Meta-analytic approaches to mapping the brain, its functions and connectivity

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Background

Why meta-analytic approaches?

Limitation of neuroimaging data

Small samples

Compared to other fields of cognitive and social science and particularly to clinical research

Indirect measures of neuronal activity

Reliability is limited by biological, technical and methodological confounds

Publication of isolated findings

Due to logistic expenses, additional experiments for confirmation and extension are rare

Generalisation of context-specific findings

Inference on brain function and pathomechanisms is based on a specific observed difference between two conditions

Advantages of neuroimagig data

BUT

There are many studies

Recent estimate

14.000 fMRT and PET Paper

>1200 Articles on Schizophrenia, Depression und Autism

All report standardised results!

Year	# of hits
1991-1995	57
1996	57
1997	85
1998	183
1999	263
2000	379
2001	497
2002	573
2003	770
2004	964
2005	1245
2006	1369
2007	1466
Total	7908

Derrfuss & Mar 2009

Image based meta analyses

Mega-analyses

jointly analyze the raw data of all experiments

Multi-Study Conjunctions

Overlap between significant effects

Third-level analyses

Statistical test on the between-experiment effects

Compilation of original data rarely feasible, usually accompanied with strong biases

Coordinate based meta-analyses

Based on published maxima-coordinates

Sparse representation of results

May integrate the entire literature

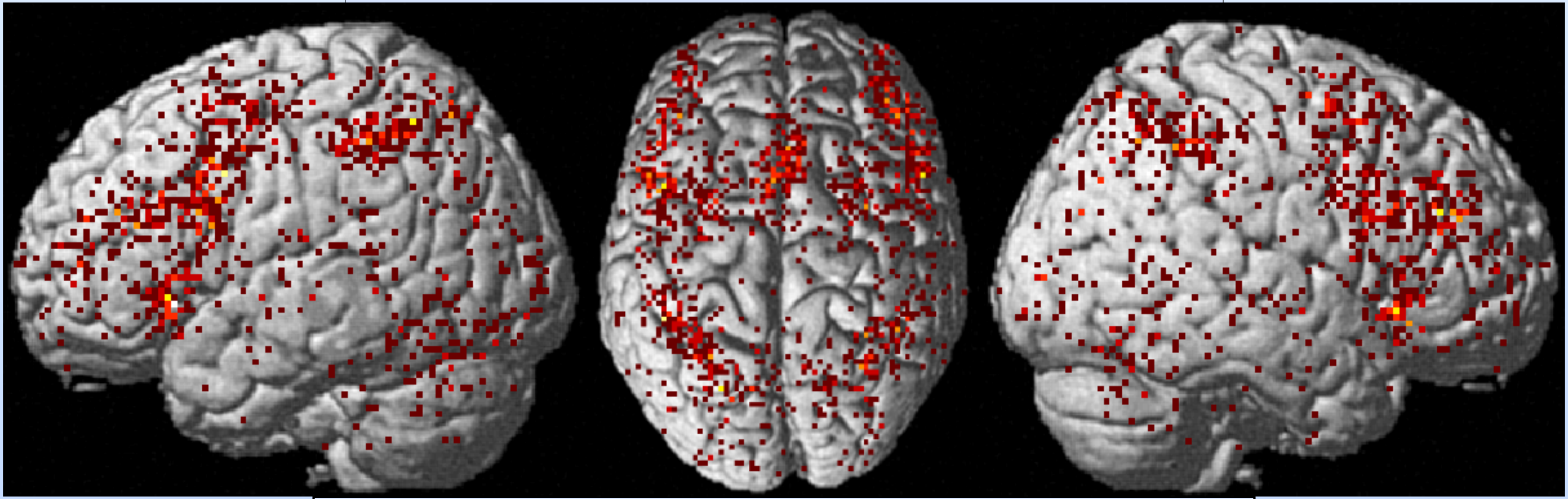
The “where” approach

Meta-Analyses

Activation likelihood estimation (ALE)

189 neuroimaging experiments on working memory

Location of activation foci



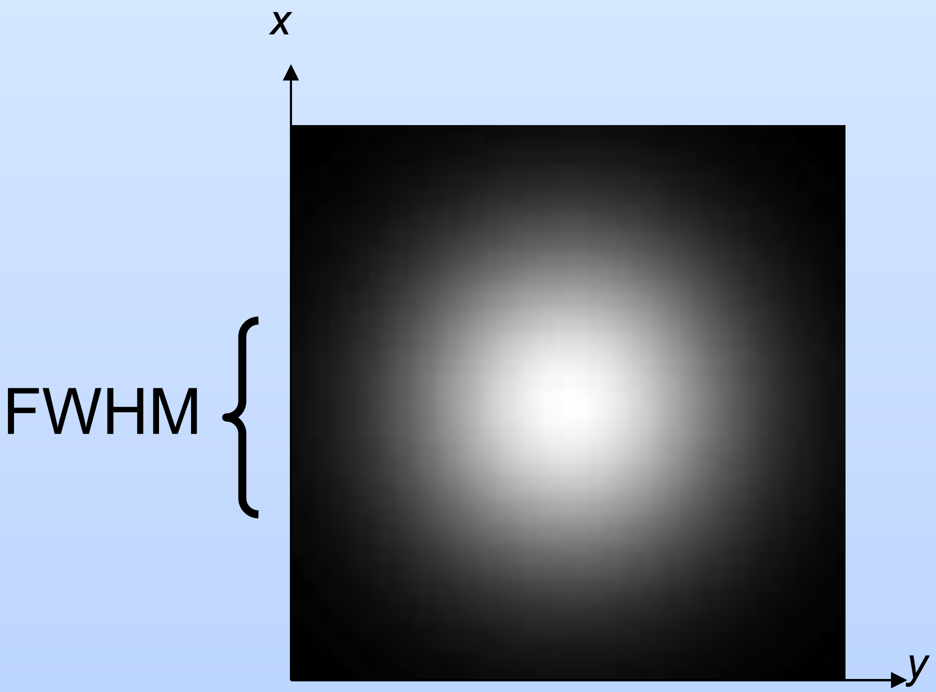
Where do these foci converge ?

Activation likelihood estimation (ALE)

The reported coordinates are not treated as points but centres of probability distributions

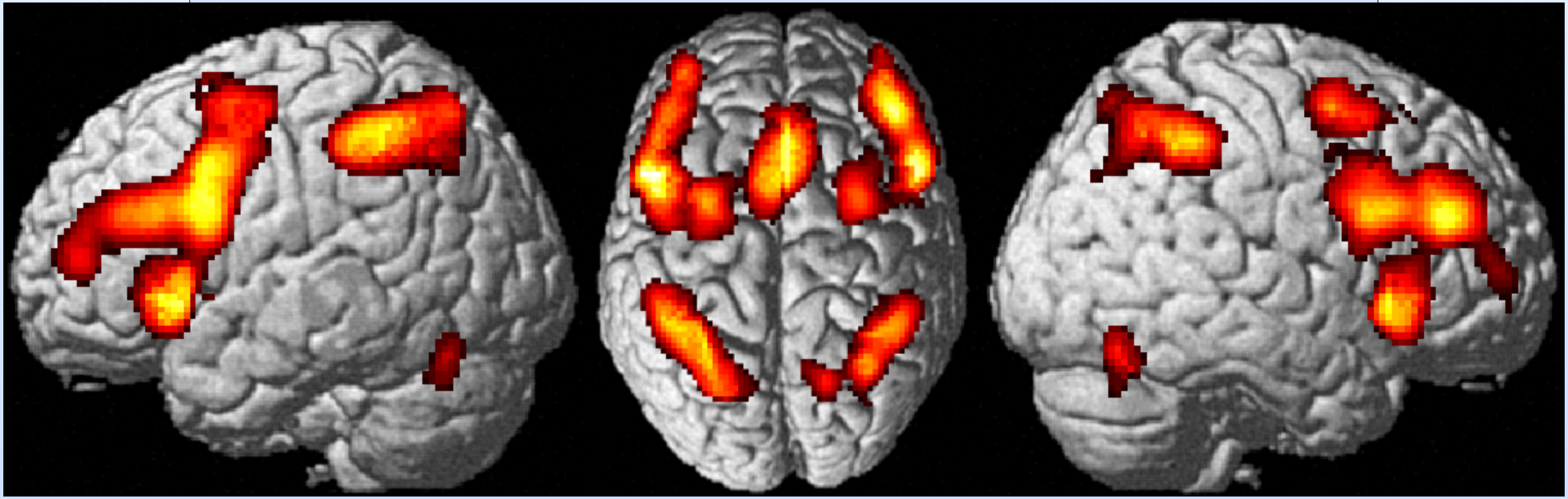
The “true” location of each reported activation is modelled by a 3D Gaussian

Empirical model of spatial uncertainty associated with neuroimaging data



Activation likelihood estimation (ALE)

ALE defined by the union over all experiments



Which of these values are significant?

