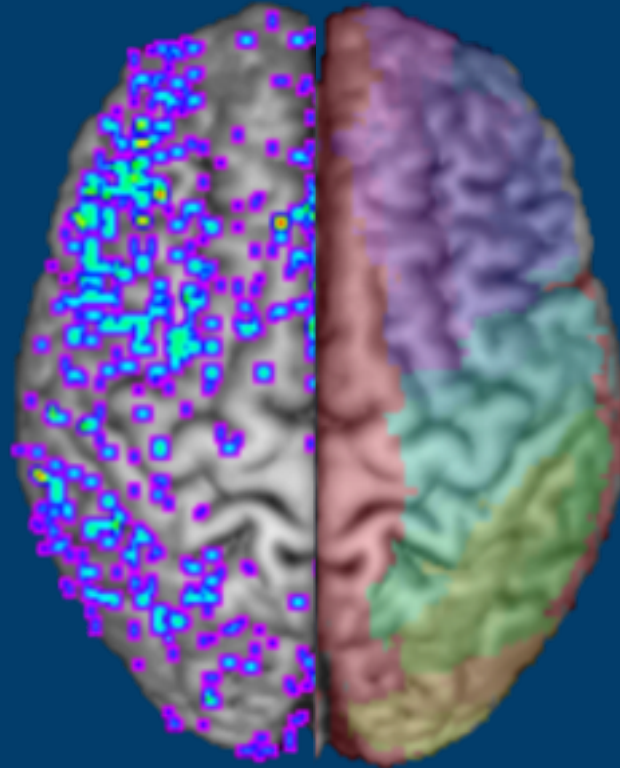


# Co-activation mapping and Parcellation



**Sarah Genon**

**Brain & Behaviour**

# META-ANALYSES

- **Topic based meta-analyses:**

derive brain regions consistently found across studies investigating a specific behavioral function



- **Location based meta-analyses:**

# META-ANALYSES

- **Topic based meta-analyses:**

derive brain regions consistently found across studies investigating a specific behavioral function

- **Location based meta-analyses:**

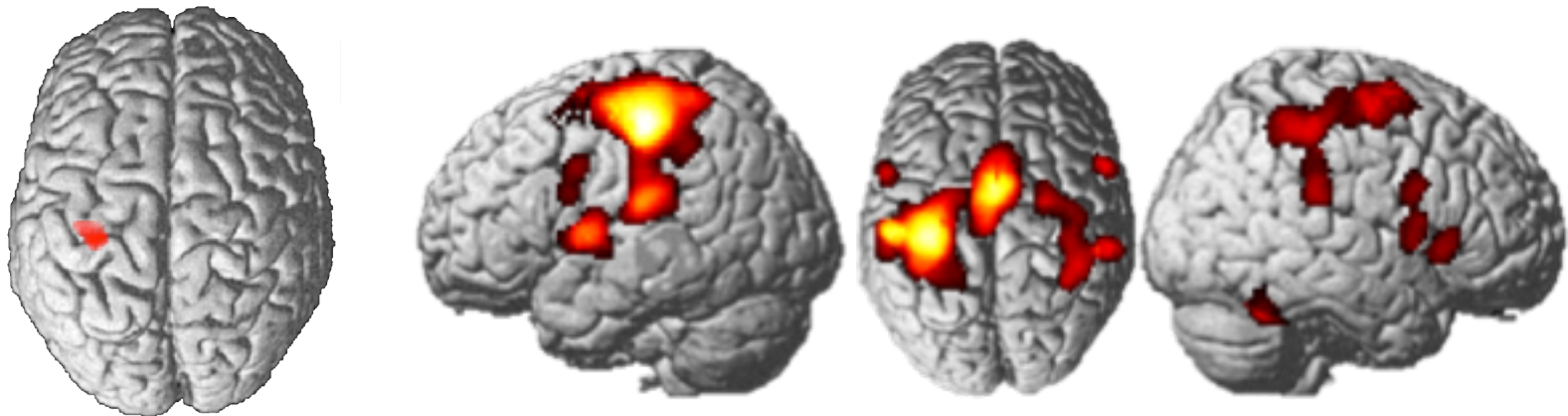
derive brain regions consistently found to activate together with a specific region across studies investigating different behavioral functions

# META-ANALYSES

- **Topic based meta-analyses:**

derive brain regions consistently found across studies investigating a specific function

- **Location based meta-analyses:**



„ left M1 functional network „



# MRI/PET-BASED CONNECTIVITY

**Structural/anatomical:**  
**Diffusion MRI**

**Functional:**  
**Functional MRI & PET**

**Data**

Diffusion MRI

Resting state fMRI  
(no behavioral task !)

Task-based fMRI & PET  
(behavioral task !)

**Concept**

Diffusion-based:  
Estimation of fiber  
direction

Resting-state:  
Signal fluctuations  
at rest

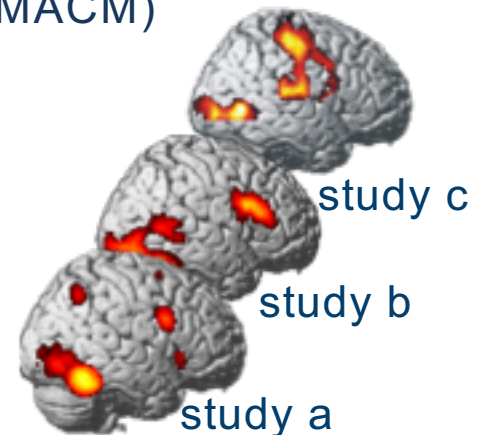
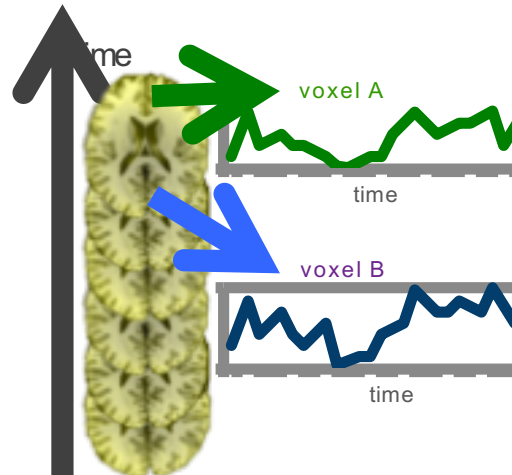
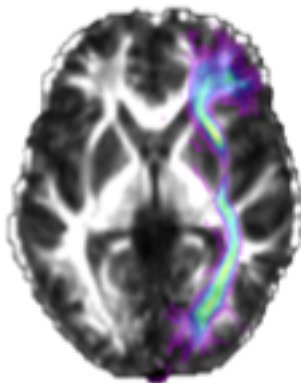
Task-based:  
Activation during task

**How ?**

E.g. : probabilistic  
diffusion tractography

Correlation in signal  
fluctuations

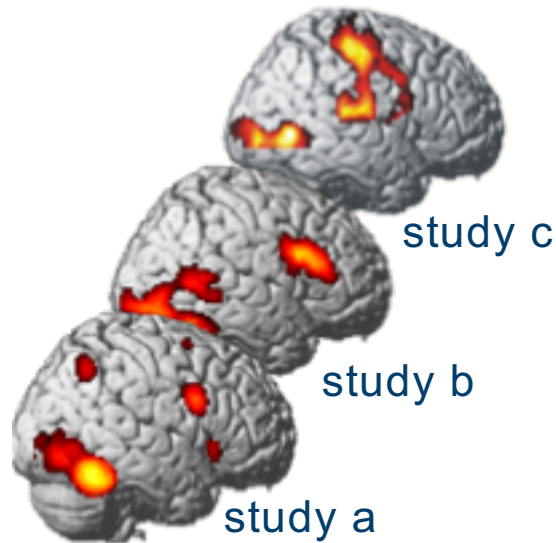
E.g.: Meta-Analytic  
Connectivity Modeling  
(MACM)



# MACM

## Location based meta-analyses:

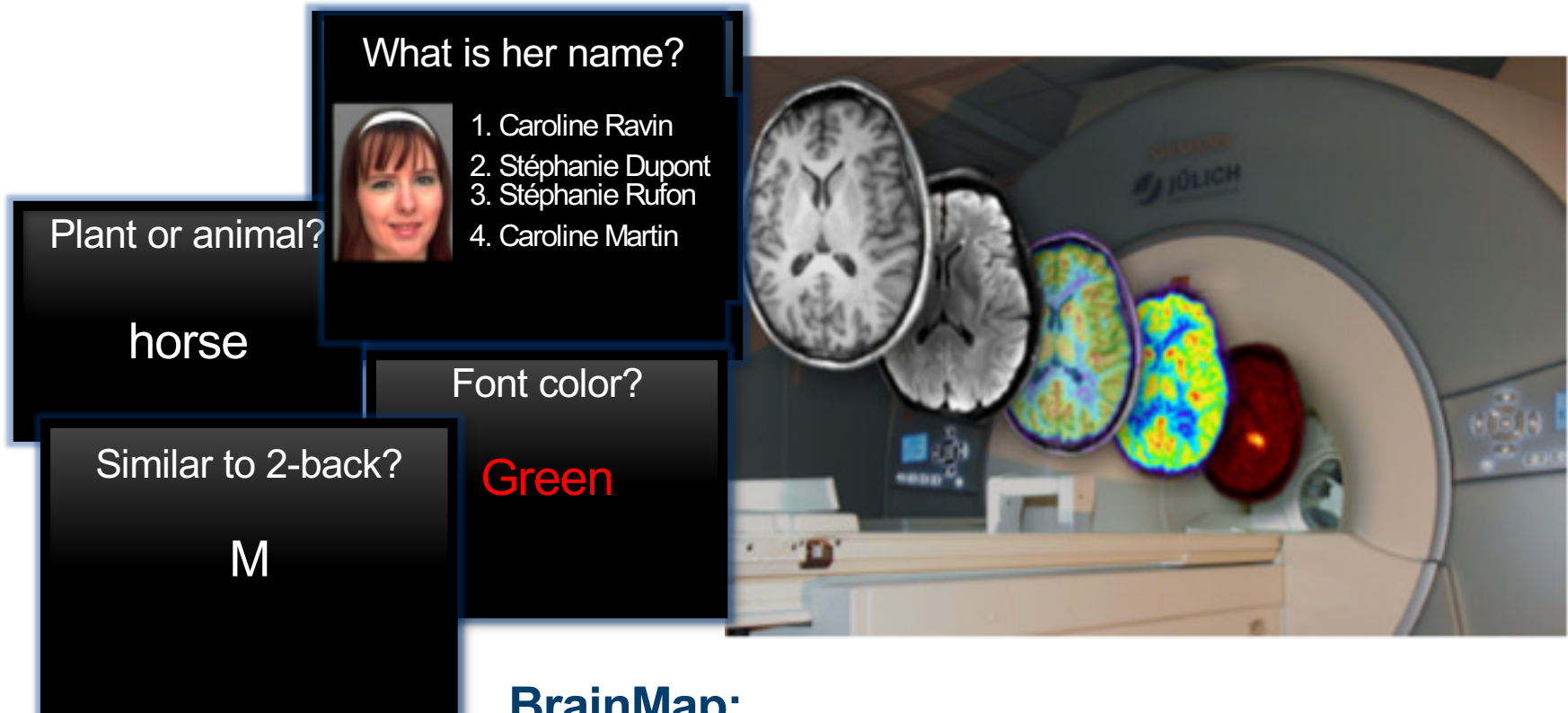
- Co-activations consistently found across different experiments
- Meta-analysis as a tool to derive functional connectivity



