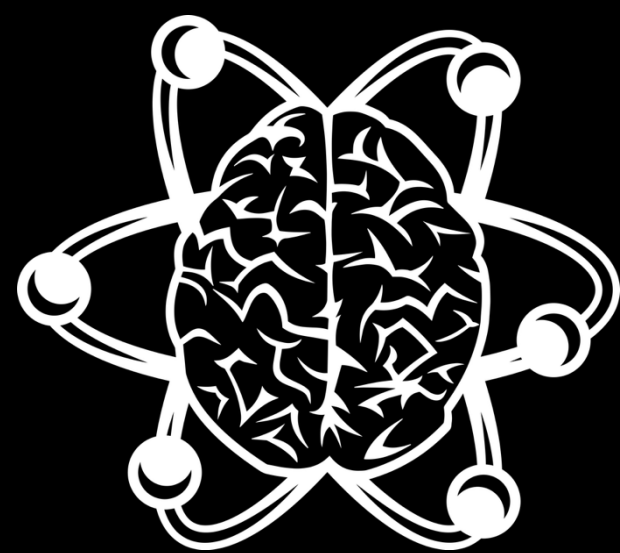
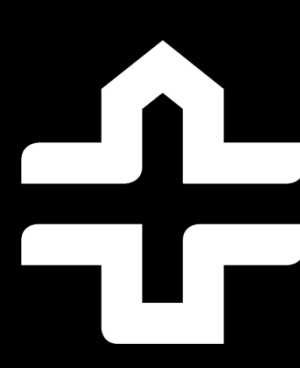




EXPERIMENTAL DESIGNS FOR FUNCTIONAL NEUROIMAGING

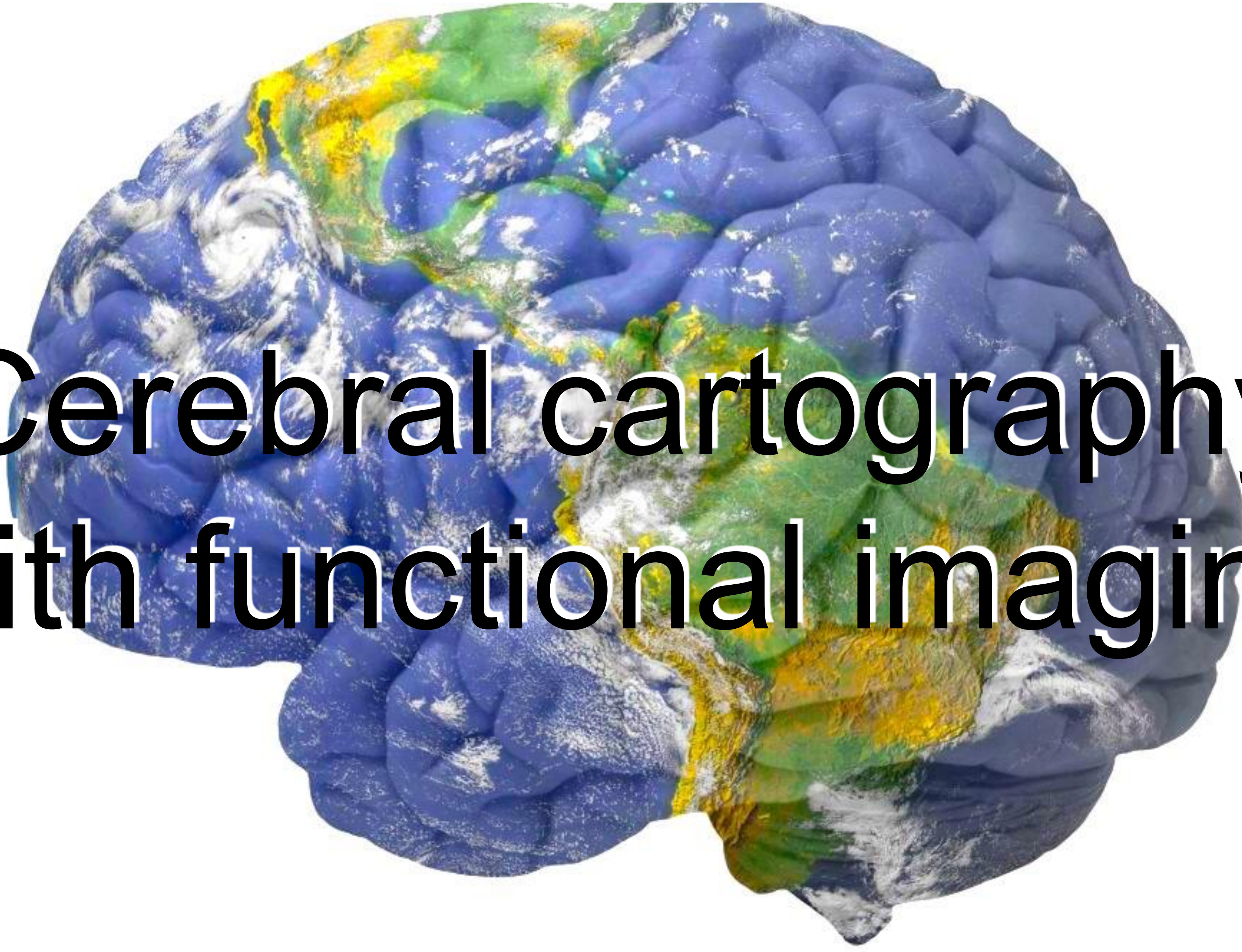
Turku PET Centre Brain Imaging Course 2026

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

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

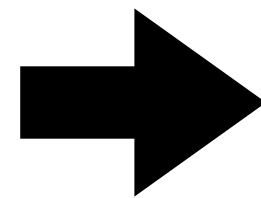


Experiment: Linking stimulation model with measurements

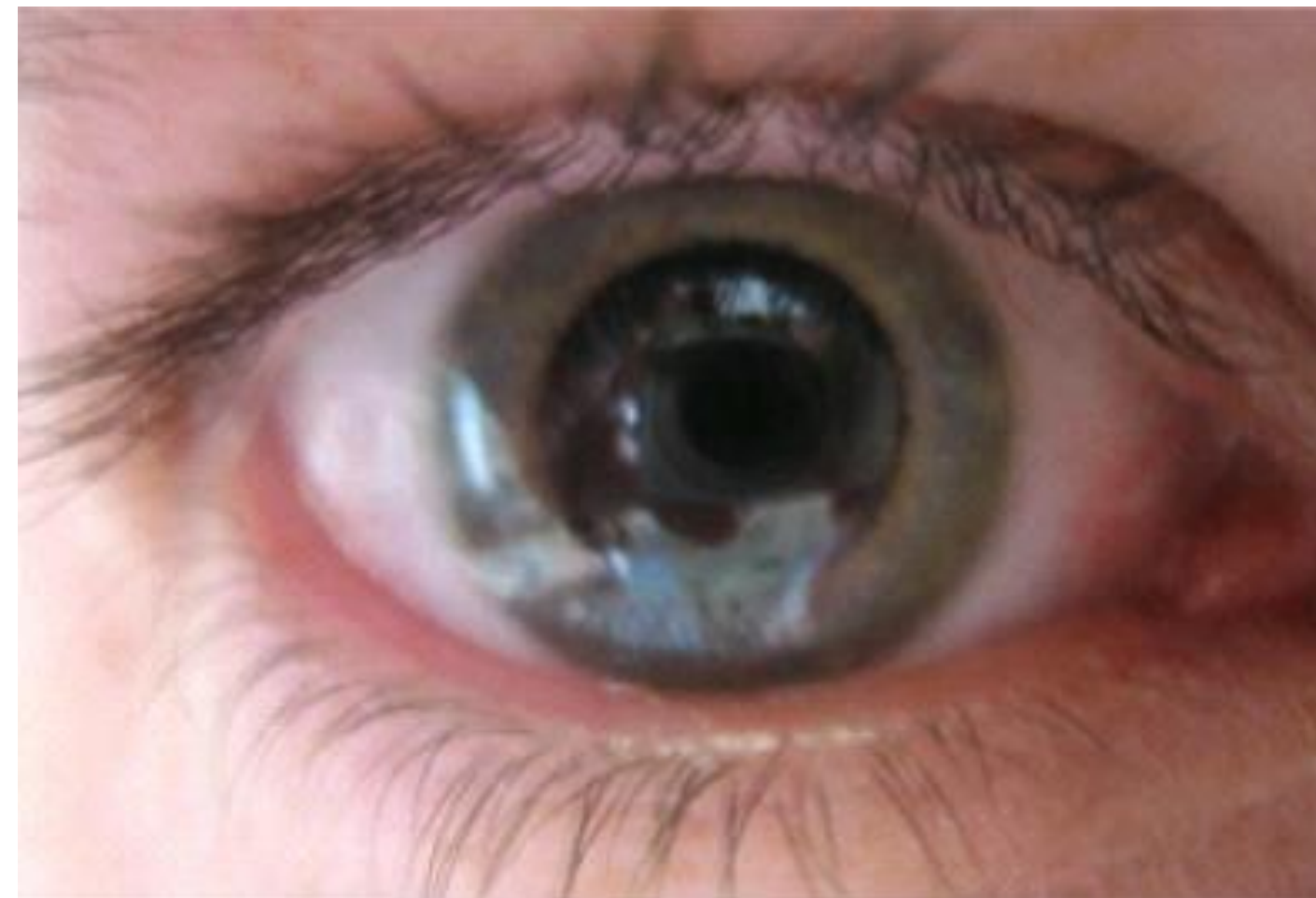
BACKGROUND LUMINOSITY



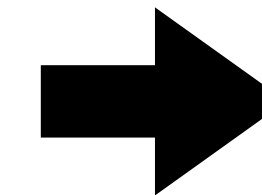
Independent variable
Controlled by experimenter



