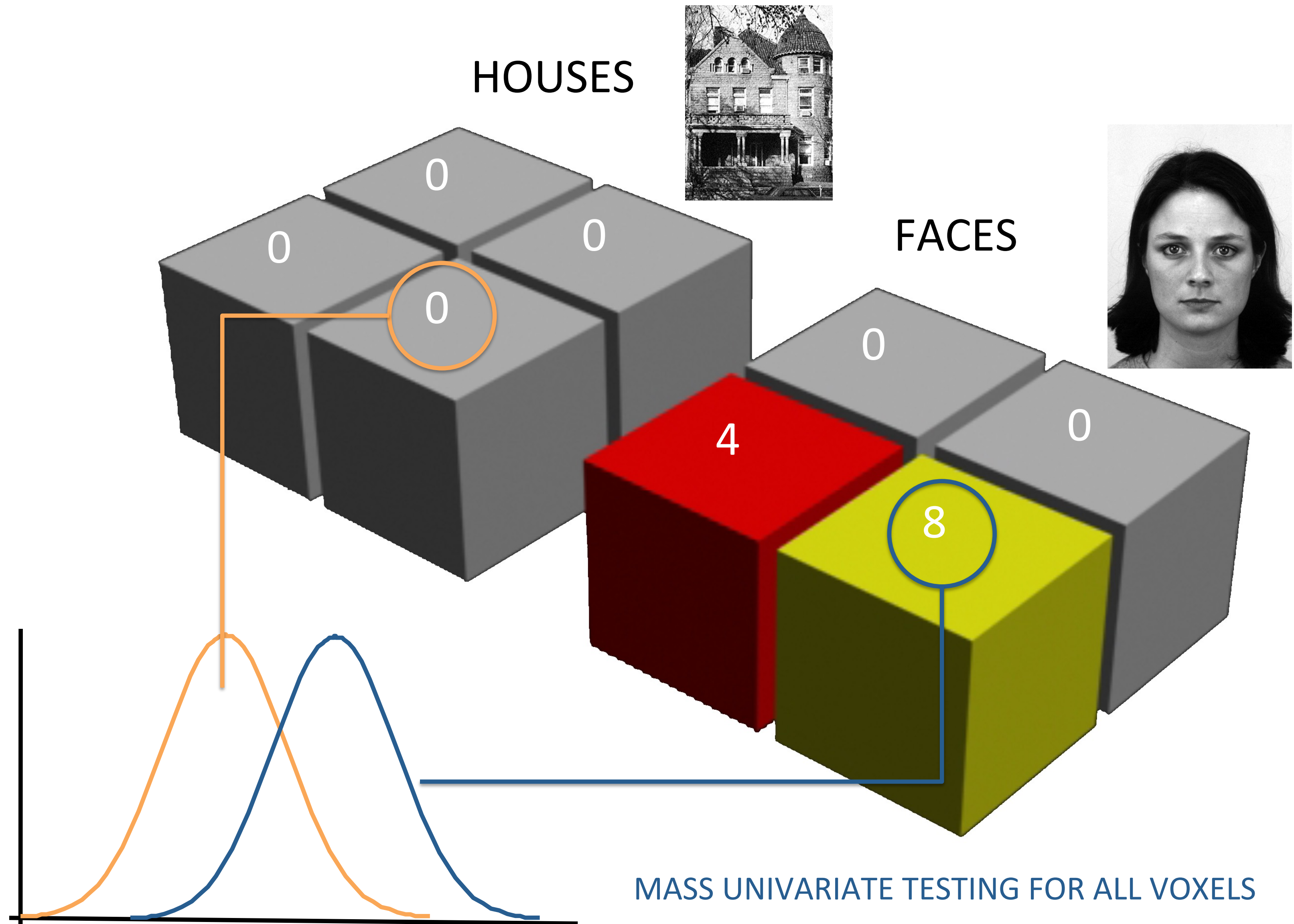


FACES





# First level model with LEGO brains



# Basic tool 1: Boxcar design



**AIM:** Localize brain regions that are more involved in process 1 vs. process 2

**DESIGN:** Blocked experiment using cognitive subtraction assuming pure insertion

**ADVANTAGES:** Simple, powerful, often short experiments

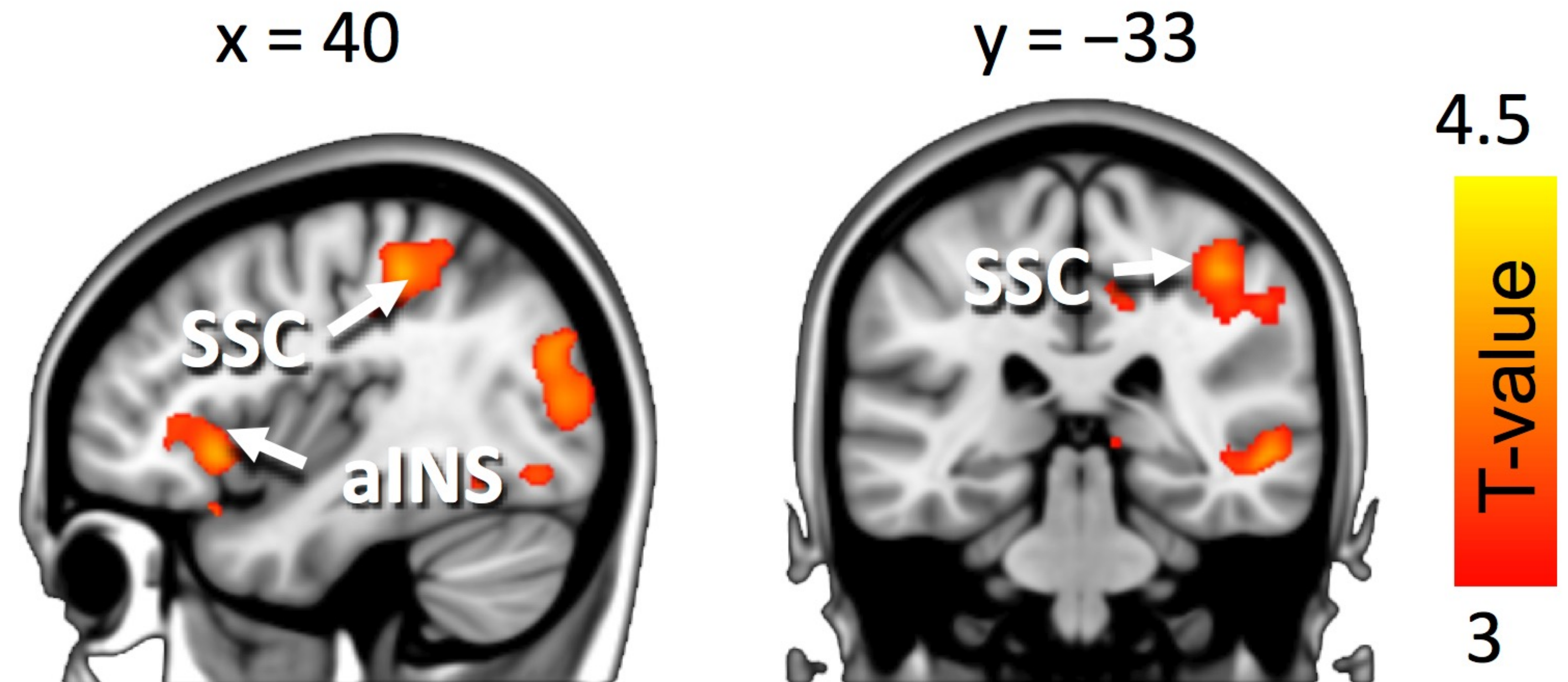


# Networks for vicarious pain perception

Feel pain trial