## Meta-Analytic Connectivity Modeling (MACM)

# Aggregation of activation experiments

## $10^4$ activations experiments



**BrainMap:**

> 3200 papers (> 16380 experiments)

**Neurosynth:**

> 11400 papers

# BrainMap database

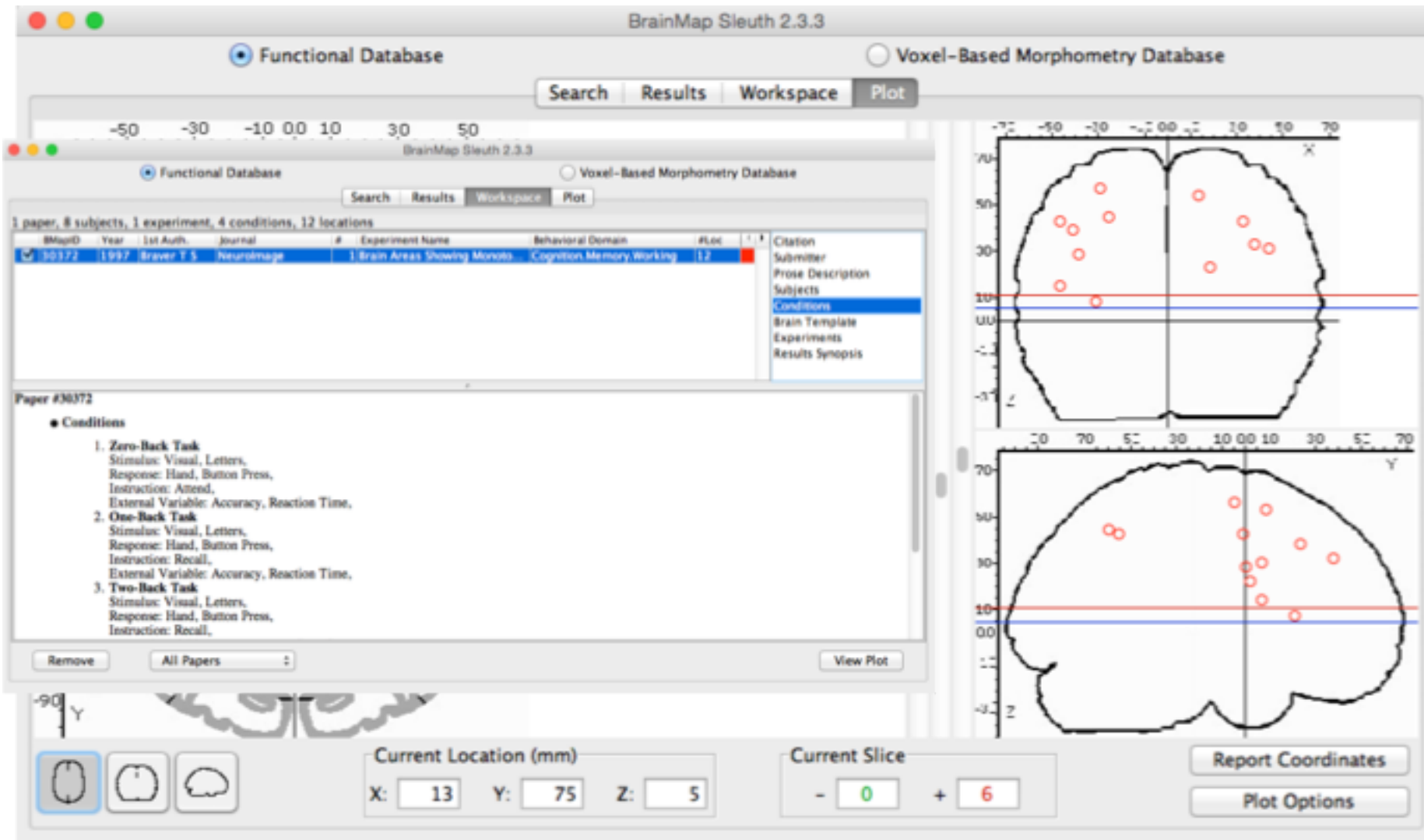


3294 papers  
16383 experiments  
127210 locations

<http://brainmap.org/>

- Coordinates in stereotactic space
- Experimental information

# BrainMap database

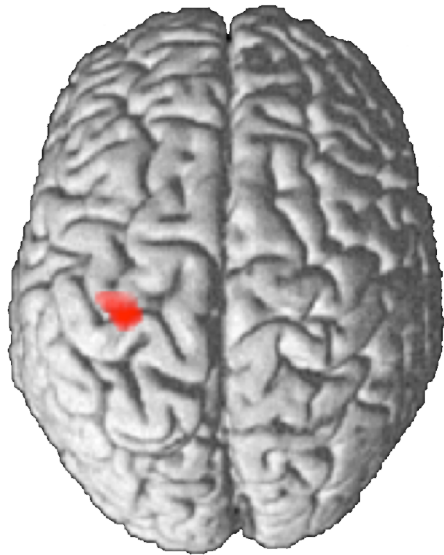


brainmap.org

# MACM : WORKFLOW

- Identification of all experiments activating the seed region
- General and specific inclusion/exclusion criteria
- Extraction of all coordinates reported in identified experiments
- Performing a meta-analysis across identified experiments

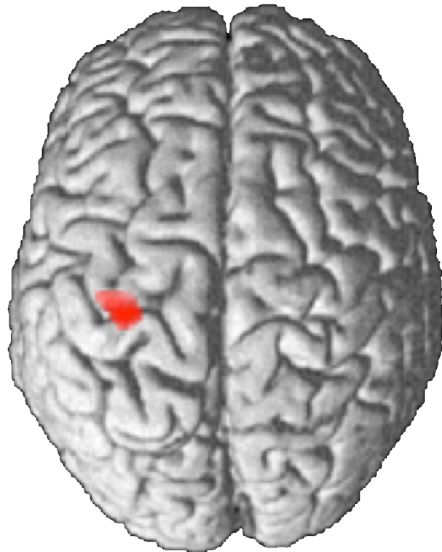
# CO-ACTIVATION OF LEFT M1



Which brain regions are functionally connected to left M1 ?

# Co-activation of left M1

- Identify all experiments activating the seed region



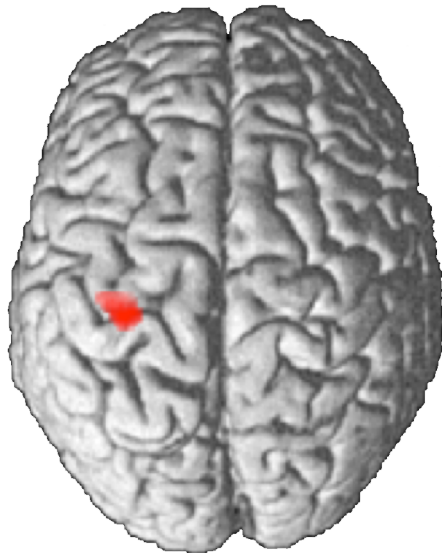
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<input checked="" type="checkbox"/> 30015	2000	Desmurget M	Experimental Brain Re...	4	RAND - STAT	Perception.Vision.Moti...	5
<input type="checkbox"/> 30016	2001	Desmurget M	Journal of Neuroscience	1	Overall hand-reaching effect	Action.Execution,Perce...	17
<input checked="" type="checkbox"/> 30016	2001	Desmurget M	Journal of Neuroscience	2	Strict hand-reaching effect	Action.Execution	14
<input type="checkbox"/> 30016	2001	Desmurget M	Journal of Neuroscience	3	Eye error correction effect	Perception.Vision.Moti...	3
<input type="checkbox"/> 30020	2000	Ehrsson H H	European Journal of N...	1	Foot vs. Rest	Action.Execution	9
<input checked="" type="checkbox"/> 30020	2000	Ehrsson H H	European Journal of N...	2	Hand vs. Rest	Action.Execution	14
<input type="checkbox"/> 30020	2000	Ehrsson H H	European Journal of N...	3	Simultaneous vs. Rest	Action.Execution	17
<input checked="" type="checkbox"/> 30020	2000	Ehrsson H H	European Journal of N...	4	Hand vs. Foot	Action.Execution	5
<input type="checkbox"/> 30020	2000	Ehrsson H H	European Journal of N...	5	Foot vs. Hand	Action.Execution	4
<input type="checkbox"/> 30020	2000	Ehrsson H H	European Journal of N...	6	Conjunction Analysis	Action.Execution	13
<input type="checkbox"/> 30020	2000	Ehrsson H H	European Journal of N...	7	{(Hand - Rest) + (Foot - Rest)} - (Simultaneous...	Action.Execution	3
<input type="checkbox"/> 30022	2001	Gosain A K	Plastic and Reconstruct...	1	Smile vs. Rest	Action.Execution	2
<input checked="" type="checkbox"/> 30022	2001	Gosain A K	Plastic and Reconstruct...	2	Finger-tapping vs. Rest	Action.Execution	2
<input checked="" type="checkbox"/> 300;							
<input type="checkbox"/> 300;							
<input type="checkbox"/> 300;							
<input type="checkbox"/> 300;							
<input type="checkbox"/> 300;							
<input type="checkbox"/> 30026	1998	Sadato N	Brain	6	Discrimination-Sweep (Sighted)	Perception.Somesthesi...	10
<input type="checkbox"/> 30026	1998	Sadato N	Brain	7	Sweep-Rest (Blind)	Perception.Somesthesi...	3
<input type="checkbox"/> 30026	1998	Sadato N	Brain	8	Discrimination-Rest (Blind)	Perception.Somesthesi...	10
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<input type="checkbox"/> 30026	1998	Sadato N	Brain	10	Blind > Sighted (Non-Braille discrimination com...	Perception.Somesthesi...	7
<input type="checkbox"/> 30026	1998	Sadato N	Brain	11	Sighted > Blind (Non-Braille discrimination com...	Perception.Somesthesi...	8
<input type="checkbox"/> 30026	1998	Sadato N	Brain	12	Blind > Sighted (Rest)	Action.Rest	8
<input type="checkbox"/> 30026	1998	Sadato N	Brain	13	Sighted > Blind (Rest)	Action.Rest	2
<input checked="" type="checkbox"/> 30033	2001	Indovina I	Experimental Brain Re...	1	Move vs. No-Move	Action.Execution	15
<input type="checkbox"/> 30033	2001	Indovina I	Experimental Brain Re...	2	Move-Attend vs. No-Move	Action.Execution,Cogni...	23
<input type="checkbox"/> 30033	2001	Indovina I	Experimental Brain Re...	3	Move-Attend vs. Move	Cognition.Attention,Acti...	15
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<input checked="" type="checkbox"/> 30045	2001	Mayer A R	Neuroreport	1	Right Hand > Foot	Action.Execution	2
<input type="checkbox"/> 30045	2001	Mayer A R	Neuroreport	2	Right Foot > Hand	Action.Execution	2
<input type="checkbox"/> 30054	1997	Rao S M	Journal of Neuroscience	1	Synchronization-300 vs. Rest	Action.Execution	3
<input type="checkbox"/> 30054	1997	Rao S M	Journal of Neuroscience	2	Continuation-300 vs. Rest	Action.Execution	7
<input checked="" type="checkbox"/> 30054	1997	Rao S M	Journal of Neuroscience	3	Listening-300 vs. Rest	Perception.Audition	2
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<input type="checkbox"/> 30054	1997	Rao S M	Journal of Neuroscience	5	Synchronization-600 vs. Rest	Action.Execution	3
<input type="checkbox"/> 30054	1997	Rao S M	Journal of Neuroscience	6	Continuation-600 vs. Rest	Action.Execution	7

