NeuroImaging Training Program

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Studying brain organization via spontaneous fMRI signal

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UCLA Neuroimaging Summer Course

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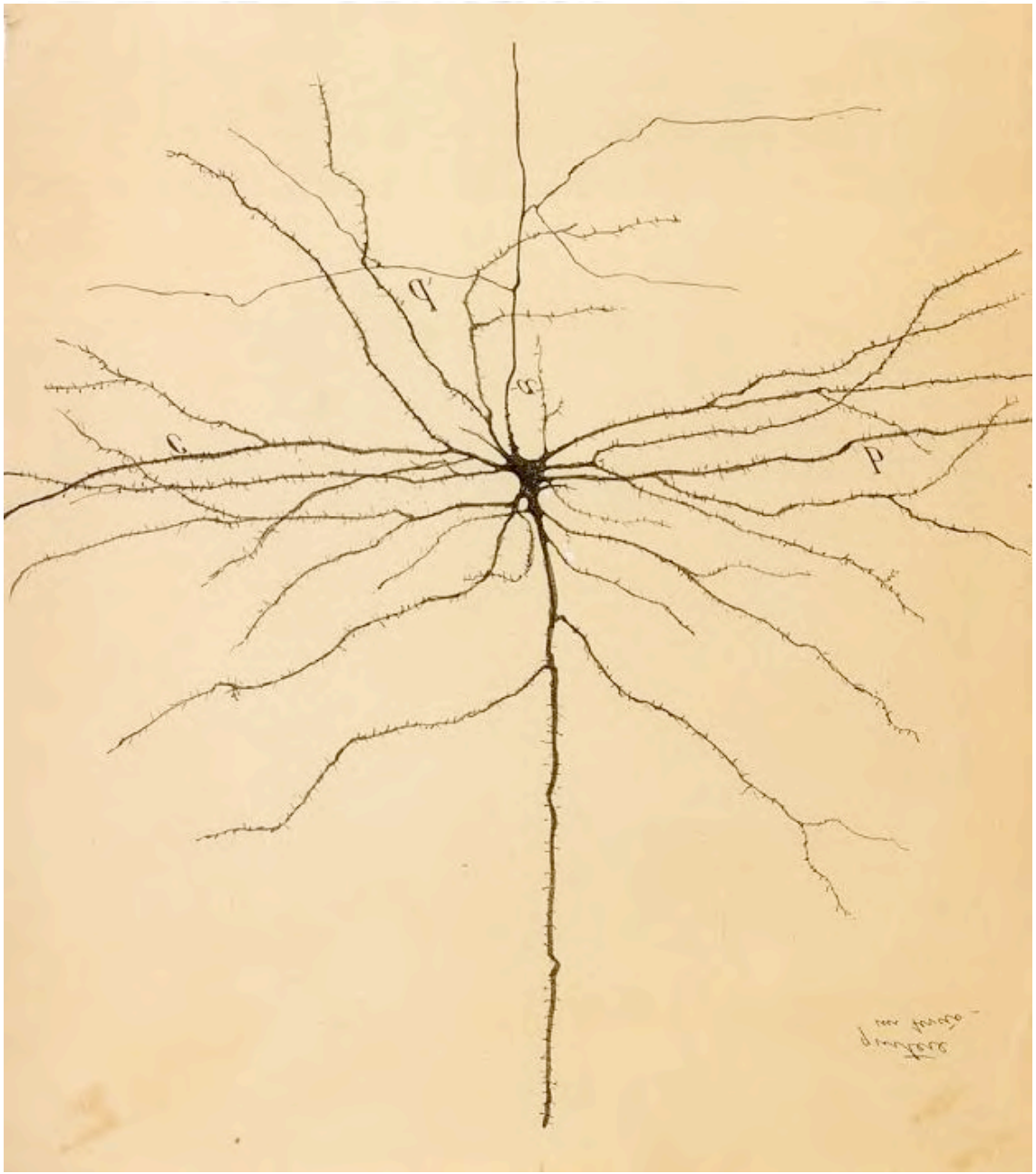
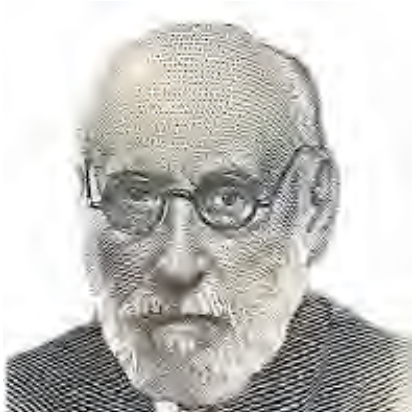
Washington University in St. Louis

NIMH National Institute of Mental Health

How is the brain organized?