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

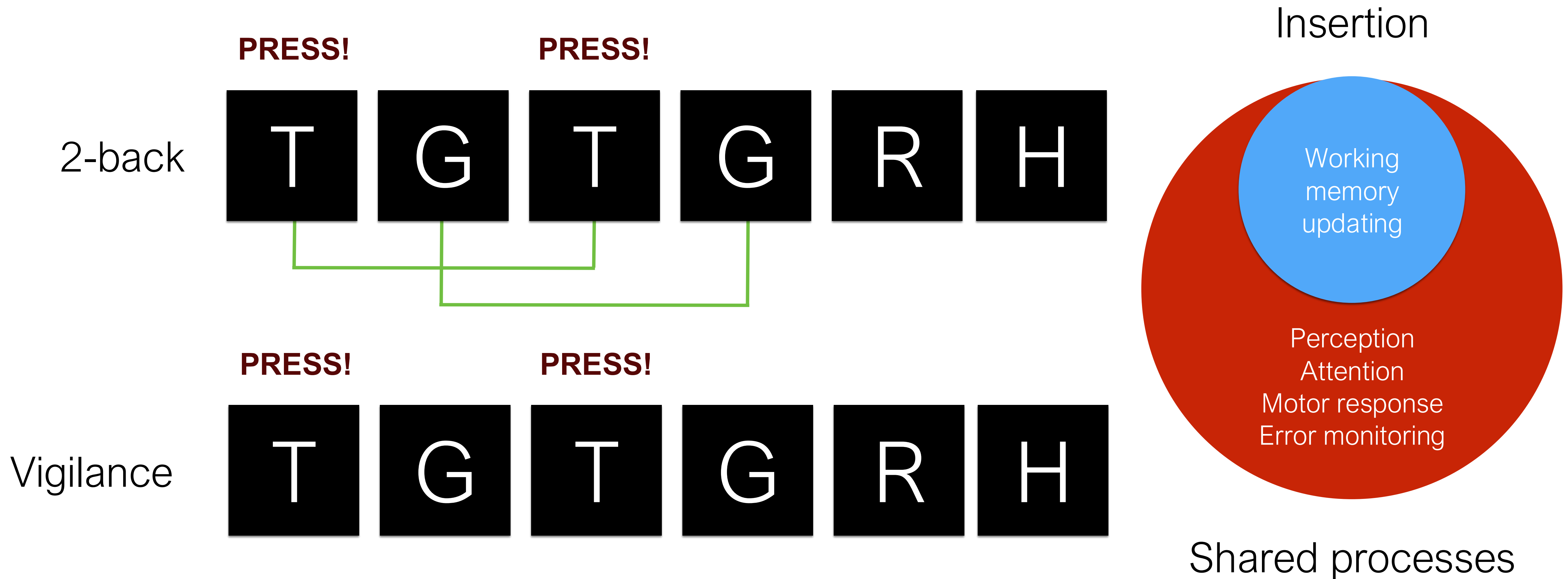
STATISTICS = SEPARATING NOISE FROM SIGNAL IN A PROBABILISTIC FASHION

Cognitive subtraction



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

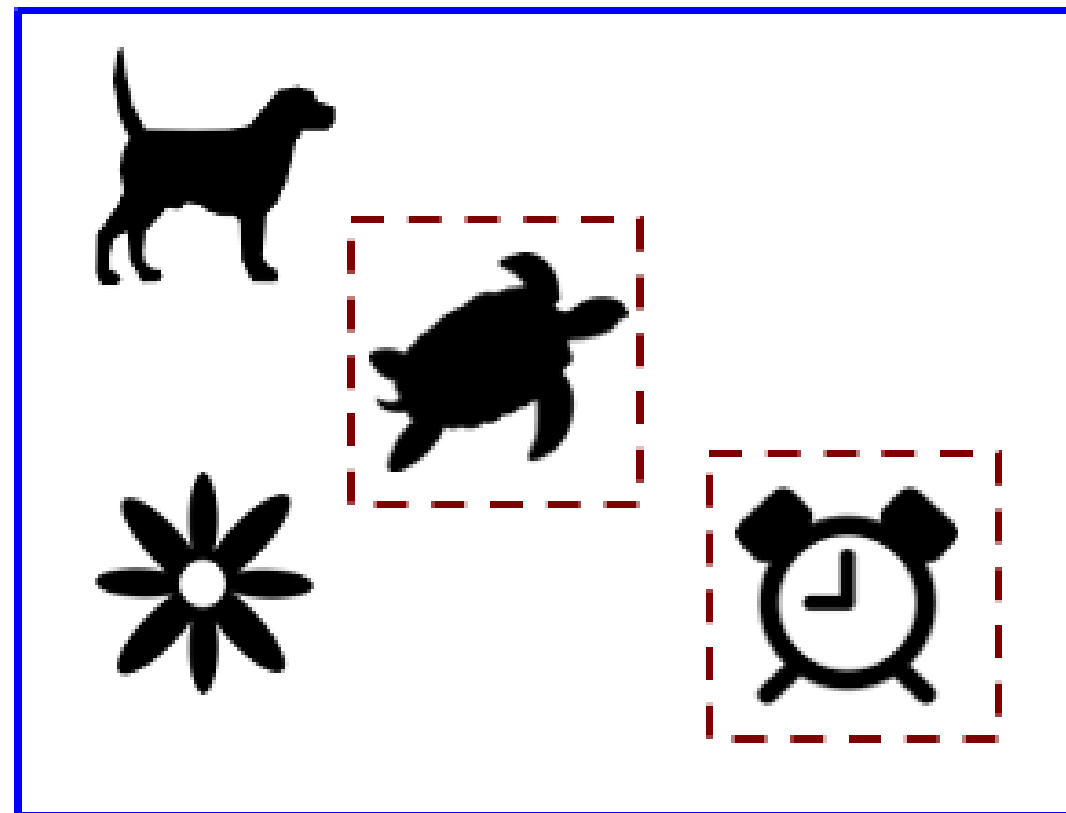
Problem: assumption of pure insertion



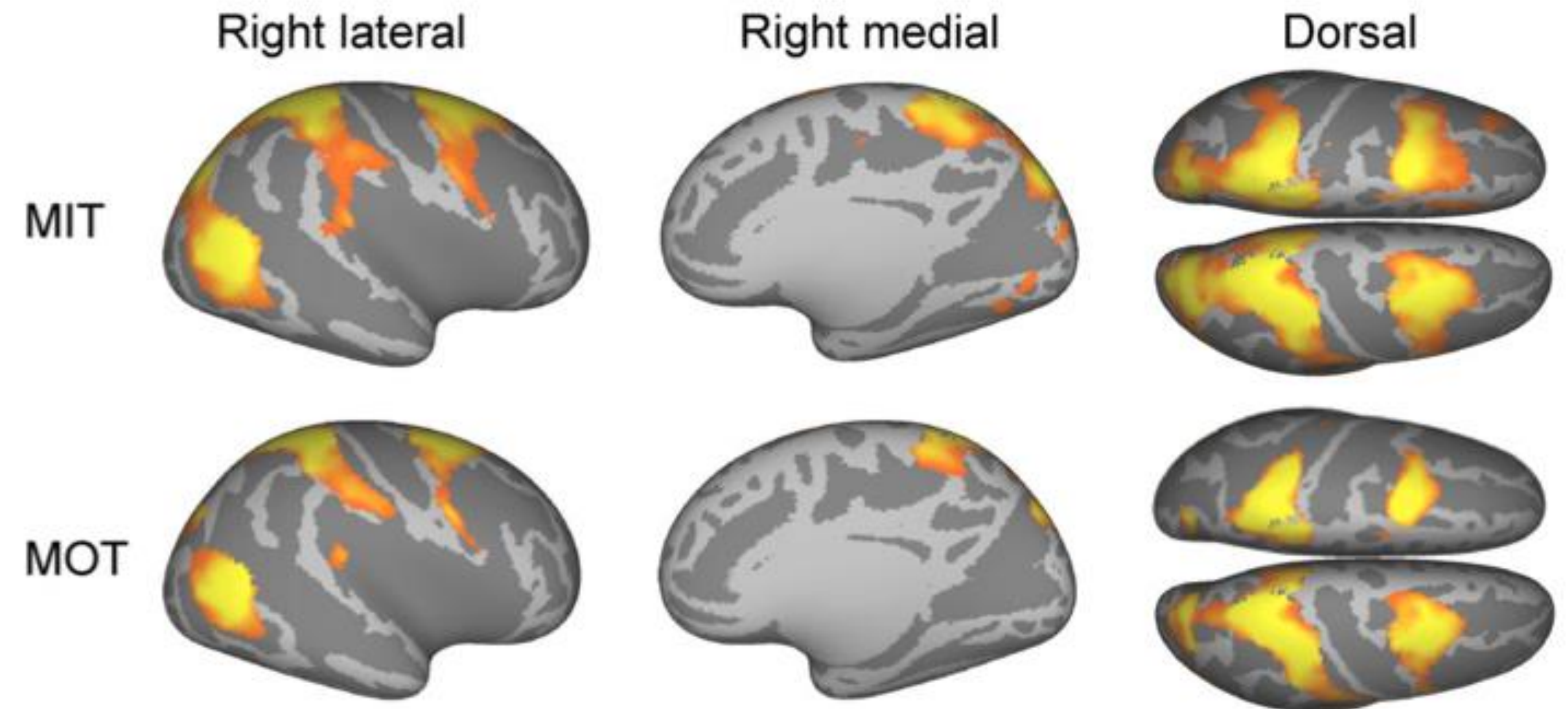
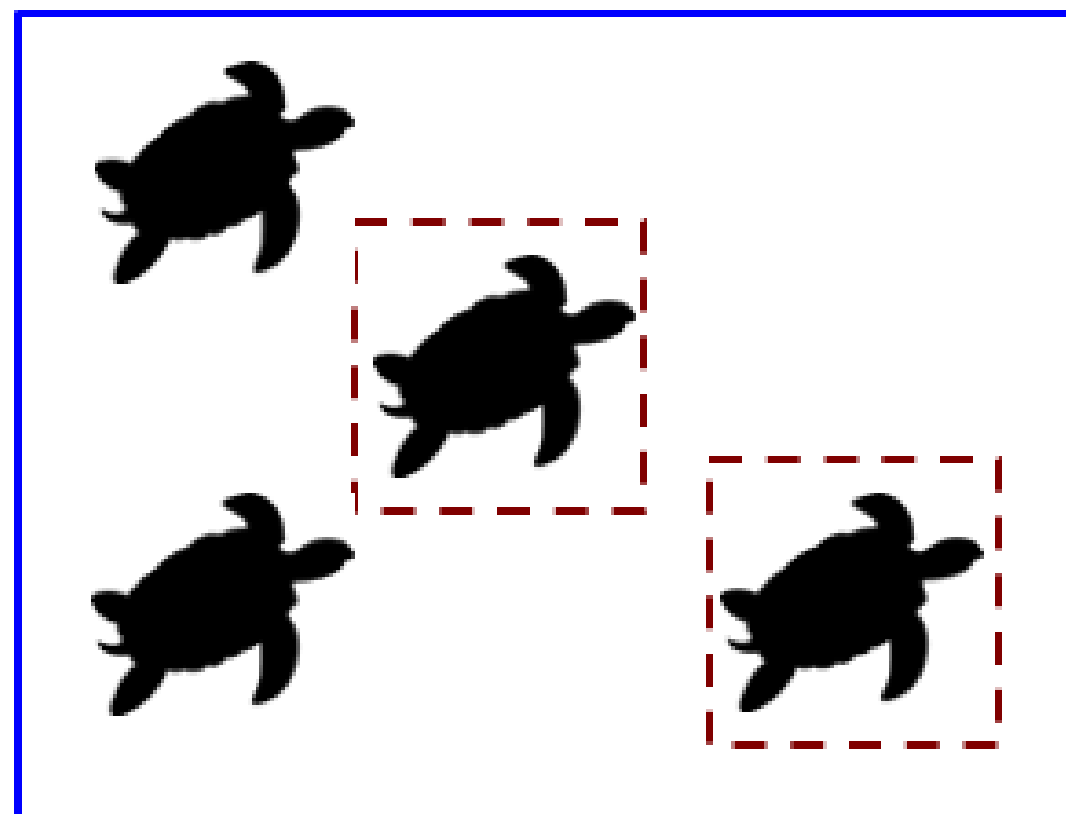
Pure insertion: assumption that inserting another component to the task does not affecting the remaining process

A) Multiple Identity Tracking (MIT)