155 experiments activating left M1



# Co-activation of left M1

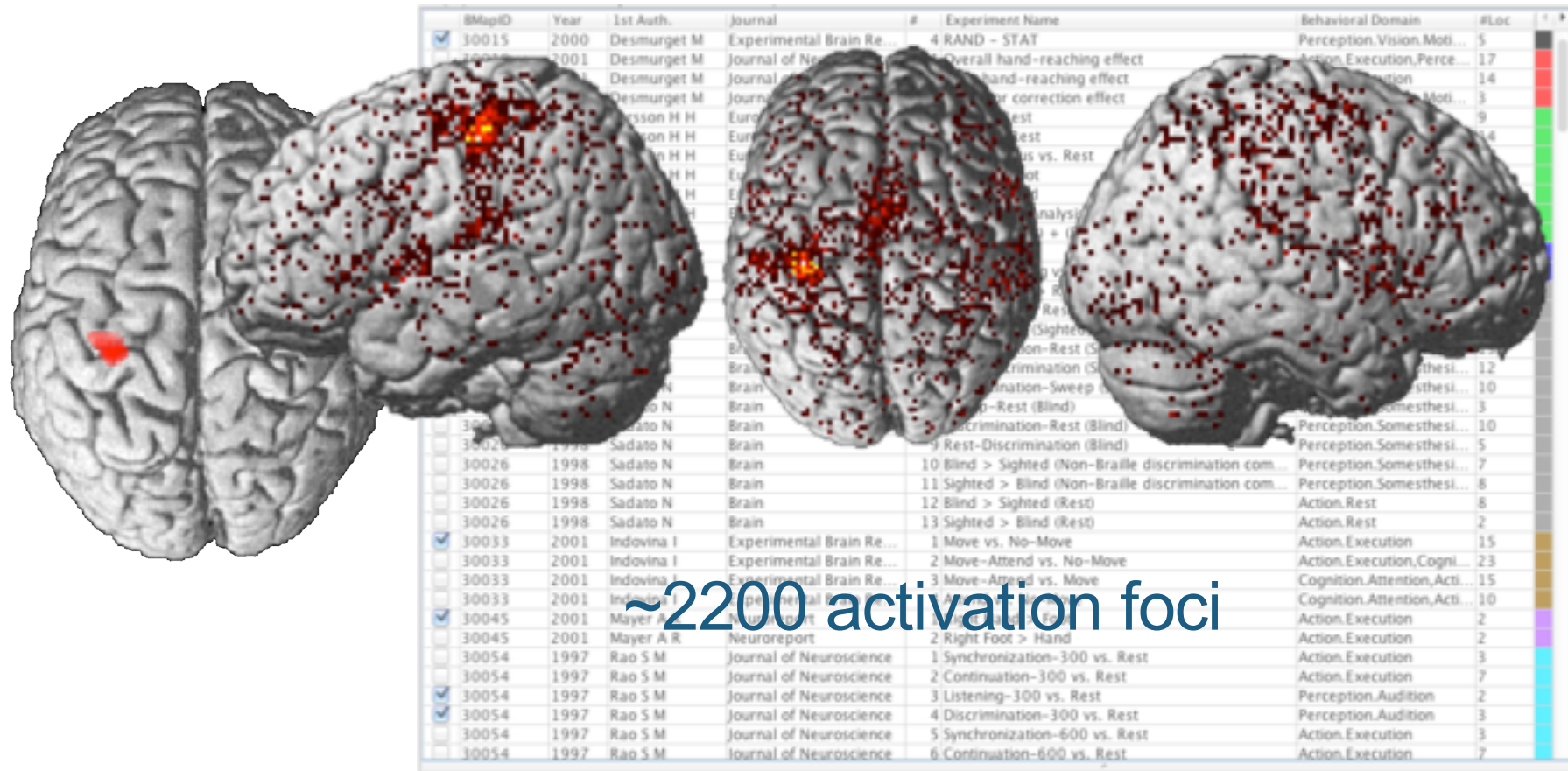
- Extract all coordinates



BMapID	Year	1st Auth.	Journal	#	Experiment Name	Behavioral Domain	#Loc
<input checked="" type="checkbox"/>	30015	2000	Desmurget M	Experimental Brain Re...	4 RAND - STAT	Perception.Vision.Moti...	5
<input type="checkbox"/>	30016	2001	Desmurget M	Journal of Neuroscience	1 Overall hand-reaching effect	Action.Execution,Perce...	17
<input checked="" type="checkbox"/>	30016	2001	Desmurg			Action.Execution	14
<input type="checkbox"/>	30016	2001	Desmurg			Perception.Vision.Moti...	3
<input type="checkbox"/>	30020	2000	Ehrsson			Action.Execution	9
<input checked="" type="checkbox"/>	30020	2000	Ehrsson			Action.Execution	14
<input type="checkbox"/>	30020	2000	Ehrsson			Action.Execution	17
<input checked="" type="checkbox"/>	30020	2000	Ehrsson			Action.Execution	5
<input type="checkbox"/>	30020	2000	Ehrsson			Action.Execution	4
<input type="checkbox"/>	30020	2000	Ehrsson			Action.Execution	13
<input type="checkbox"/>	30022	2001	Gosain A			Action.Execution	3
<input checked="" type="checkbox"/>	30022	2001	Gosain A			Action.Execution	2
<input checked="" type="checkbox"/>	30026	1998	Sadato N			Perception.Somesthesi...	27
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<input type="checkbox"/>	30026	1998	Sadato N			Perception.Somesthesi...	7
<input checked="" type="checkbox"/>	30026	1998	Sadato N			Perception.Somesthesi...	15
<input type="checkbox"/>	30026	1998	Sadato N			Perception.Somesthesi...	12
<input type="checkbox"/>	30026	1998	Sadato N			Perception.Somesthesi...	10
<input type="checkbox"/>	30026	1998	Sadato N			Perception.Somesthesi...	3
<input type="checkbox"/>	30026	1998	Sadato N			Perception.Somesthesi...	10
<input type="checkbox"/>	30026	1998	Sadato N			Perception.Somesthesi...	5
<input type="checkbox"/>	30026	1998	Sadato N			Perception.Somesthesi...	7
<input type="checkbox"/>	30026	1998	Sadato N	Brain	12 Sighted > Blind (non-braine discrimination con...	Perception.Somesthesi...	8
<input type="checkbox"/>	30026	1998	Sadato N	Brain	12 Blind > Sighted (Rest)	Action.Rest	8
<input type="checkbox"/>	30026	1998	Sadato N	Brain	13 Sighted > Blind (Rest)	Action.Rest	2
<input checked="" type="checkbox"/>	30033	2001	Indovina I	Experimental Brain Re	1 Move vs. No-Move	Action.Execution	15
<input type="checkbox"/>	30033	2001	Indovina I	Experimental Brain Re...	2 Move-Attend vs. No-Move	Action.Execution,Cogni...	23
<input type="checkbox"/>	30033	2001	Indovina I	Experimental Brain Re...	3 Move-Attend vs. Move	Cognition.Attention,Acti...	15
<input type="checkbox"/>	30033	2001	Indovina I	Experimental Brain Re...	4 Attend vs. No-Move	Cognition.Attention,Acti...	10
<input checked="" type="checkbox"/>	30045	2001	Mayer A R	Neuroreport	1 Right Hand > Foot	Action.Execution	2
<input type="checkbox"/>	30045	2001	Mayer A R	Neuroreport	2 Right Foot > Hand	Action.Execution	2
<input type="checkbox"/>	30054	1997	Rao S M	Journal of Neuroscience	1 Synchronization-300 vs. Rest	Action.Execution	3
<input type="checkbox"/>	30054	1997	Rao S M	Journal of Neuroscience	2 Continuation-300 vs. Rest	Action.Execution	7
<input checked="" type="checkbox"/>	30054	1997	Rao S M	Journal of Neuroscience	3 Listening-300 vs. Rest	Perception.Audition	2
<input checked="" type="checkbox"/>	30054	1997	Rao S M	Journal of Neuroscience	4 Discrimination-300 vs. Rest	Perception.Audition	3
<input type="checkbox"/>	30054	1997	Rao S M	Journal of Neuroscience	5 Synchronization-600 vs. Rest	Action.Execution	3
<input type="checkbox"/>	30054	1997	Rao S M	Journal of Neuroscience	6 Continuation-600 vs. Rest	Action.Execution	7

