EXPERIMENTAL DESIGNS FOR FUNCTIONAL NEUROIMAGING

Turku PET Centre Brain Imaging Course 2024

Lauri Nummenmaa, Turku PET Centre

Lecture contents

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

WELCOME TO THE PET NEUROIMAGING COURSE

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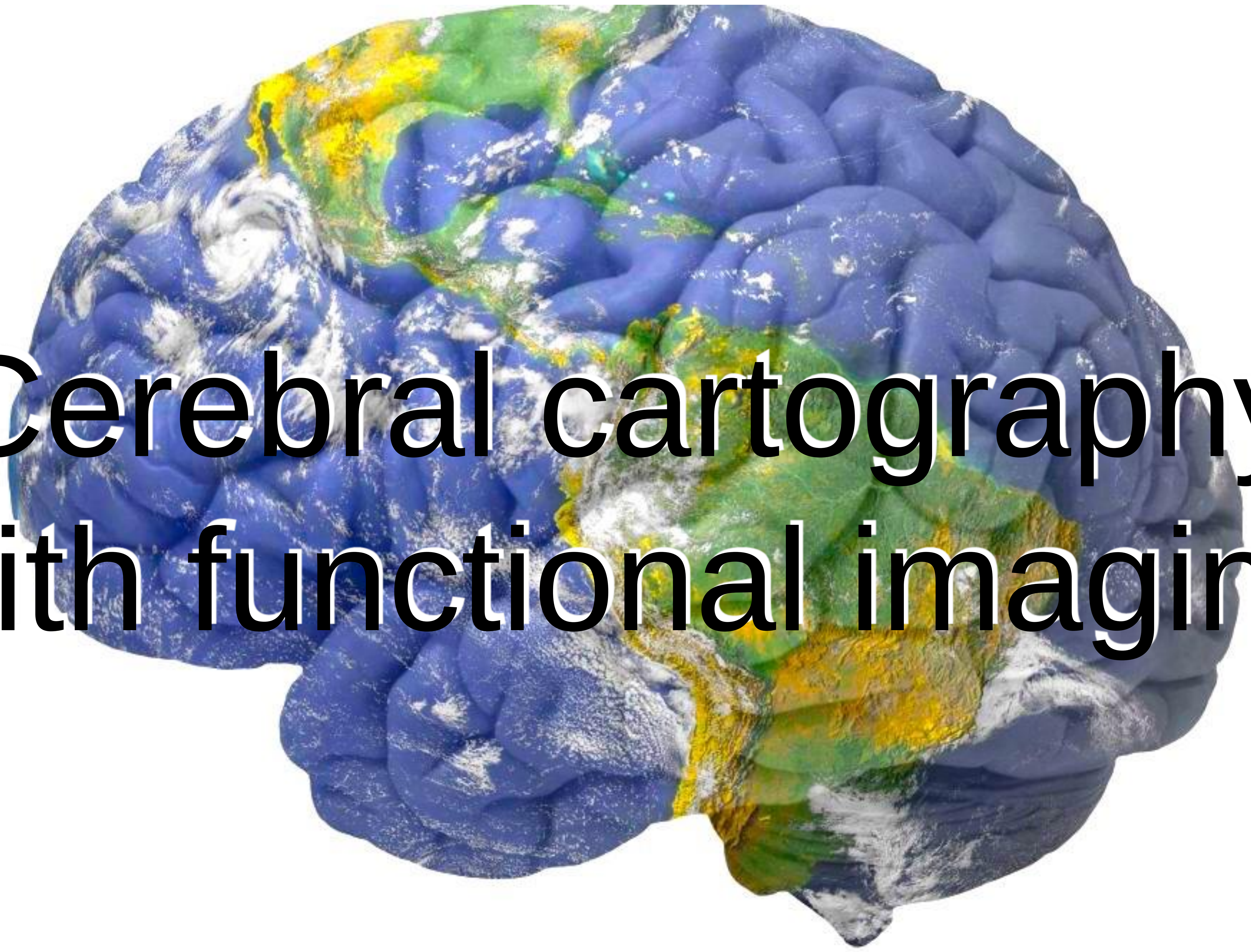
Cerebral cartography with functional imaging



Magnetic resonance imaging (MRI)

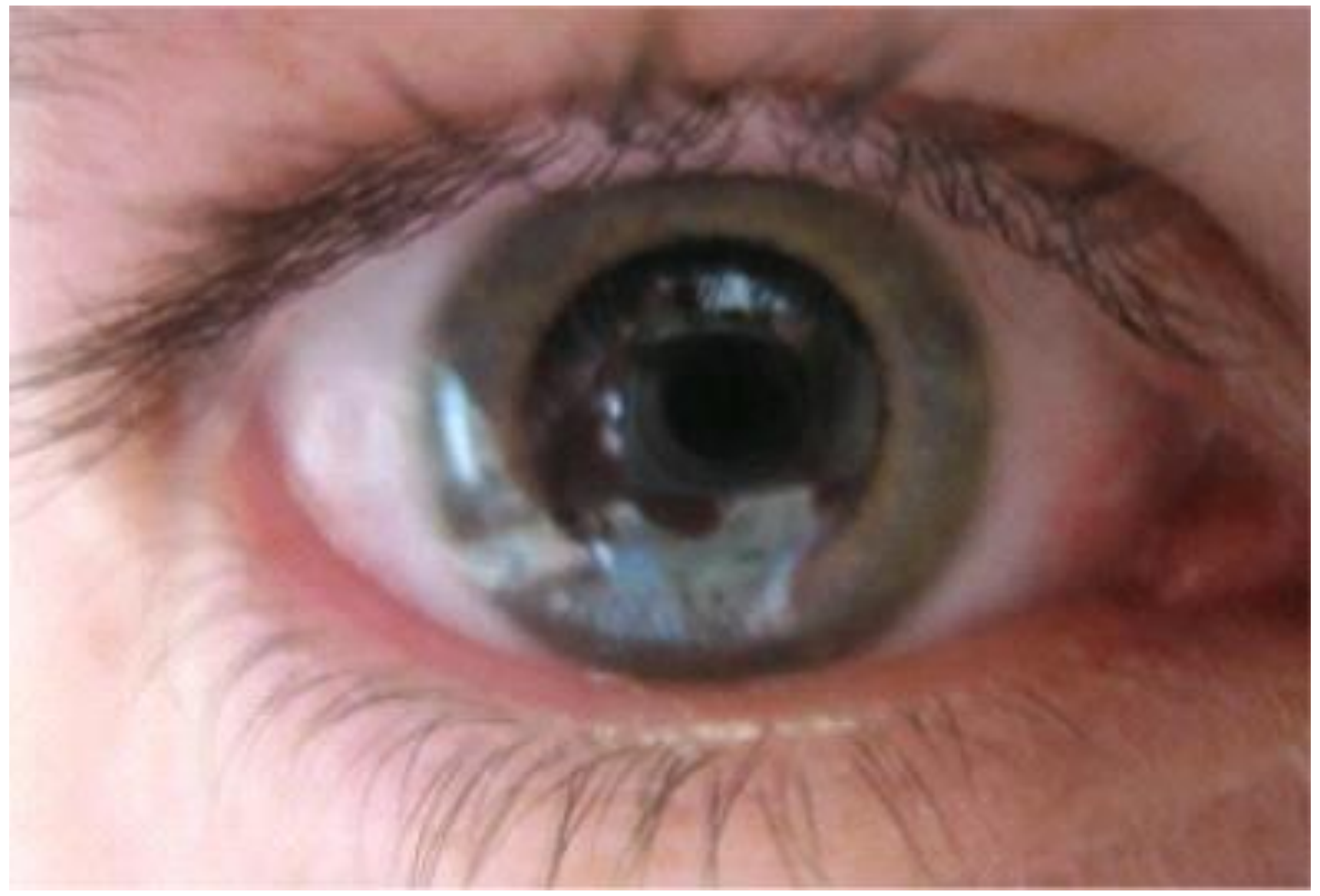
- Based on the magnetic resonance of the hydrogen nuclei
- Measuring the behaviour of hydrogen nuclei in the strong magnetic field of the MRI device allows studying different tissues in vivo
- Adjusting imaging sequence allows highlighting different tissues or their different characteristics

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

+

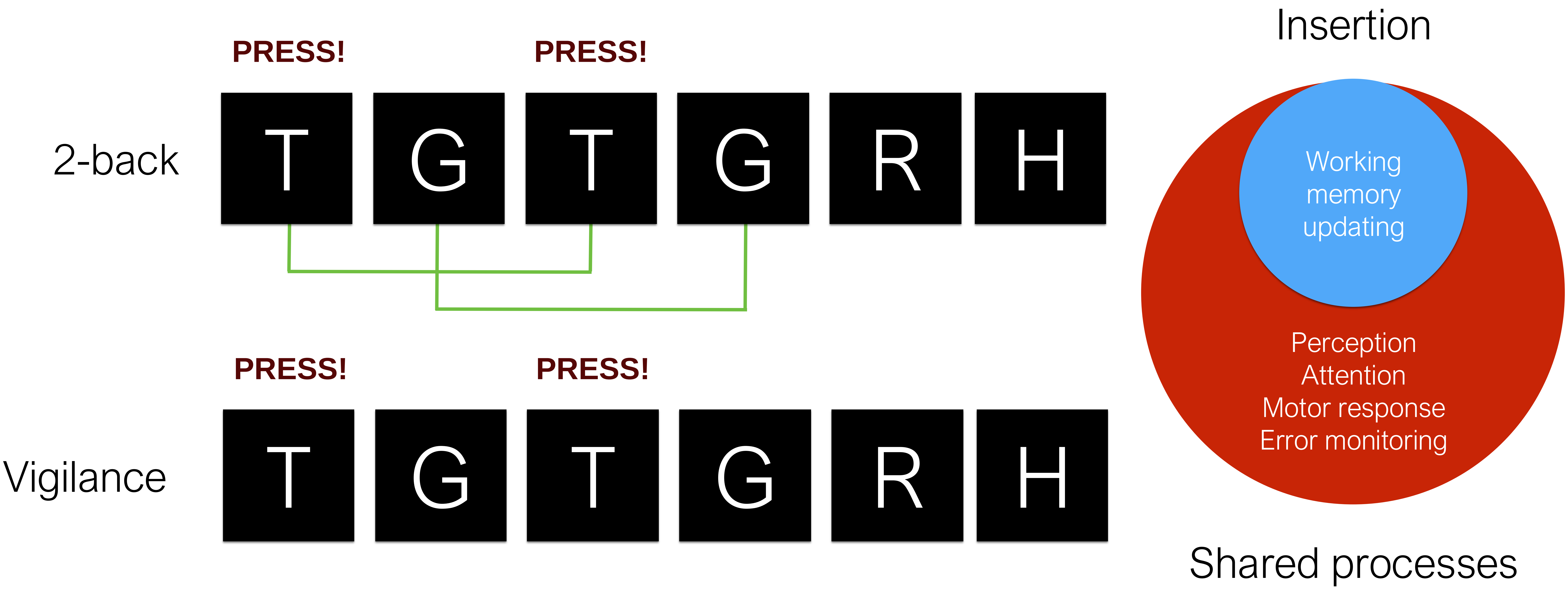
NOISE
Errors in measurement, individual differeneces