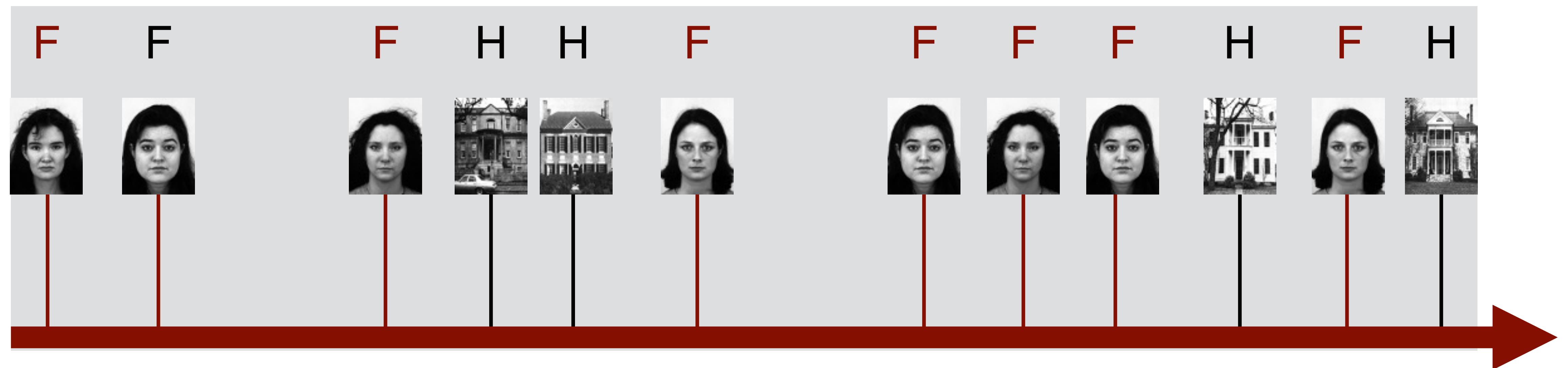


Cause pain trial



Nummenmaa et al (2014 J Neurosci)

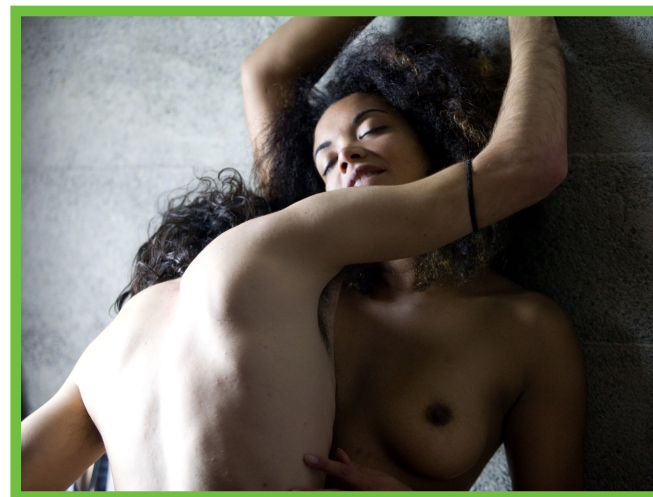
# Basic tool 2: Event-related design



**AIM:** Localize brain regions that are more sensitive to process 1 vs. process 2  
**DESIGN:** Event-related design with cognitive subtraction assuming pure insertion  
**ADVANTAGES:** More accurate model, trial wise analysis, randomisation