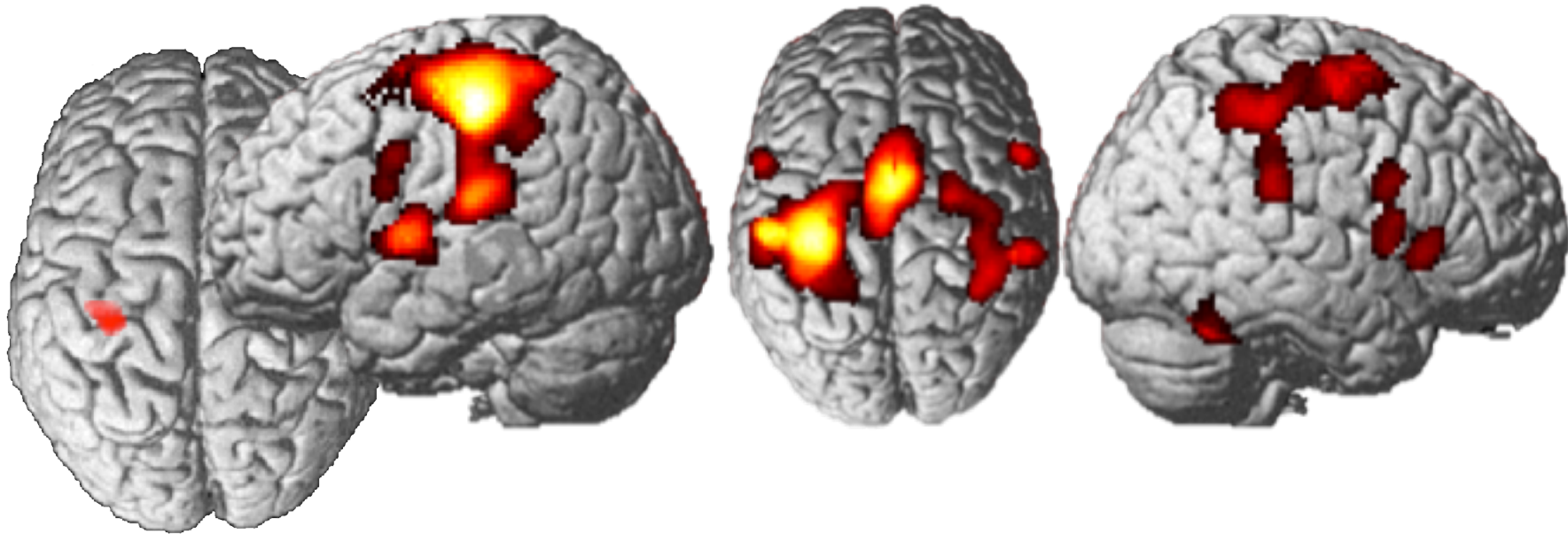
# Co-activation of left M1

- Extract all coordinates from 155 experiments



# CO-ACTIVATION OF LEFT M1

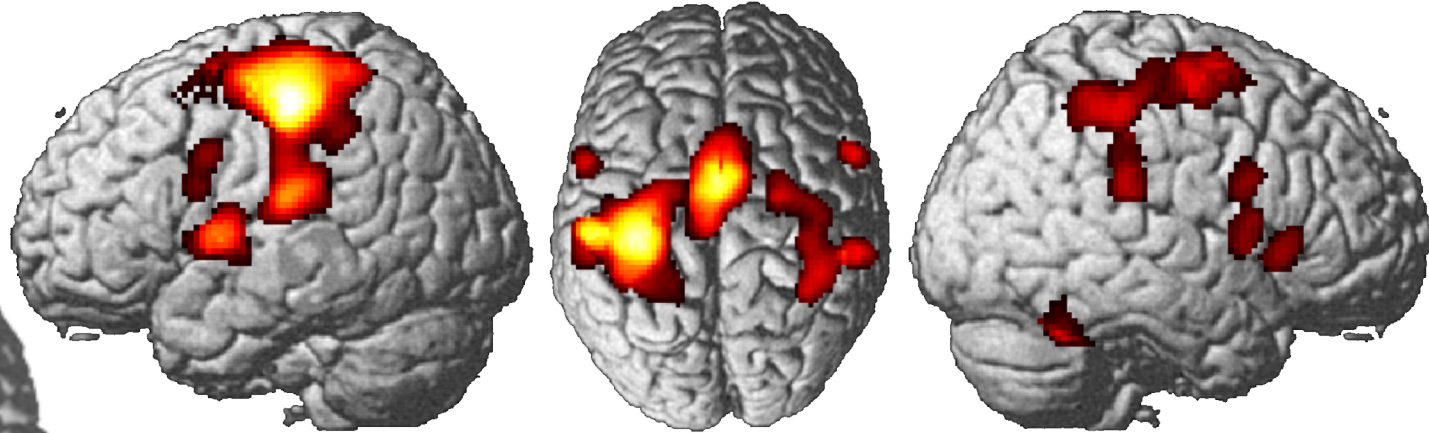
- Perform a meta-analysis across identified experiments



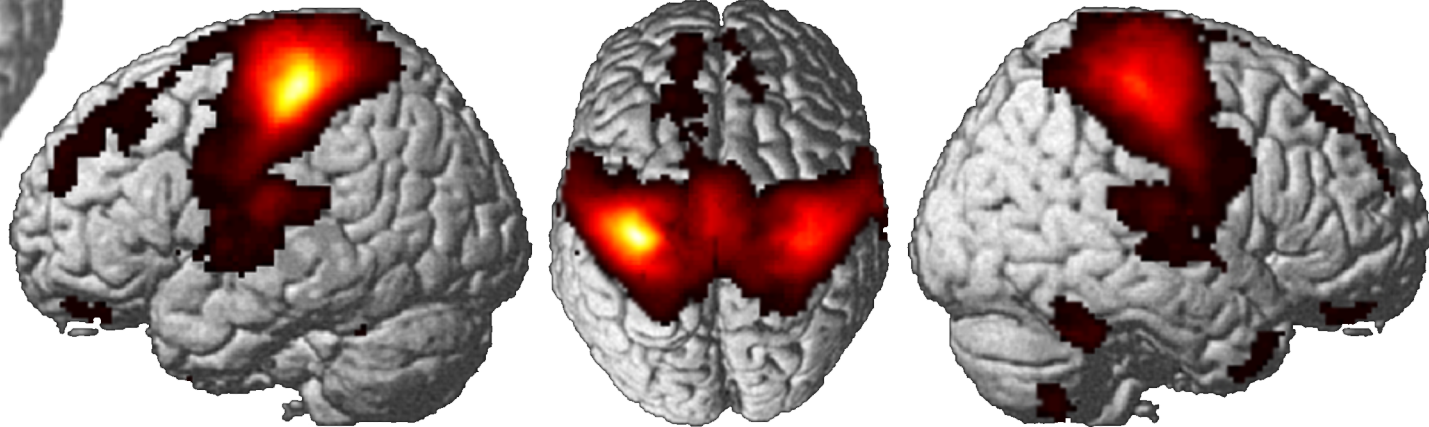
Network significantly co-activating with M1

# COMPARISON TO RESTING STATE FUNCTIONAL CONNECTIVITY

MACM



Resting-State

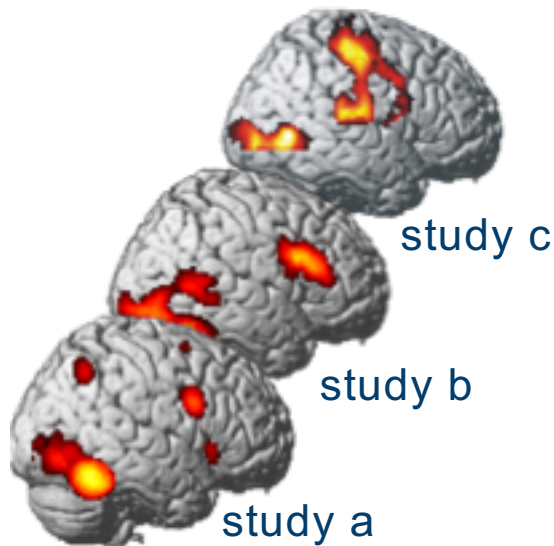




# MACM

## Location based meta-analyses:

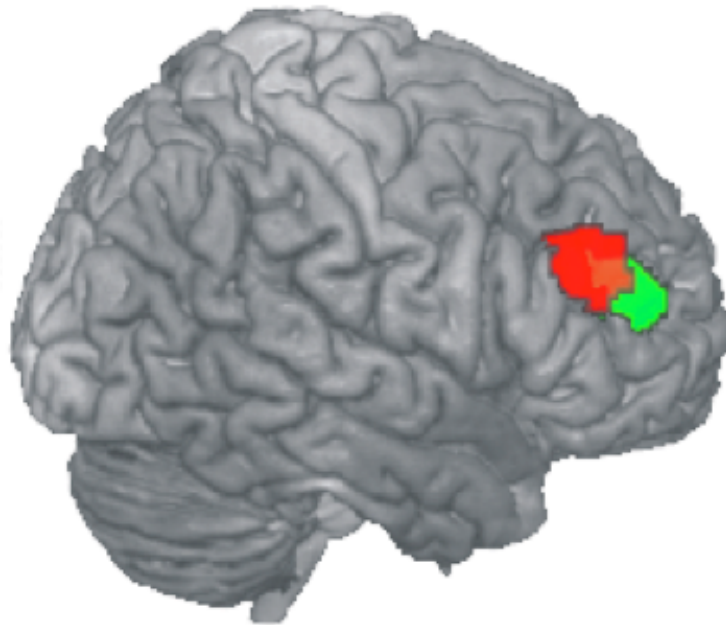
- Co-activations consistently found across different experiments
- Meta-analysis as a tool to derive functional connectivity