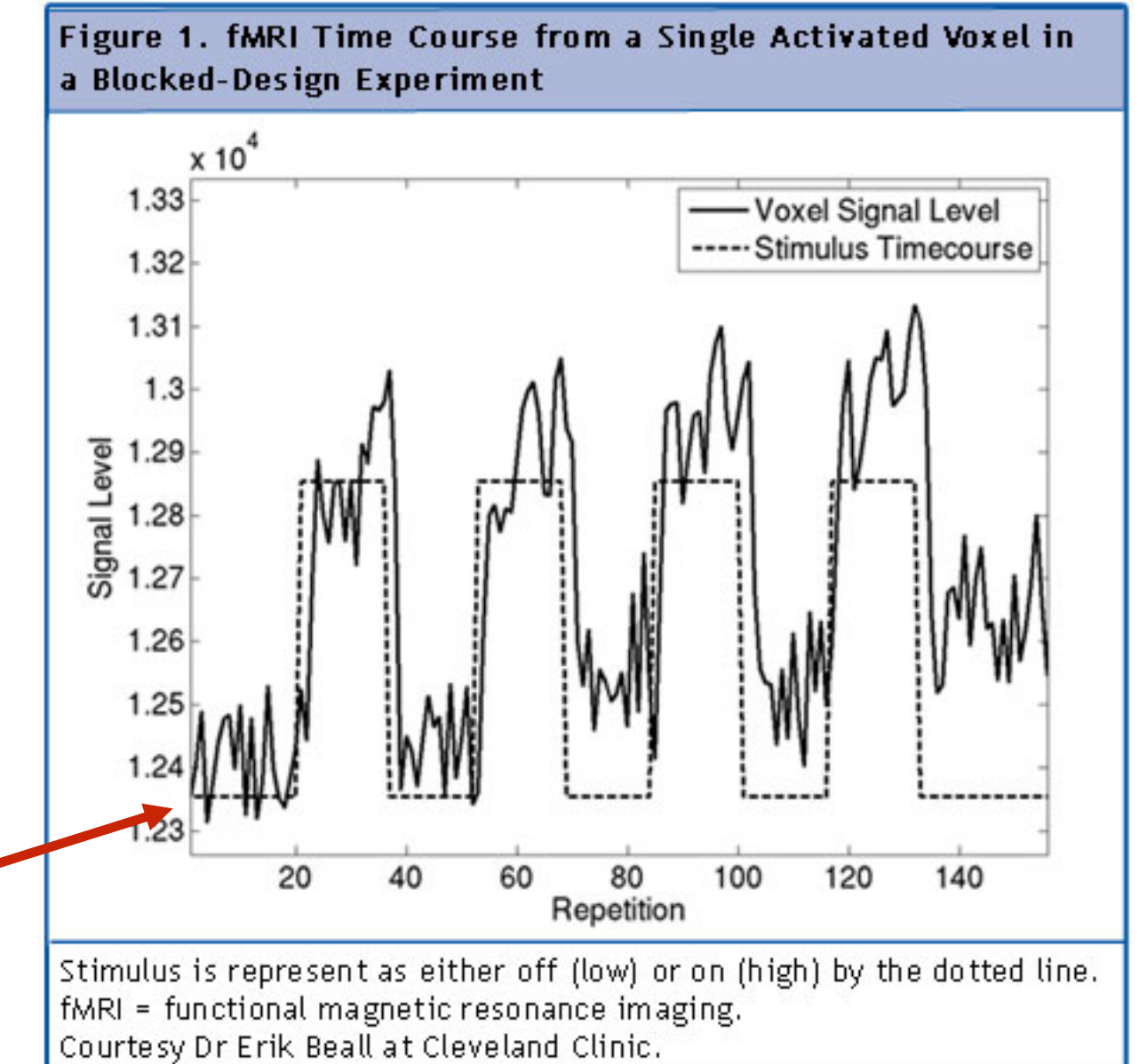
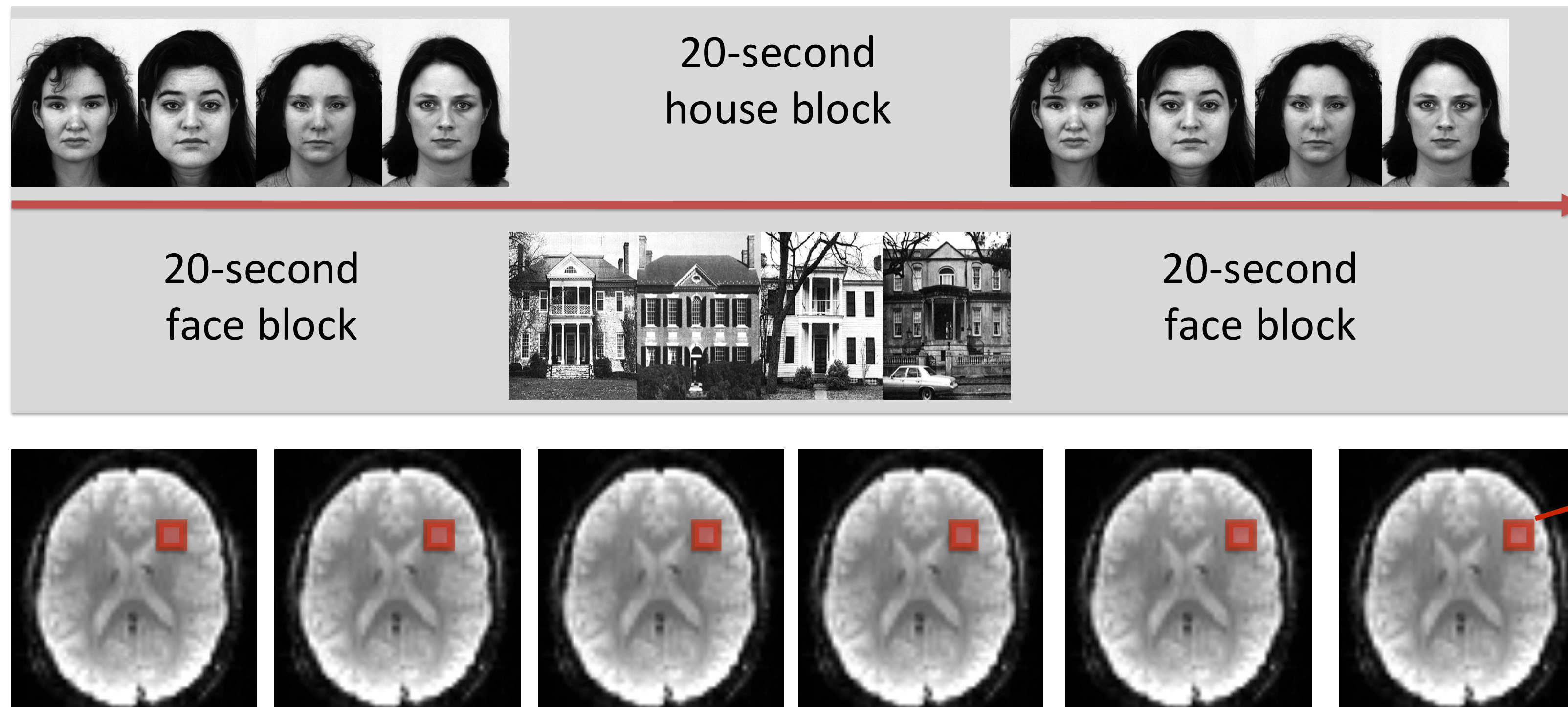
4 s



B) Multiple Object Tracking (MOT)



Typical fMRI experiment

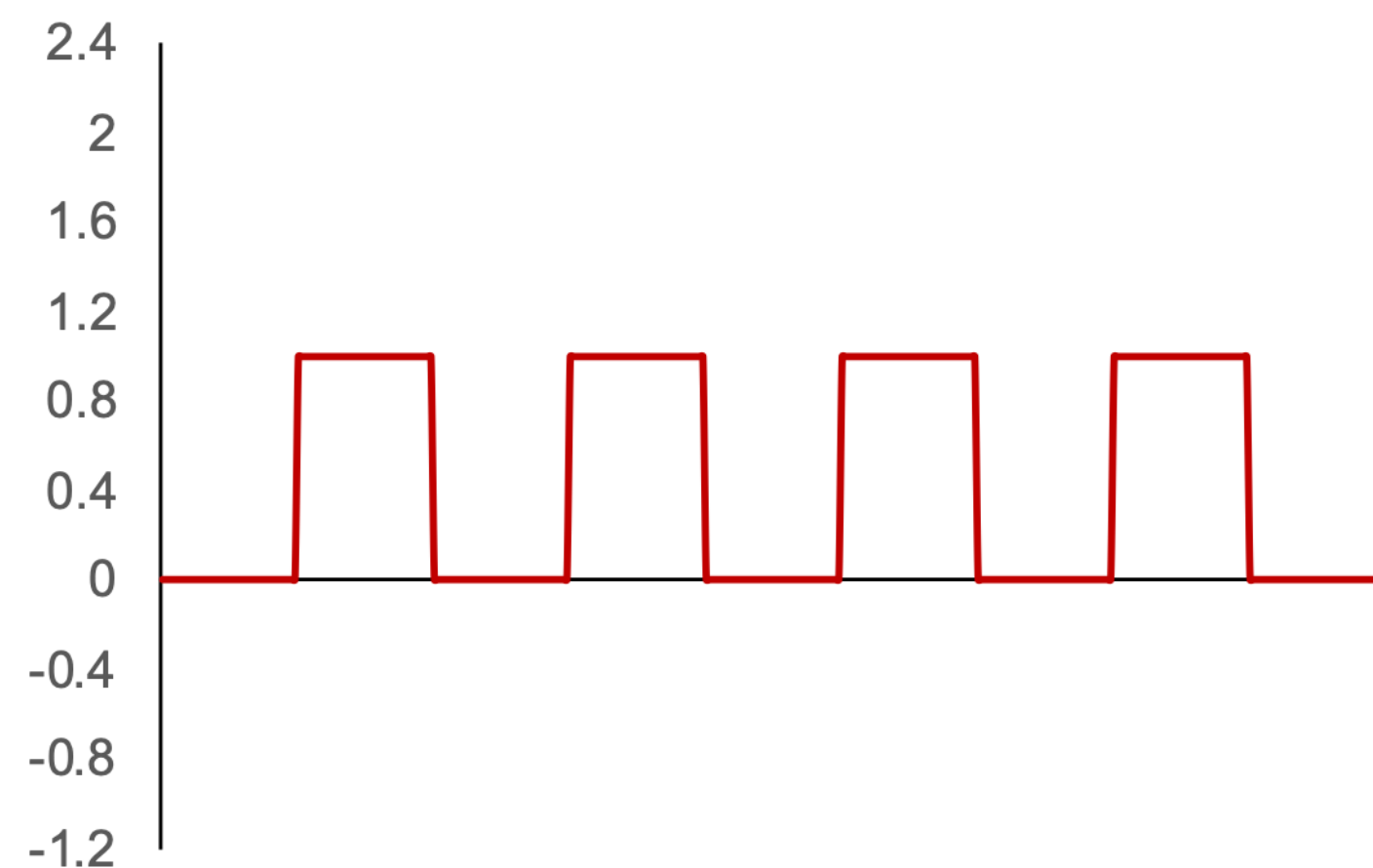


Acquiring one 3D functional volume takes about 1.5 seconds

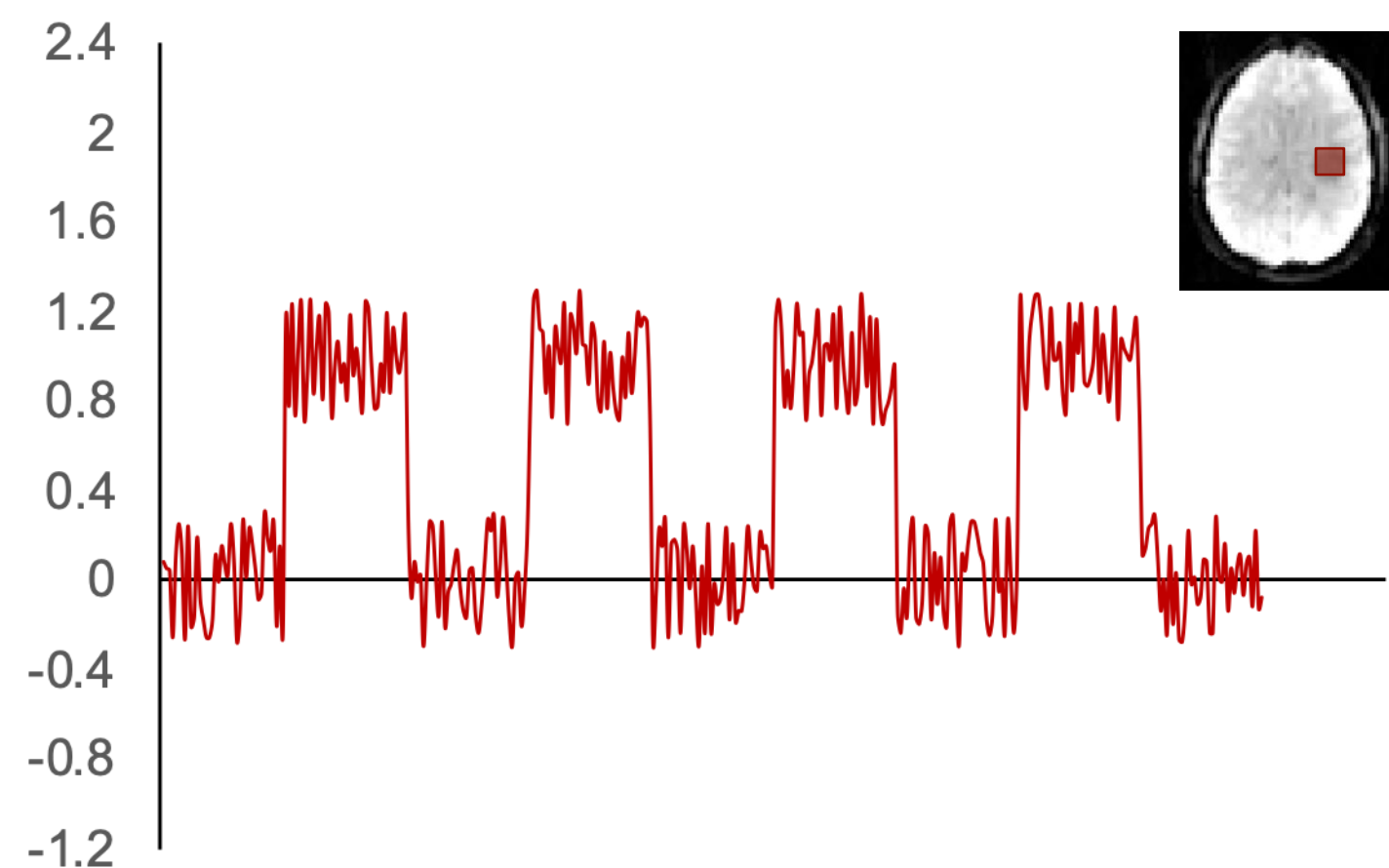
We can distinguish events $\sim 100\text{ms}$ apart, yet their actual timing can be resolved with about 2-s accuracy