1s



1s



1s



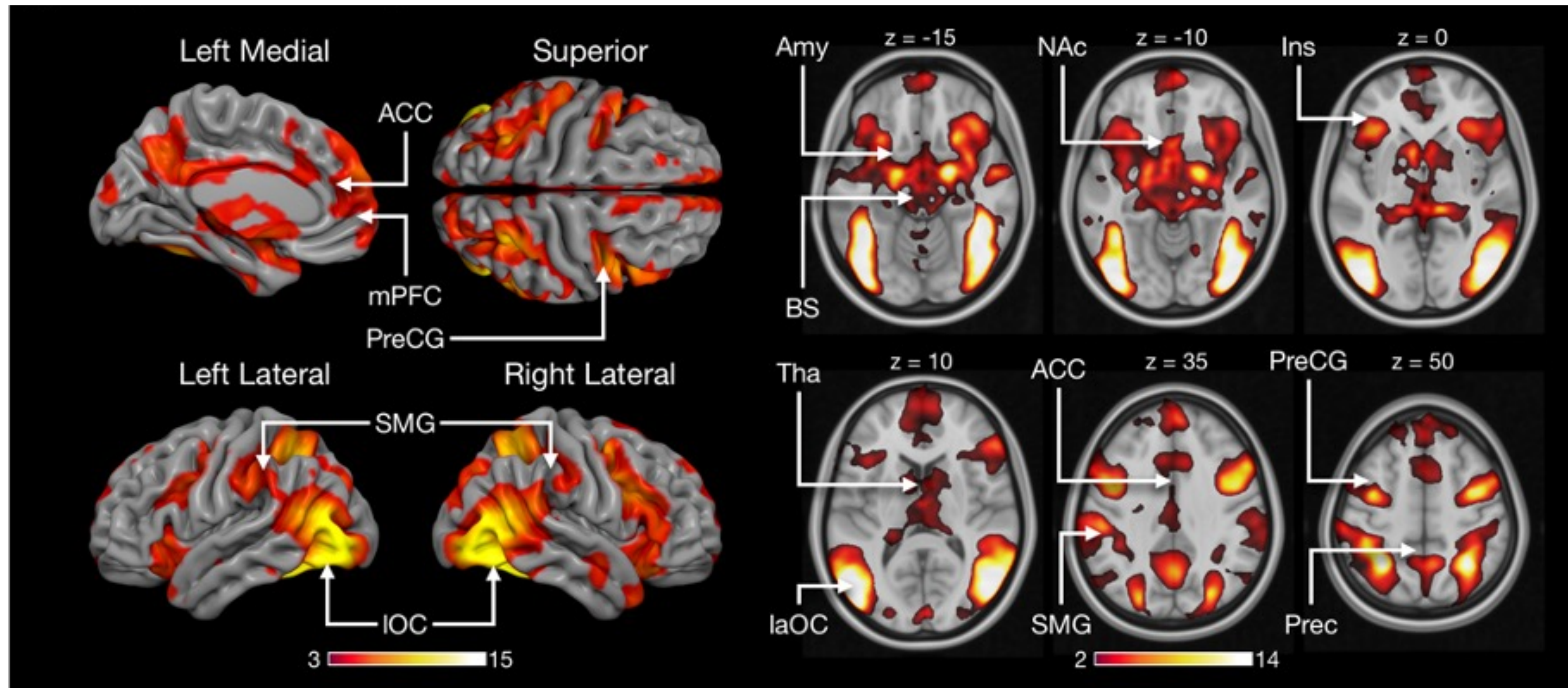
1s



1s



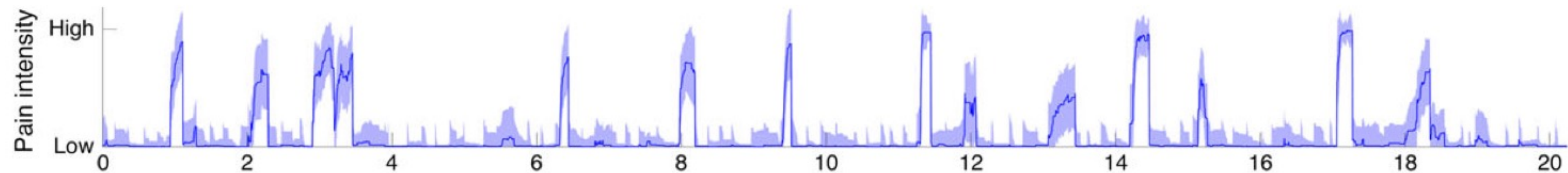
1s



Putkinen et al (submitted)