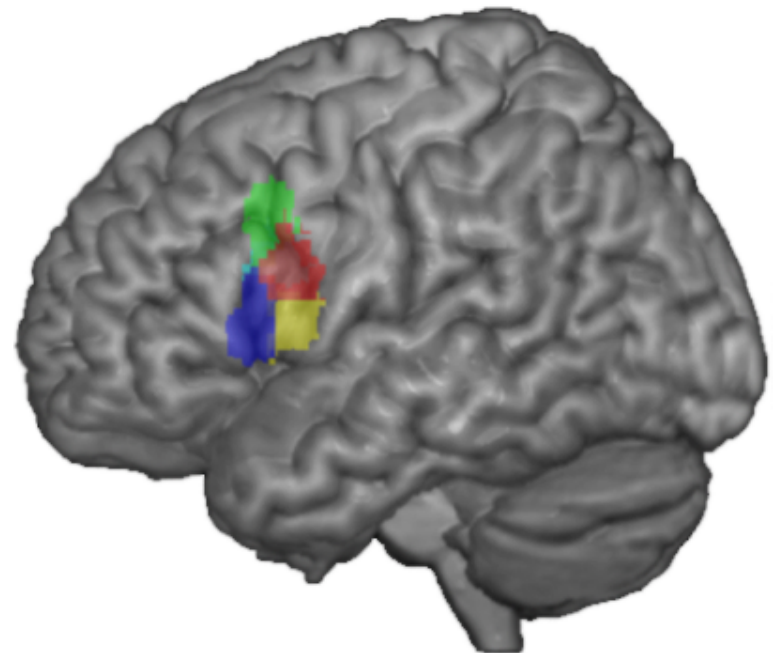
## Meta-Analytic Connectivity Modeling (MACM)

➔ **Functional connectivity to parcellate the brain**

# CONNECTIVITY BASED PARCELLATION (CBP)



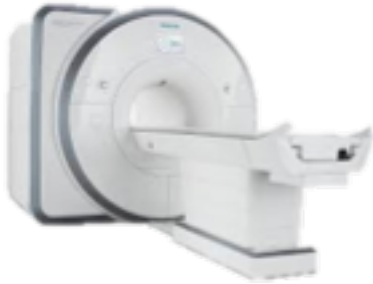
Cieslik et al., 2013



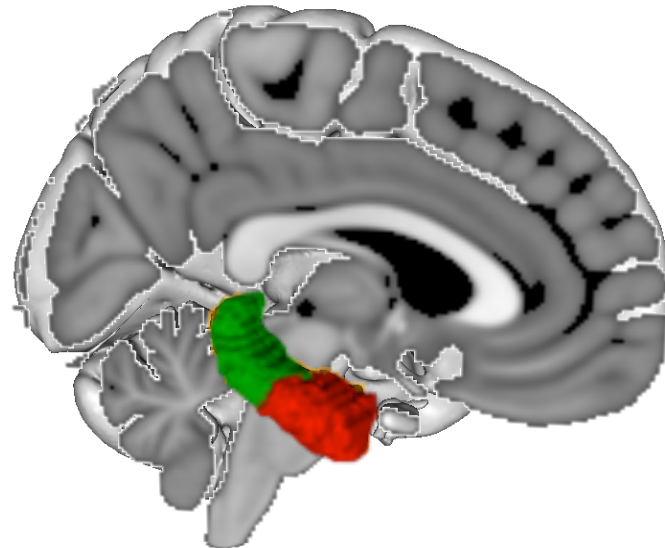
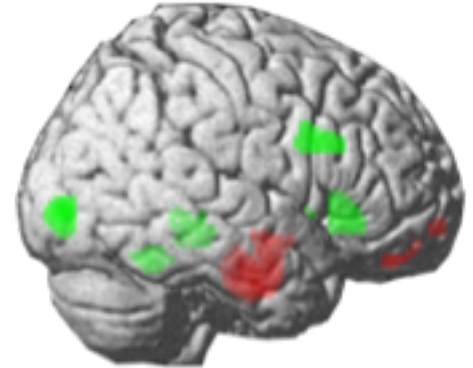
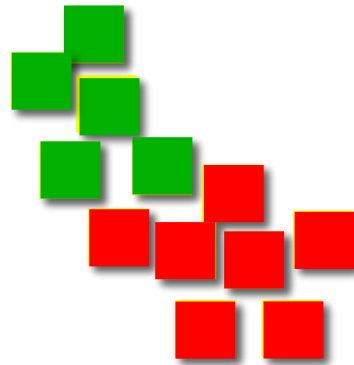
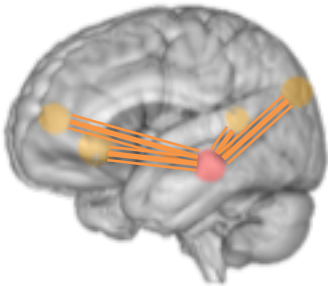
Clos et al., 2013

# Connectivity-based parcellation (CBP)

Neuroimaging  
scanner



Connectivity

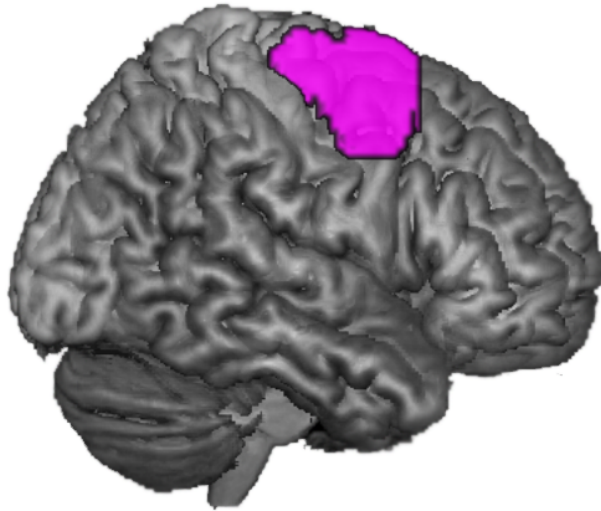


# MACM-CBP : WORKFLOW

- Perform a MACM analysis for every individual voxel of the ROI
  - Connectivity matrix: Probability of co-activation for every voxel of the ROI with all voxels of the brain
- Examination of distances in connectivity between each pair of voxels within the VOI
  - (Dis)Similarity matrix: Correspondence between profiles
- Clustering: e.g. K-mean clustering



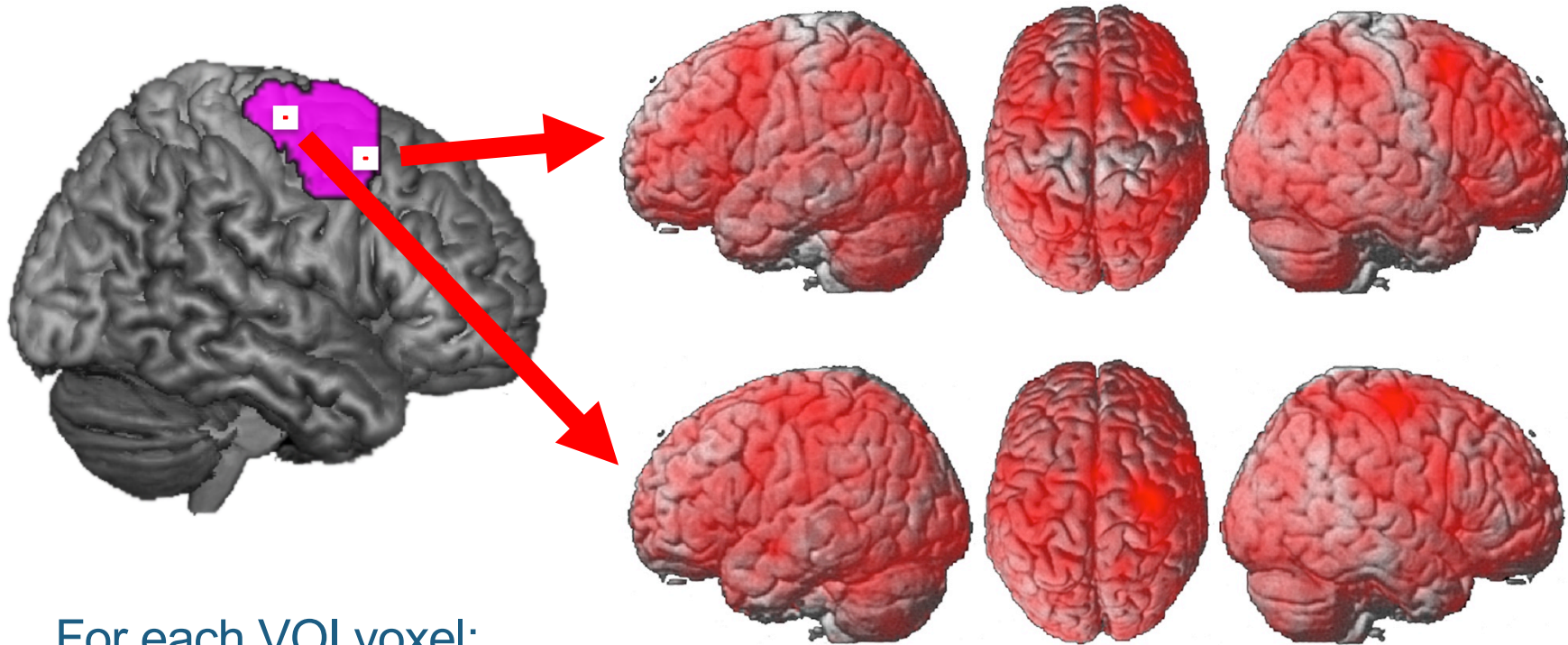
# MACM-CBP OF DORSAL PREMOTOR CORTEX (PMD)



Are there functionally distinct subregions within the dorsal premotor cortex ROI ?