STATISTICS = SEPARATING NOISE FROM SIGNAL IN A PROBABILISTIC FASHION

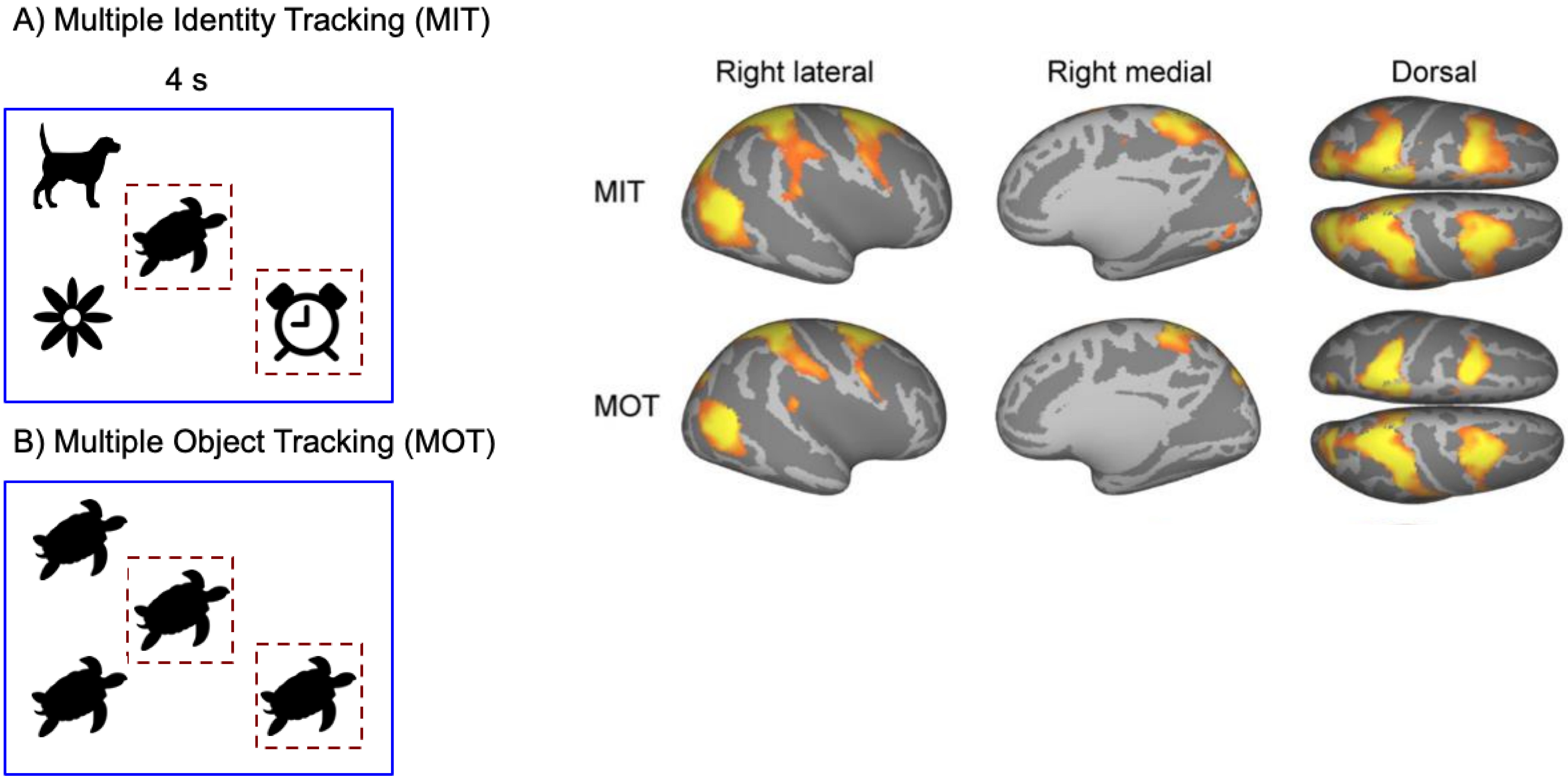
Cognitive subtraction

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



Nummenmaa et al (2018 Cereb Cortex)

Typical fMRI experiment

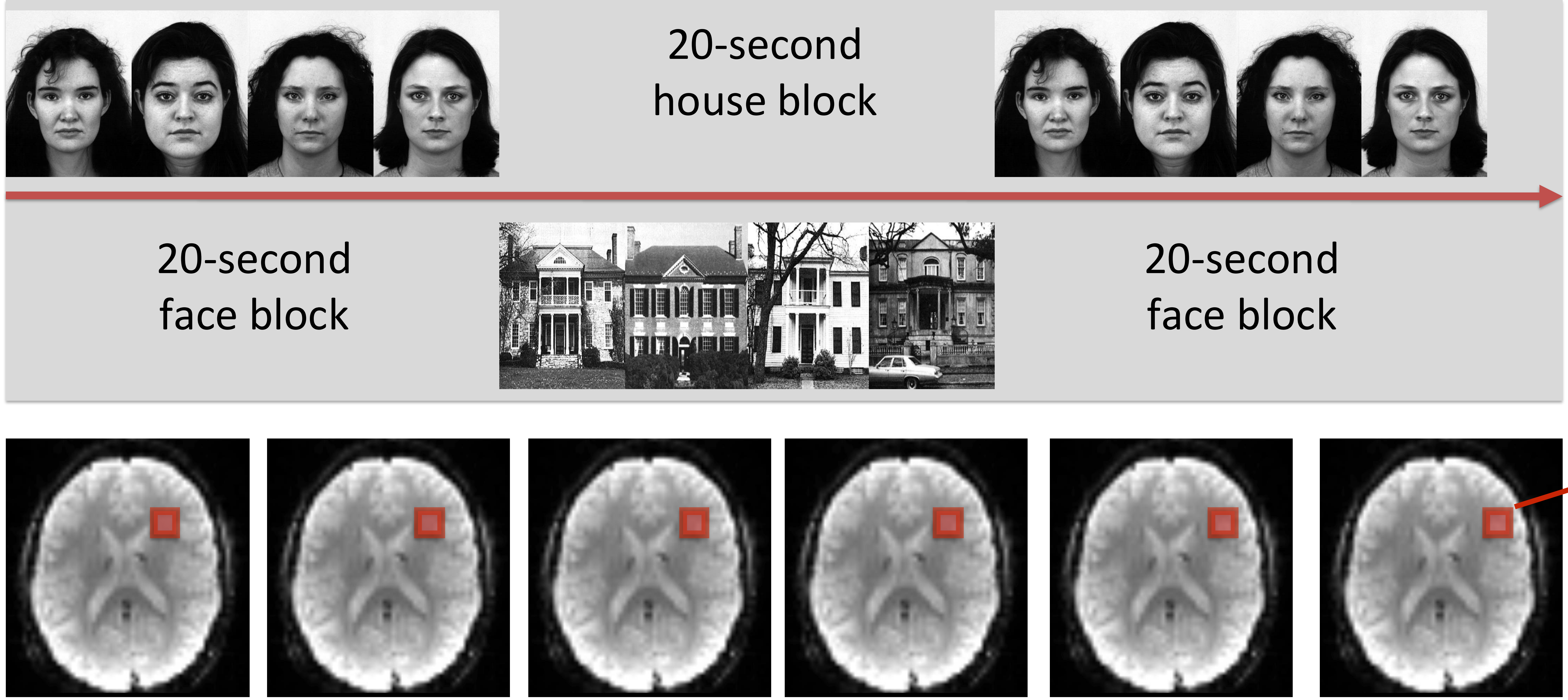
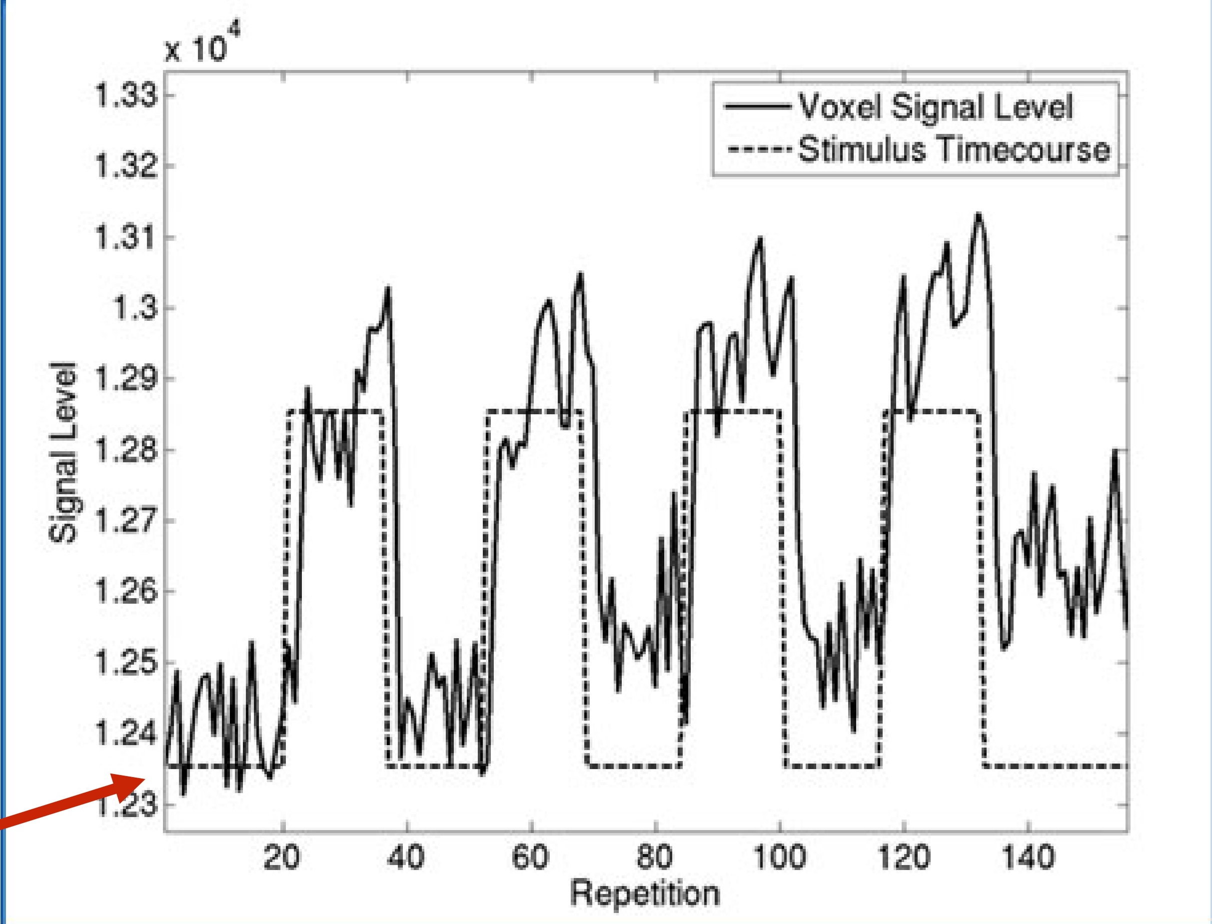