# Basic tool 3: Parametric design

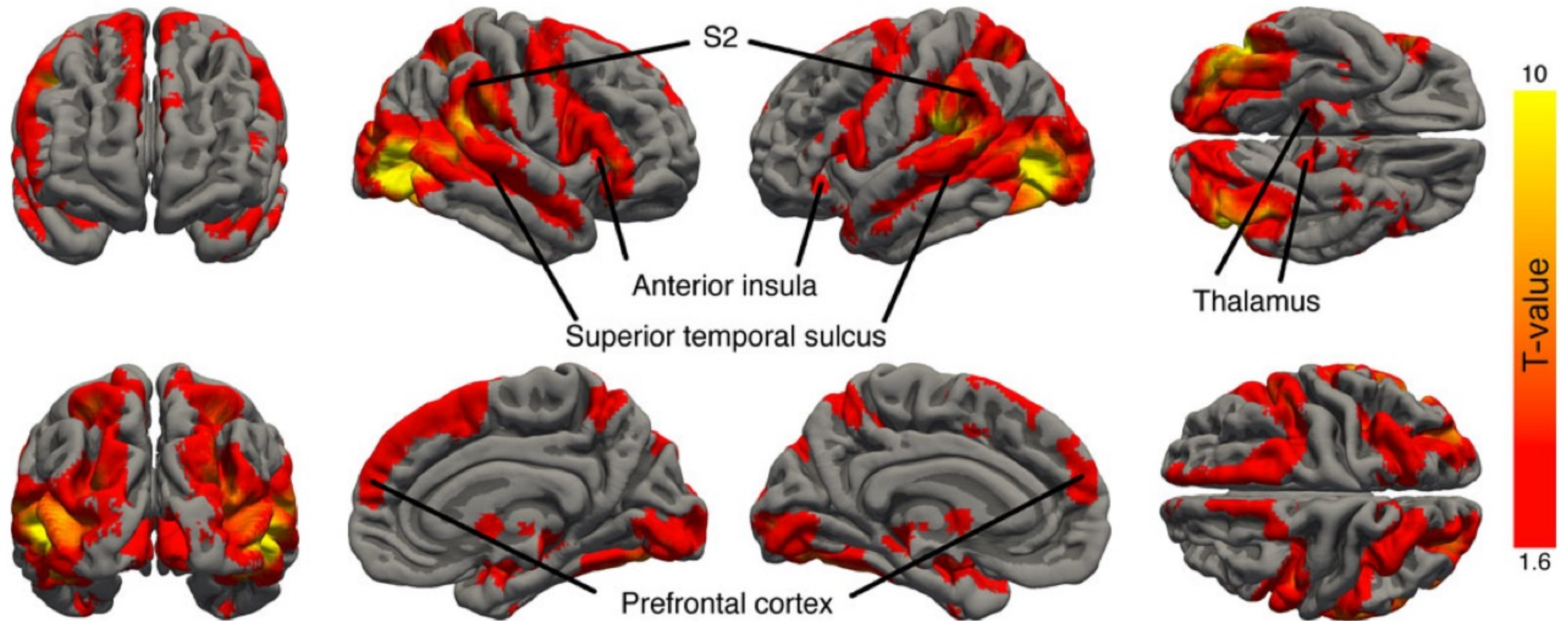


**AIM:** Localize brain regions that respond to vicarious pain

**DESIGN:** Parametric design with continuous stimulation