Fitting the model to the data

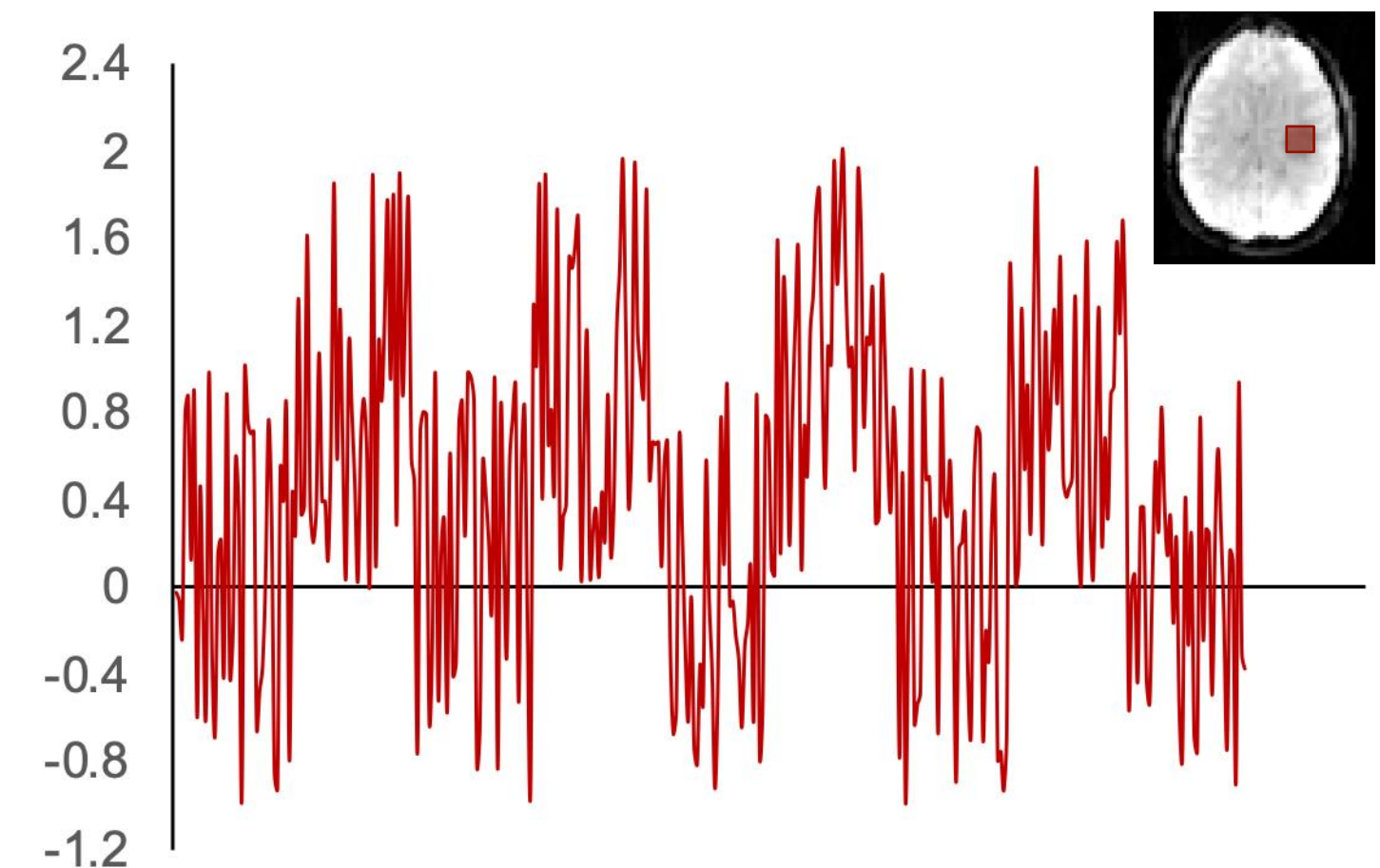
Stimulation model (boxcar)



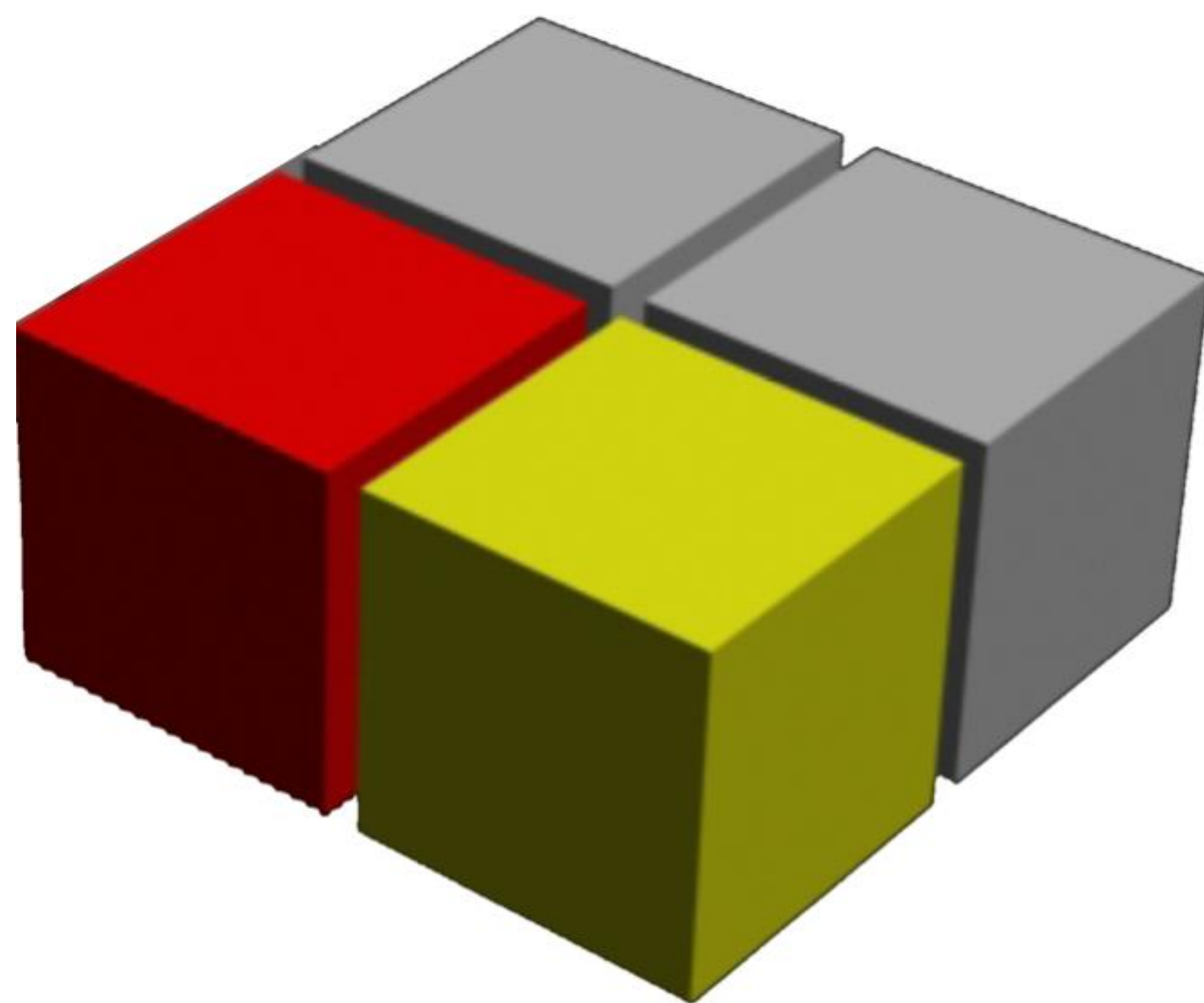
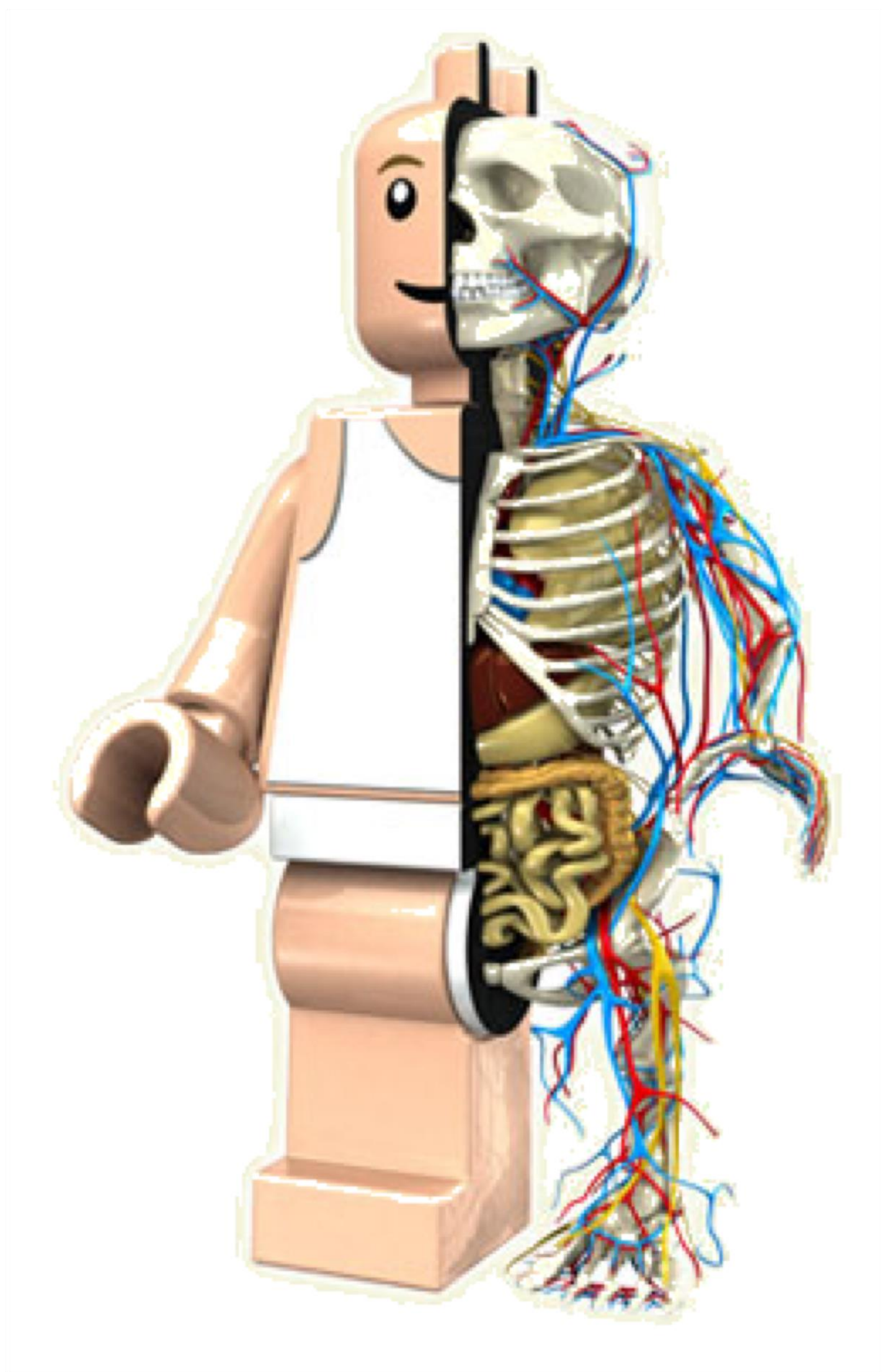
Clean data