Figure 1. fMRI Time Course from a Single Activated Voxel in a Blocked-Design Experiment

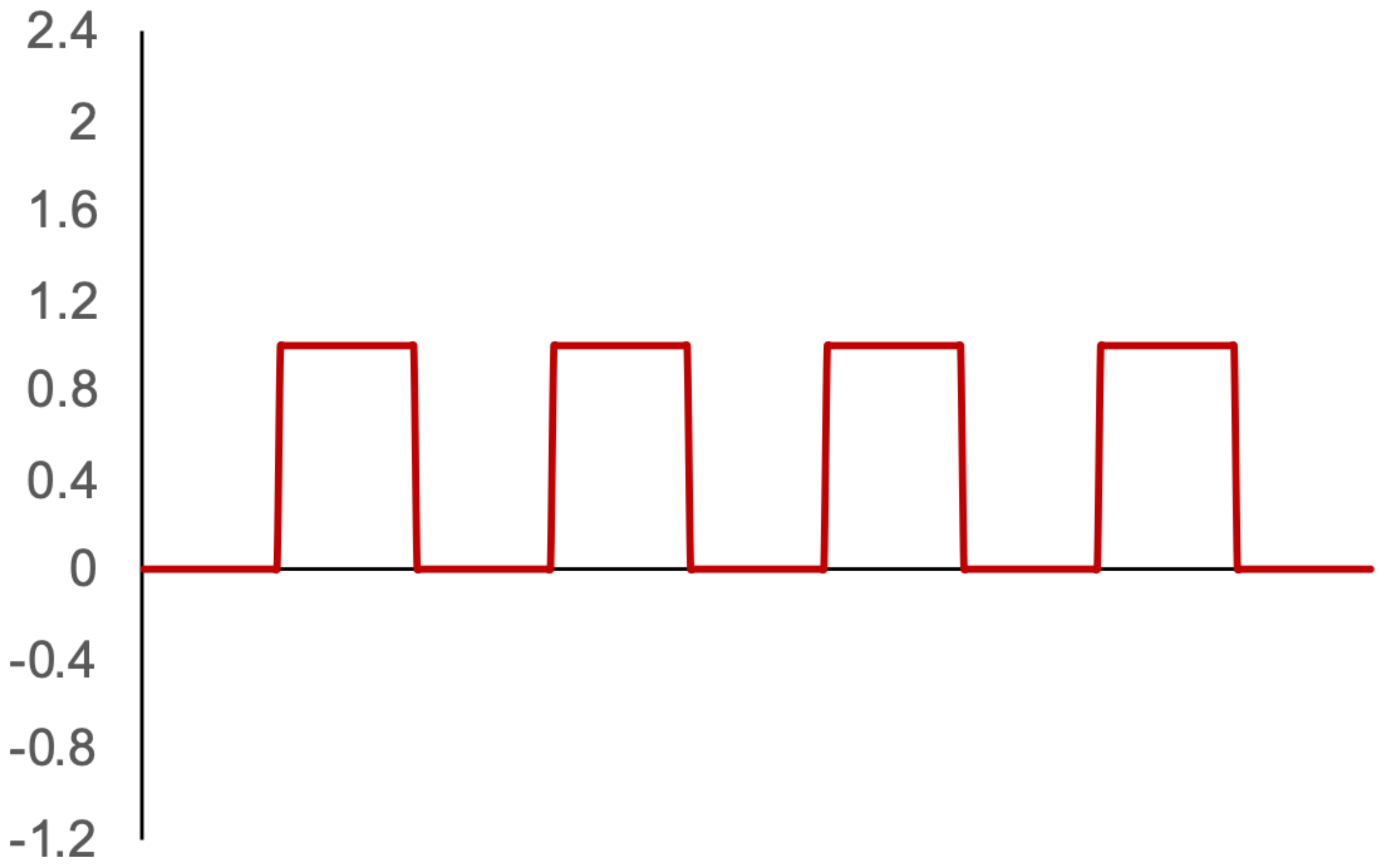


Stimulus is represent as either off (low) or on (high) by the dotted line.
fMRI = functional magnetic resonance imaging.
Courtesy Dr Erik Beall at Cleveland Clinic.

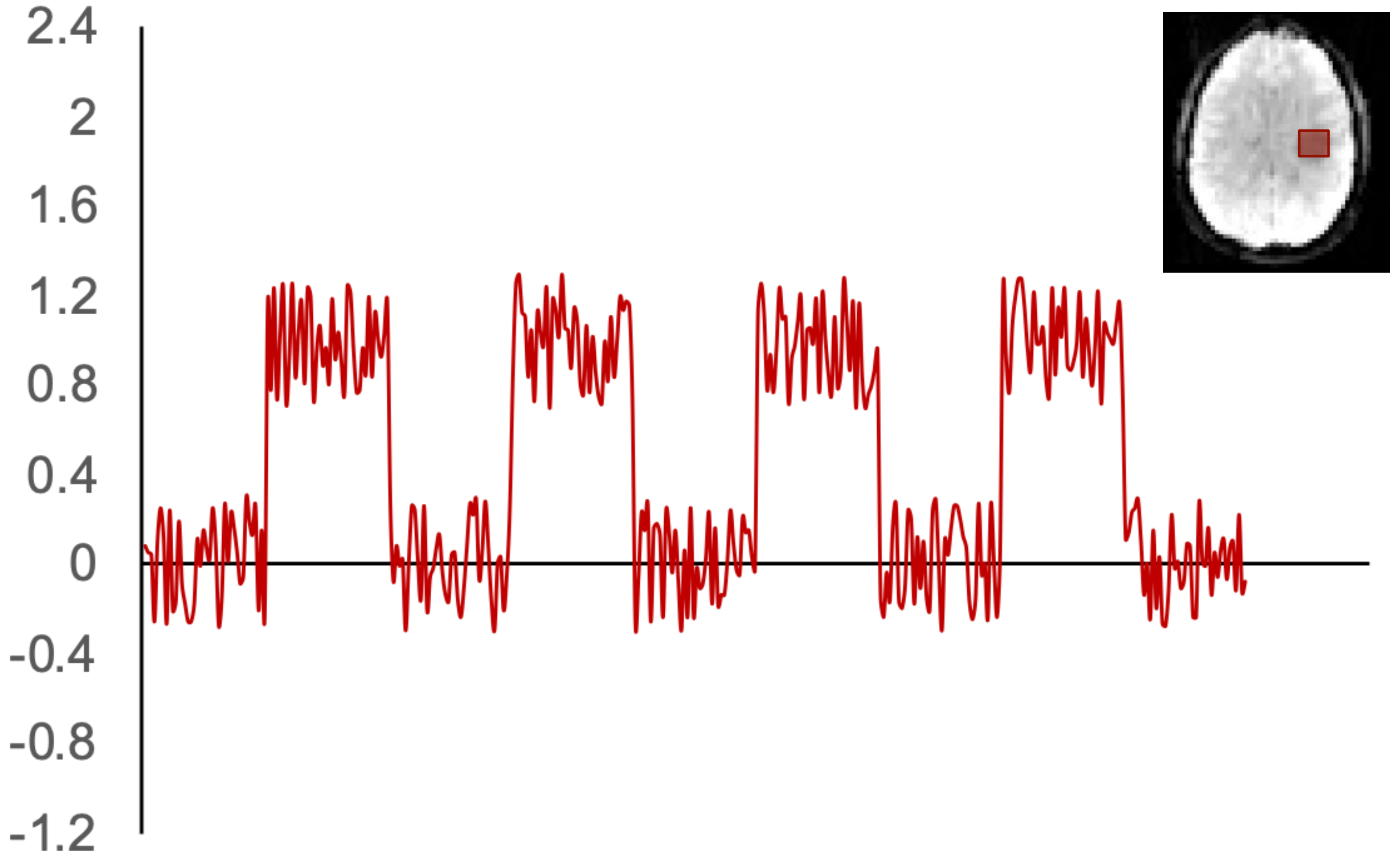
Acquiring one 3D functional volume takes about 1.5 seconds
We can distinguish events ~100ms apart, yet their actual timing can be resolved with about 2-s accuracy