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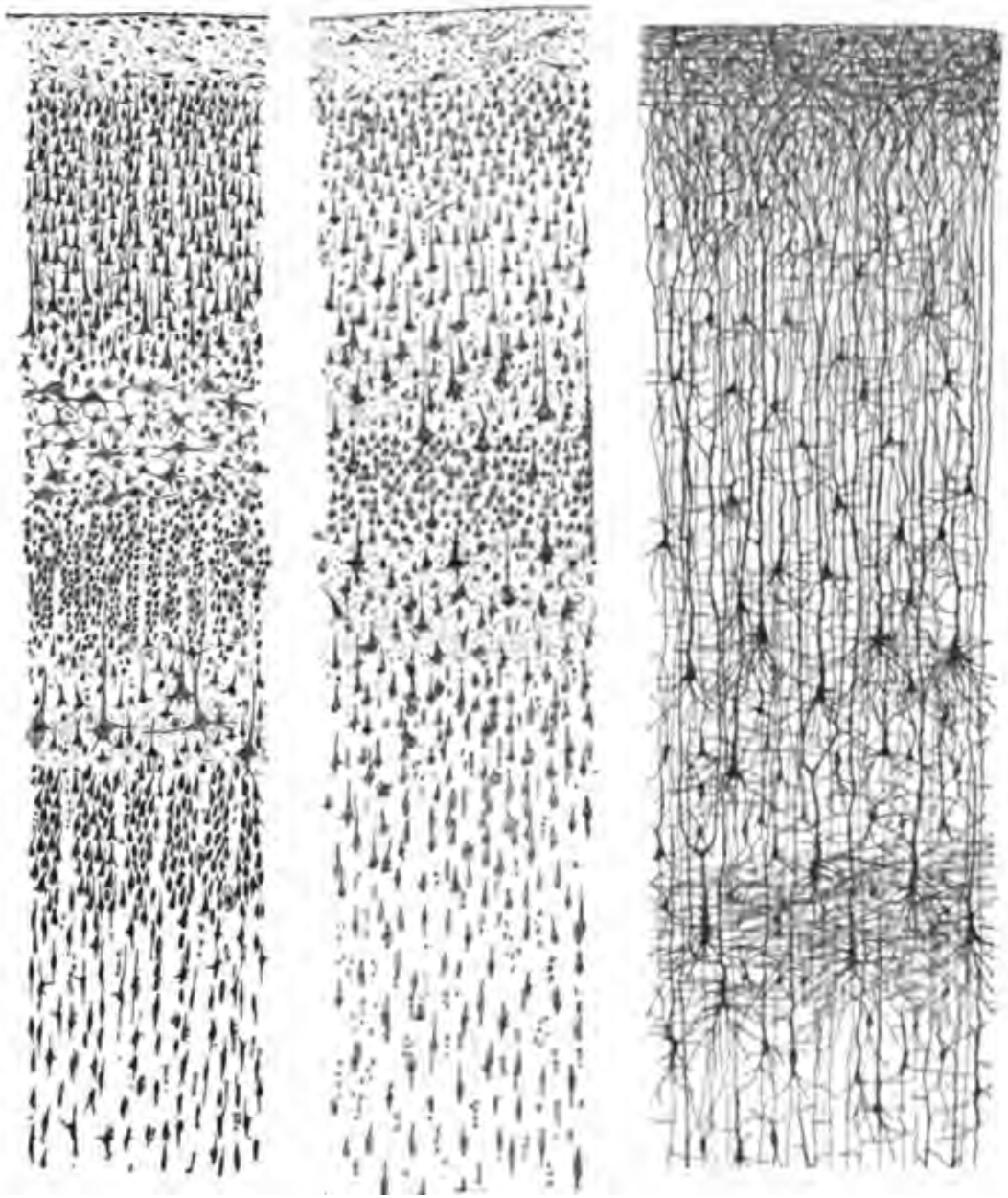