# MACM-CBP OF PMD

- Perform a MACM analysis for every individual voxel of the PMd ROI

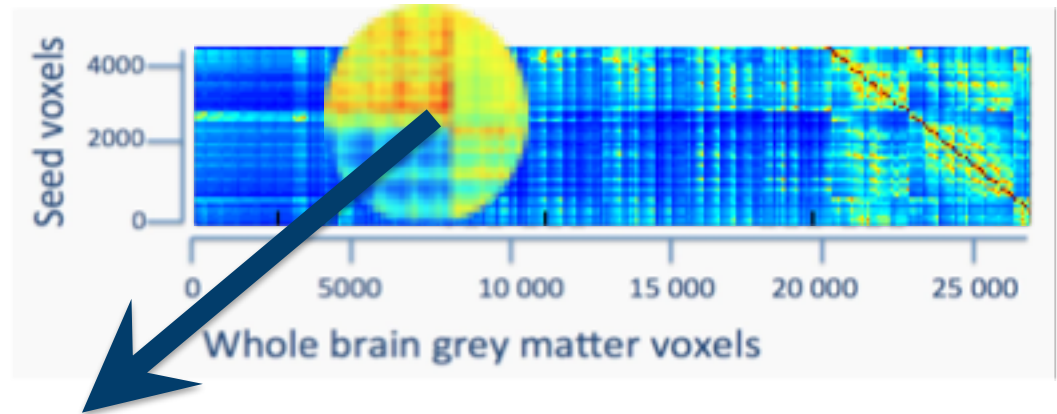
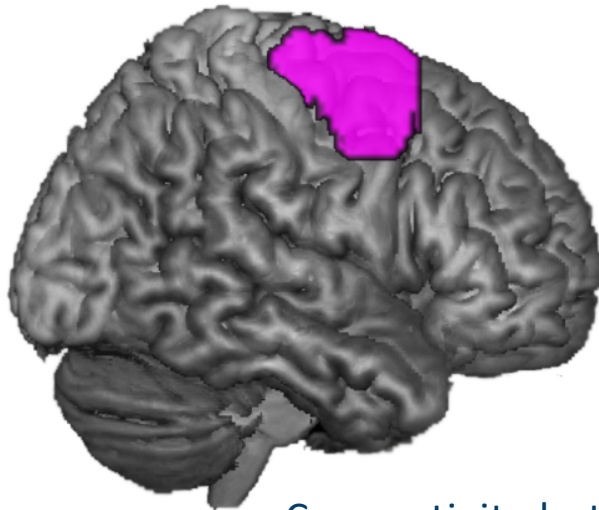


For each VOI voxel:

- Identification of all experiments activating that voxel
- Computation of across-experiment convergence of co-activations

# MACM-CBP OF PMD

- Perform a MACM analysis for every individual voxel of the PMd ROI → connectivity matrix



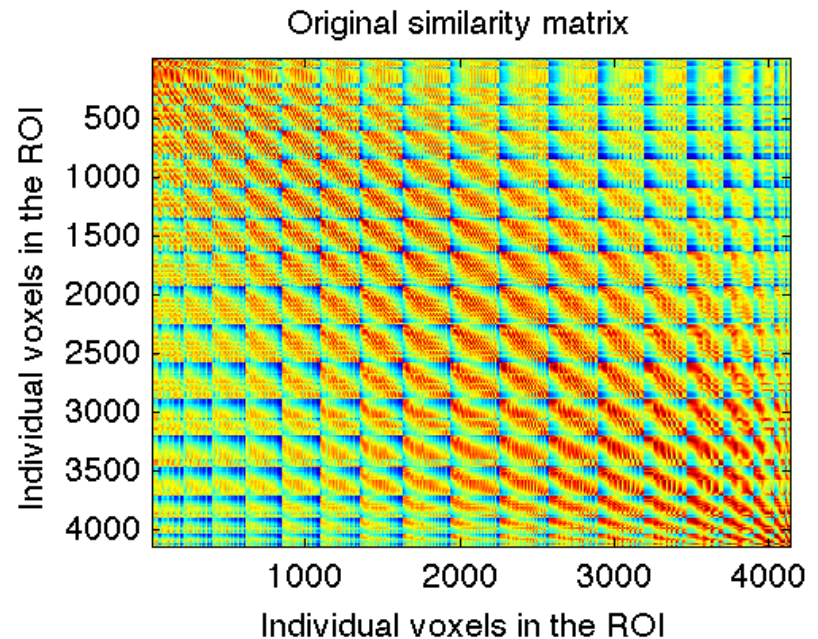
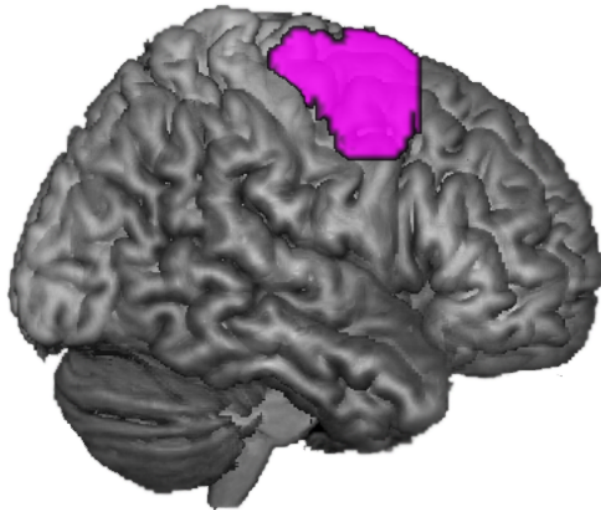
Connectivity between ROI voxel „x“ and brain voxel „y“

For each VOI voxel:

- Its connectivity profile (fingerprint)

# MACM-CBP OF PMD

- Calculation of distance in connectivity between each voxel pair of the PMd

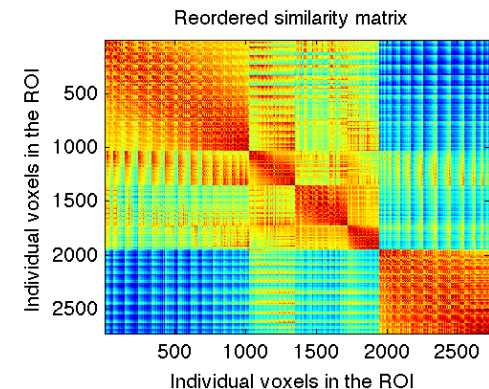
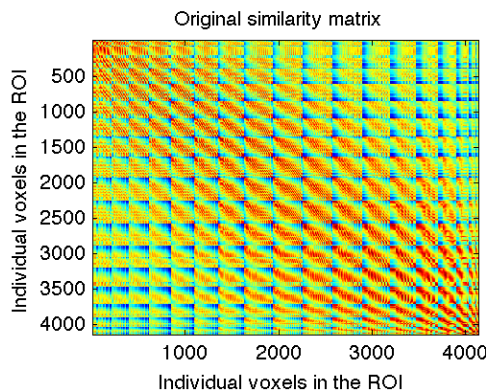
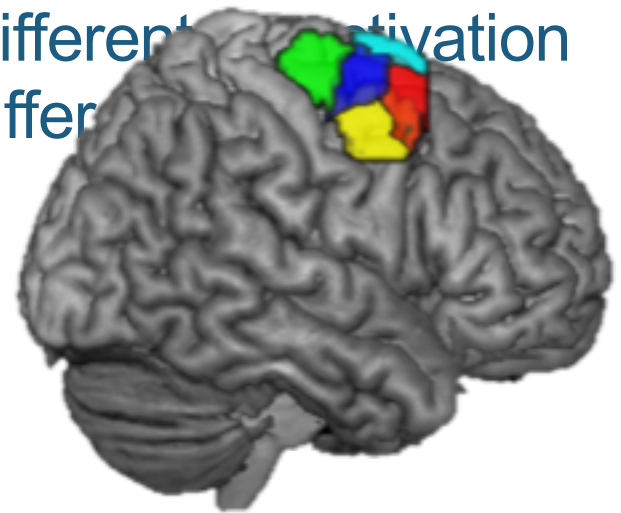
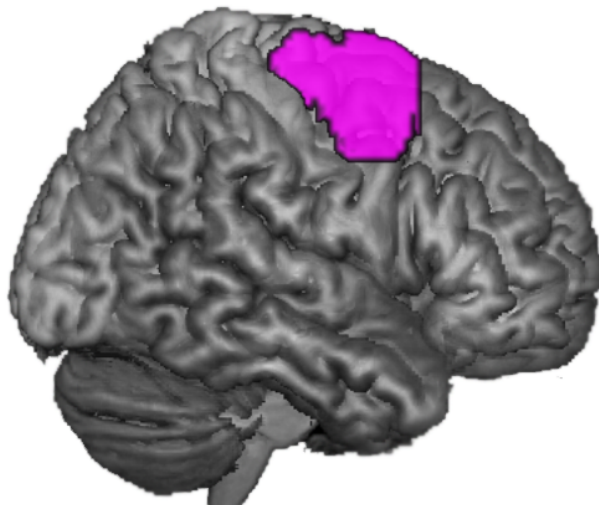