Fitting the model to the data

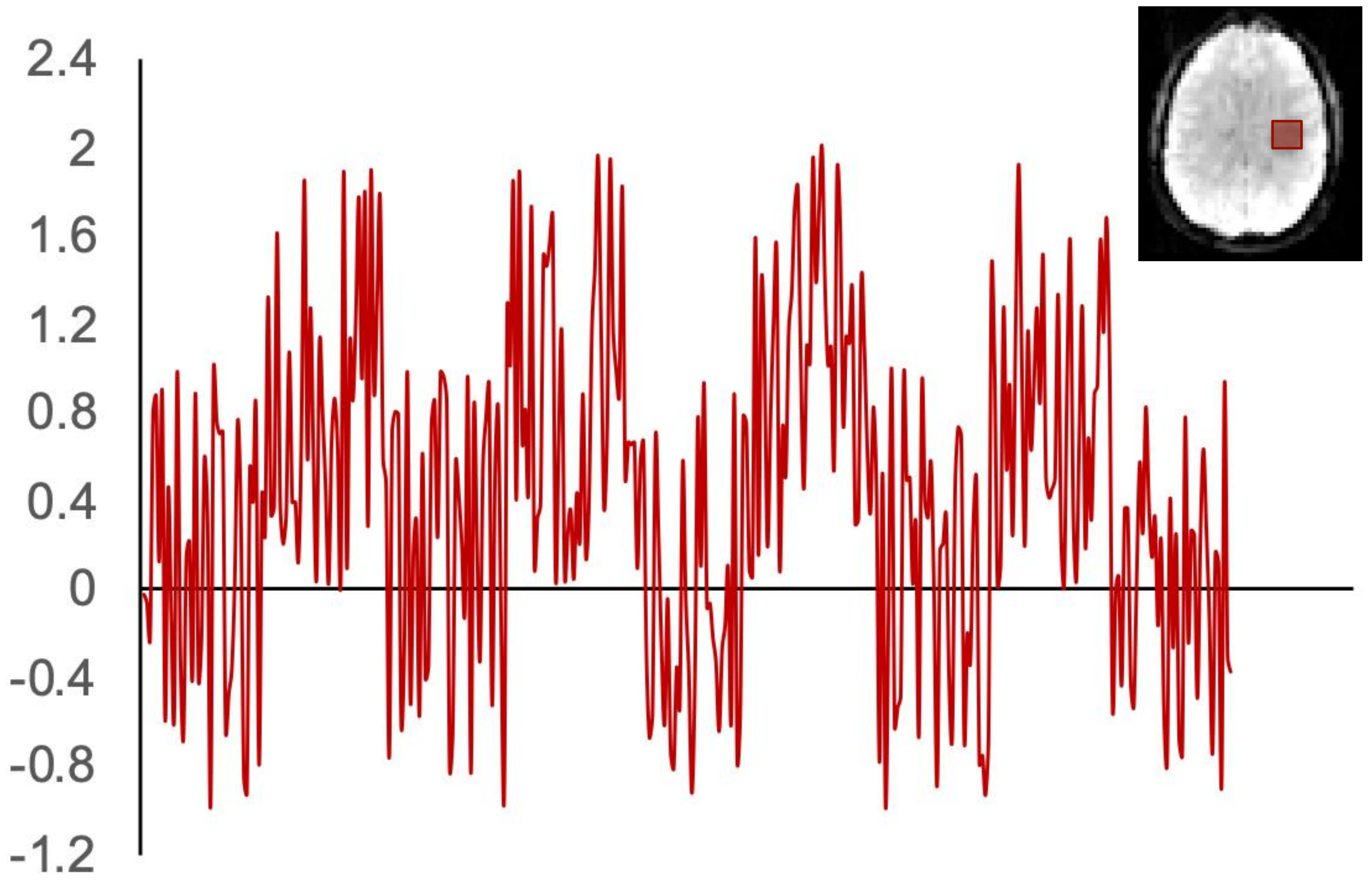
Stimulation model (boxcar)