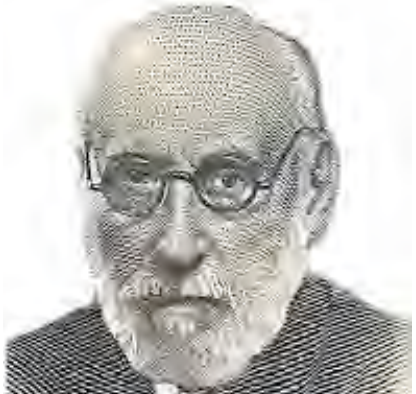

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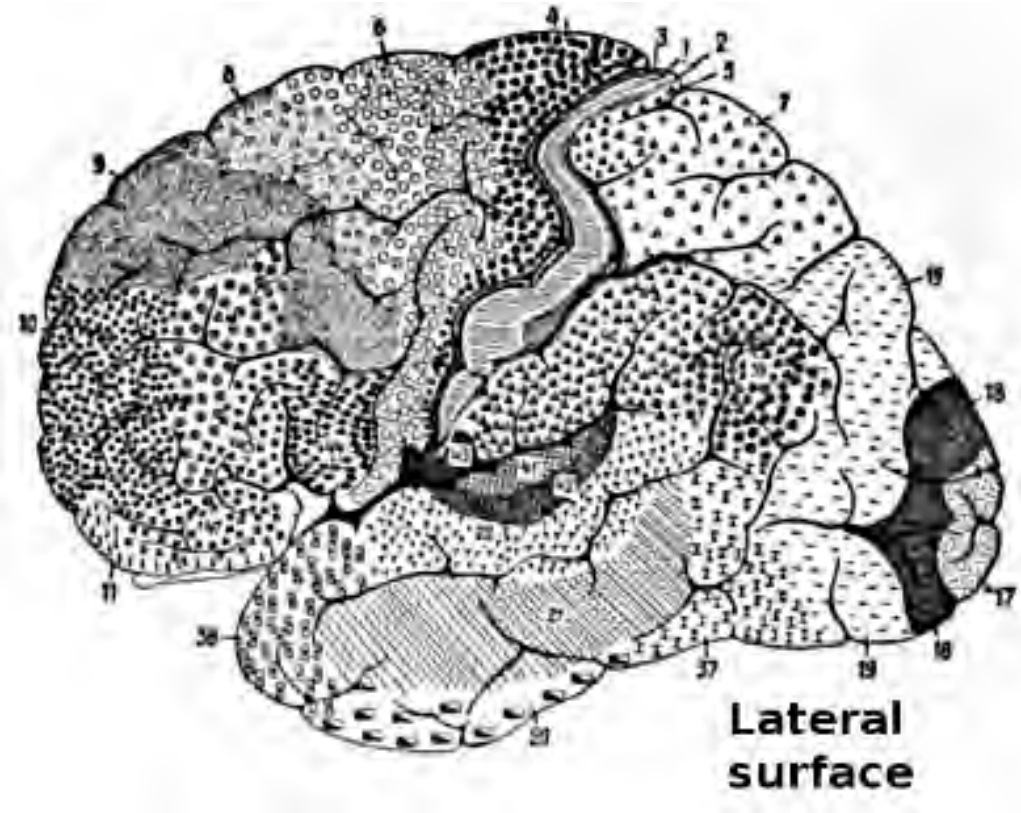
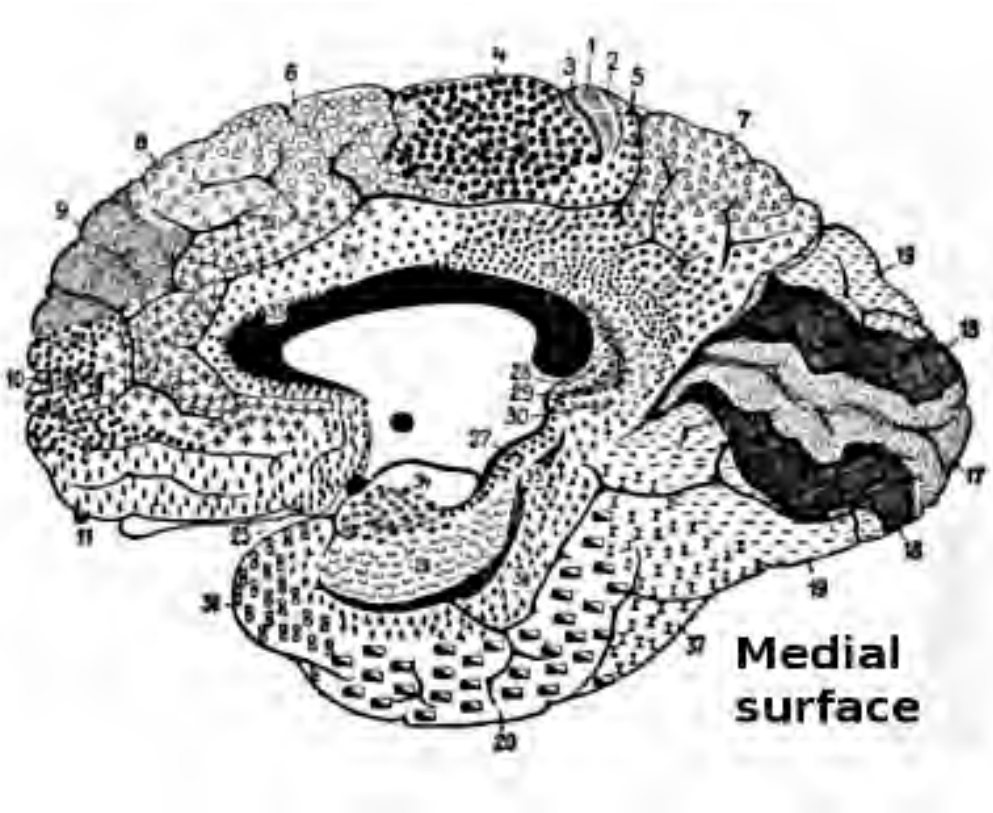
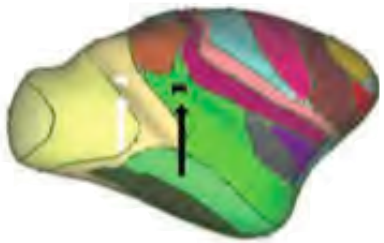




How is the brain organized?

Brodman 1905
macaque, 28 areas/hemi



Bonin & Bailey 1947
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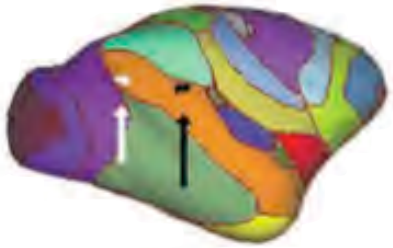
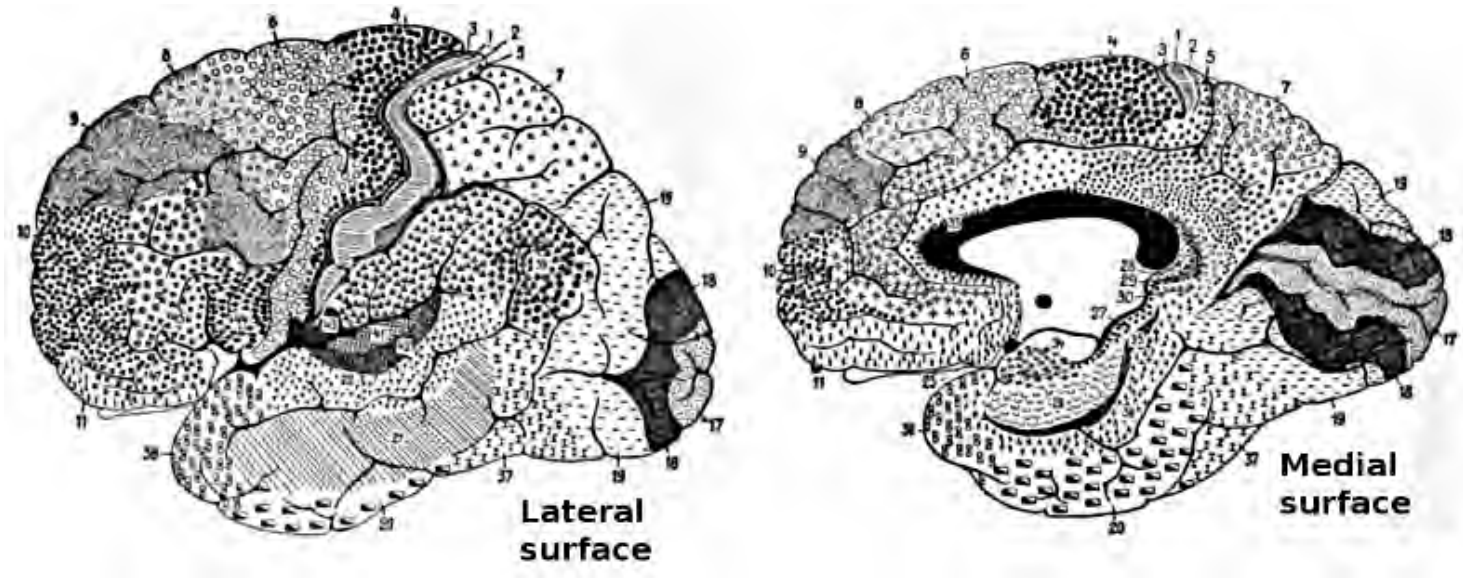