model

**ADVANTAGES:** Quantitative stimulation model, high statistical power



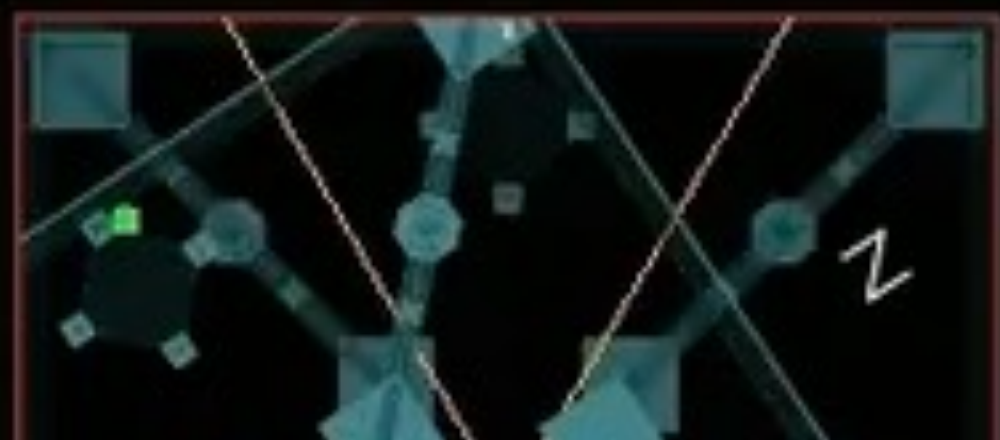
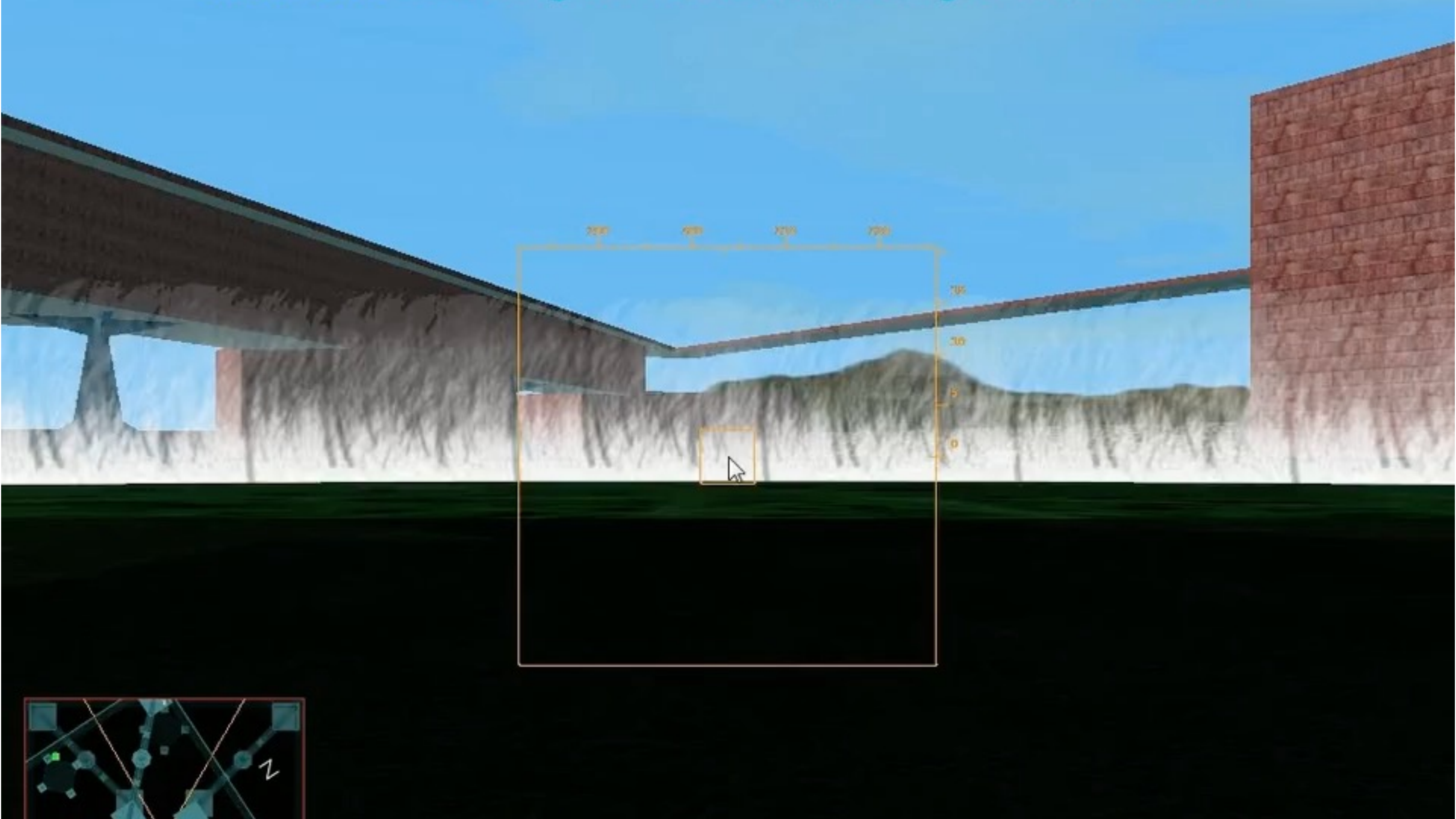


Karjalainen et al (2018 Cereb Cortex)