Permutation procedure testing null-hypothesis of random spatial association

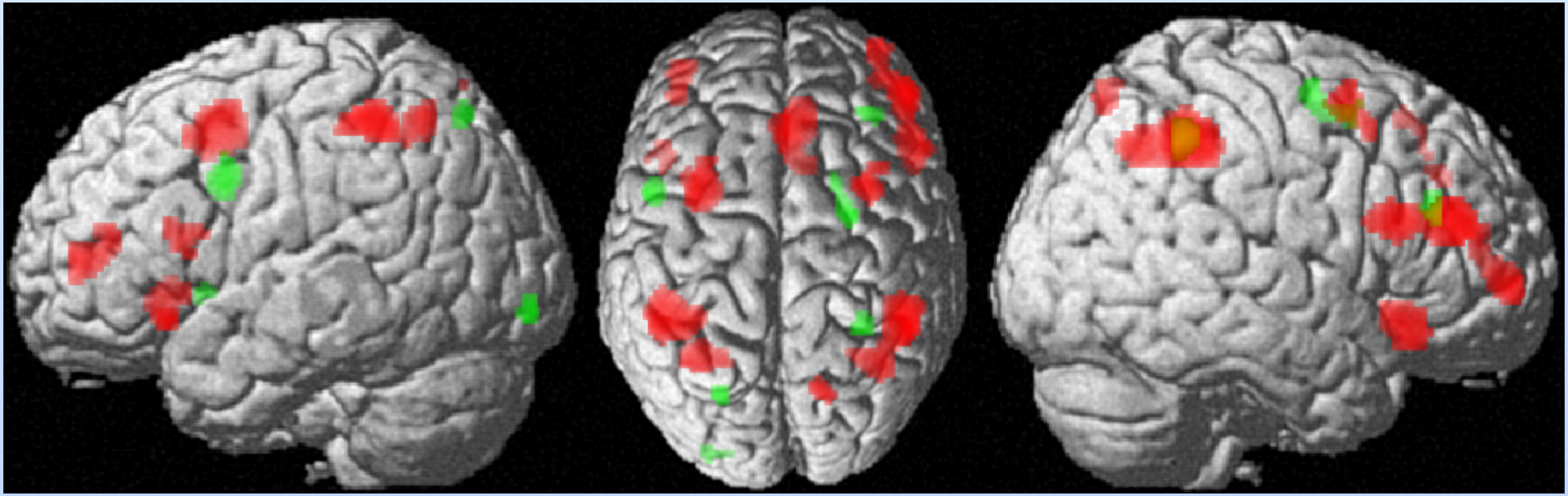
Eickhoff et al., Hum Brain Mapp 2009
Eickhoff et al., Neuroimage 2012

Meta-analytic contrasts

Where is the convergence for set A higher than for set B

Is A more likely to result in activation at this voxel than B?

n-back vs. Sternberg



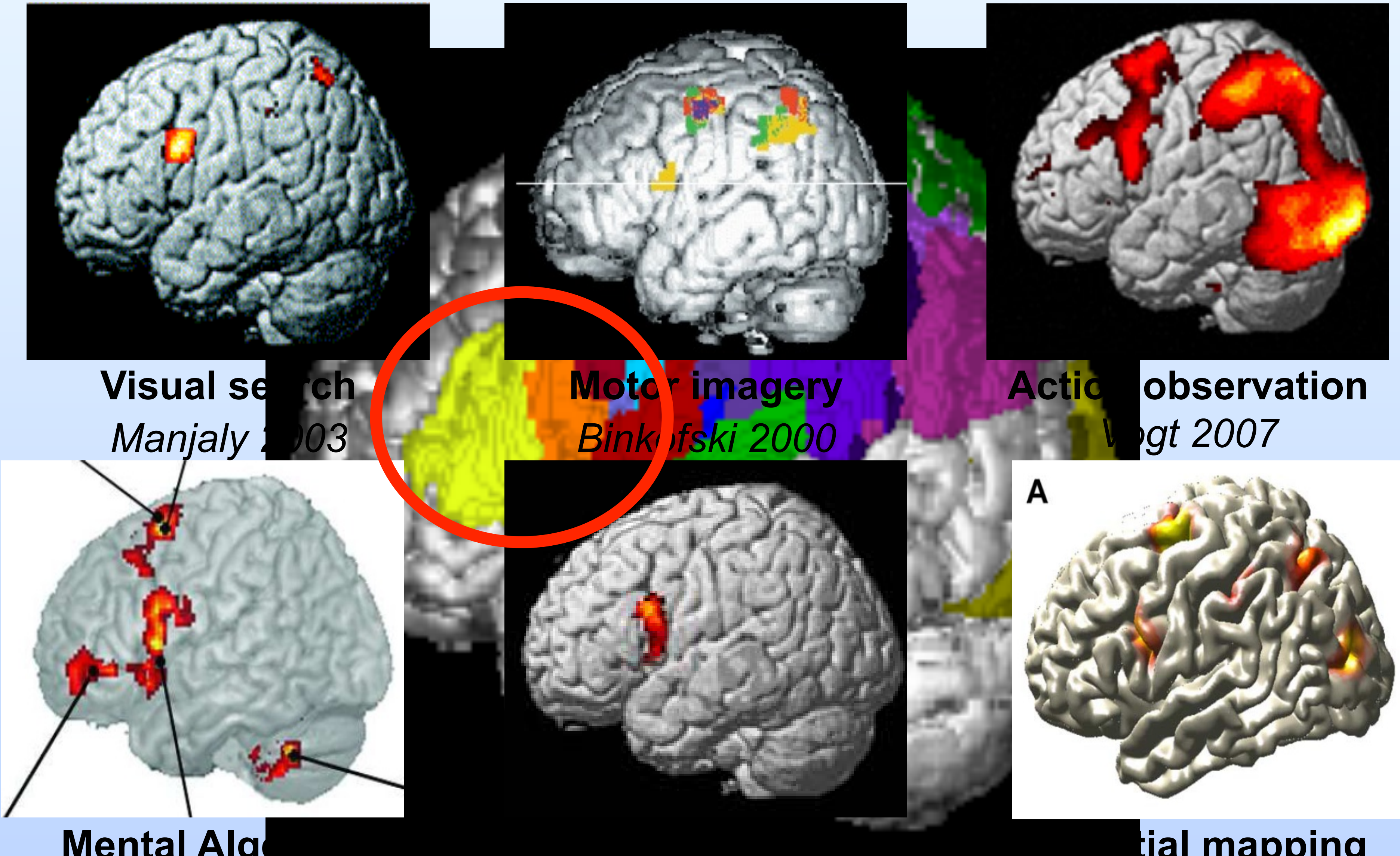
The choice of task may bias your results !

Rottschy et al., Neuroimage 2012

The “what” approach

Functional characterization

The problem of functional inference



Wu 2009

Heim 2006

Grol 2007

The BrainMap database

BrainMap Paradigm Classes

Action Observation
Acupuncture
Anti-Saccades
Braille Reading
Breath-Holding
Classical Conditioning
Counting/Calculation
Cued Explicit Recognition
Deception Task
Deductive Reasoning
Delayed Match to Sample
Divided Auditory Attention
Drawing
Eating
Encoding
Episodic Recall
Face Monitor/Discrimination
Film Viewing
Finger Tapping
Fixation
Flanker Task
Flashing Checkerboard
Flexion/Extenion
Free Word List Recall
Go/No-Go
Grasping
Imagined Movement
Imagined Objects/Scenes
Isometric Force
Mental Rotation
Micturition Task
Music Comprehension/Production
n-back
Naming (Covert)
Naming (Overt)
Non-Painful Electrical Stimulation
Non-Painful Thermal Stimulation
Oddball Discrimination
Olfactory Monitor/Discrimination
Orthographic Discrimination
Pain Monitor/Discrimination
Paired Associate Recall
Passive Listening
Passive Viewing
Phonological Discrimination
Pitch Monitor/Discrimination
Pointing
Posner Task
Reading (Covert)
Reading (Overt)
Recitation/Repetition (Covert)
Recitation/Repetition (Overt)
Rest
Reward Task
Saccades
Semantic Discrimination
Sequence Recall/Learning
Simon Task
Spatial/Location Discrimination
Sternberg Task
Stroop Task
Syntactic Discrimination
Tactile Monitor/Discrimination
Task Switching
Theory of Mind Task
Tone Monitor/Discrimination
Transcranial Magnetic Stimulation
Vibrotactile Monitor/Discrimination
Visual Distractor/Visual Attention
Visual Pursuit/Tracking
Wisconsin Card Sorting Test
Word Generation (Covert)
Word Generation (Overt)
Word Stem Completion (Covert)
Word Stem Completion (Overt)
Writing