Felleman & Van Essen 1991
macaque, 80 areas/hemi

Van Essen et al., 2011
macaque, 129 areas/hemi

Brodmann, 1905



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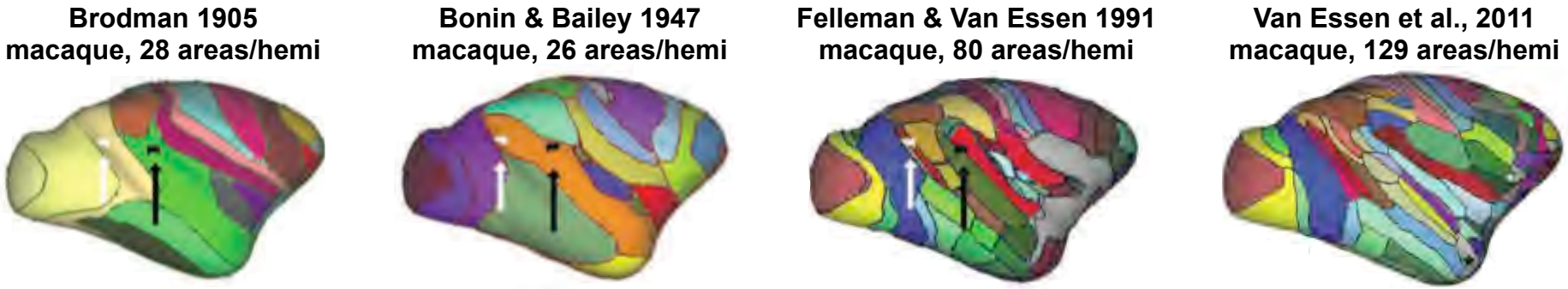
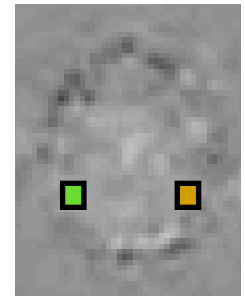
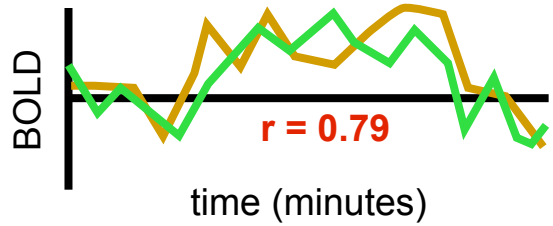


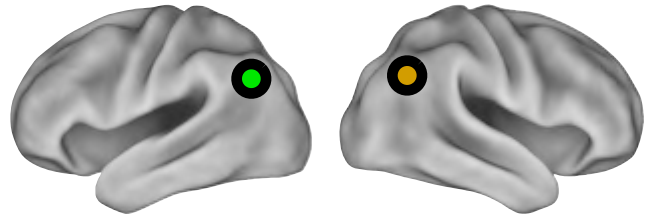
- Progress in humans slower
- Invasive techniques cant be used: tracers, penetrations, etc.
- Limitations of non-invasive techniques
  - Spatial resolution: EEG, MEG
  - Temporal resolution: PET, fMRI
- Newer non-invasive techniques may accelerate progress
  - Resting state functional connectivity MRI (RSFC)