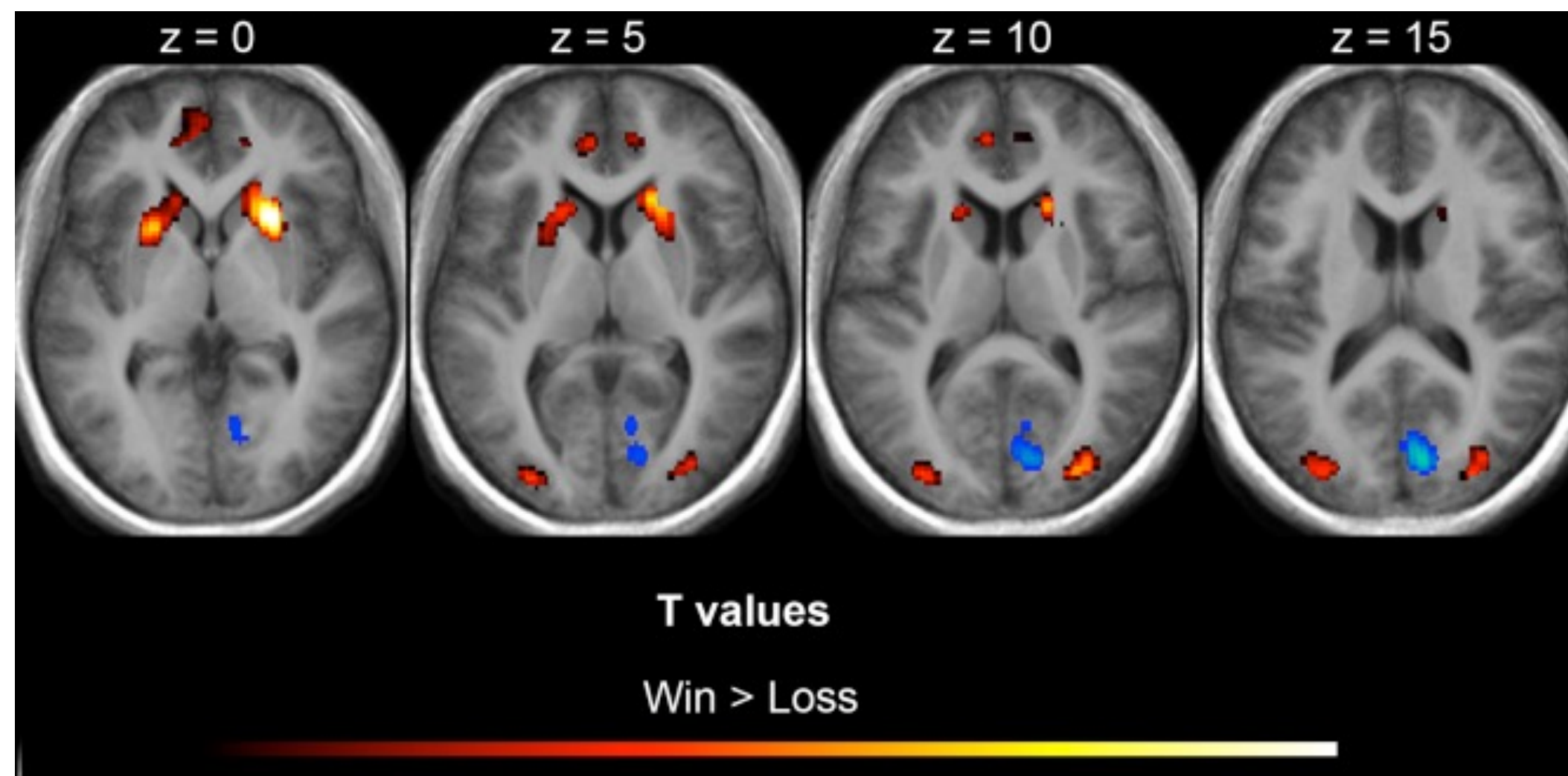
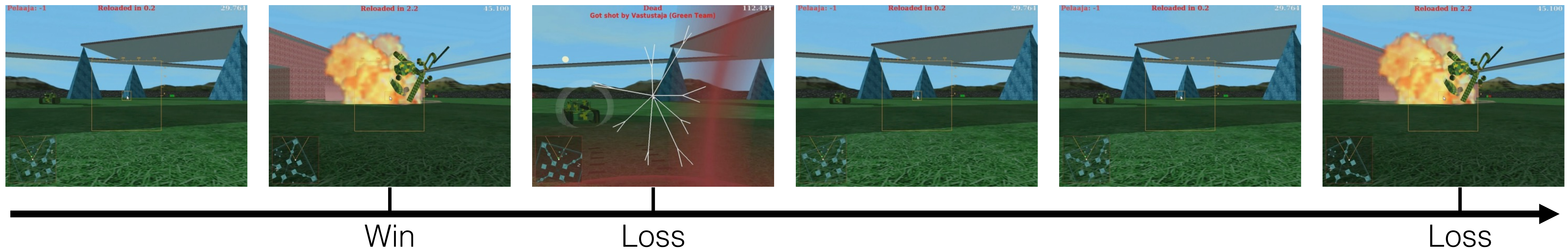
Basic tool 4: Unconstrained  
conditions and active experiments