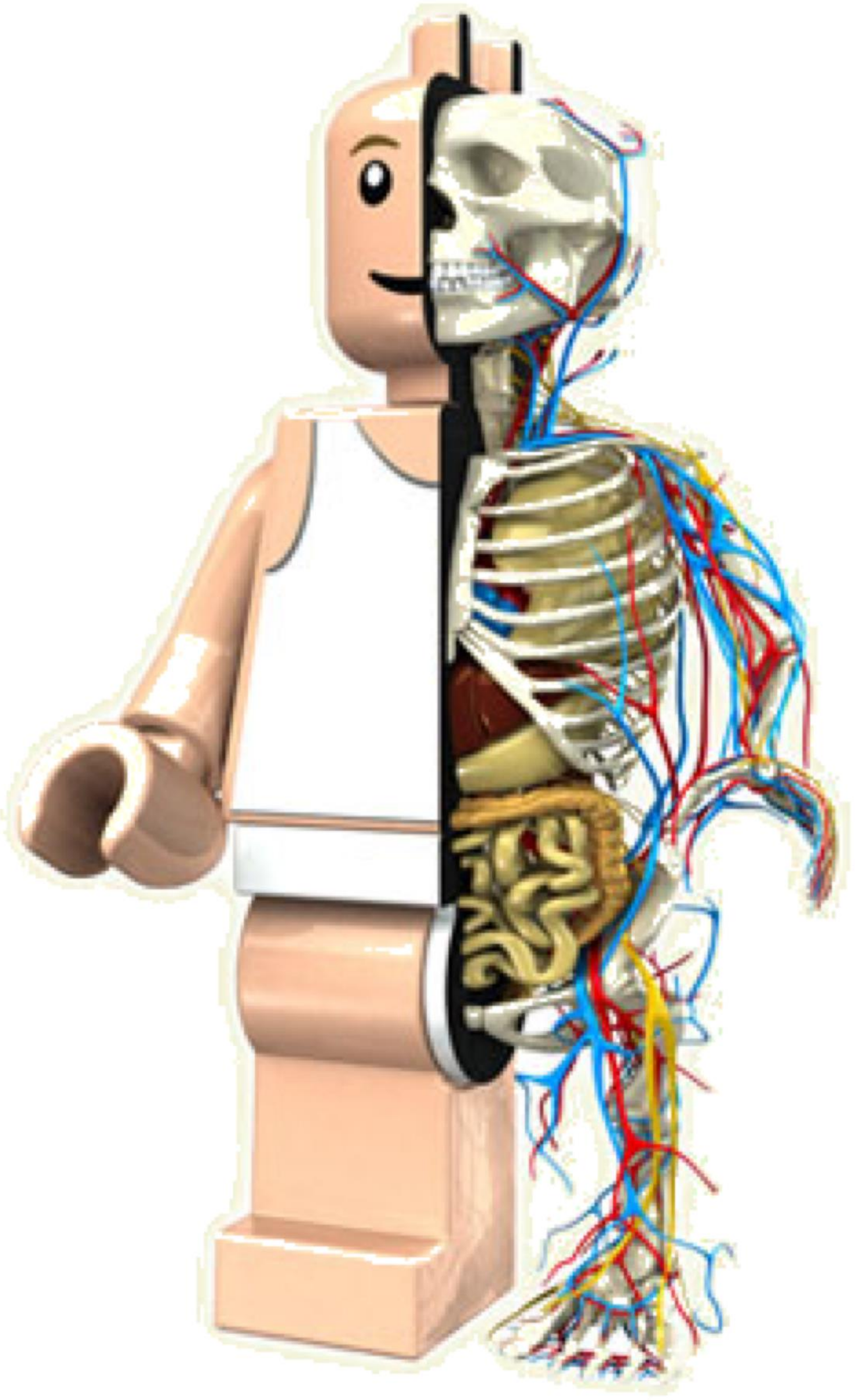
Clean data

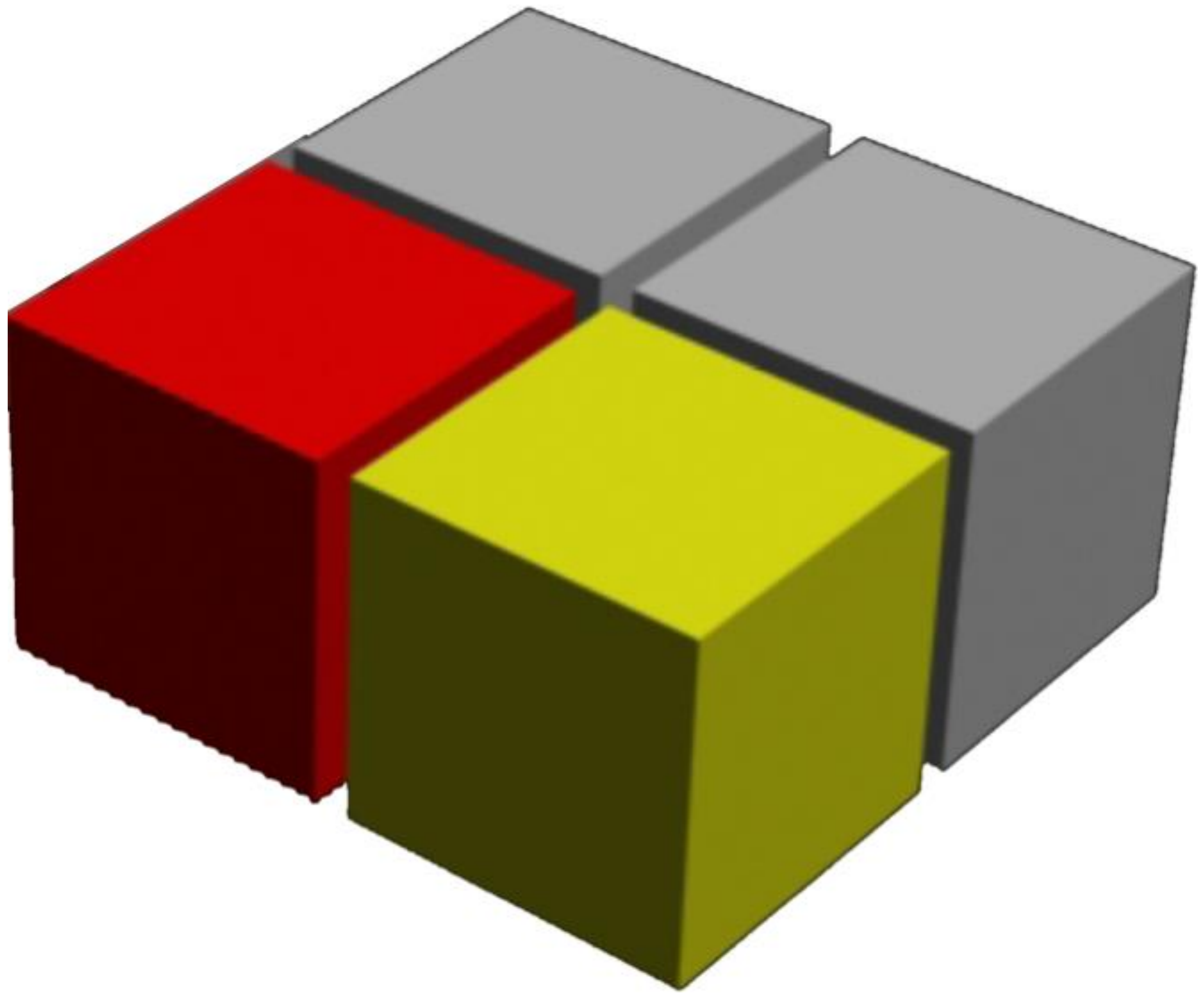


Noisy data



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

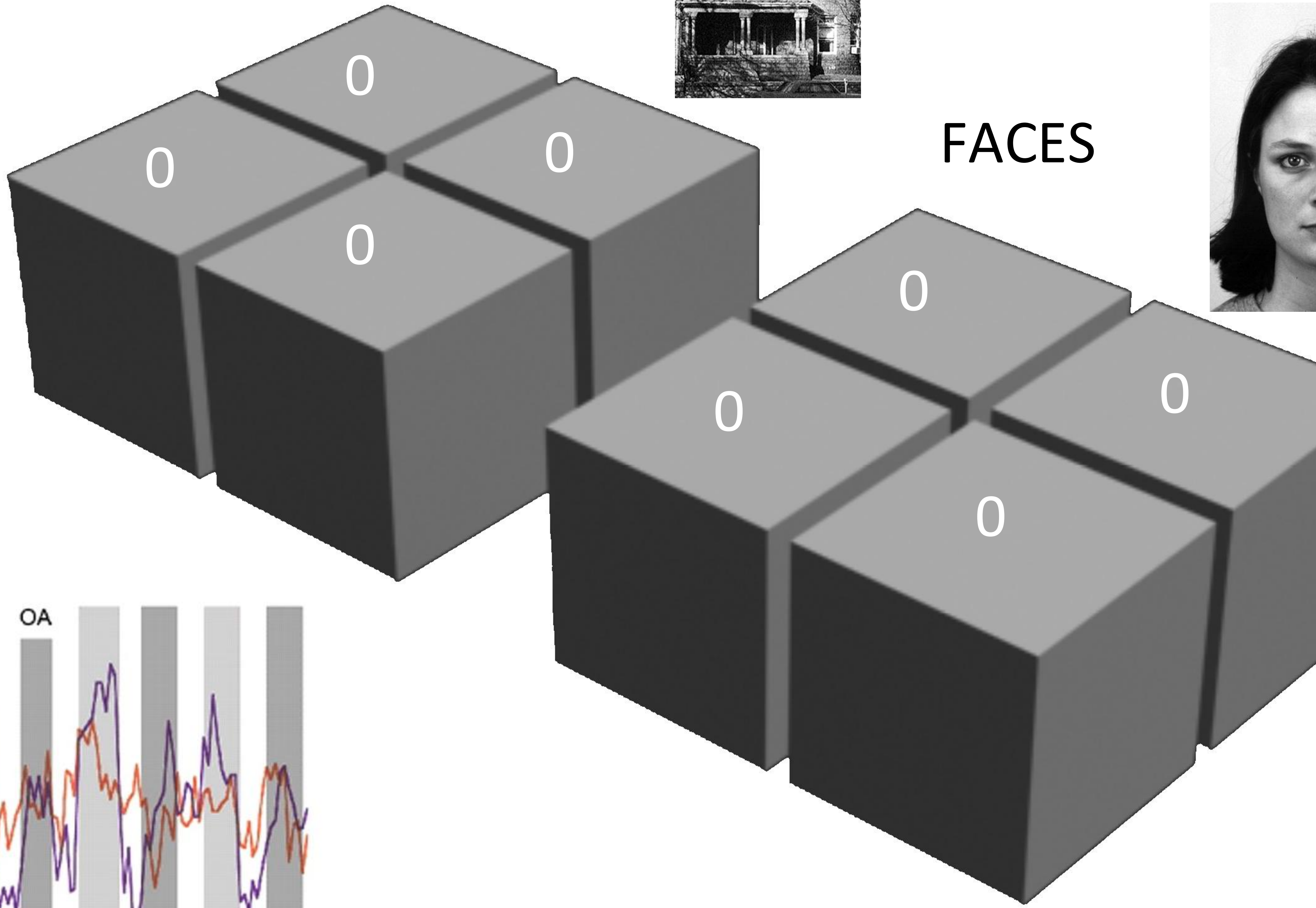


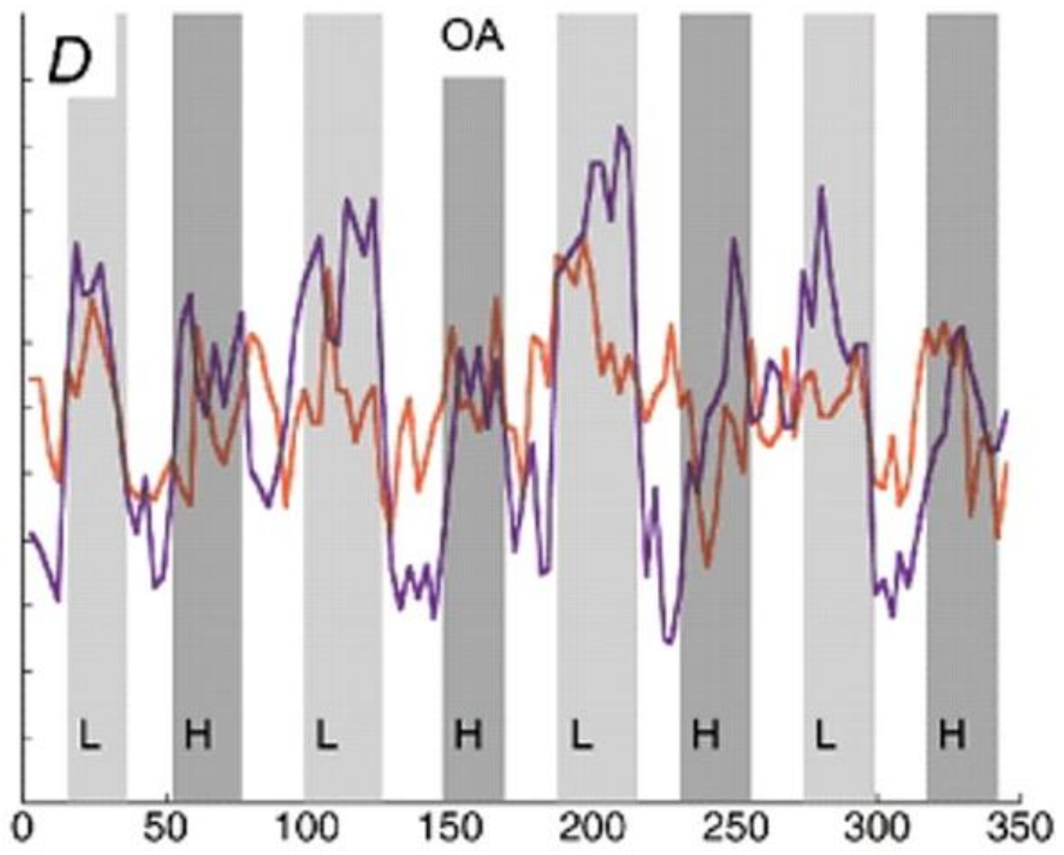


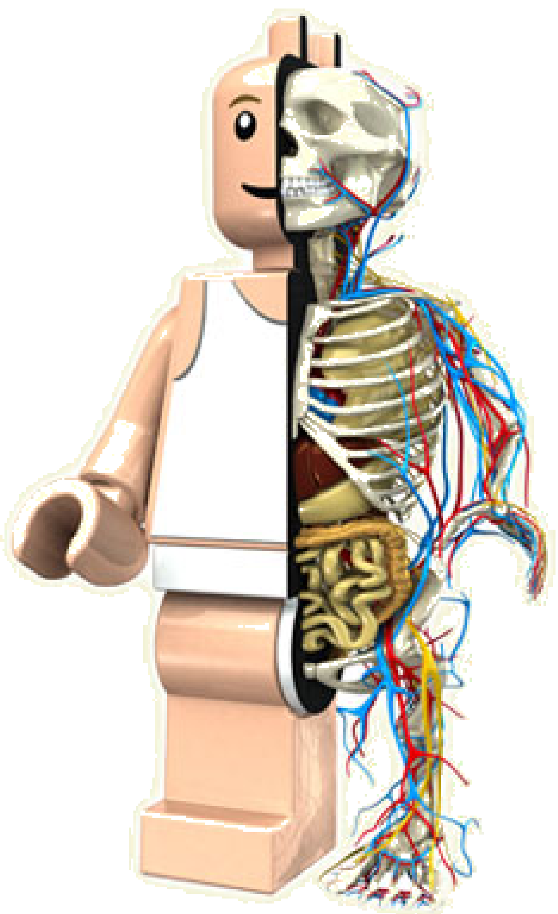
First level model with LEGO brains

HOUSES

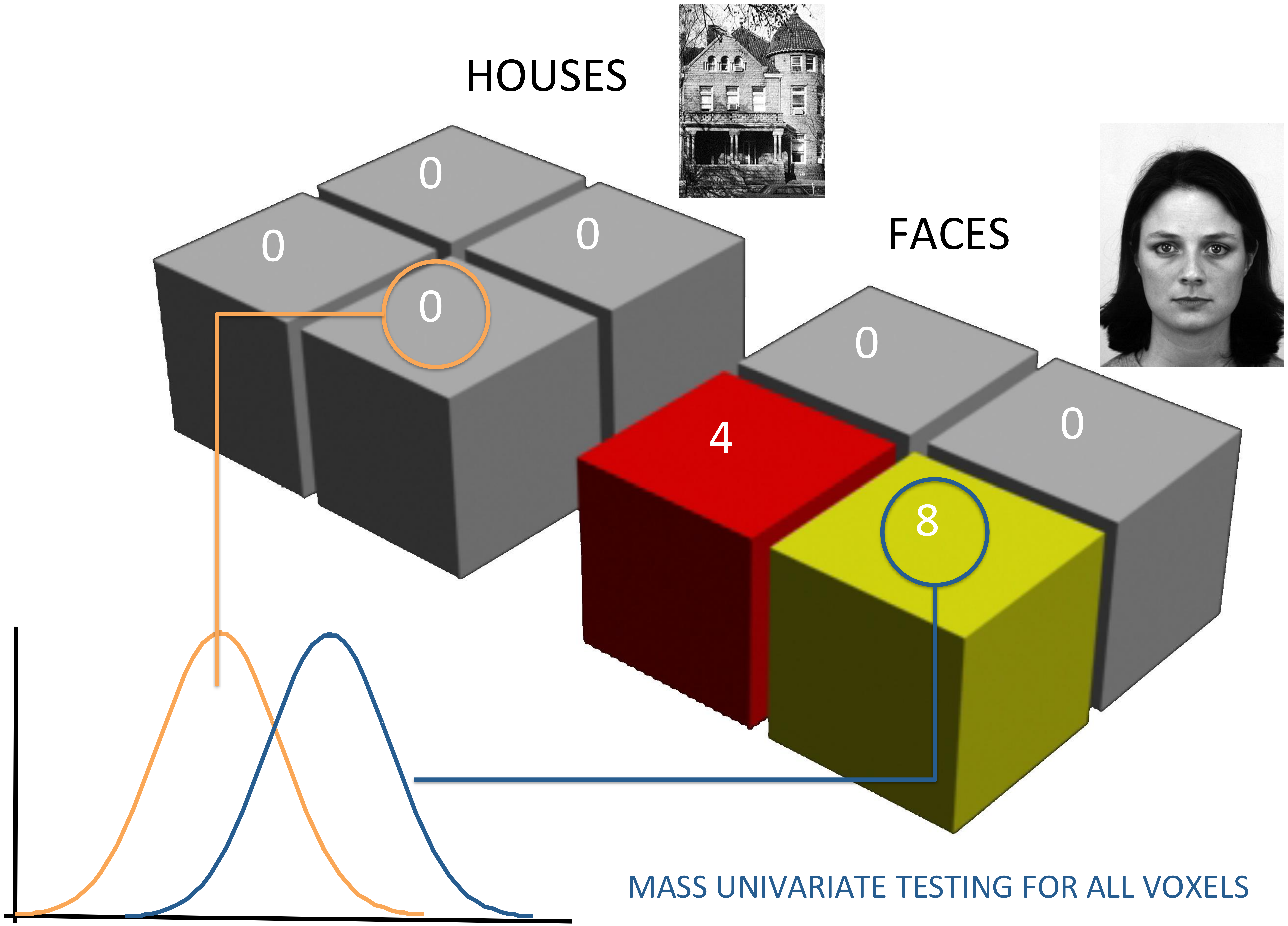
FACES







First level model with LEGO brains



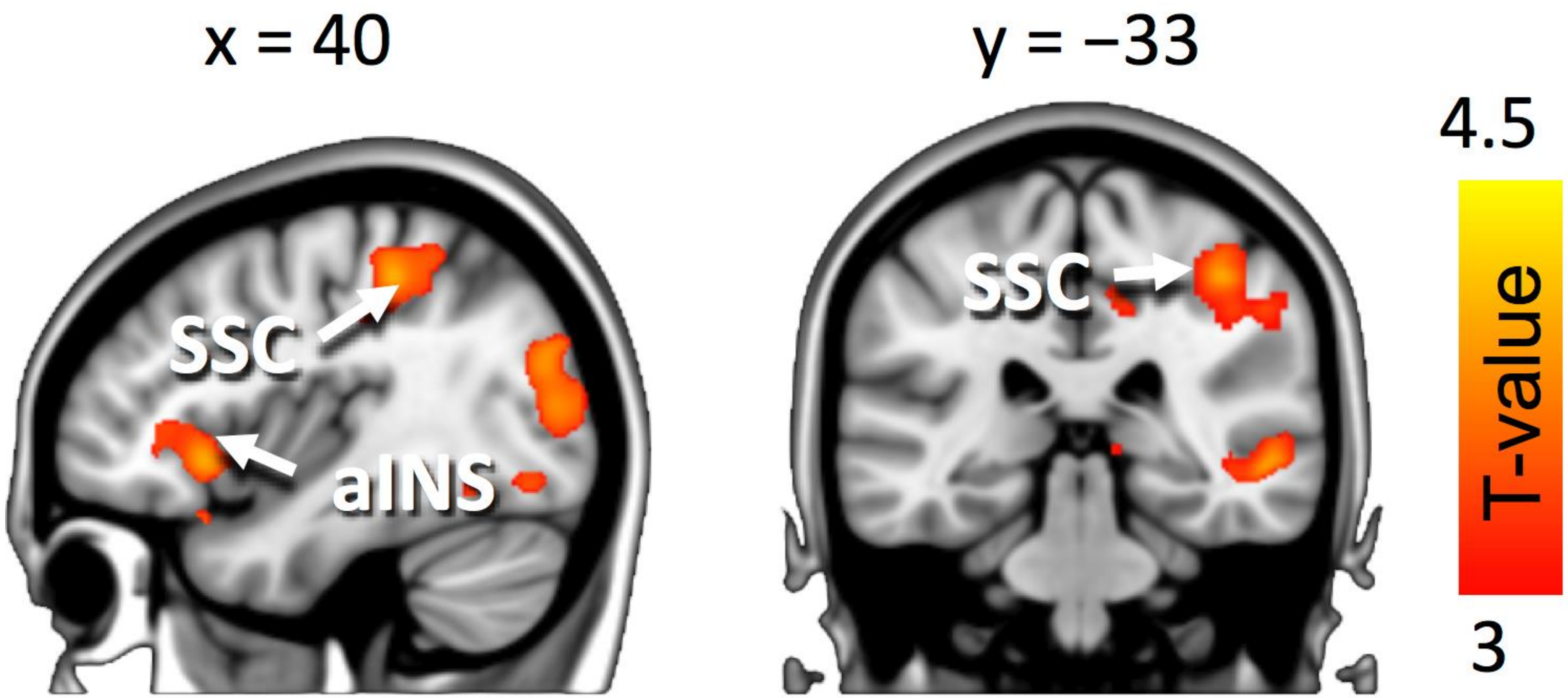
Basic tool 1: Boxcar design