Noisy data

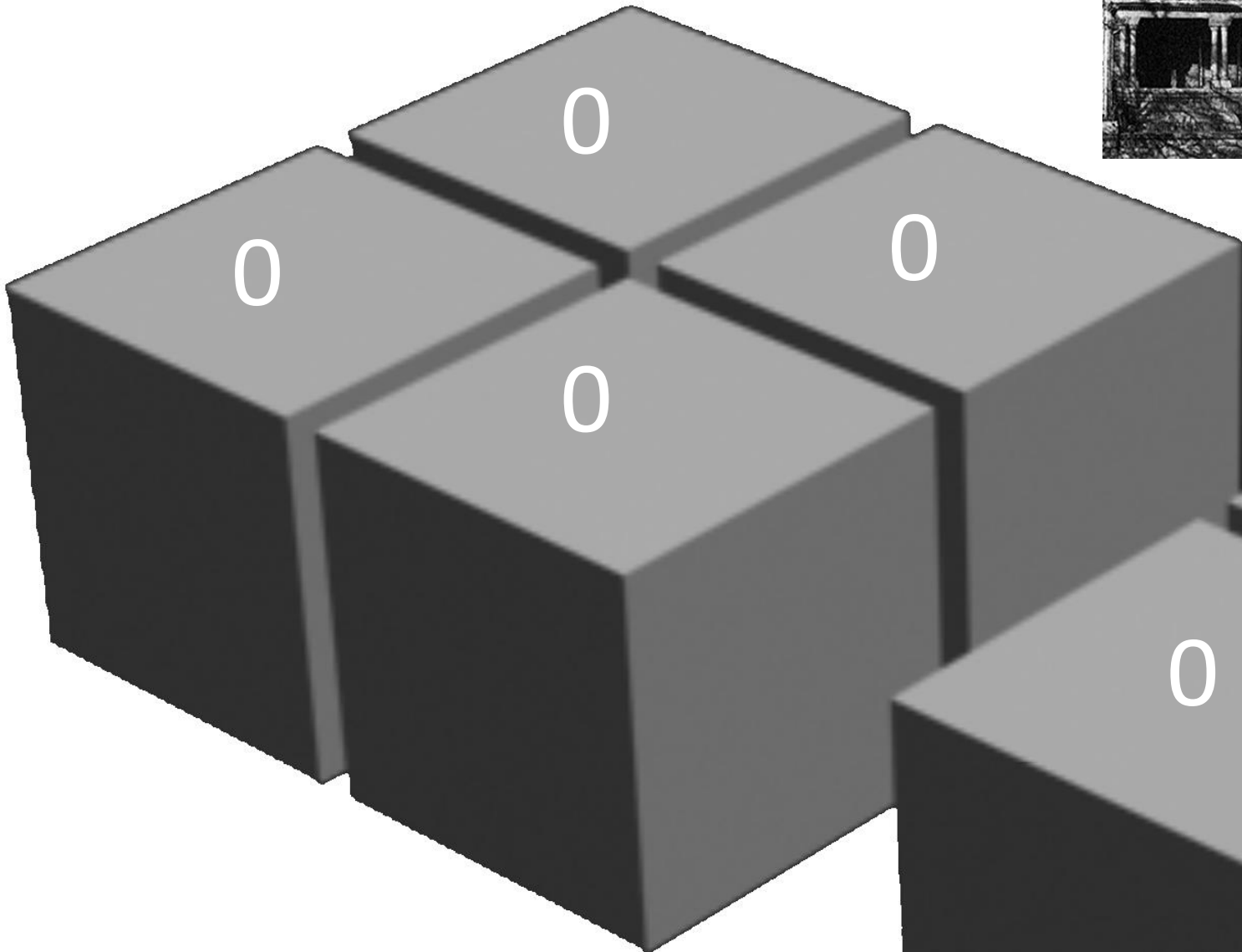


Basic idea: model how well the stimulation model predicts BOLD time course at each voxel

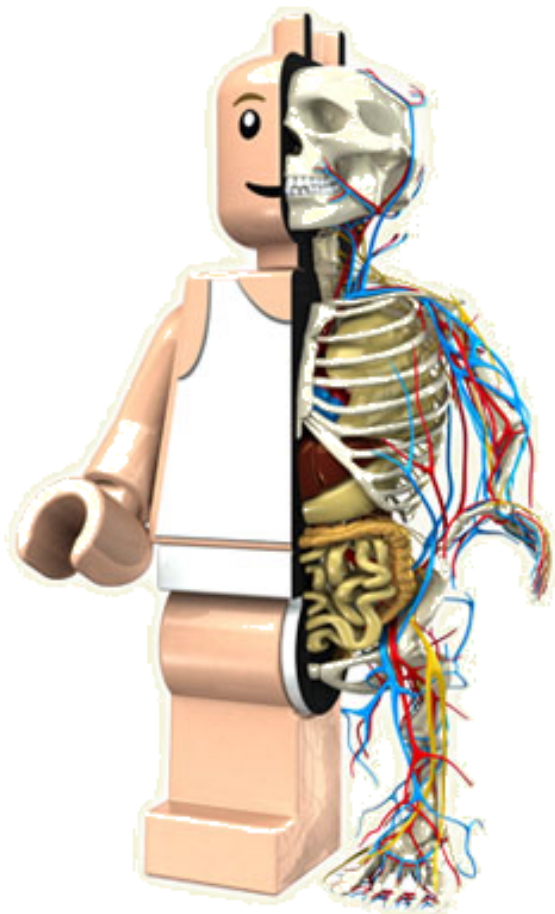
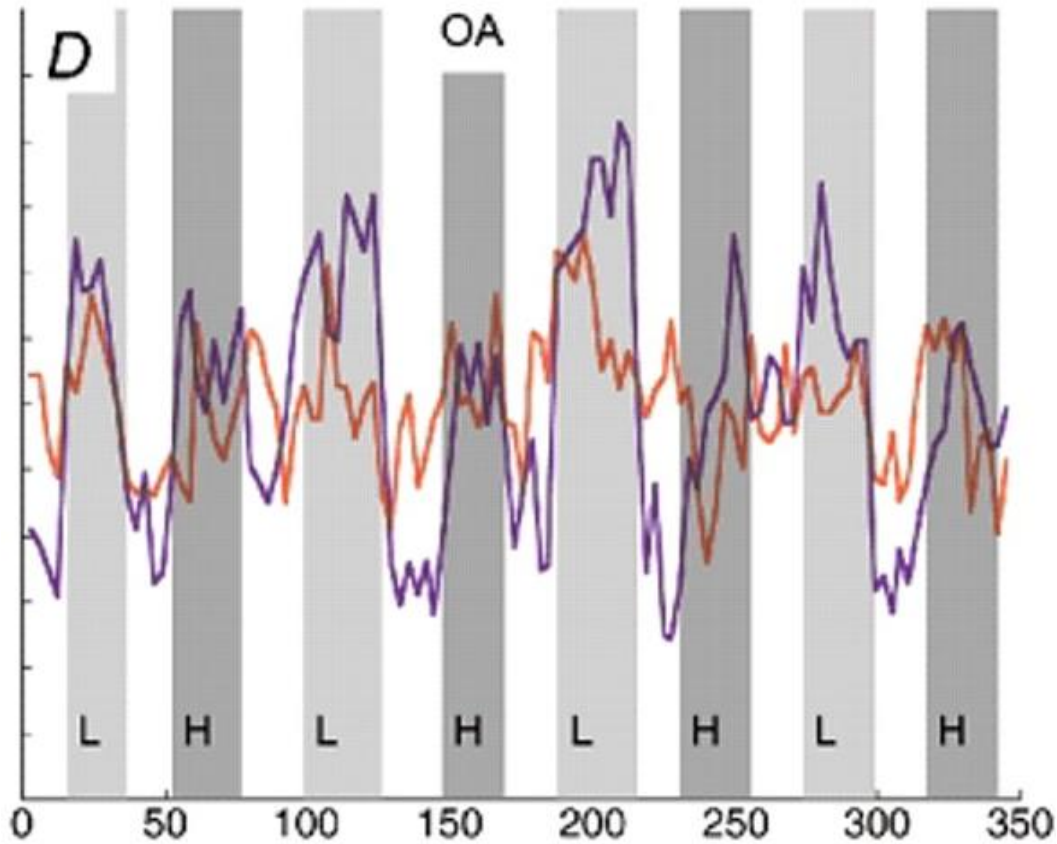
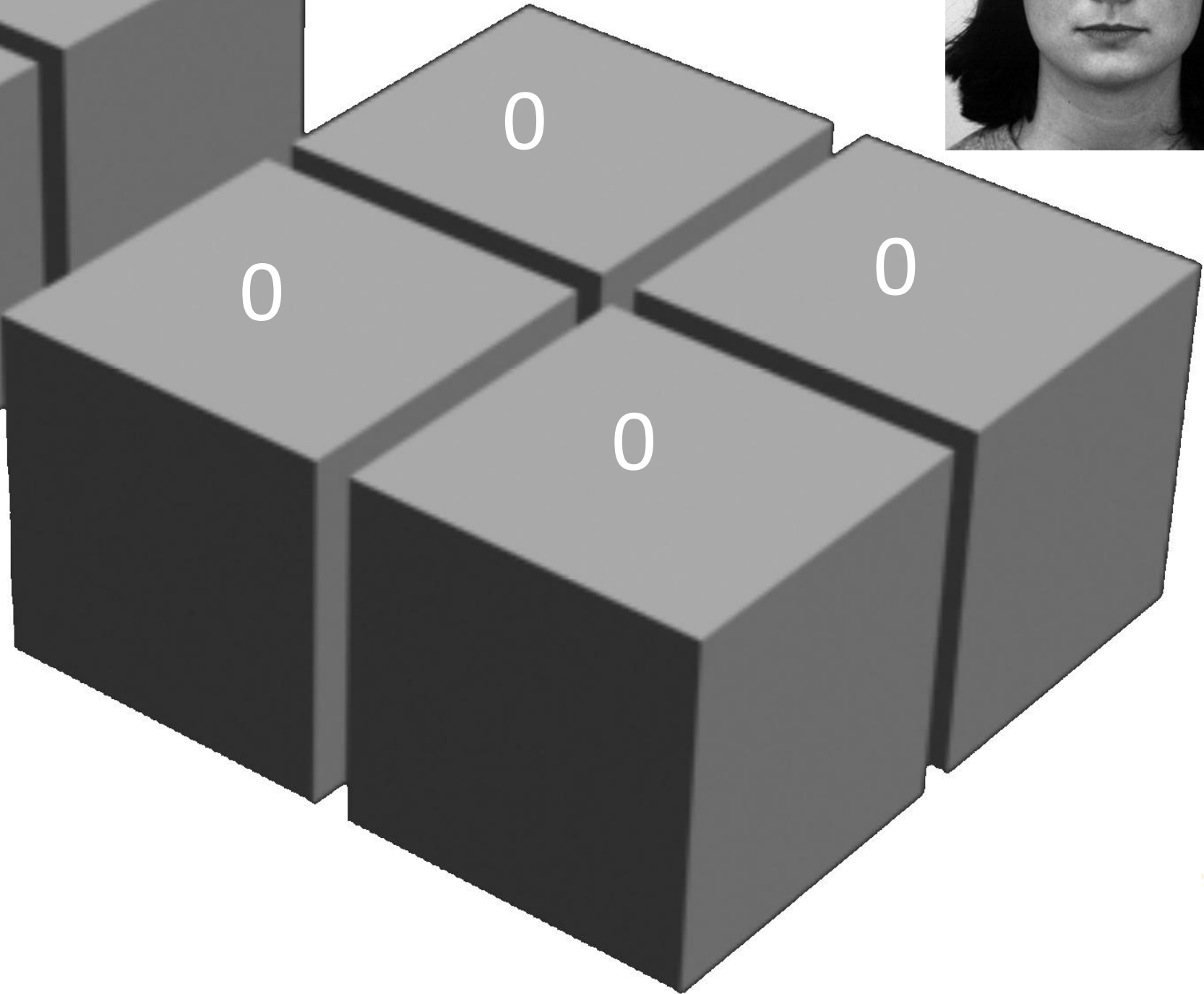