# Model-based analysis of an unstructured gameplay session



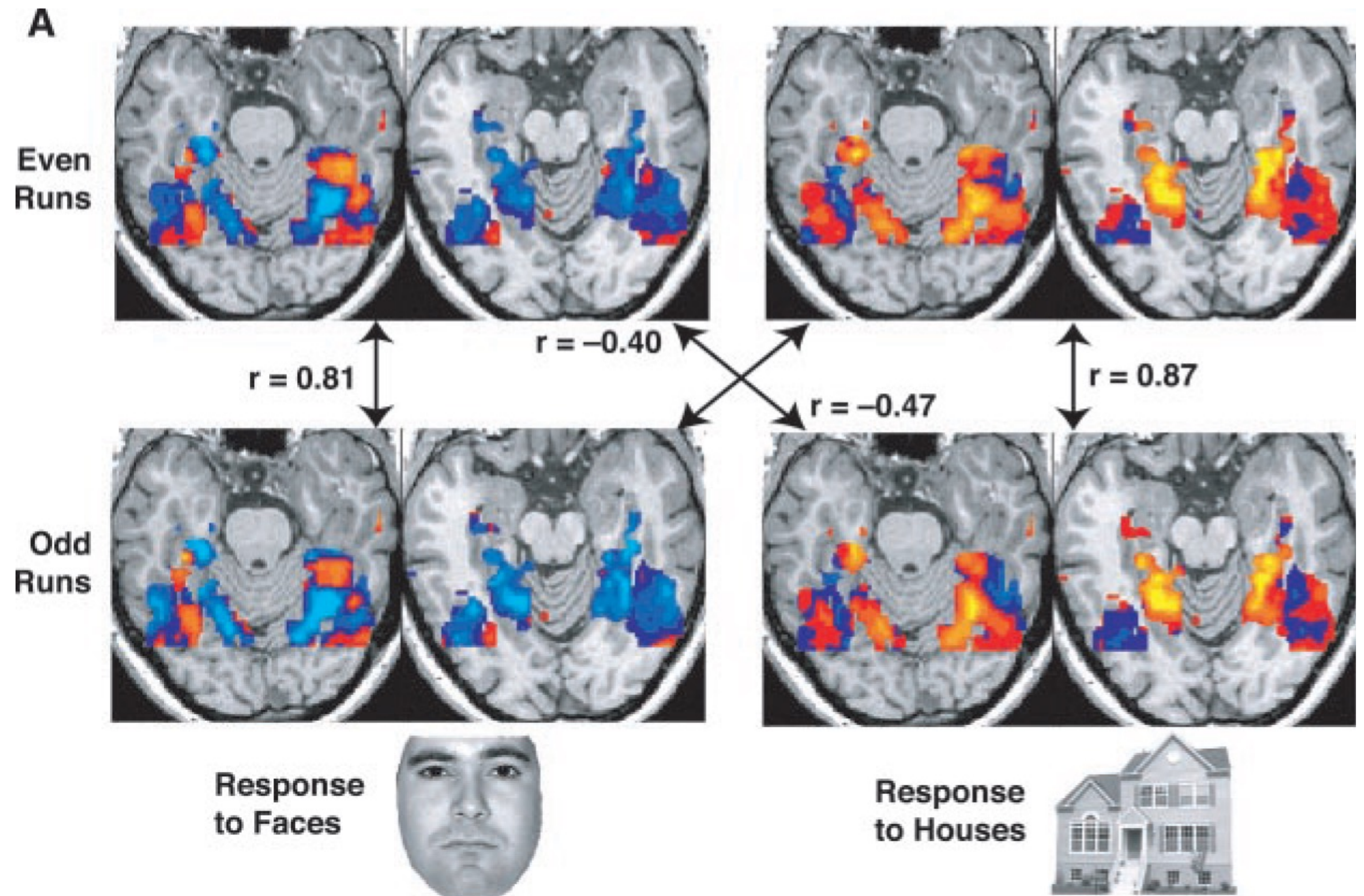
- Stimulus model is stored based on player behaviour
- Events of interest modelled as
- Stick functions
- Everyone free to play as they want,
- But gameplay is parsed into similar event



# Response variability across session

## Sources of variation

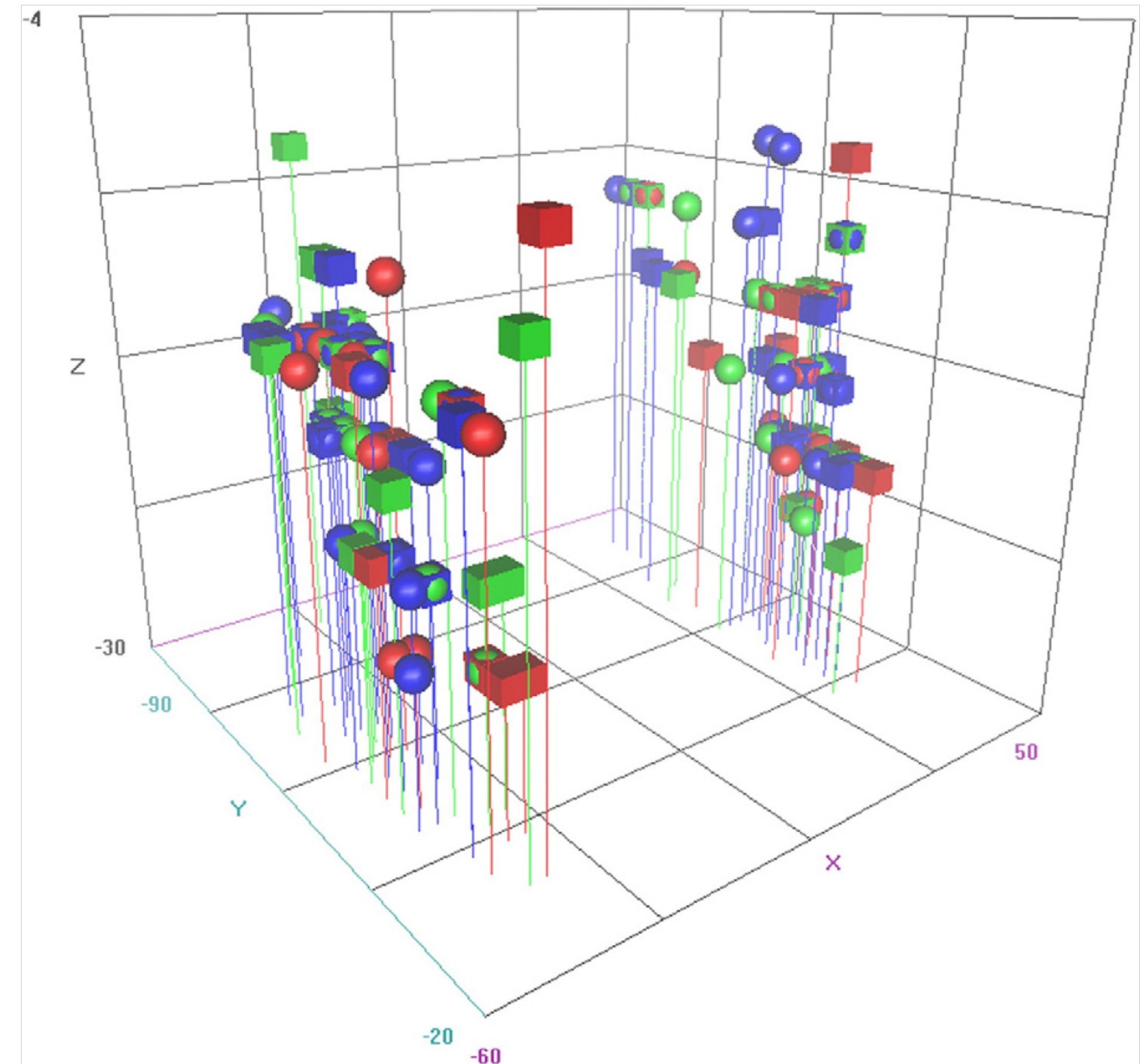
- Random variation (noise)
- Physiological state
- Arousal level
- Attention
- Learning effects
- Stimulus / event differences