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

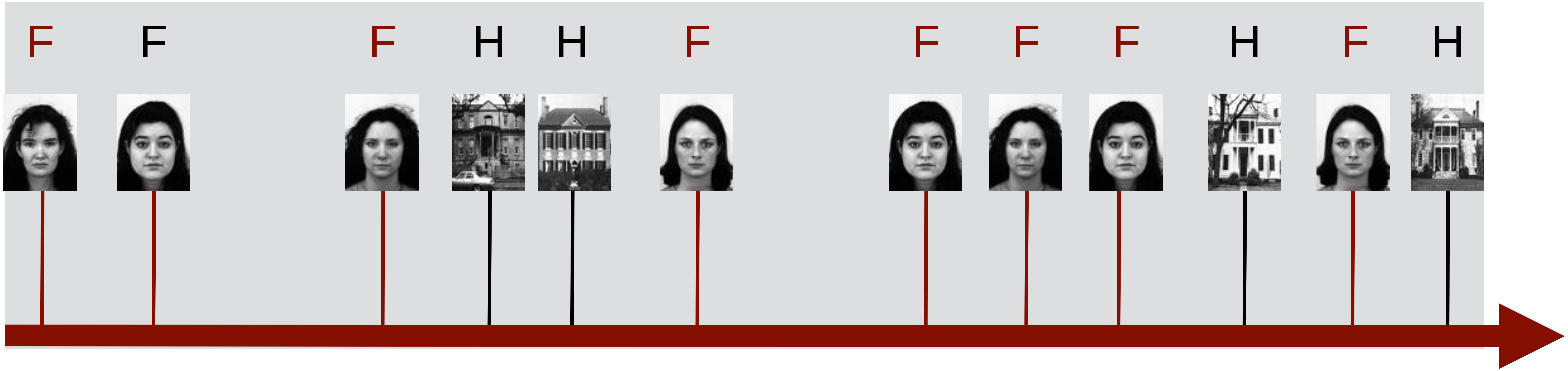
Feel pain trial

Cause pain trial

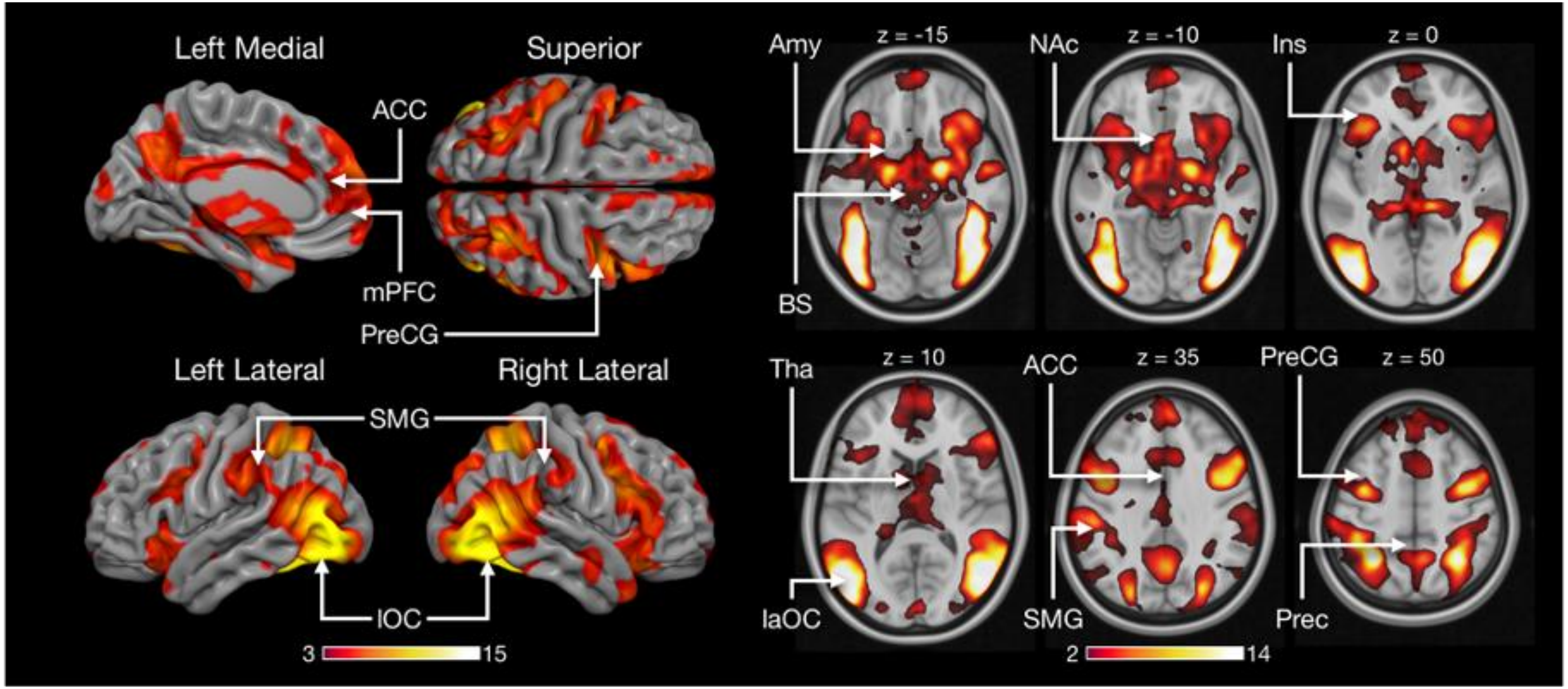


Nummenmaa et al (2014 J Neurosci)

Basic tool 2: Event-related design

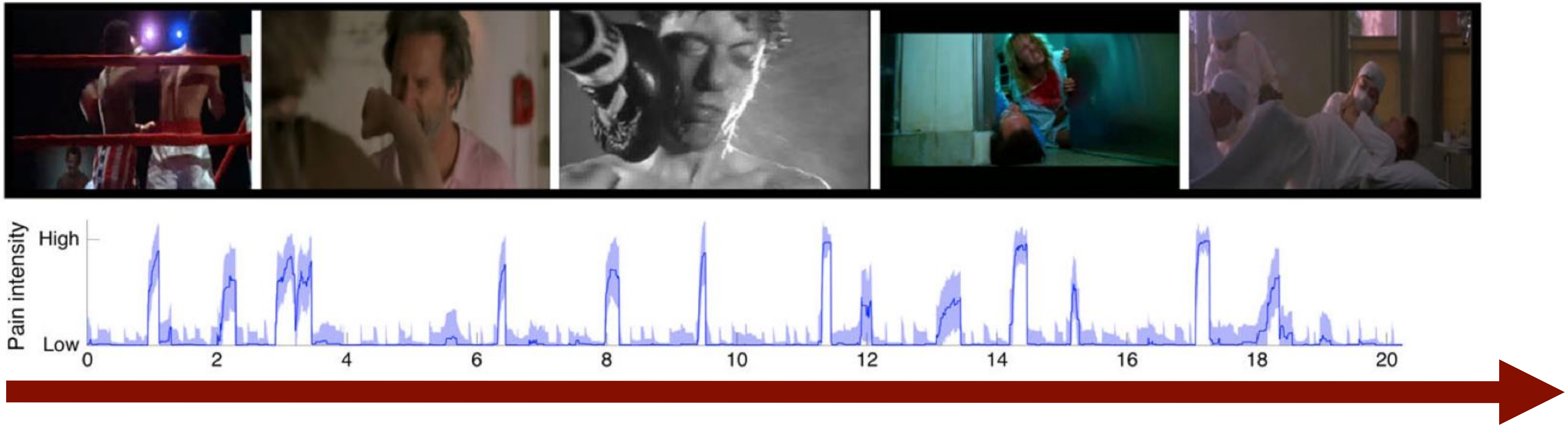


AIM: Localize brain regions that are more sensitive to process 1 vs. process 2
DESIGN: Event-related design with cognitive subtraction assuming pure insertion
ADVANTAGES: More accurate model, trial wise analysis, randomisation