BrainMap Behavioral Domains

<u>Action</u>
- Execution
  - Speech
- Imagination
- Inhibition
- Motor Learning
- Observation
- Preparation
- Rest

<u>Cognition</u>
- Attention
- Language
  - Orthography
  - Phonology
  - Semantics
  - Speech
  - Syntax
- Memory
  - Explicit
  - Implicit
  - Working
- Music
- Reasoning
- Soma
- Space
- Time

<u>Emotion</u>
- Anger
- Anxiety
- Disgust
- Fear
- Happiness
  - Humor
- Sadness

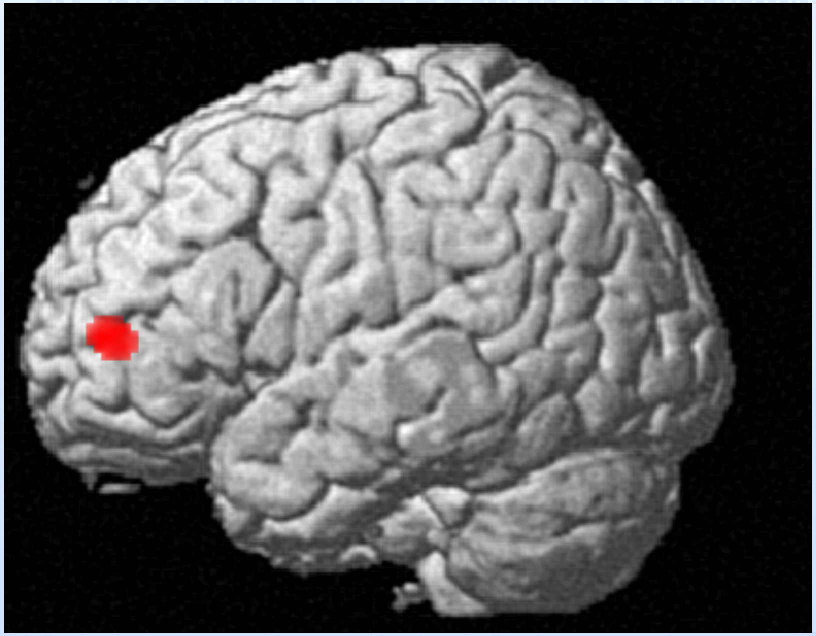
<u>Interoception</u>
- Air-Hunger
- Baroregulation
- Bladder
- Hunger
- Osmoregulation
- Sexuality
- Sleep
- Thermoregulation
- Thirst

<u>Perception</u>
- Audition
- Gustation
- Olfaction
- Somesthesis
  - Pain
- Vision
  - Color
  - Motion
  - Shape

<u>Pharmacology</u>
- Alcohol
- Amphetamines
- Caffeine
- Capsaicin
- Cocaine
- Ketamine
- Marijuana
- Nicotine
- NSAIDs
- Psychiatric Medications
  - Anti-Depressants
  - Anti-Psychotics
- Steroids and Hormones

Forward inference

How likely is a particular type of experiments to activate this region?



Identify all experiments in BrainMap
that activate in the ROI

222 Experiments in BrainMap
(2944 subjects, 3445 foci)

Proportion of experiments from domain X activating ROI
vs. a priori probability of activating ROI

Were experiments of a given domain more likely to activate this ROI than chance? Is the number of activations higher than expected?

Reverse inference

How likely was a particular domain present when the ROI activates?

Inference on domain-specificity

Decoding of functional recruitment

Depends on forward probability and baserate of the domain

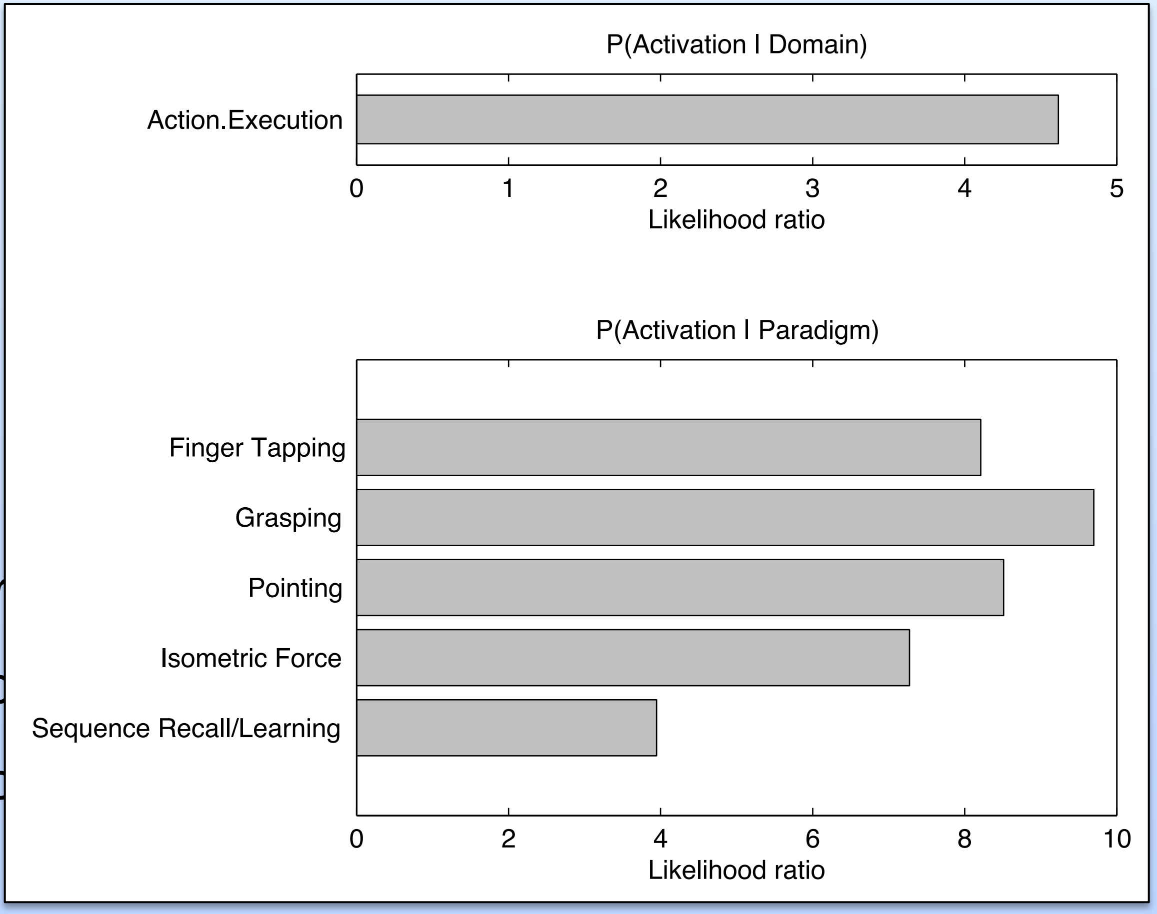
$$P(\text{Domain}|\text{Activation}) = \frac{P(Activation|Domain) * P(Domain)}{P(Activation)}$$

Dependent on the a priori probability for the given domain

168 experiments reported activation in left M1

Forward inference

P(Activation | Task)