First level model with LEGO brains

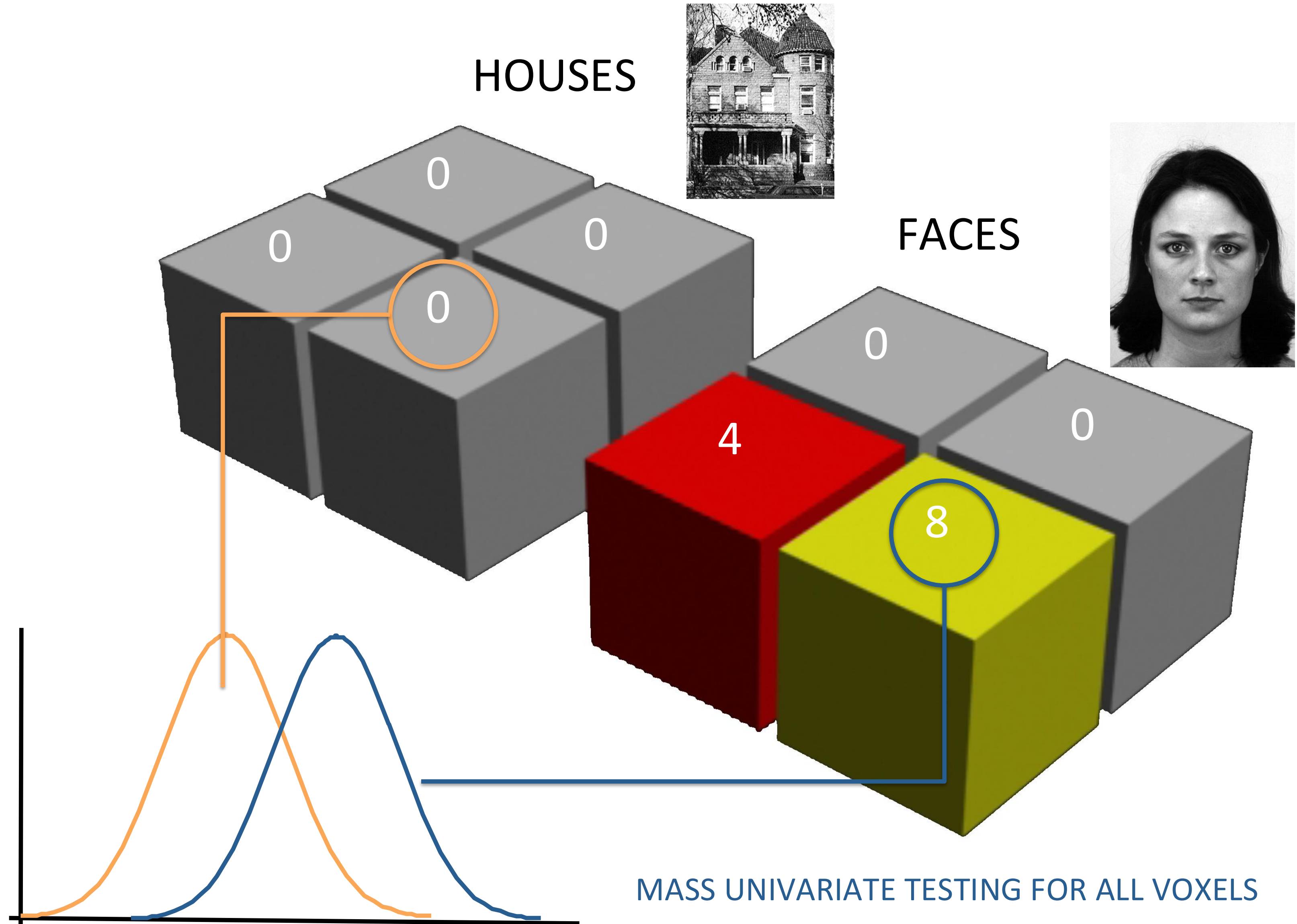
HOUSES



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

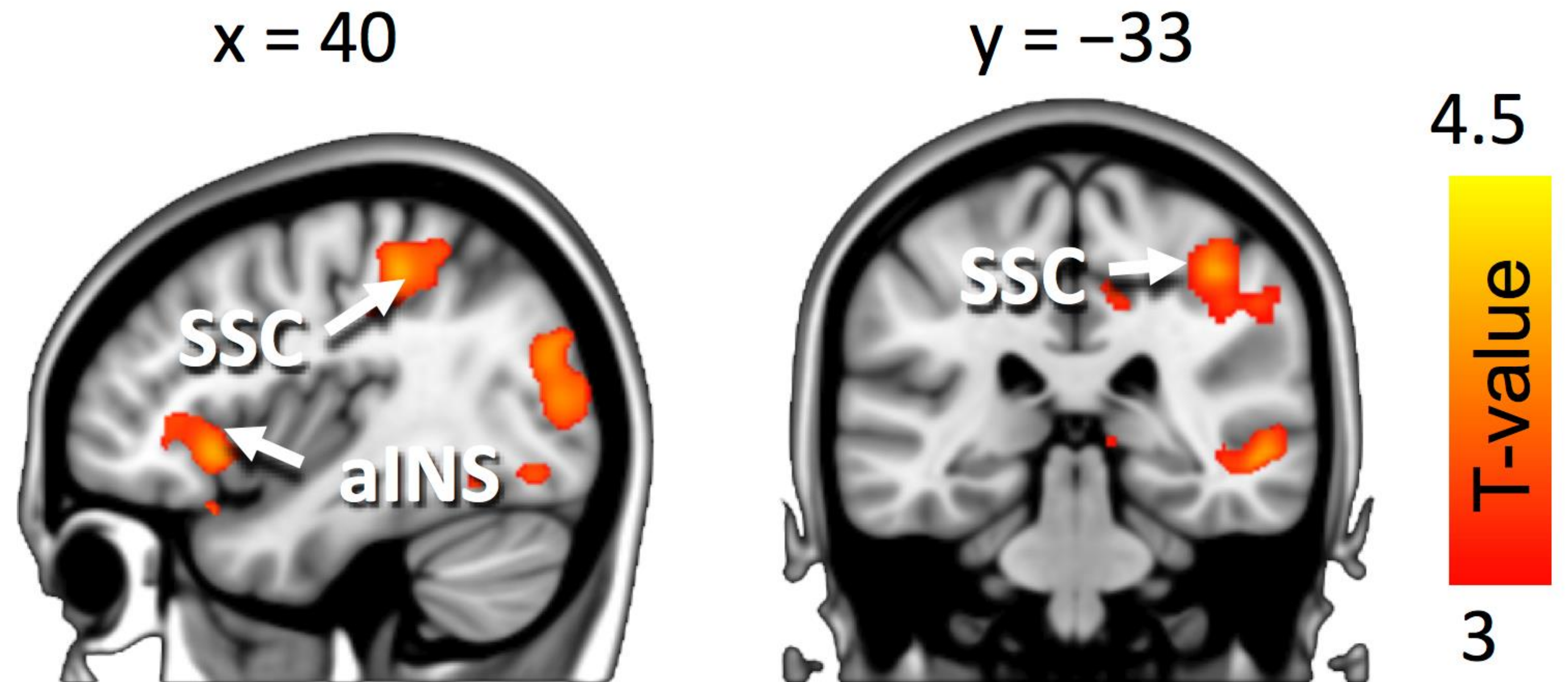
ADVANTAGES: Simple, powerful, often short experiments

Networks for vicarious pain perception

Feel pain trial

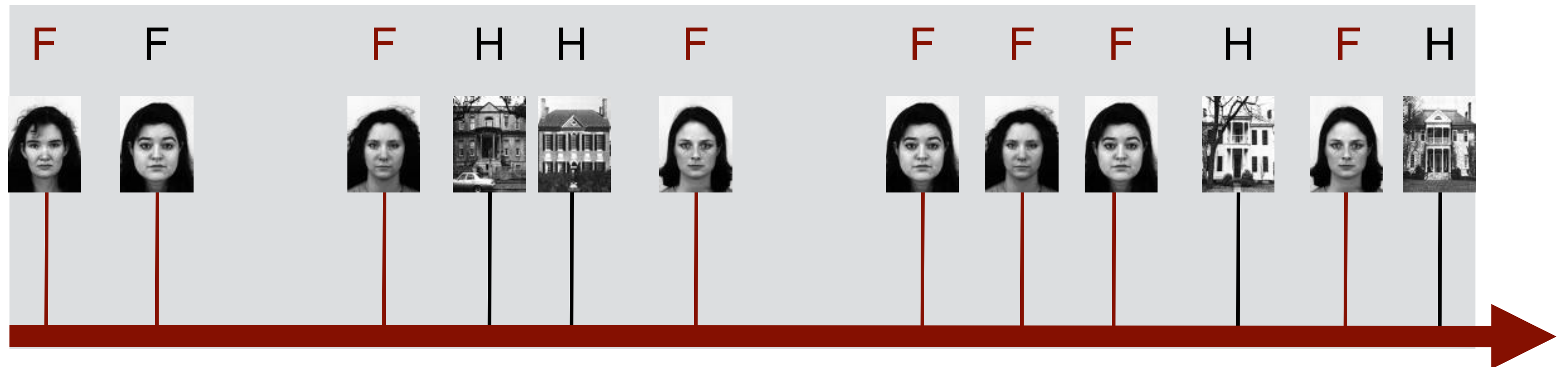


Cause pain trial



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

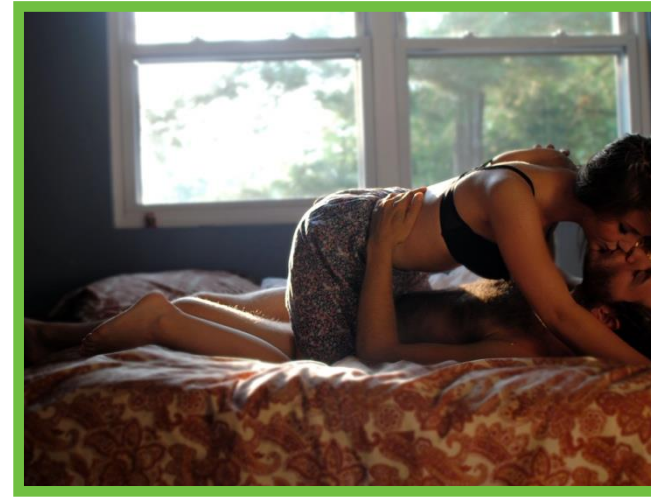
DESIGN: Event-related design with cognitive subtraction assuming pure insertion