Resting state functional connectivity MRI

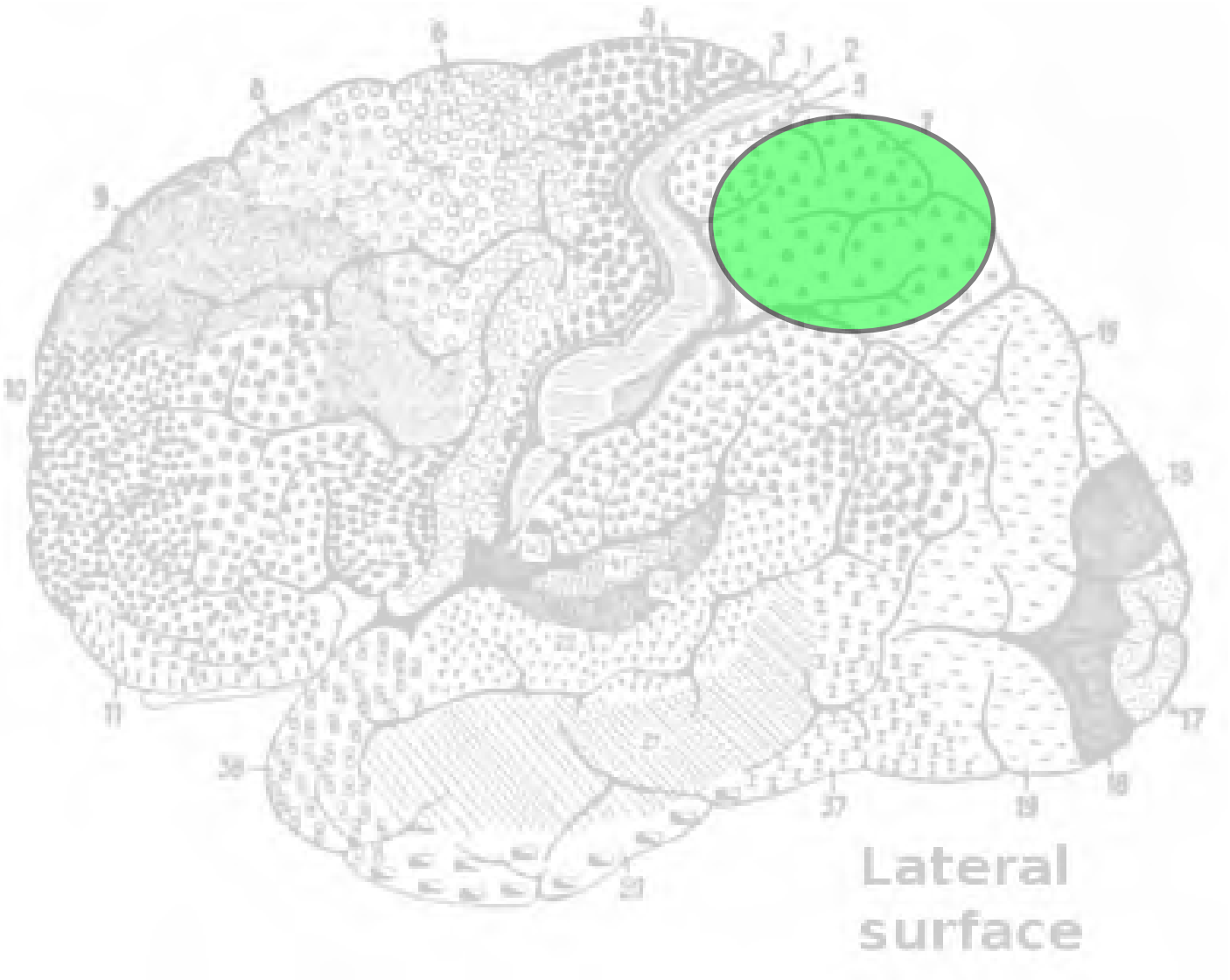
- Subjects lie in the scanner
- Record spontaneous T2* signal
- Brain volume every 2-3 sec (or less)
- ~3 mm cubes (or less)
- Low frequencies most powerful (< 0.08 Hz)
- Analyses are correlation-based
- High correlations imply relationships

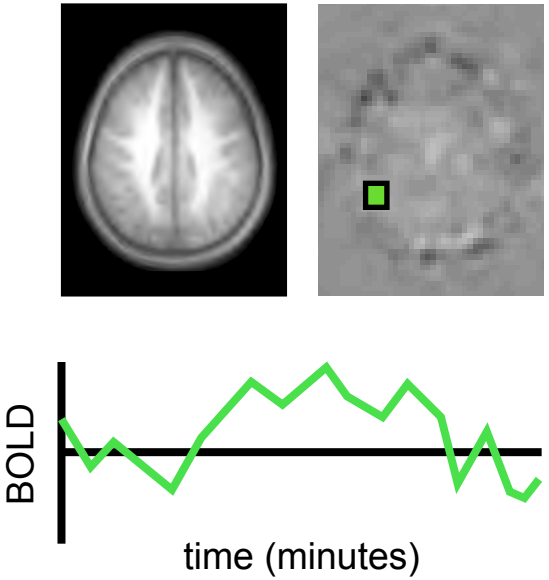






Resting state functional connectivity MRI





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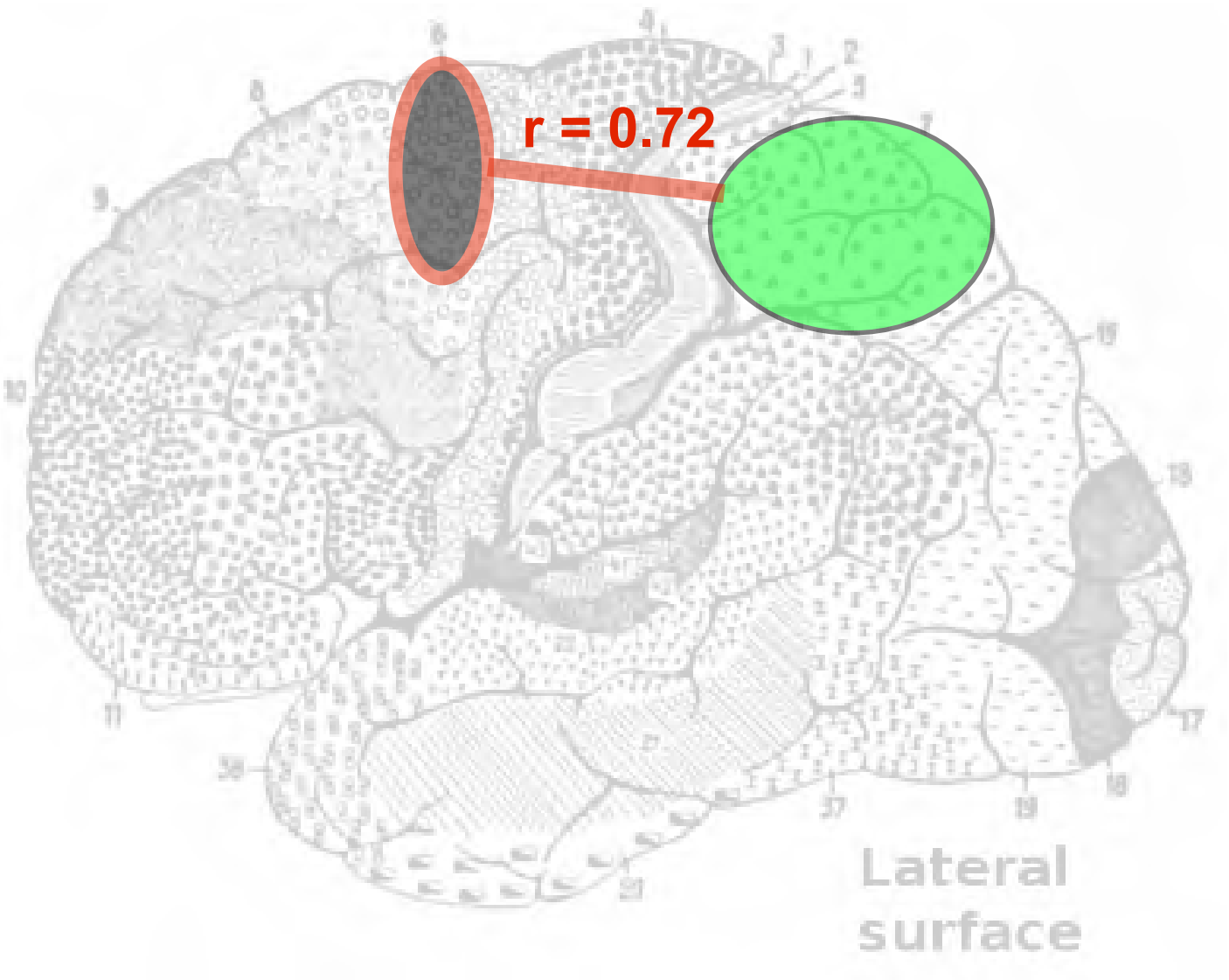