Probability for

probability o

Fo

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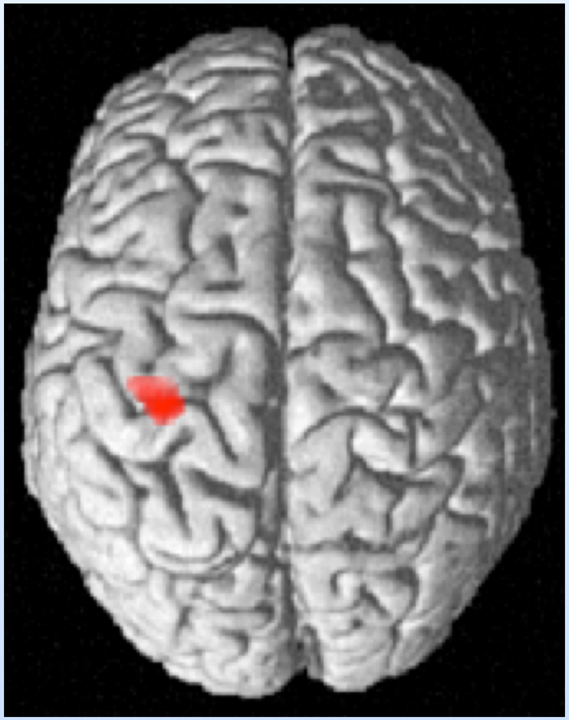
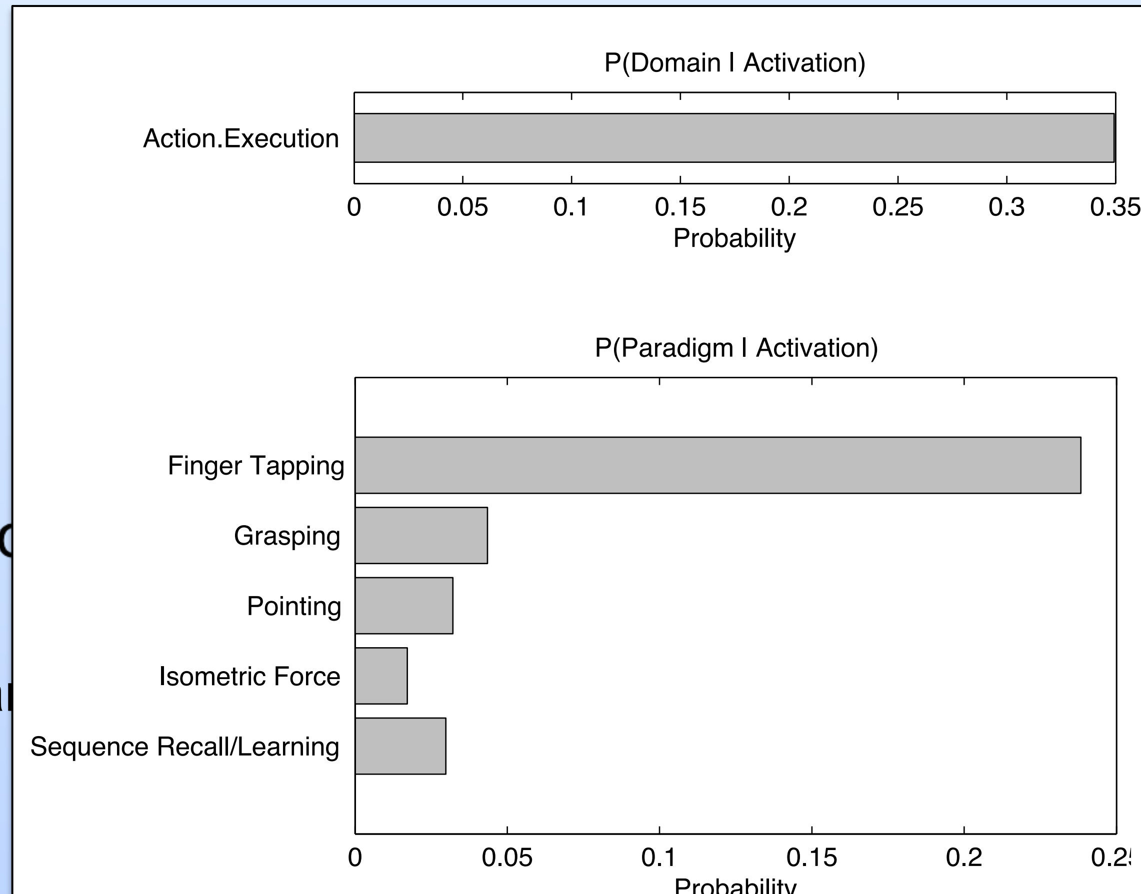


Reverse inference

P(Task | Activation)



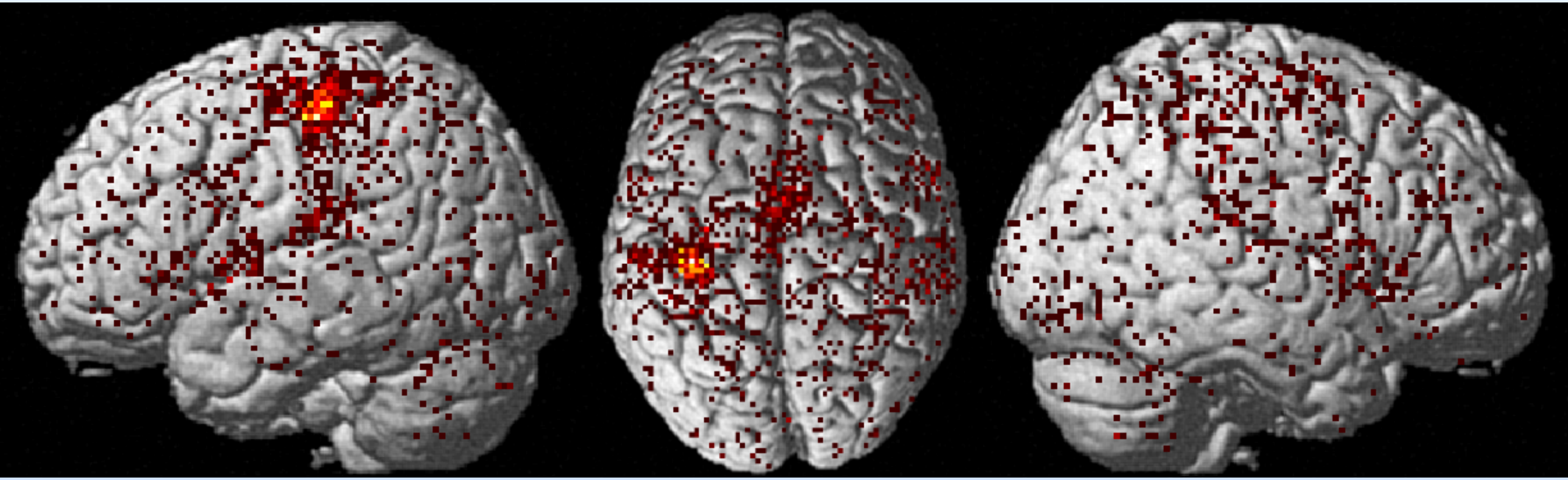
P(Domain|Activati

Depends on forwar

The “with whom” approach

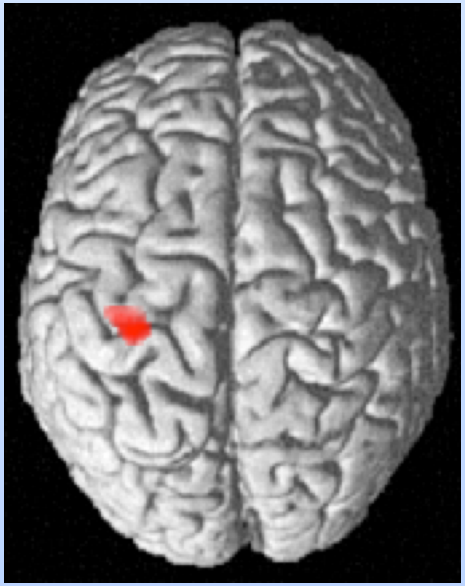
Meta-Analytic Connectivity Modelling

Meta-analytic connectivity modeling

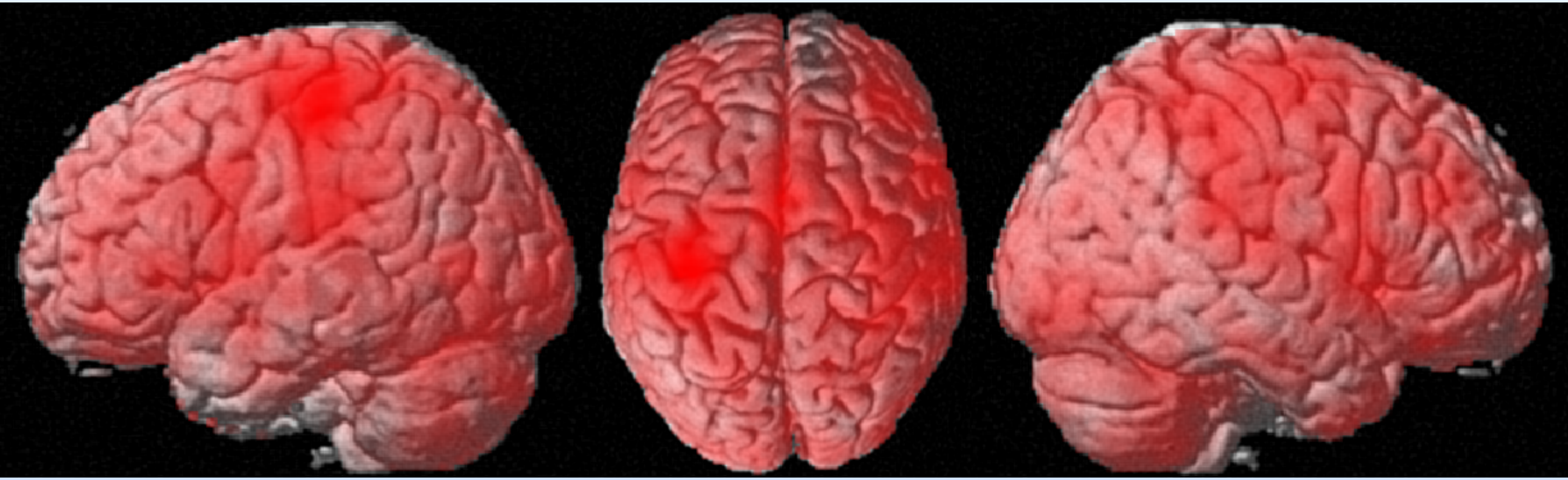


The ~2431 activation foci reported in the 168 experiments activating left M1

Experiments are only identified by the fact that they feature activation in the seed