ADVANTAGES: More accurate model, trial wise analysis, randomisation

1s



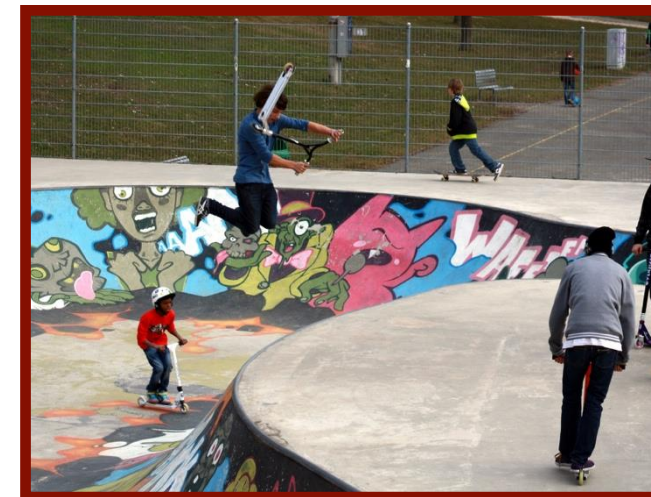
1s



1s



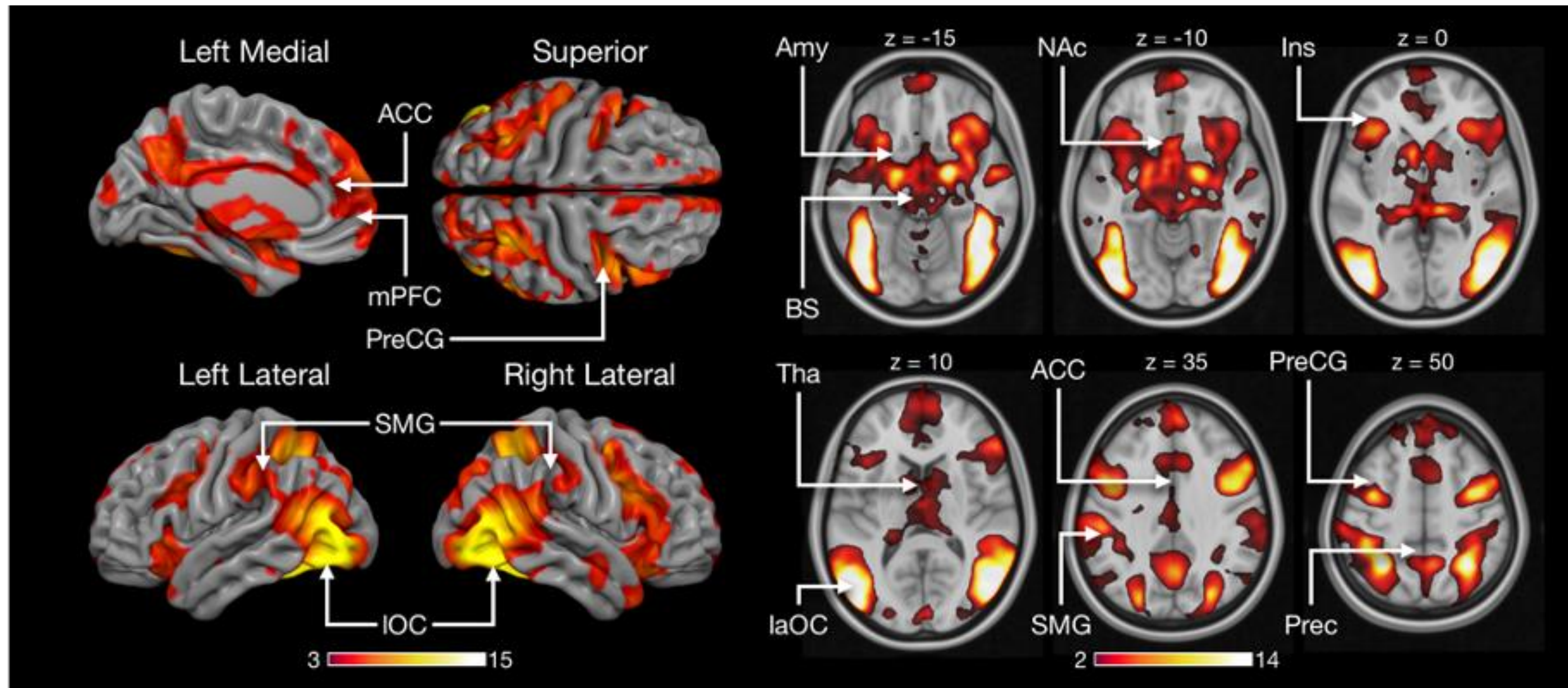
1s



1s

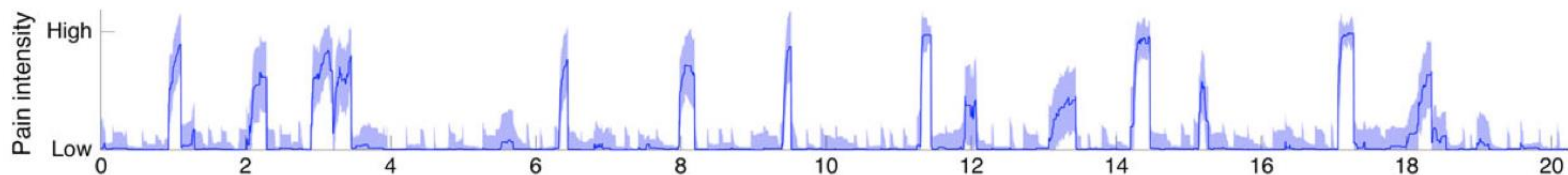


1s



Putkinen et al (submitted)

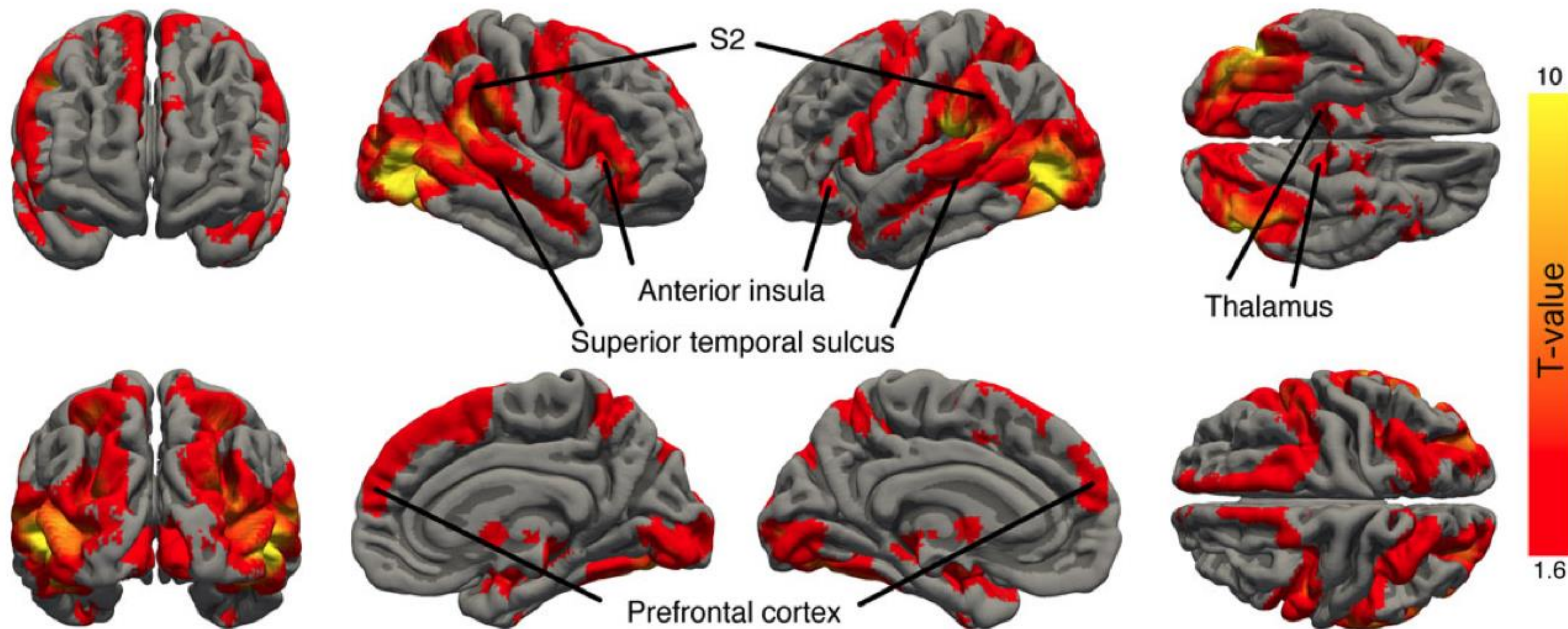
Basic tool 3: Parametric design



AIM: Localize brain regions that respond to vicarious pain

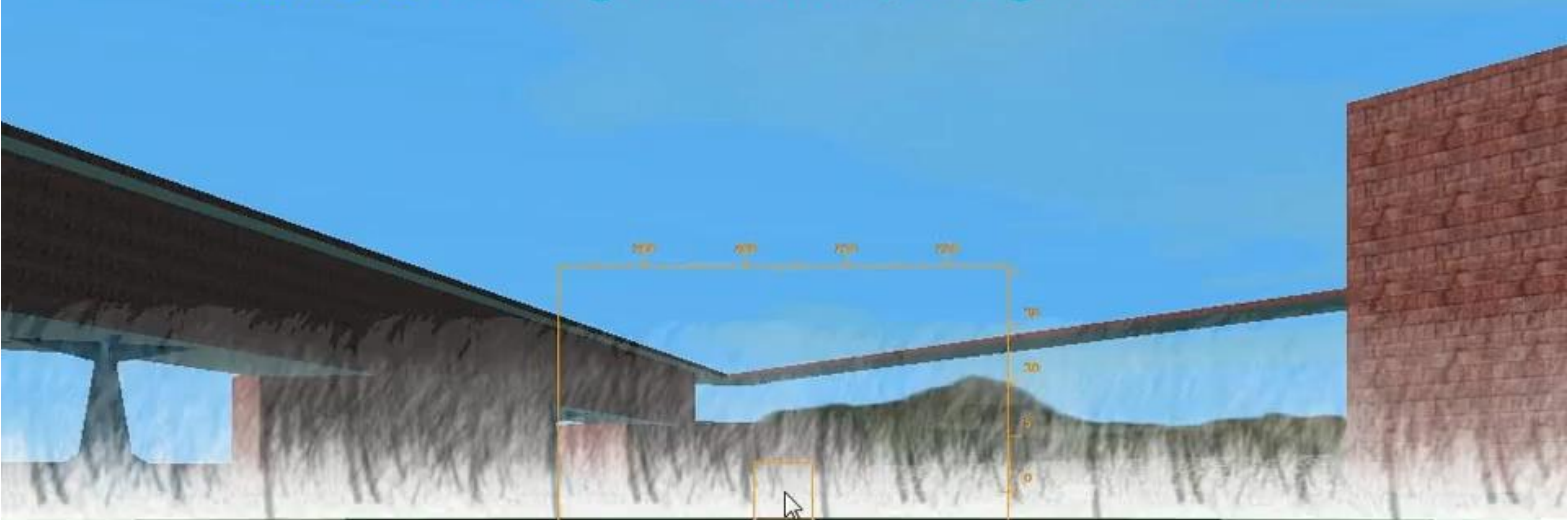
DESIGN: Parametric design with continuous stimulation model

ADVANTAGES: Quantitative stimulation model, high statistical power

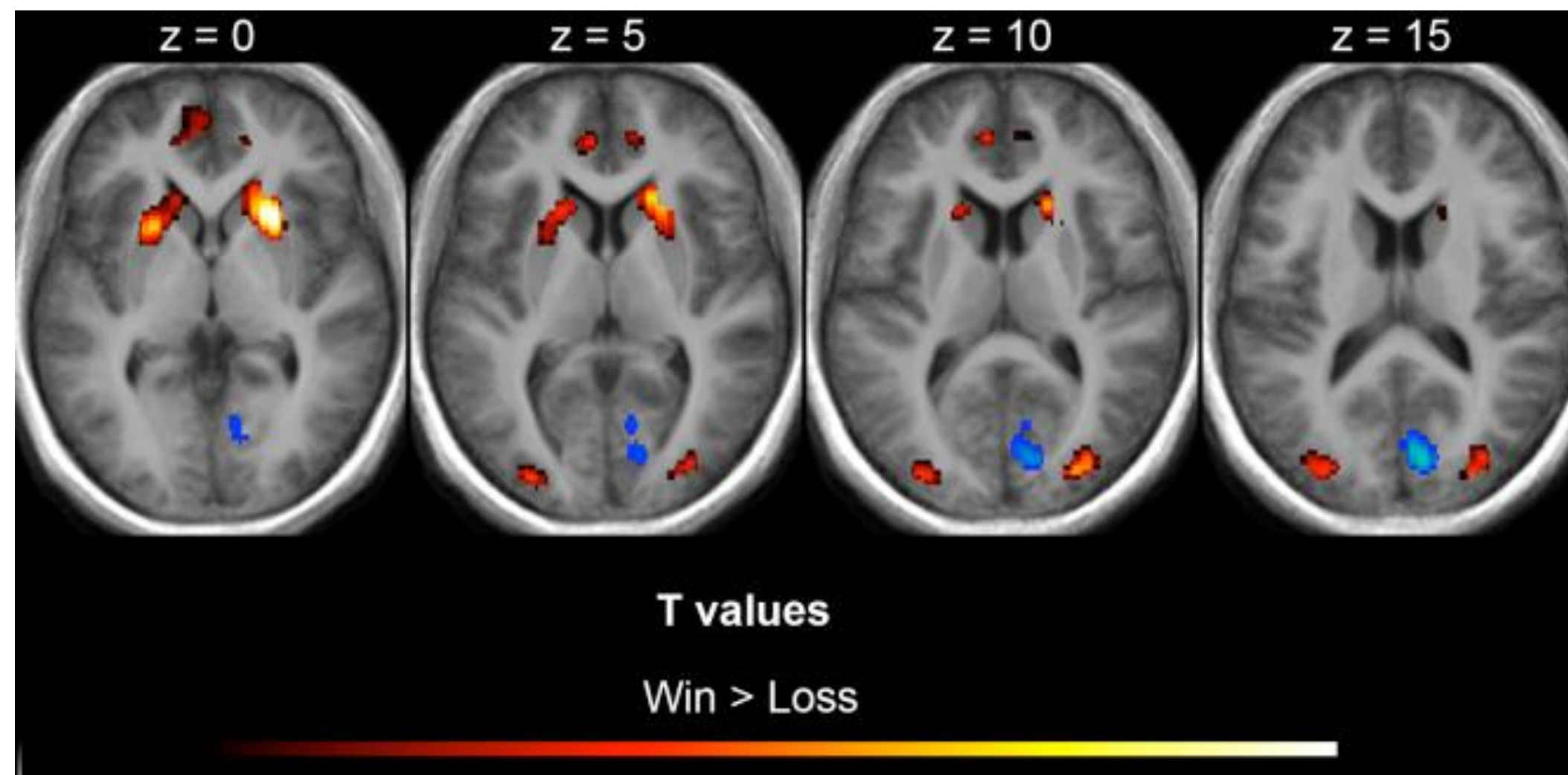
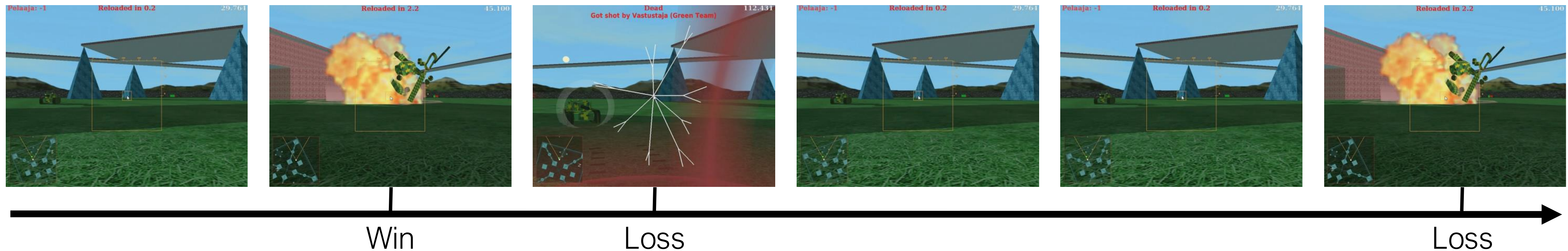