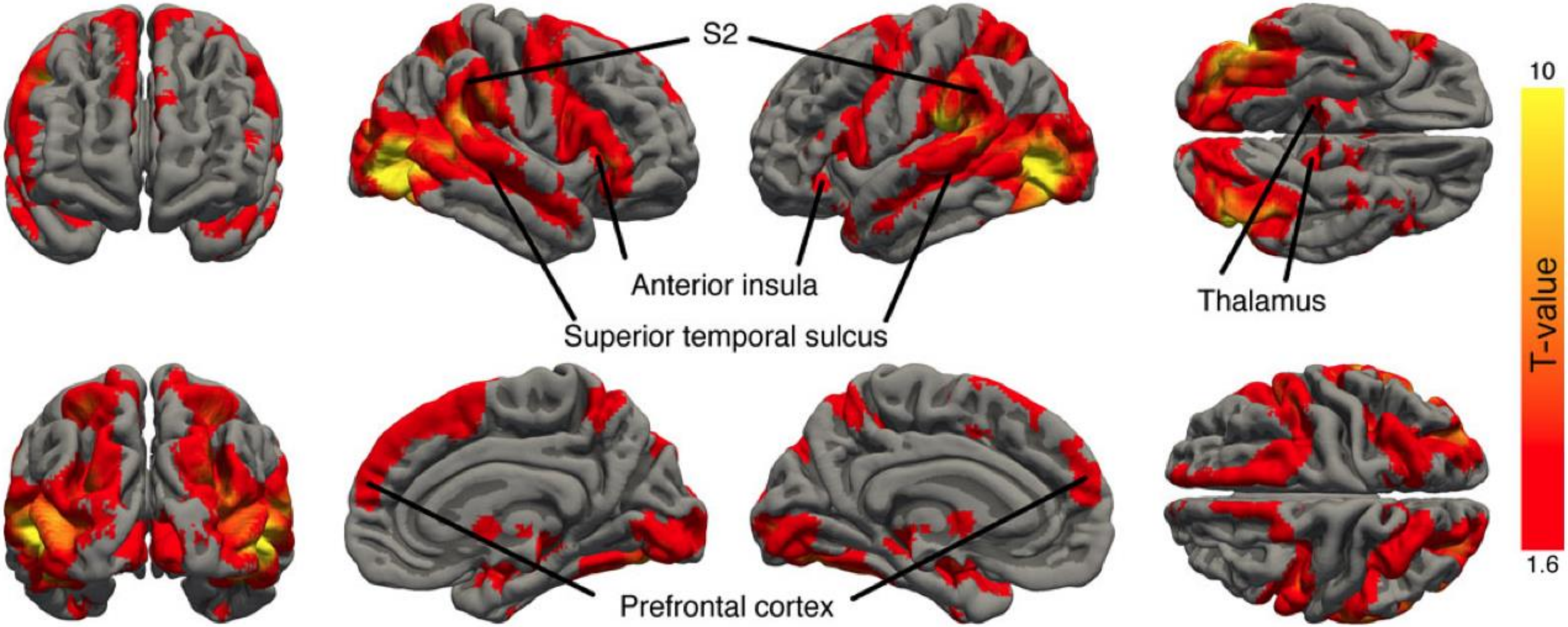


Putkinen et al (submitted)

Basic tool 3: Parametric design



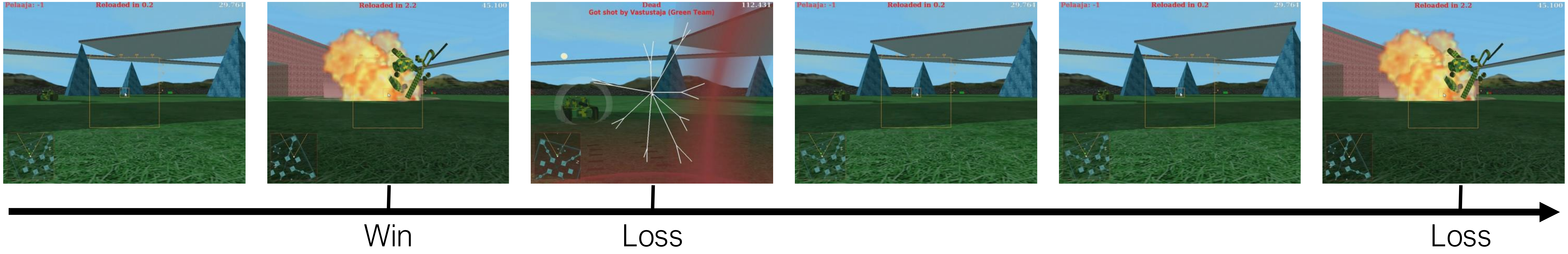
AIM: Localize brain regions that respond to vicarious pain
DESIGN: Parametric design with continuous stimulation model
ADVANTAGES: Quantitative stimulation model, high statistical power

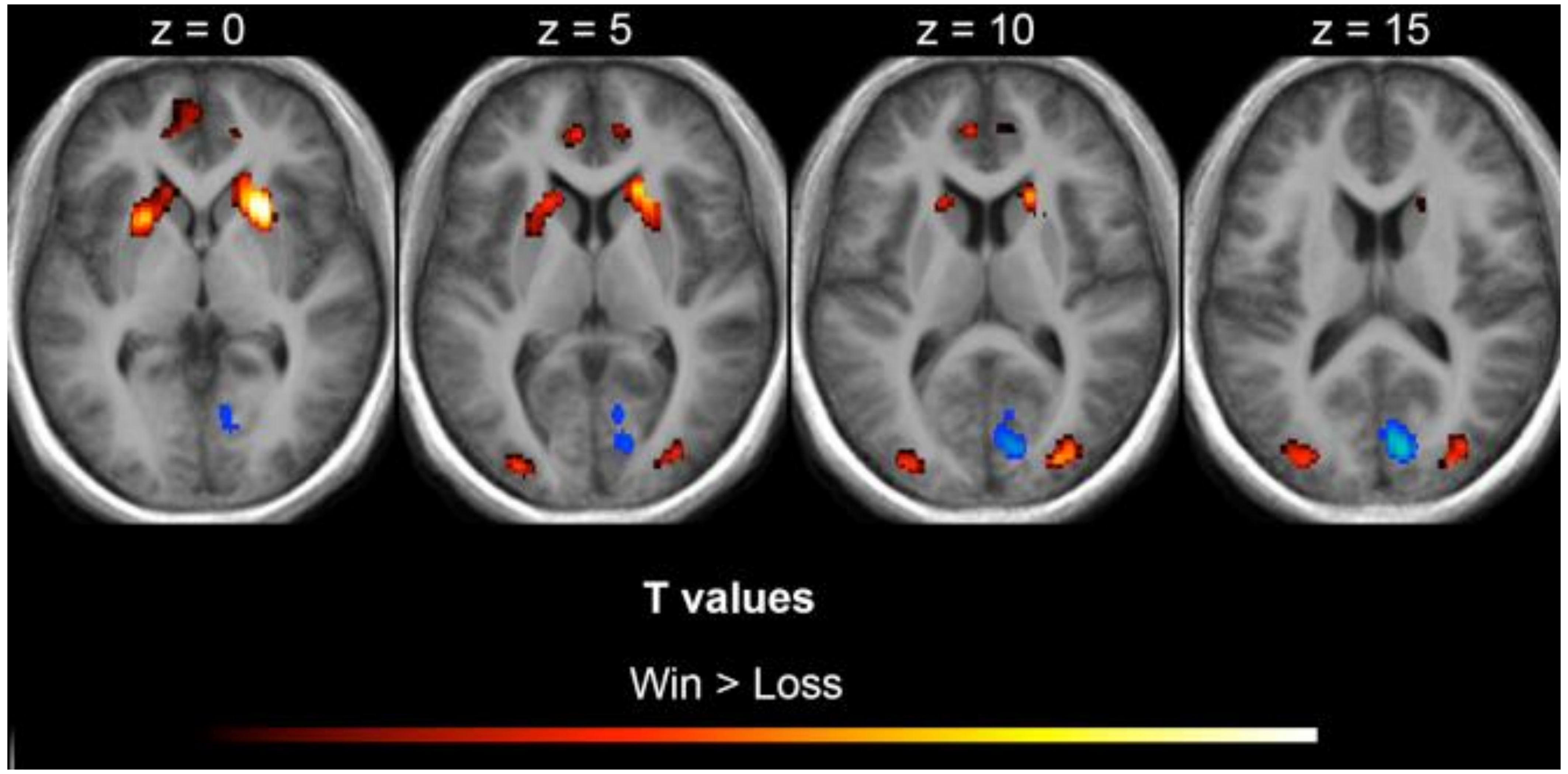


Karjalainen et al (2018 Cereb Cortex)