# Anatomical differences

- Localization of the 'fusiform face area' in 18 subjects
- Localizations vary considerably due to differences in
  - Gross anatomy
  - Functional specialization
  - Warping in normalization
- Also, consider differences in signal intensity across subjects
- All these factors are bound to lower SNR

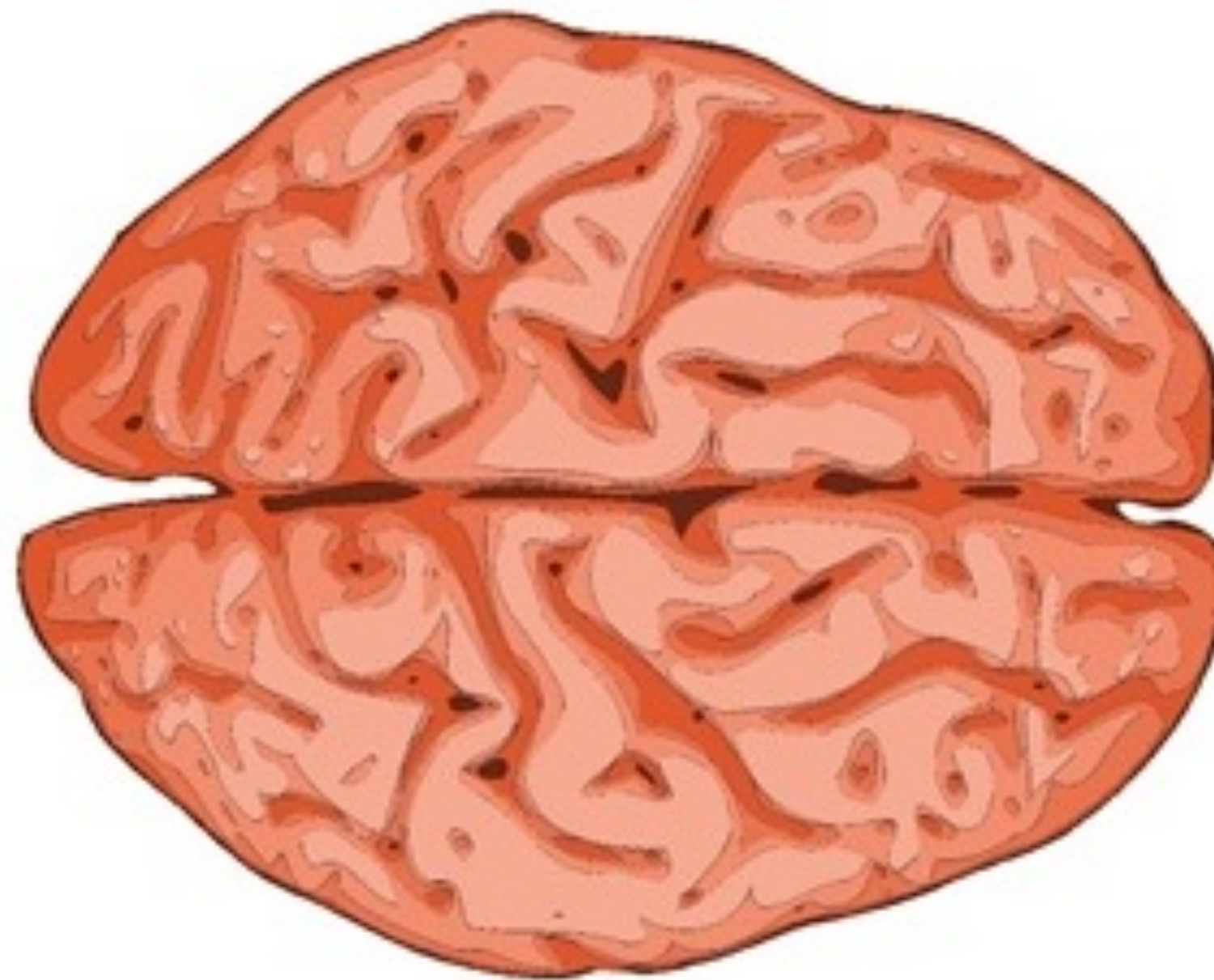




# How to improve experimental power?

1. Ask a good question
2. Improve design efficiency
3. Increase scan duration (to reasonable limits)
4. Minimize individual differences in cognitive / affective state
5. Maximize subject engagement (e.g. game > movie > picture)
6. Maximize similarity of subjects

Remember: your results are only as good as your theory!



High reliability and good SNR do not safeguard against stupid research questions and Bad Science™