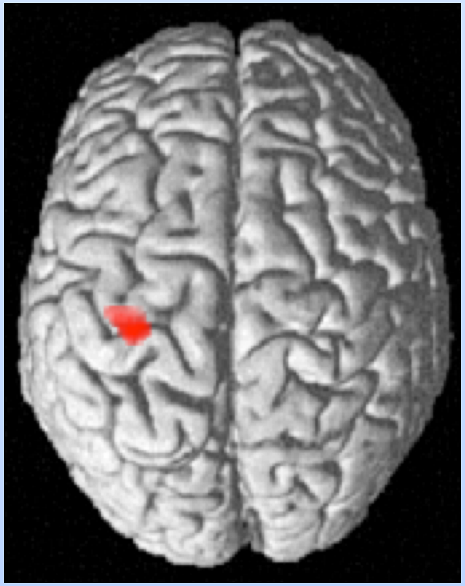
Meta-analytic connectivity modeling



Activation likelihood estimation for each voxel based on uncertainty associated with each focus

Probabilistic representation of co-activations

How likely is it that experiment activating the seed region also activates any other voxel



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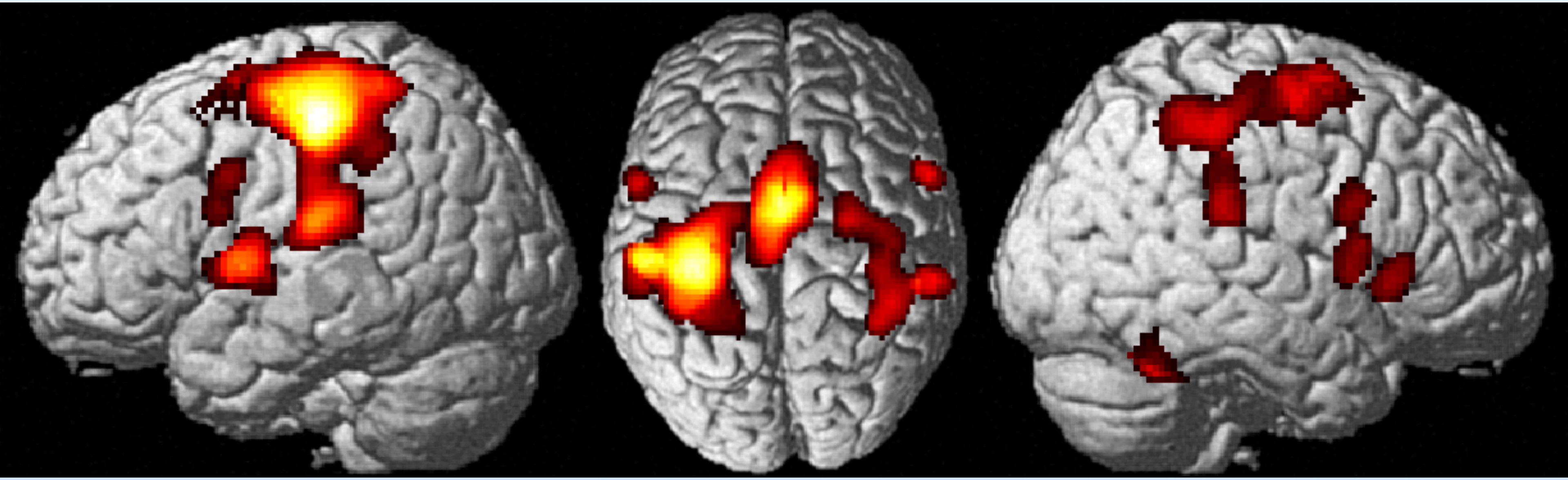

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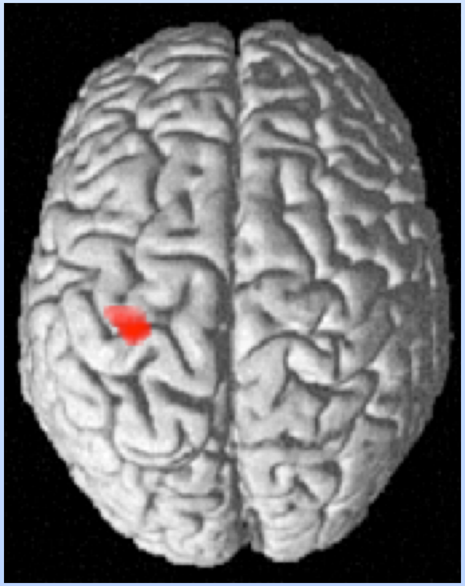
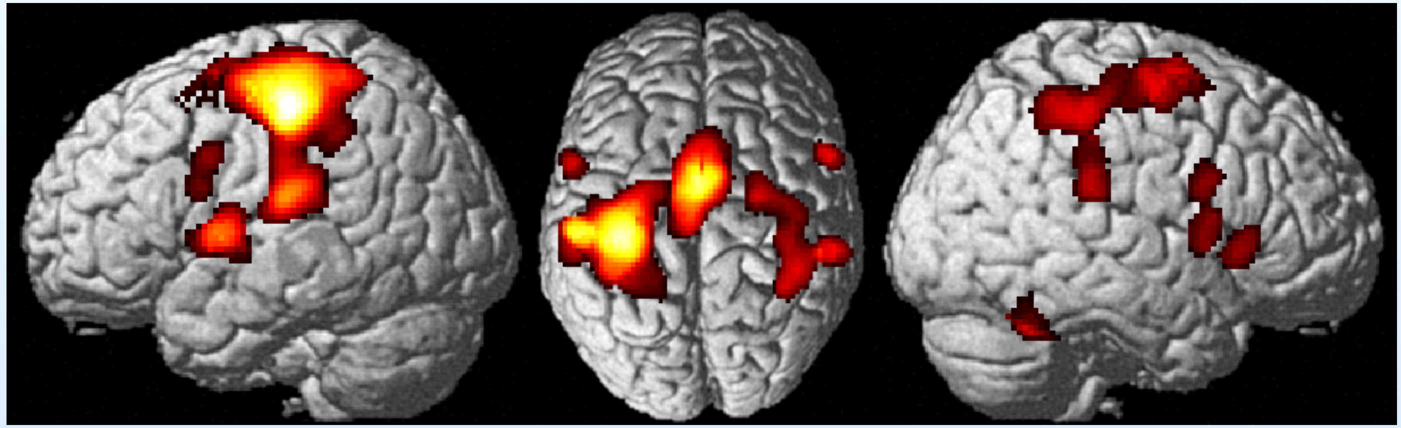
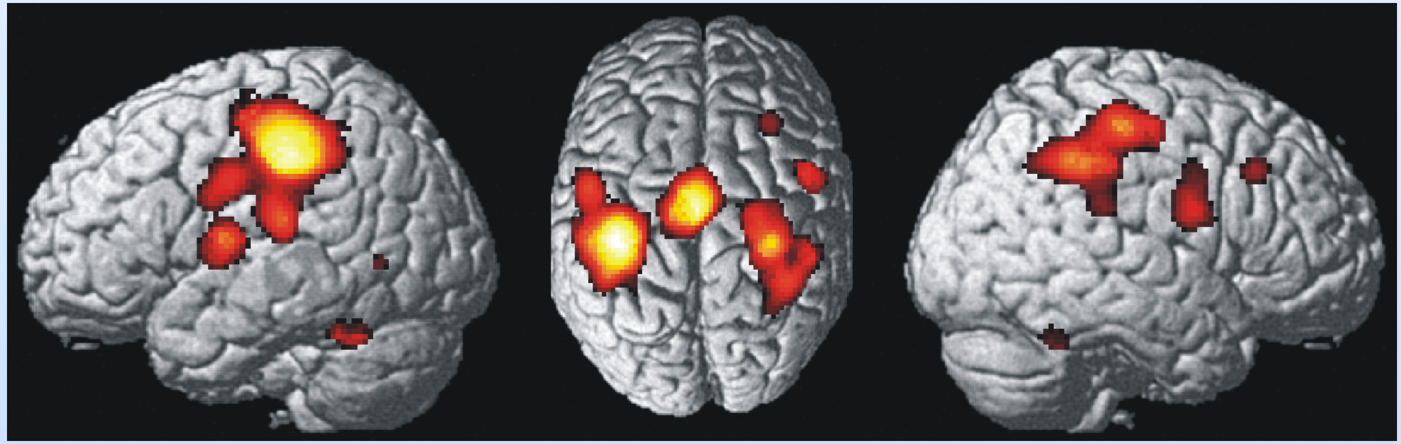