Basic tool 4: Unconstrained conditions and active experiments

Model-based analysis of an unstructured gameplay session





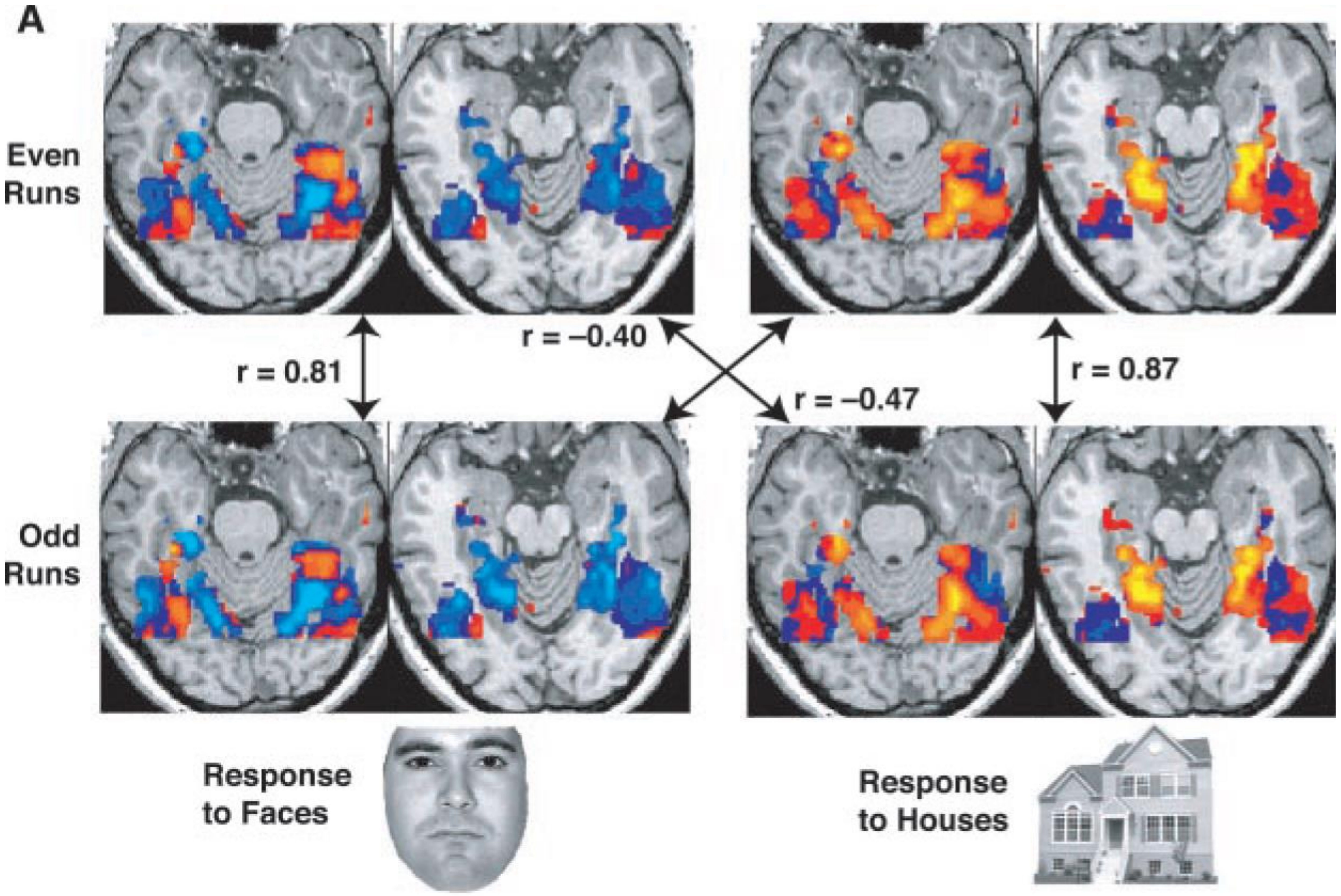
Kätsyri et al 2013 Cereb Cortex

- 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

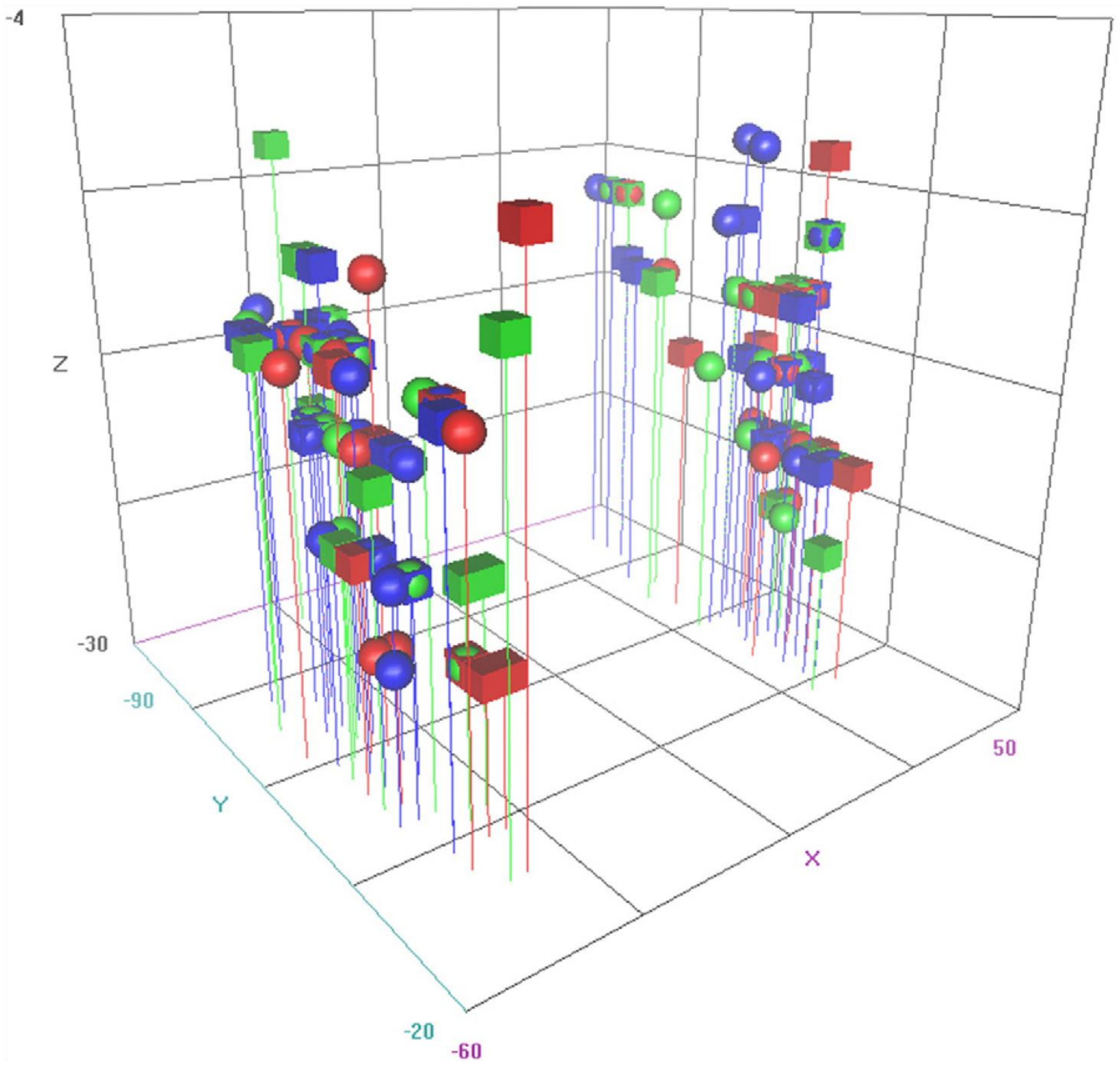
- Random variation (noise)
- Physiological state
- Arousal level
- Attention
- Learning effects
- Stimulus / event differences



Haxby et al (Science 2001)

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

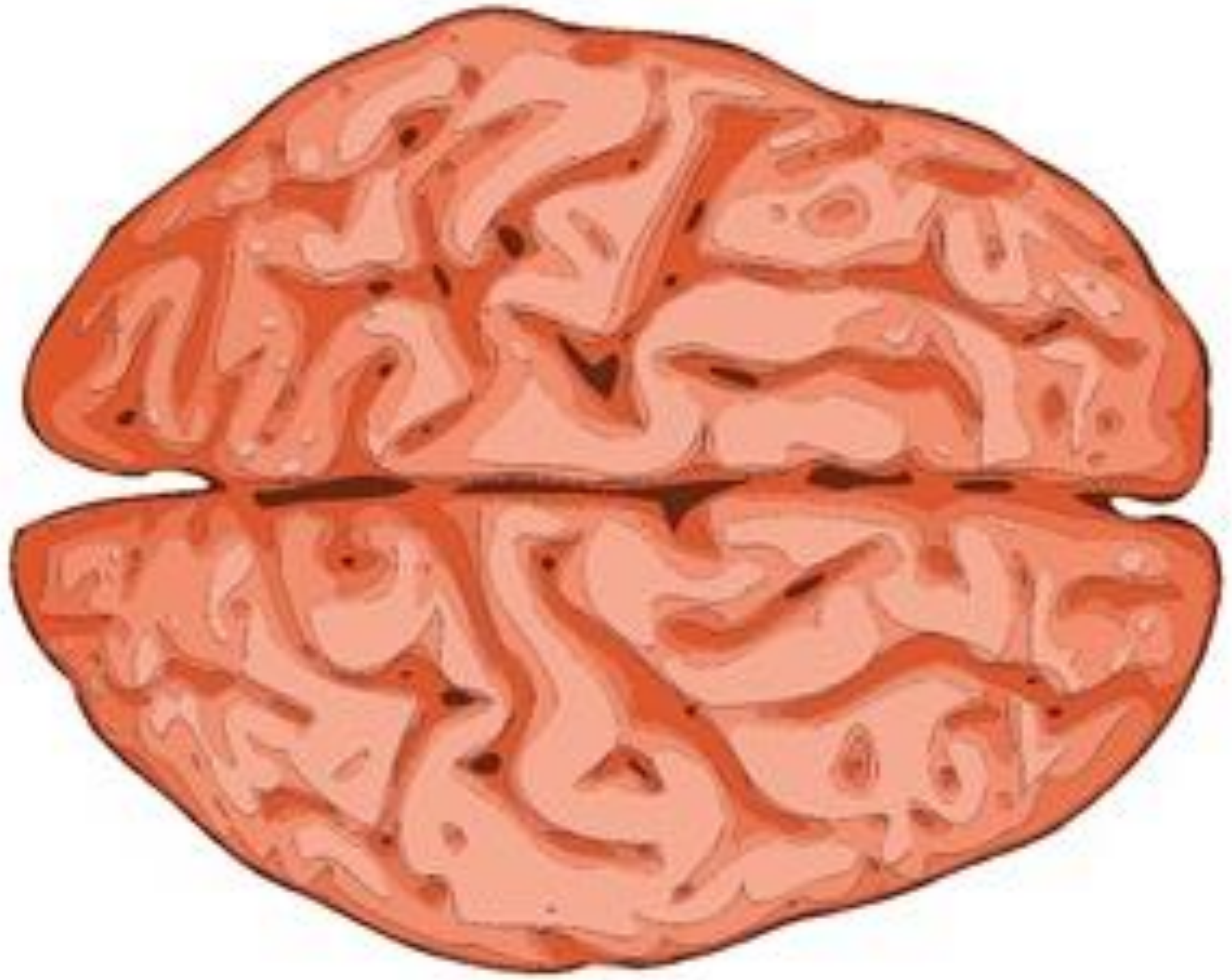


Behrens et al 2010

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™