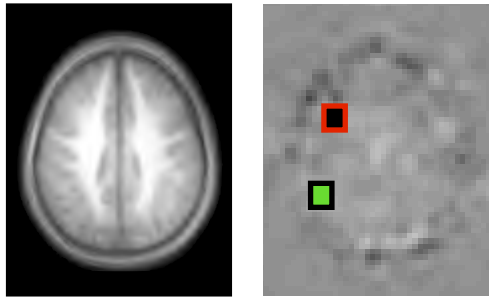

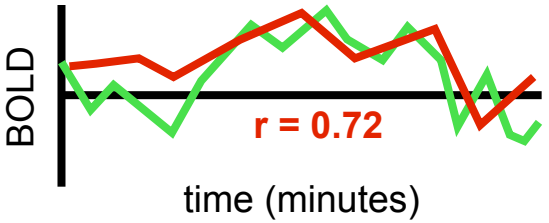

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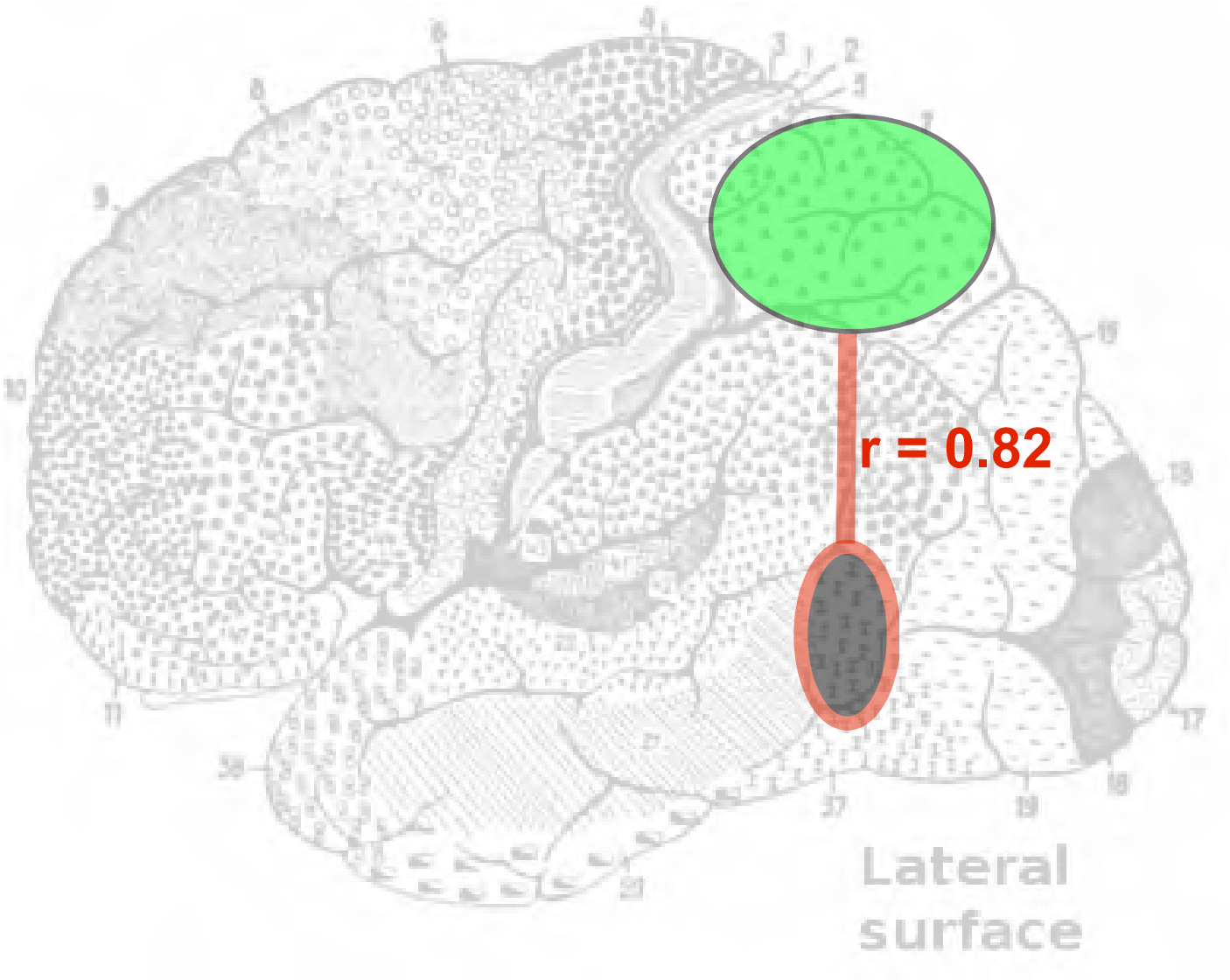