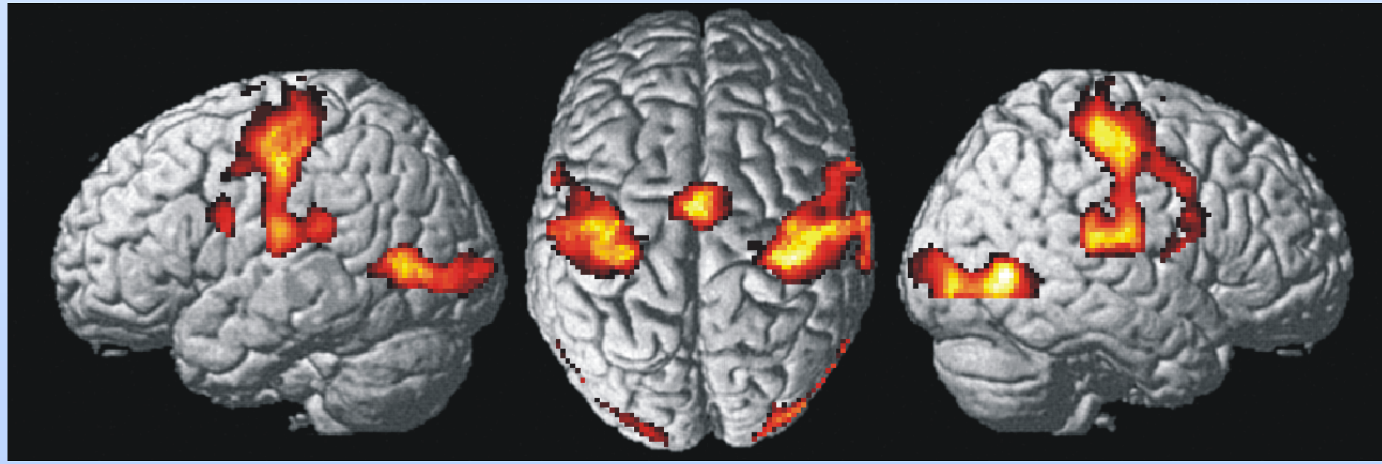
Co-activation of left M1



Meta-Analysis on finger tapping (73 experiments)



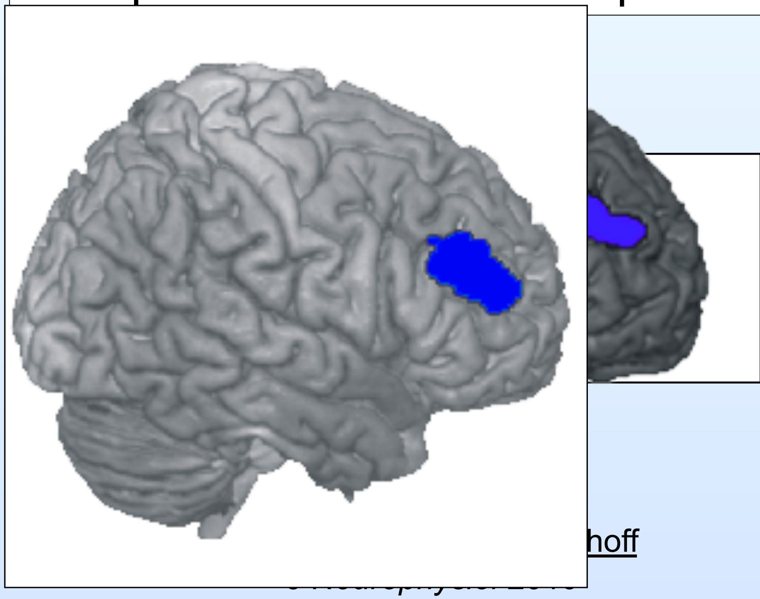
fMRI study on finger tapping (21 subjects)



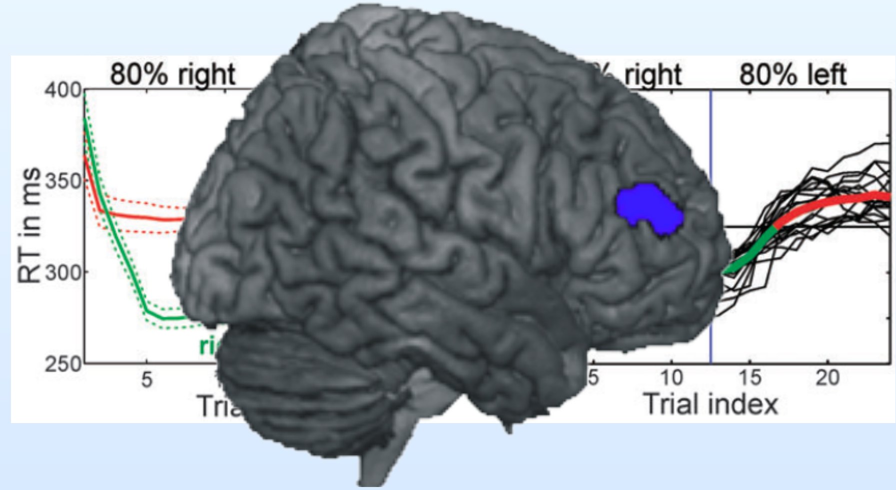
Fusion

Meta-analytic Brain Mapping

Ispi- vs. contralateral responses

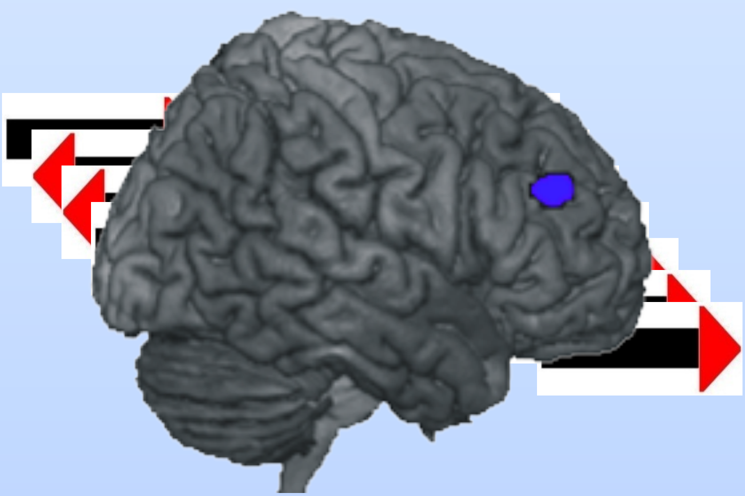


Probabilistic learning



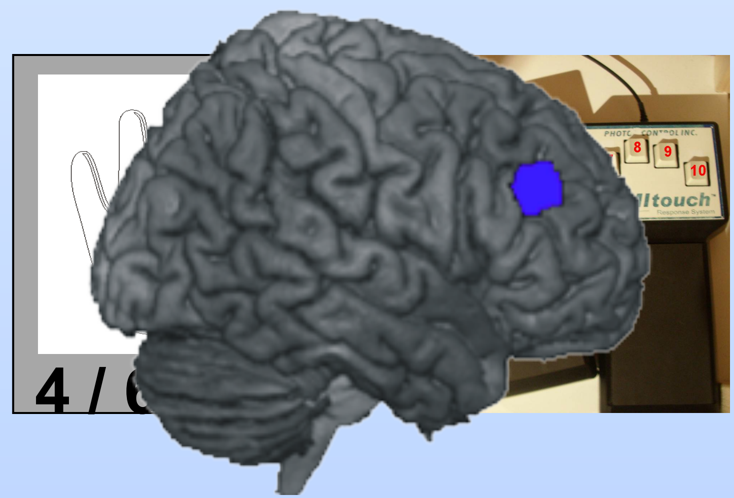
Eickhoff, Pomjanski, Jakobs, Zilles, Langner
Cerebral Cortex 2011