Karjalainen et al (2018 Cereb Cortex)

Basic tool 4: Unconstrained conditions and active experiments



Model-based analysis of an unstructured gameplay session

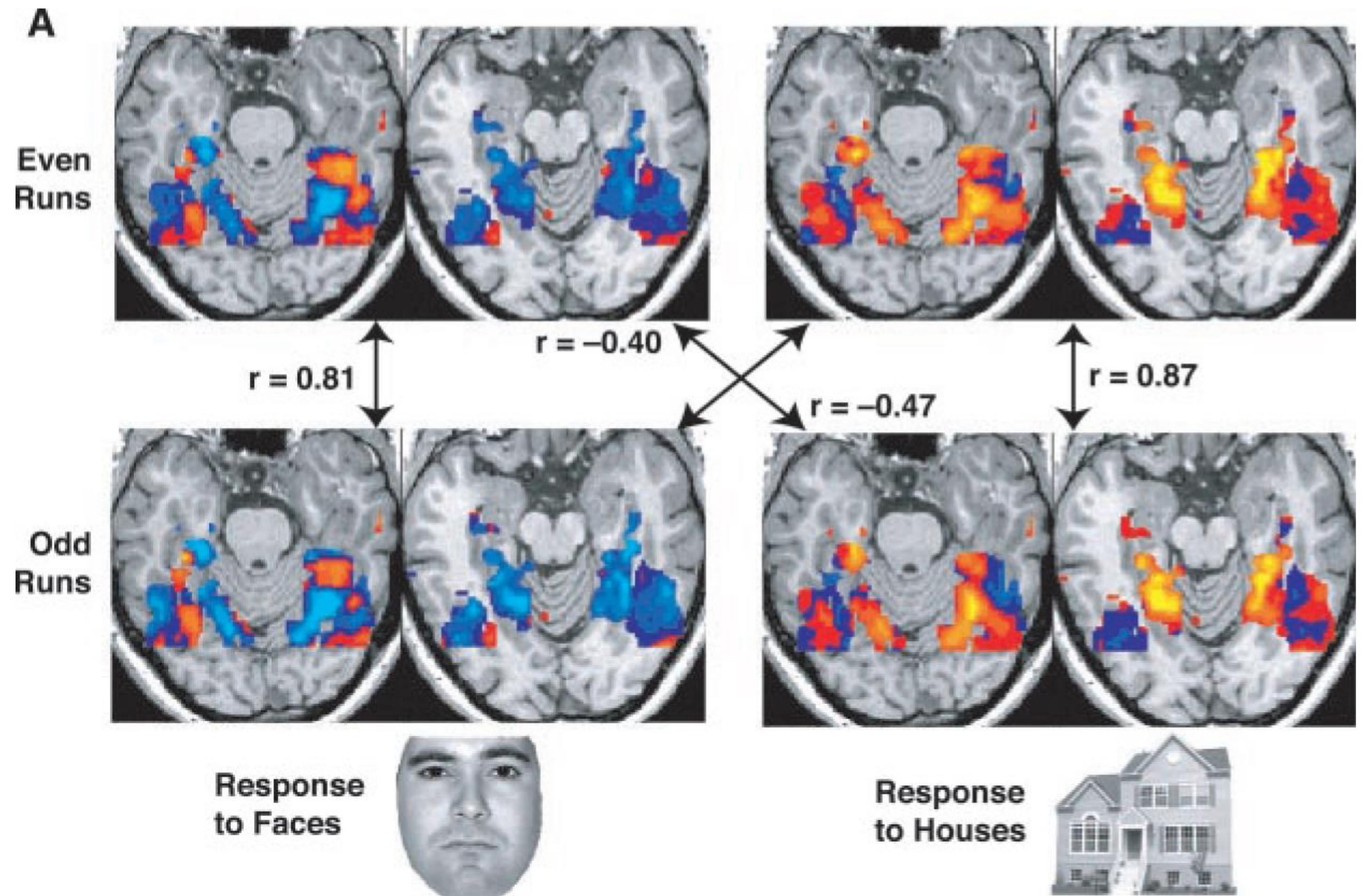


- Stimulus model is stored based on player behaviour
- Events of interest modelled as
- Stick functions
- Everyone free to play as they want,
- But gameplay is parsed into similar event

Response variability across session

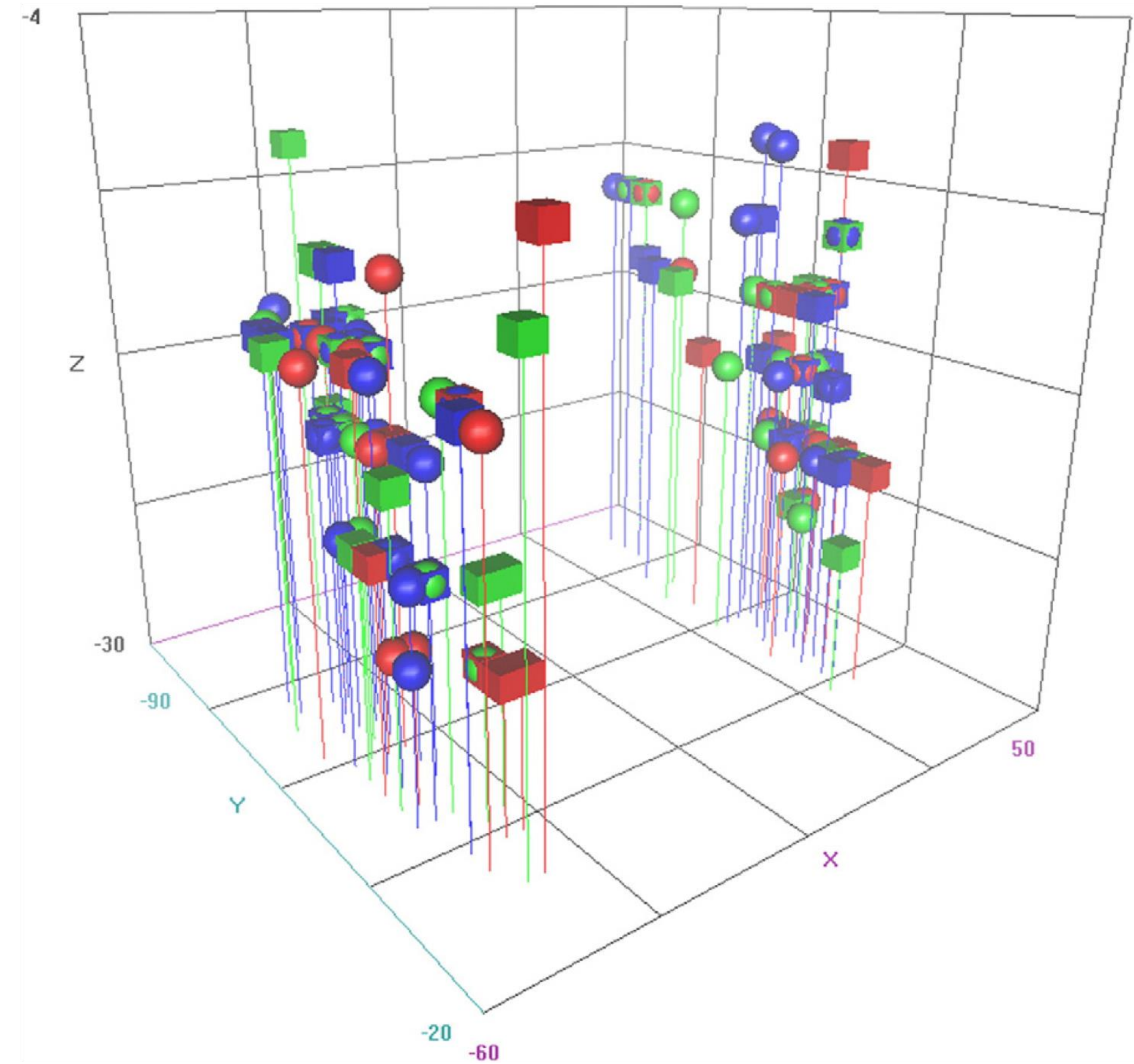
Sources of variation

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



Anatomical differences

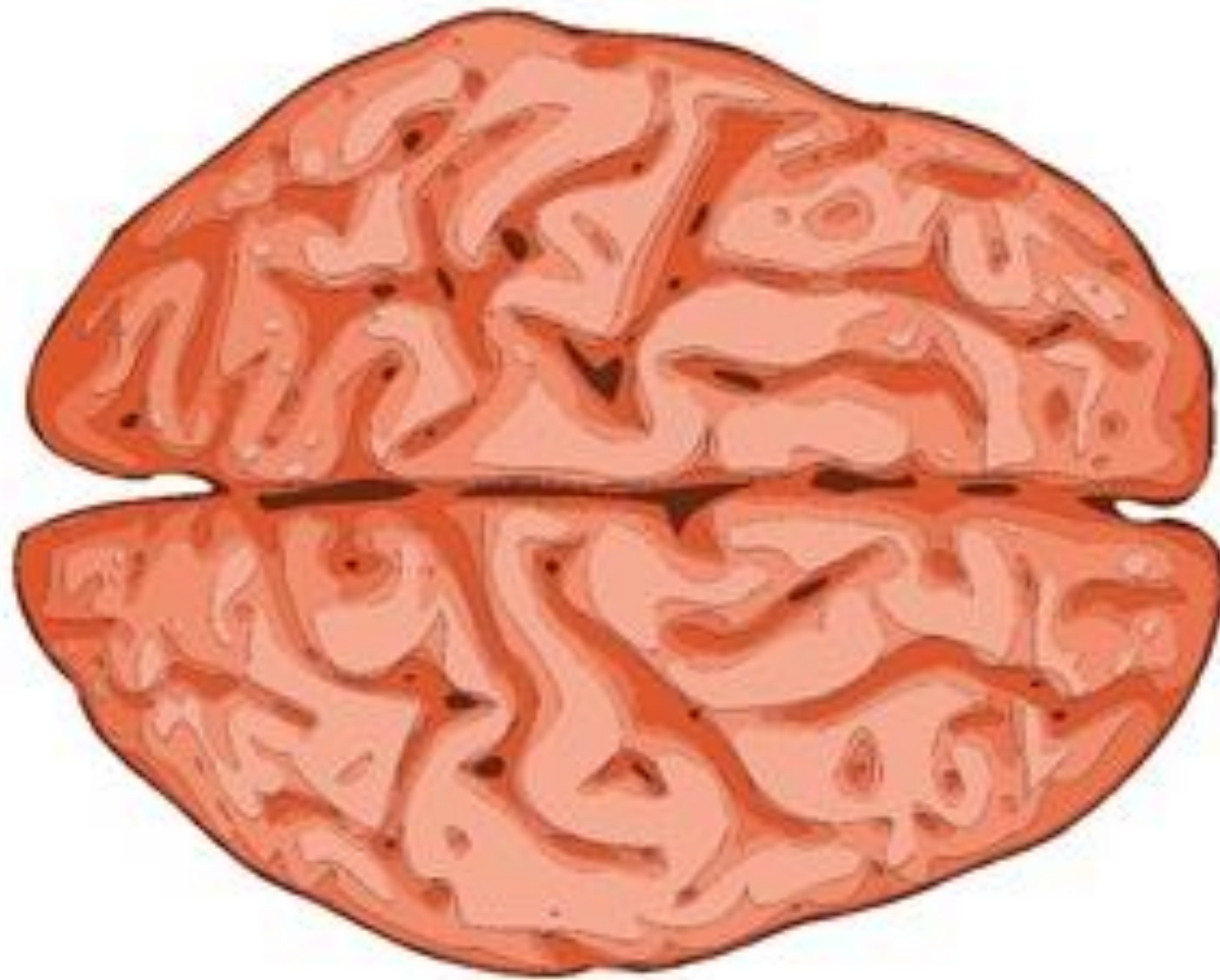
- Localization of the 'fusiform face area' in 18 subjects
- Localizations vary considerably due to differences in
 - Gross anatomy
 - Functional specialization
 - Warping in normalization
- Also, consider differences in signal intensity across subjects
- All these factors are bound to lower SNR



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™