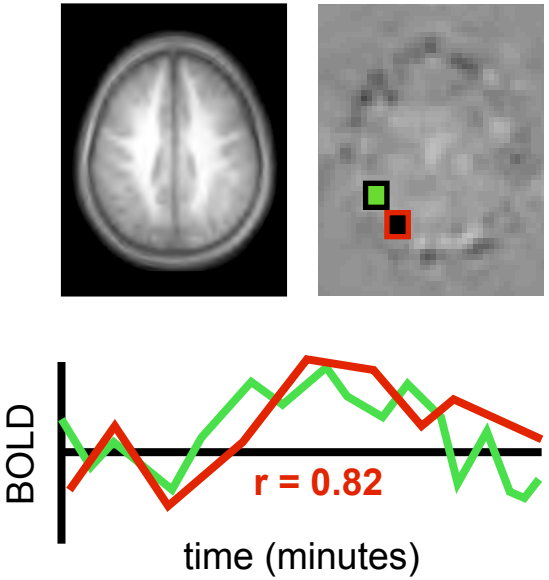

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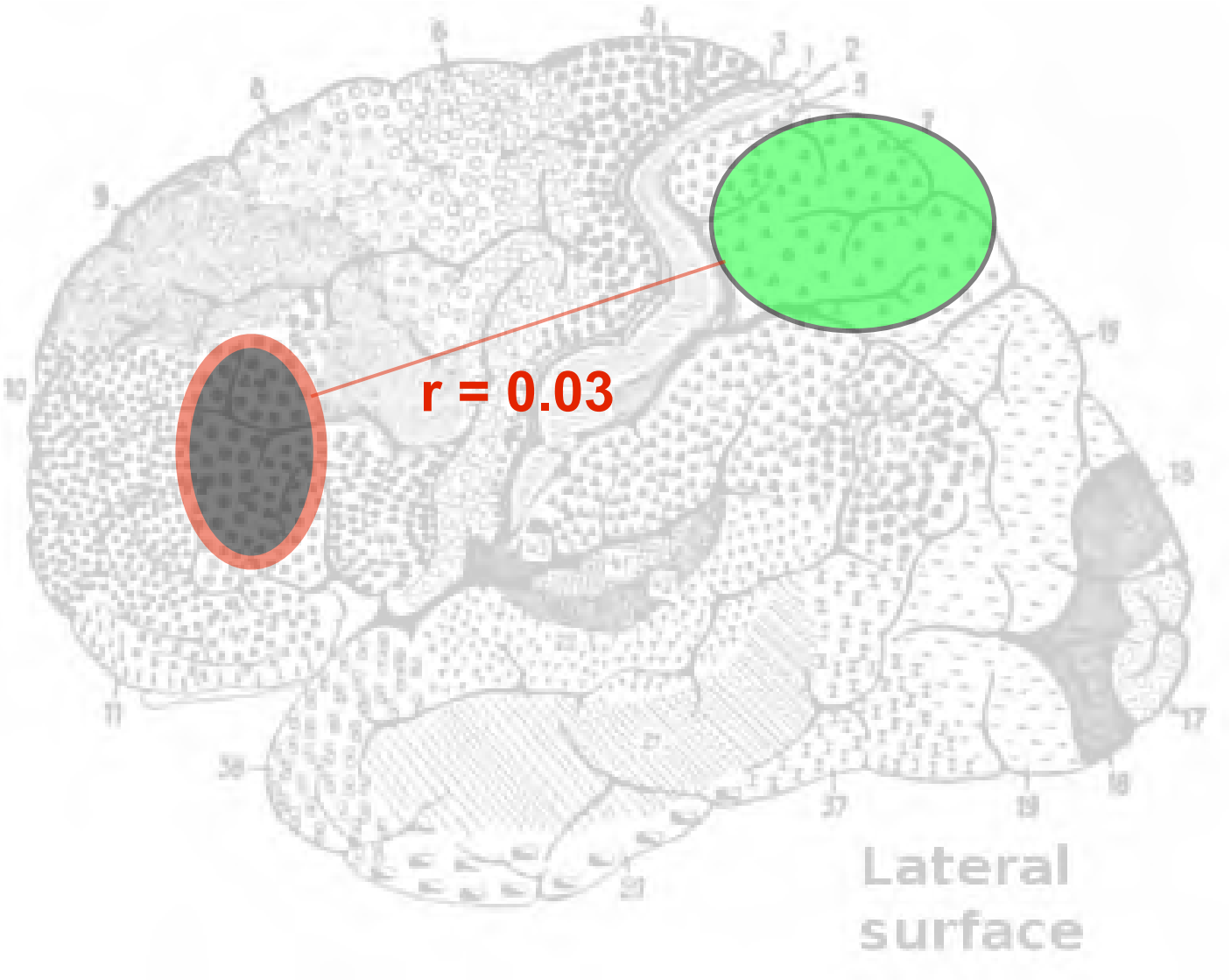