Random vs. predictable responses

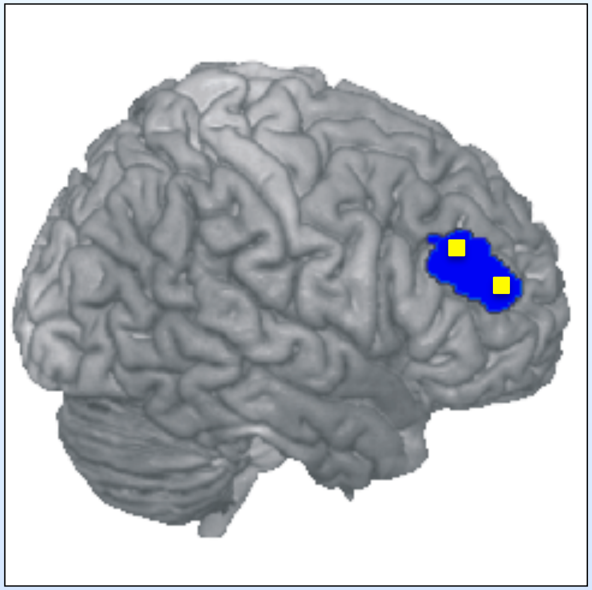


Jakobs, Wang, Dafotakis, Grefkes, Zilles, Eickhoff
NeuroImage 2009

Motor WM: 6 vs 4 items



Kellermann, Sternkopf, Schneider, Habel, Turetsky, Zilles, Eickhoff
Soc Cogn Affect Neurosci 2012



Co-activation based parcellation

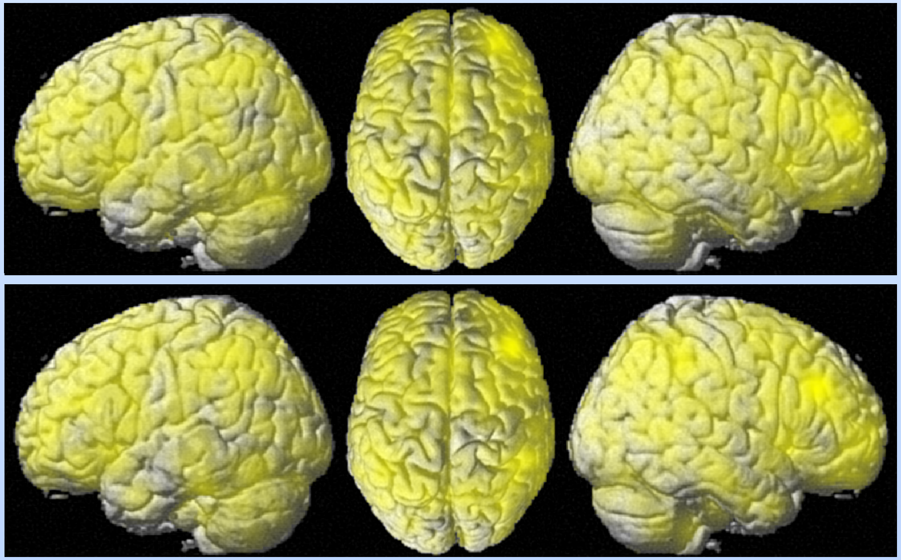
Cortical regions show distinct connectivity-profiles

Computation of each voxel's interactions
Clustering based on these profiles

Eickhoff, Bzdok, Laird, Roski, Caspers, Zilles, Fox; *Neuroimage 2011*

BrainMap Database

12.000 Neuroimaging experiments
- Coordinates for local maxima
- Meta-Data on tasks etc



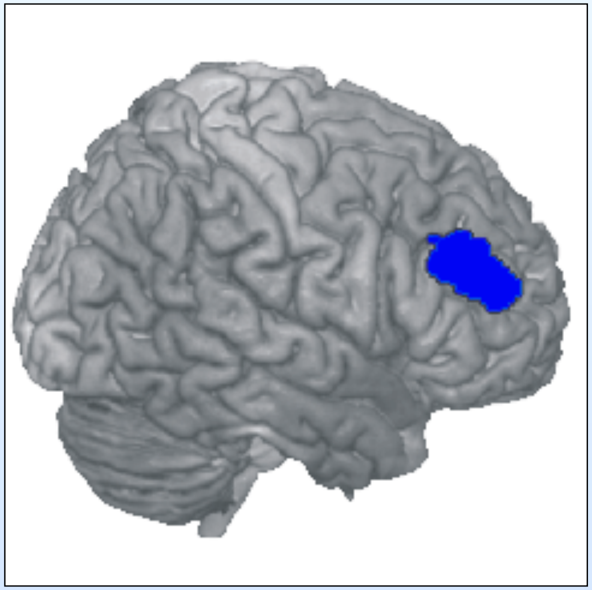
Approach (per voxel)

Identification of all experiments featuring activation at that voxel

Computation of across-experiment convergence of co-activations accommodating spatial uncertainty

Eickhoff, Bzdok, Laird, Kurth, Fox; *Neuroimage 2012*

Cieslik, Zilles, Caspers, Roski, Kellermann, Jakobs, Langner, Laird, Fox, Eickhoff, *Cerebal Cortex. ePub 2012*



Co-activation based parcellation

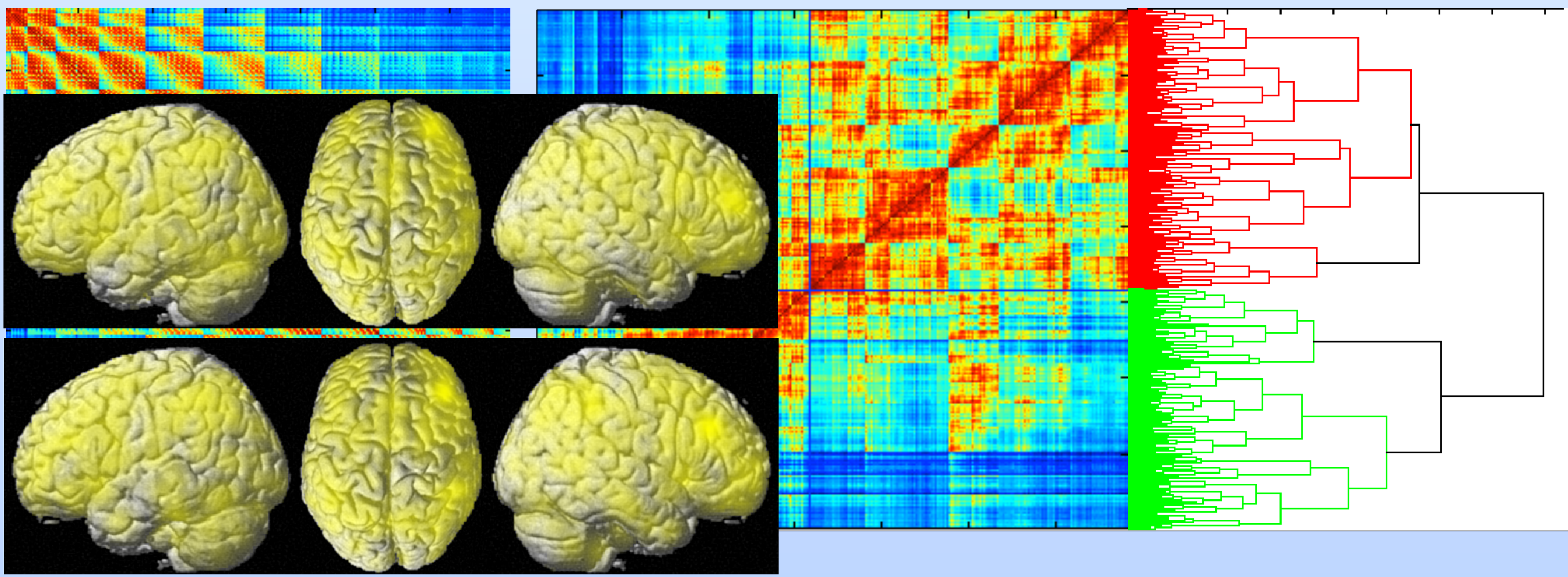
Whole-brain connectivity per voxel

Computation of cross-correlation

the co-activation patterns

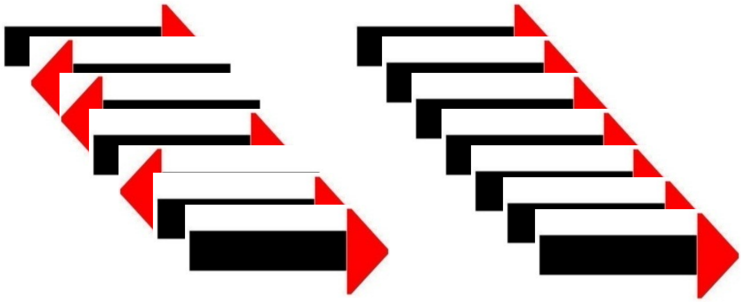
Identify groups via multivariate cluster-analyses