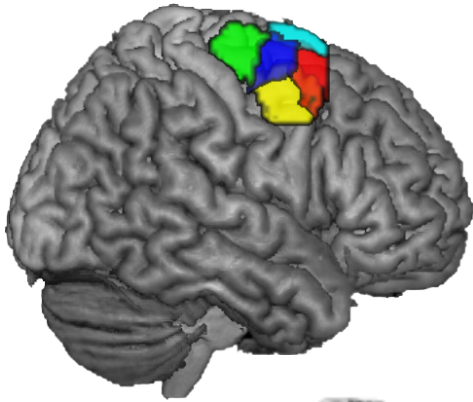
# MACM-CBP OF PMD

- Clustering:
  - Voxels with similar co-activation patterns → same cluster

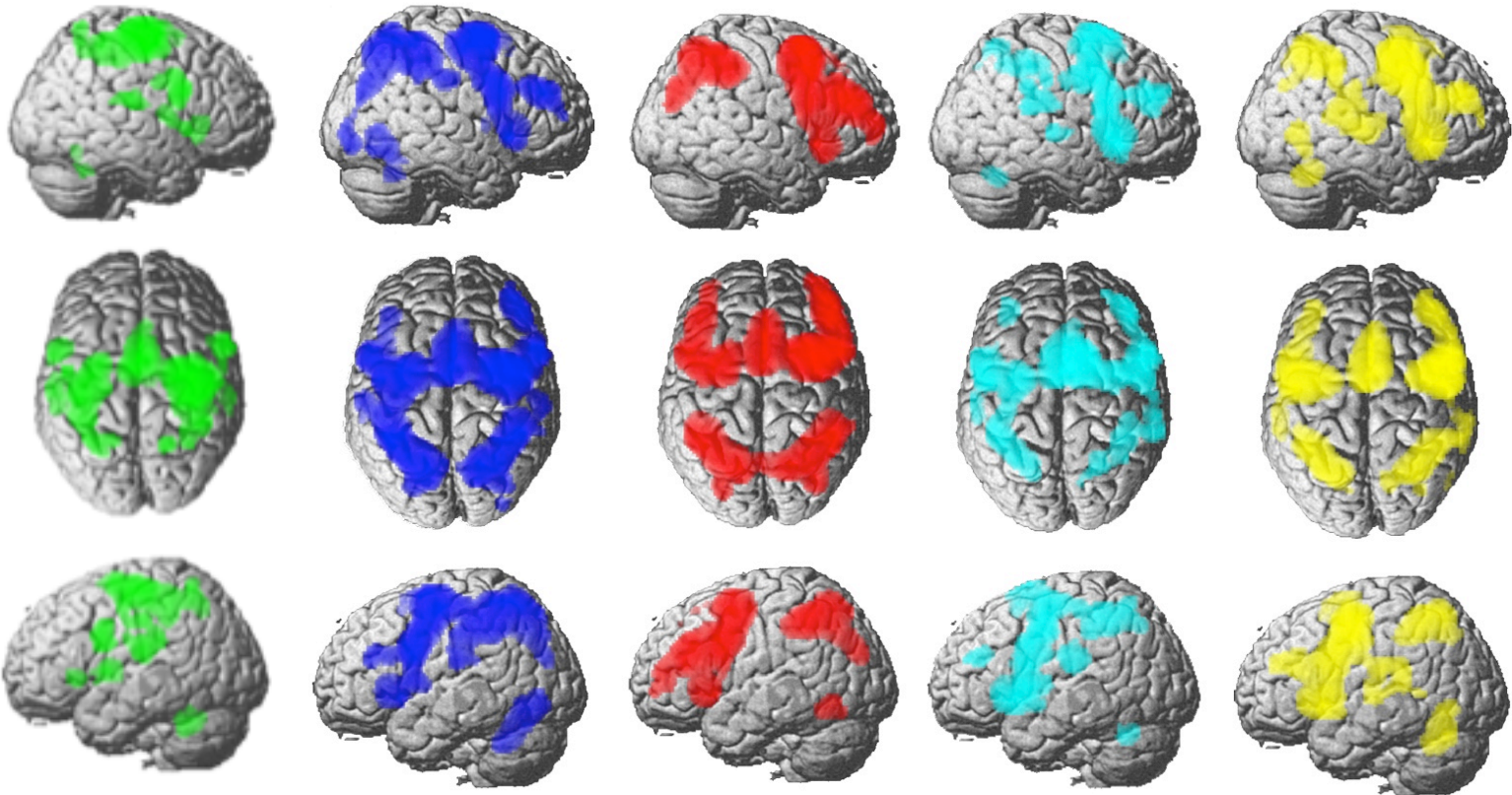
Voxels with different co-activation patterns → different clusters



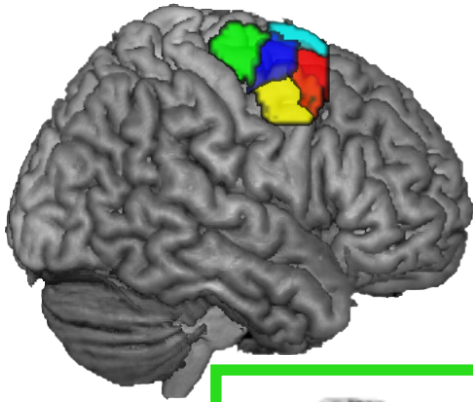
# MACM-CBP OF PMD



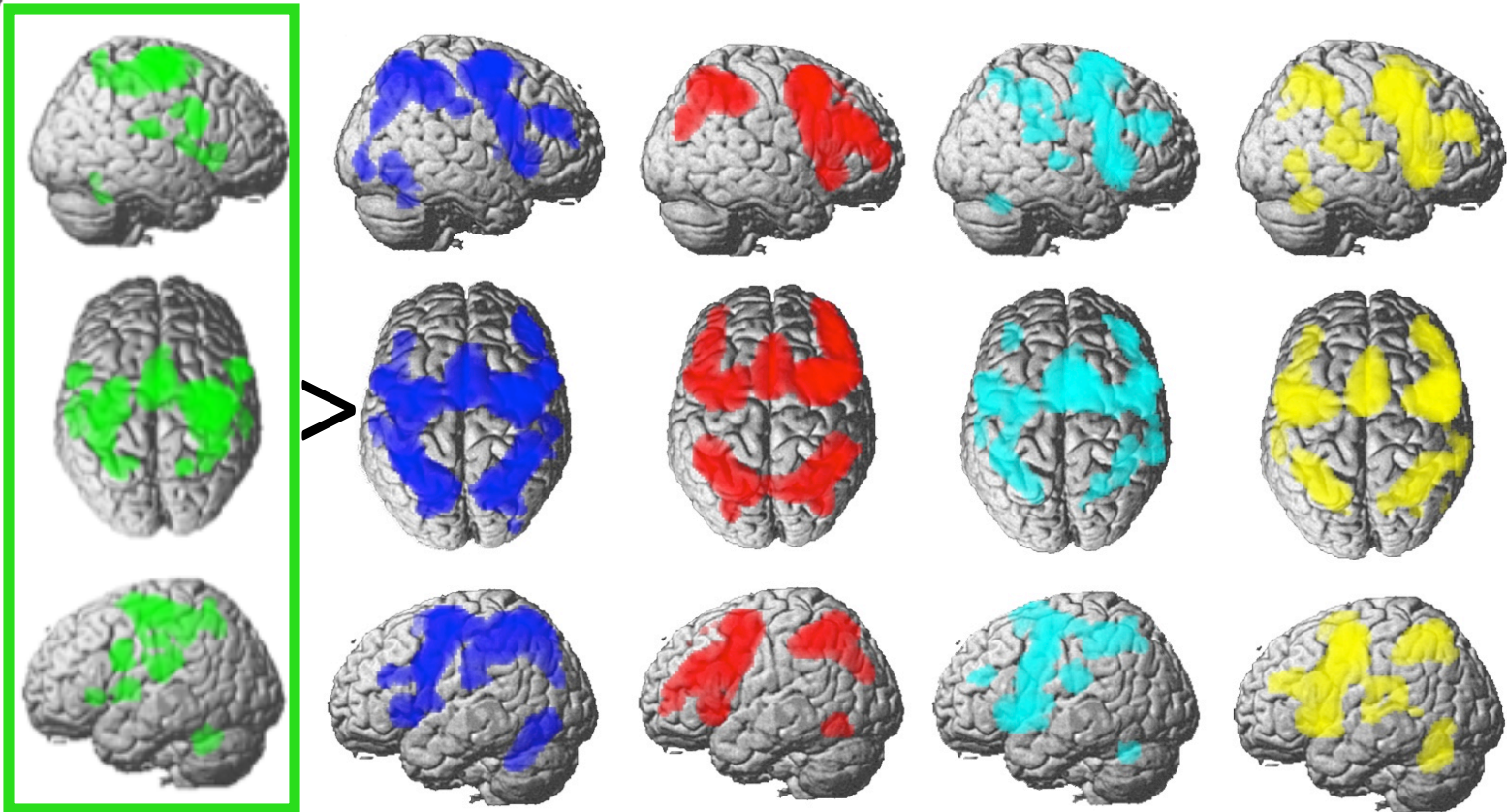
What are the connectivity differences driving this parcellation?



# MACM-CBP OF PMD

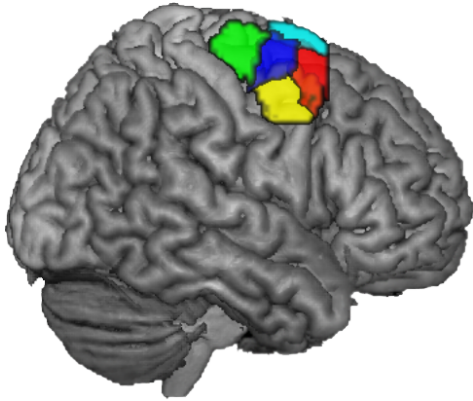


What are the connectivity differences driving this parcellation?

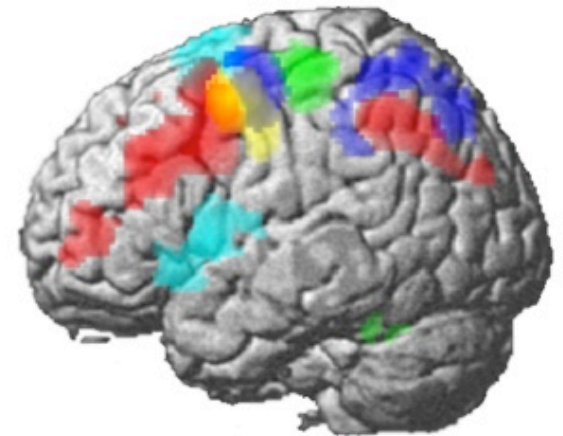
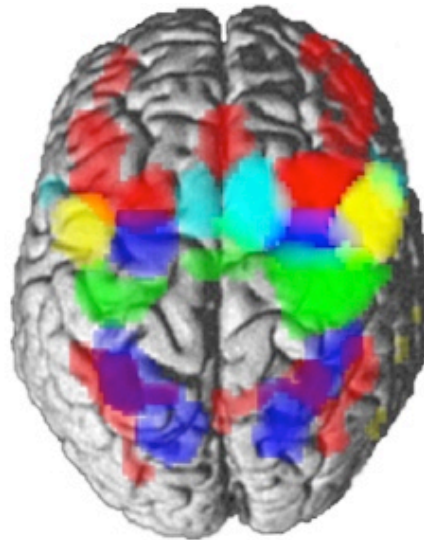
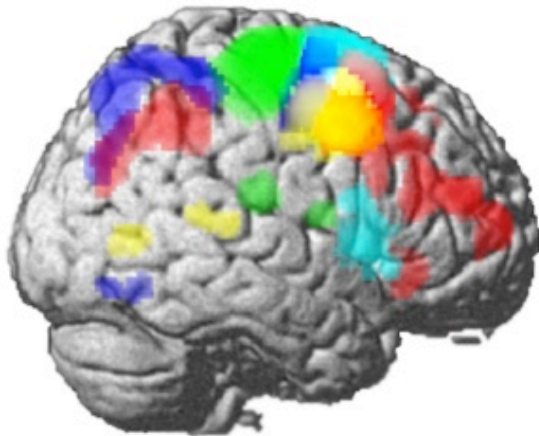




# MACM-CBP OF PMD

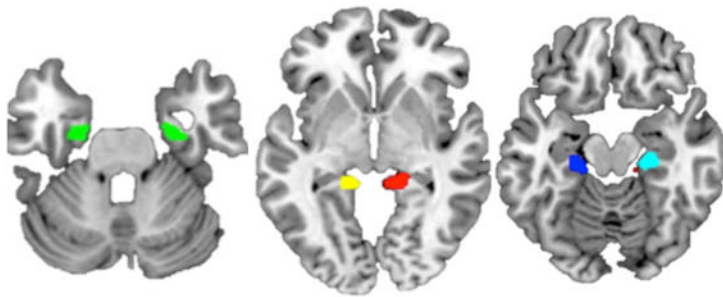


What are the connectivity differences driving this parcellation?

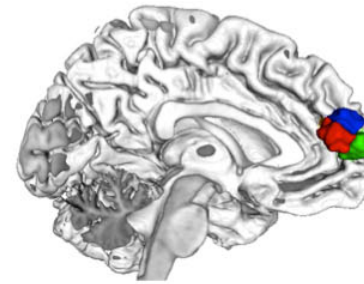




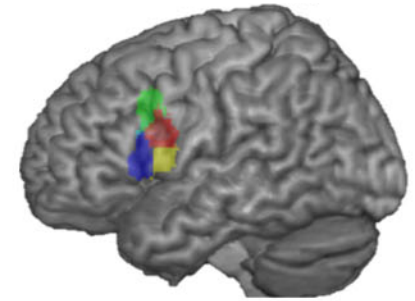
# MACM-CBP PROJECTS



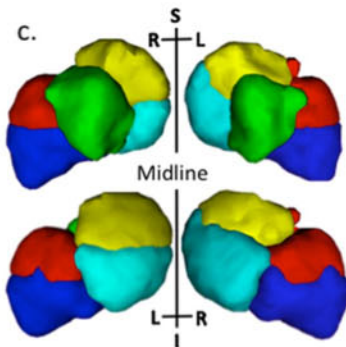
**Subiculum:** Chase et al., *Neuroimage* 2015



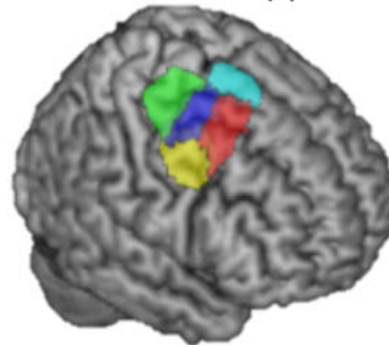
**dmPFC:** Eickhoff et al., *Cerebral Cortex* 2015



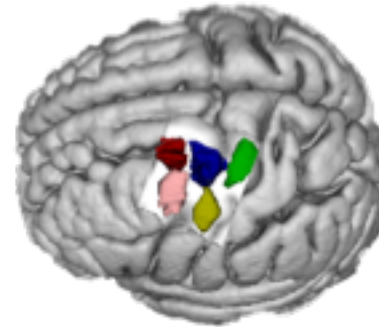
**BA 44:** Clos et al., *Neuroimage* 2015



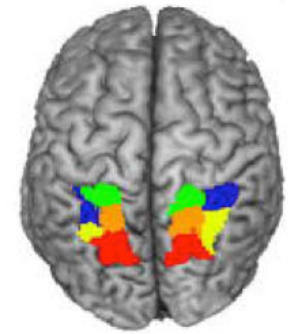
**Pulvinar:** Barron et al., *Hum Brain Mapp* 2015



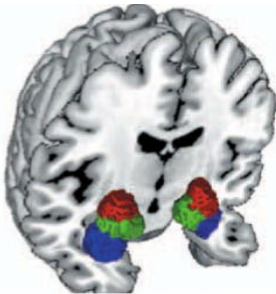
**Right PMd:** Genon et al., *Cerebral Cortex* 2017



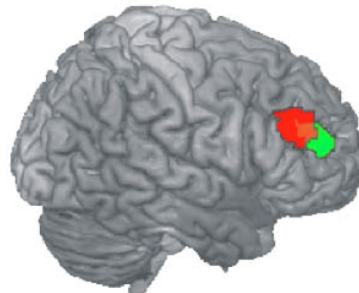
**Left PMd:** Genon et al., *NeuroImage* 2018



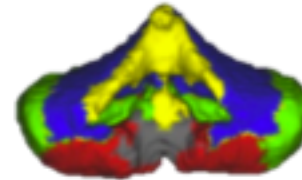
**SPL:** Wang et al., *Hum Brain Mapp* 2015



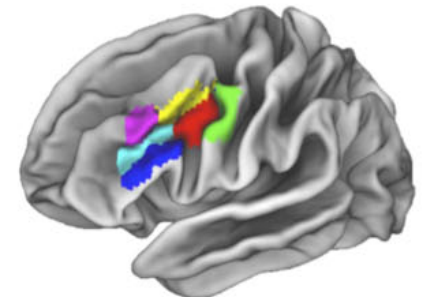
**Amygdala:** Bzdok et al., *Hum Brain Mapp* 2013



**IFS / DLPFC:** Cieslik et al., *Cerebral Cortex* 2013



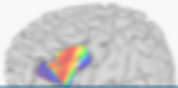
**Cerebellum:** Riedel et al., *NeuroImage* 2015




**IFJ:** Muhle-Karbe et al., *Cerebral Cortex* 2015

# DATABASE FOR META-ANALYTICAL RESULTS

Meta-analytic maps are openly shared through the ANIMA database: <http://anima.fz-juelich.de>




**ANIMA** [beta edition] 



WELCOME

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Study	Description	Size	Files
<input type="checkbox"/> <b>Cieslik et al. 2013</b> Is there "one" DLPFC in cognitive action control? Evidence for heterogeneity from co-activation-based parcellation. <i>Cerebral Cortex</i> . 23(10): 2577-2589.	This study shows that the right DLPFC as observed in 4 different experiments of executive action control may be subdivided into 2 distinct subregions -- an anterior-ventral and a posterior-dorsal one -- based on their whole-brain co-activation patterns across neuroimaging studies. The posterior subregion showed increased connectivity with bilateral intraparietal sulci, whereas the anterior subregion showed increased connectivity with the anterior cingulate cortex. Functional characterization revealed the anterior network to be more strongly associated with attention and action inhibition processes, whereas the posterior network was more strongly related to action execution and working memory.	1.6M	5 
<input type="checkbox"/> <b>Cieslik et al., 2015</b> Three key regions for supervisory attentional control evidence from neuroimaging meta-analyses. <i>Neuroscience and Biobehavioural Reviews</i> . 48: 22-34.	We here investigated the core neural correlates of cognitive action control via coordinate-based meta-analyses of brain activity reported for the Stroop, spatial interference, stop-signal and go/no-go tasks. Our study revealed evidence for a pivotal role of the right anterior insula and right inferior frontal junction in supervisory attentional control, as these were the only two regions consistently involved in all four paradigm classes. Furthermore, the anterior midcingulate cortex and pre-supplementary motor area were commonly recruited by all but the go/no-go task.	1.6M	8 
<input type="checkbox"/> <b>Clos et al. 2013</b> Tackling the multifunctional nature of Broca's region meta-analytically: co-activation-based parcellation of area 44. <i>Neuroimage</i> . 83: 174-188.	We investigated whether the functional heterogeneity of Broca's region is reflected in distinct modules within cytoarchitecturally-defined left area 44 using meta-analytic connectivity-based parcellation (CBP). Our analysis revealed five separate clusters within left area 44. A post-hoc functional characterization and functional connectivity analysis of these five clusters was then performed, revealing specific and distinct functional	2.6M	23 

# SUMMARY

- Topic based meta-analyses: identify networks associated to a specific behavioural function
- Location based meta-analyses: identify networks co-activating with a specific region across different behavioral functions
- Meta-analytic connectivity modeling offers an approach to task-based functional connectivity
- Co-activation based parcellation enables to identify cortical functional modules

# References:

Eickhoff SB, Bzdok D, Laird AR, Roski C, Caspers S, Zilles K, Fox PT (2011). **Coactivation patterns distinguish cortical modules, their connectivity and functional differentiation**. Neuroimage 57, 938–949.

Eickhoff S, Yeo T, Genon S. **Imaging-based parcellations of the human brain**. Nat Rev Neurosci. In press.

Genon S, Li H, Fan L, Müller VI, Cieslik EC, Hoffstaedter F, Reid AT, Langer R, Grefkes, C, Fox PT, Moebus S, Caspers S, Amunts K, Jiang T, Eickhoff SB (2017). **The Right Dorsal Premotor Mosaic: Organization, Functions, and Connectivity**. Cereb. Cortex, 27(3), 2095-2110.

Toro R, Fox PT, Paus T (2008). **Functional coactivation map of the human brain**. Cereb. Cortex, 18, 2553–2559.

# THANK YOU



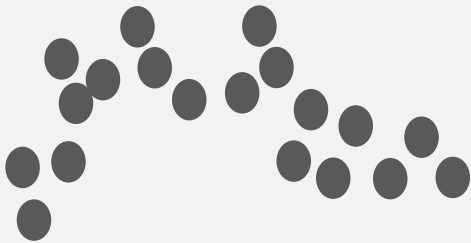
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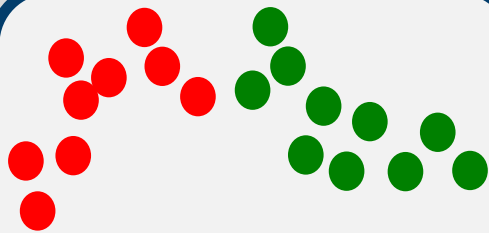
# CBP: HOW MANY CLUSTERS ?

How many  
clusters?

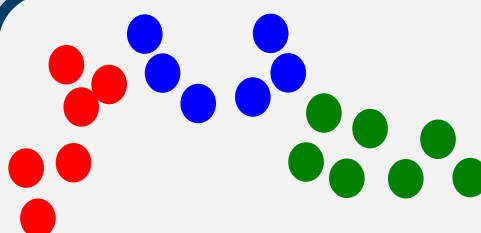


→ Search for several  $k$

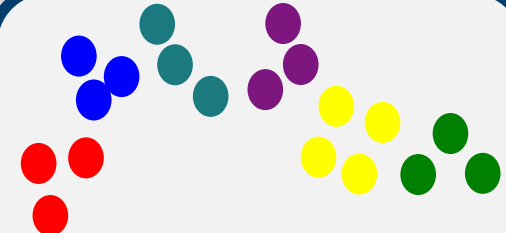
e.g.: 2 -> 8



$k = 2$



$k = 3$



$k = 6$

# CBP: HOW MANY CLUSTERS ?

Information theory

consistency

separation