Eickhoff, Bzdok, Laird, Roski, Caspers, Zilles, Fox; *Neuroimage 2011*

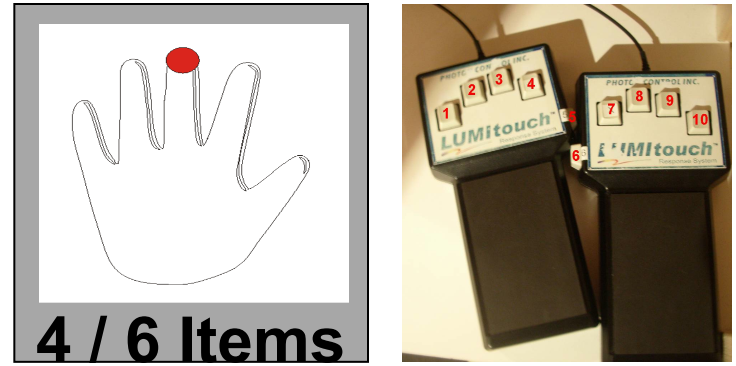


Cieslik, Zilles, Caspers, Roski, Kellermann, Jakobs, Langner, Laird, Fox, Eickhoff, *Cerebal Cortex. ePub 2012*

Random vs. predictable responses



Motor WM: 6 vs 4 items



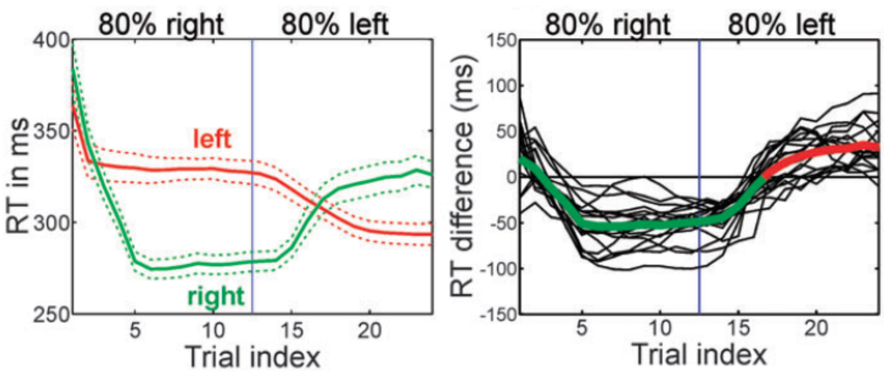
Ipsi- vs. Contralateral responses

GLEICH

GEGEN

Cieslik, Zilles, Kurth, Eickhoff
J Neurophysiol 2010

Probabilistic learning



Eickhoff, Pomjanski, Jakobs, Zilles, Langner
Cerebral Cortex 2011

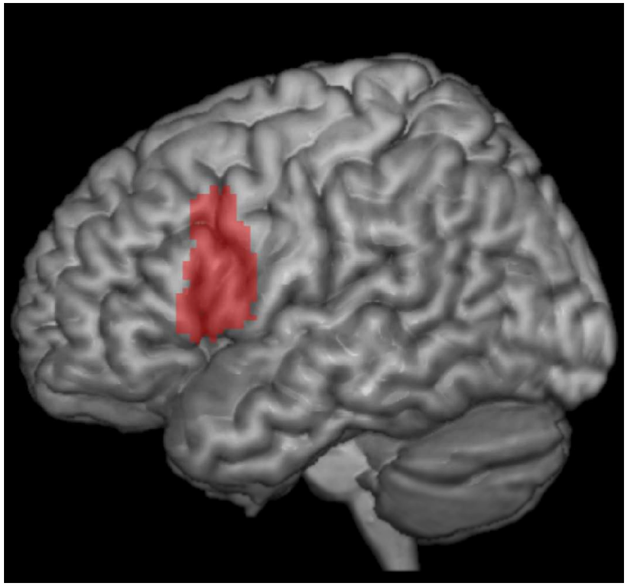
Functional decoding using the BrainMap meta-data

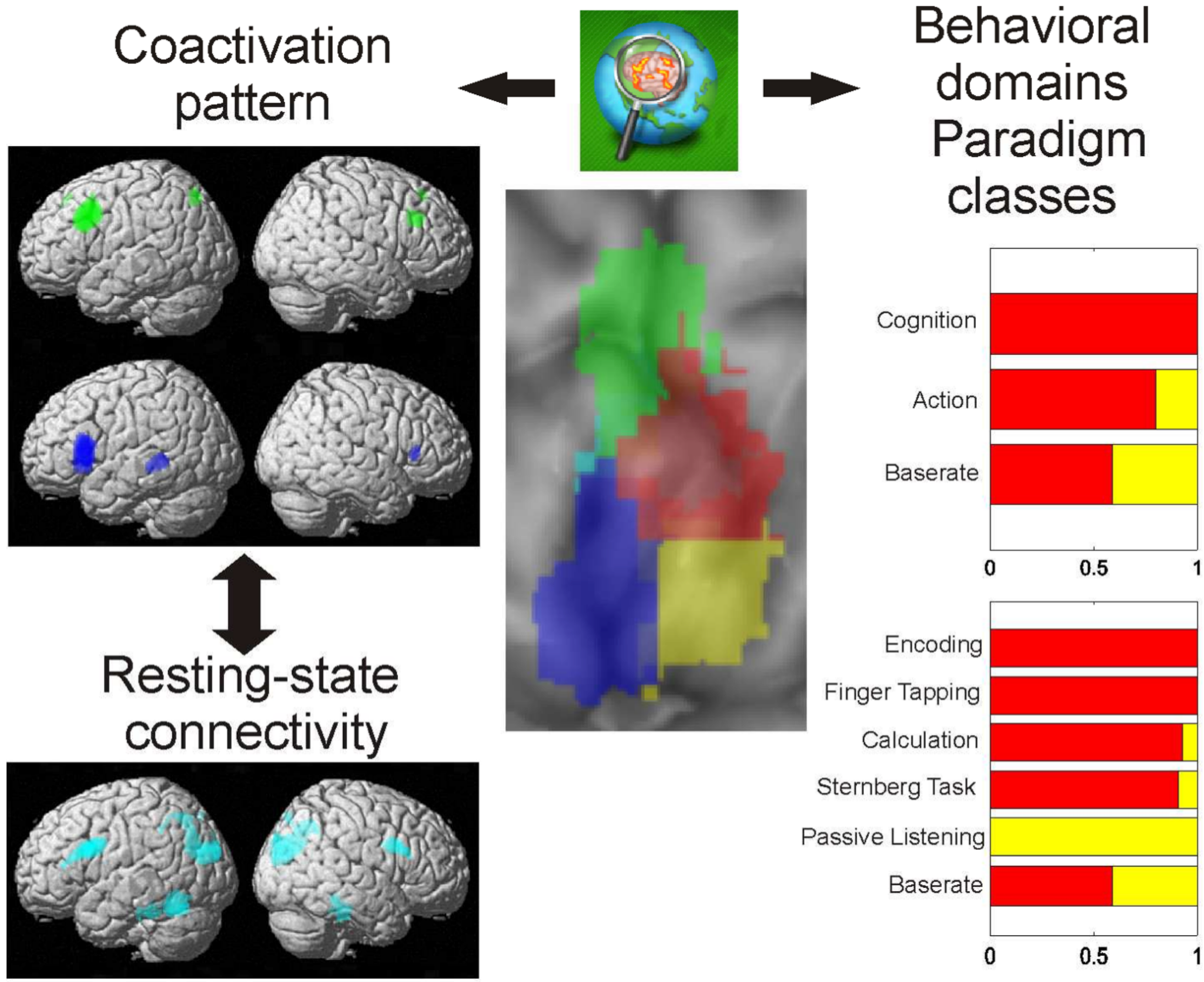
Action, Working memory

Attention, Inhibition, Conflict

Cieslik, Zilles, Caspers, Roski, Kellermann, Jakobs, Langner, Laird, Fox, Eickhoff, *Cerebal Cortex. ePub 2012*

The present and future of MACM-CBP





Mapping cortical segregation, connectivity and functions

Quantitative evaluation of each parameter

Clos et al., Neuroimage in revision

Insight from each individual neuroimaging study is limited by inherent drawbacks

High degree of standardization pooling of results allows inference on converging evidence

Coordinate-based meta-analyses provide a statistical tool for the objective integration of findings

Database driven functional decoding allows objective forward and reverse inference

Meta-analytic connectivity modelling offers a new approach to task-based functional connectivity

Co-activation based parcellation enables to identify cortical modules in a data-driven fashion

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