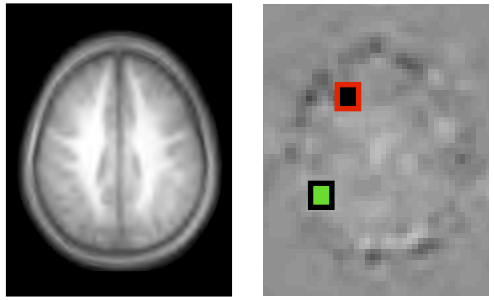

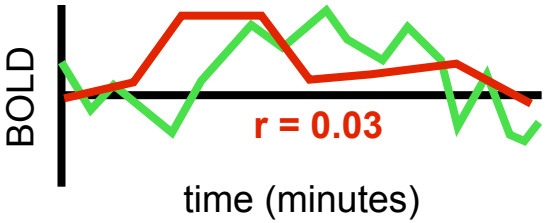

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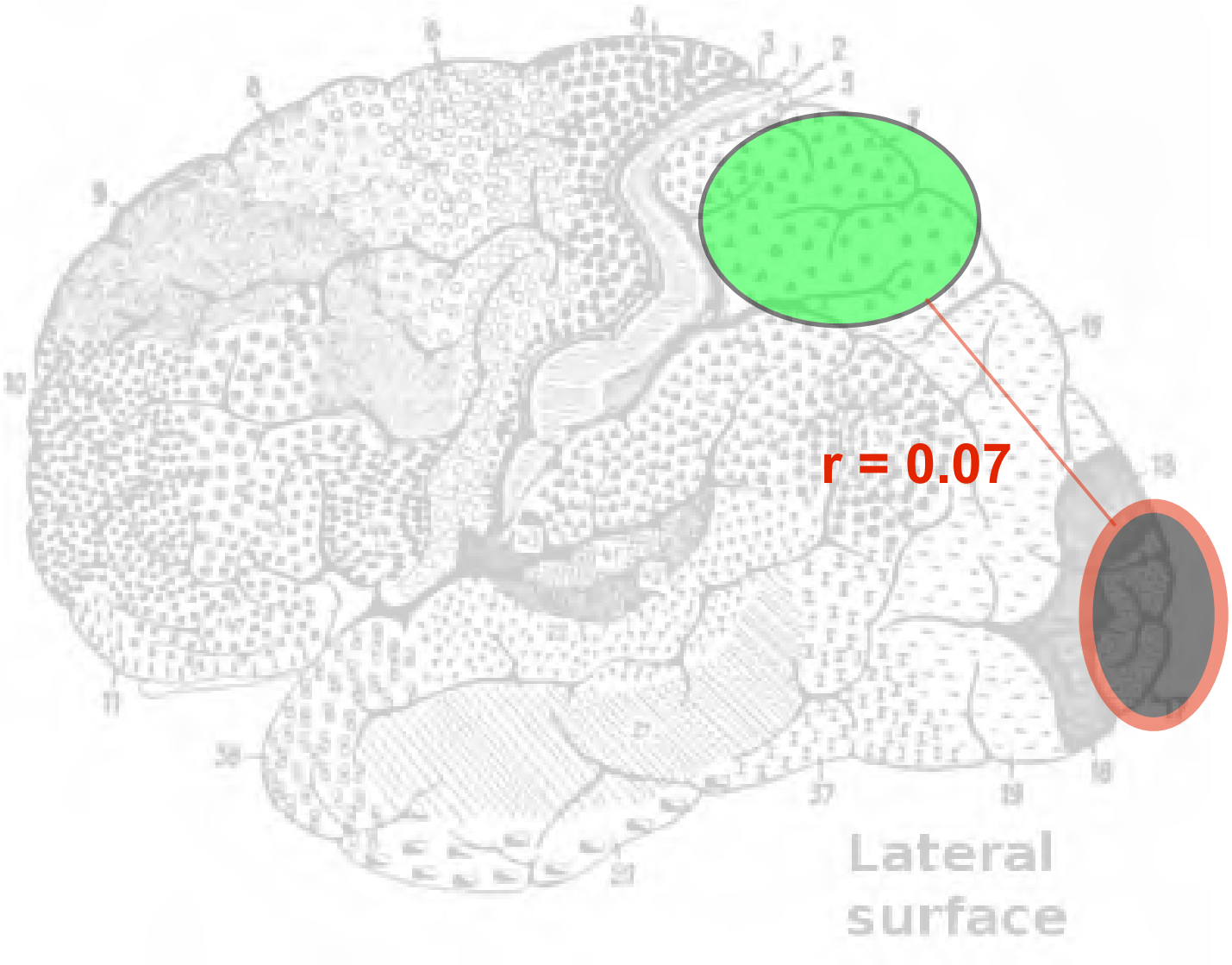

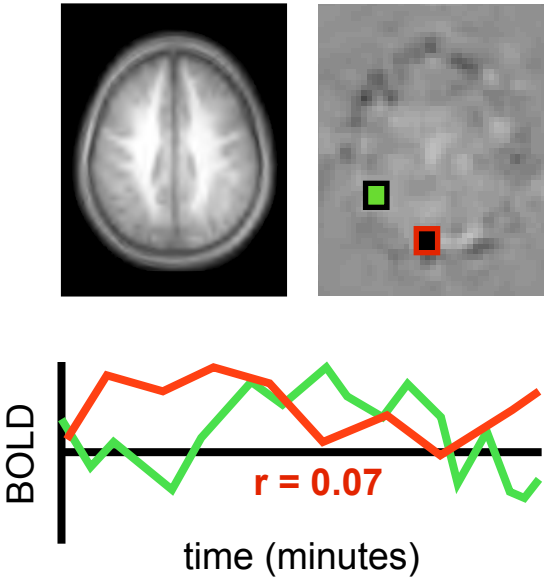

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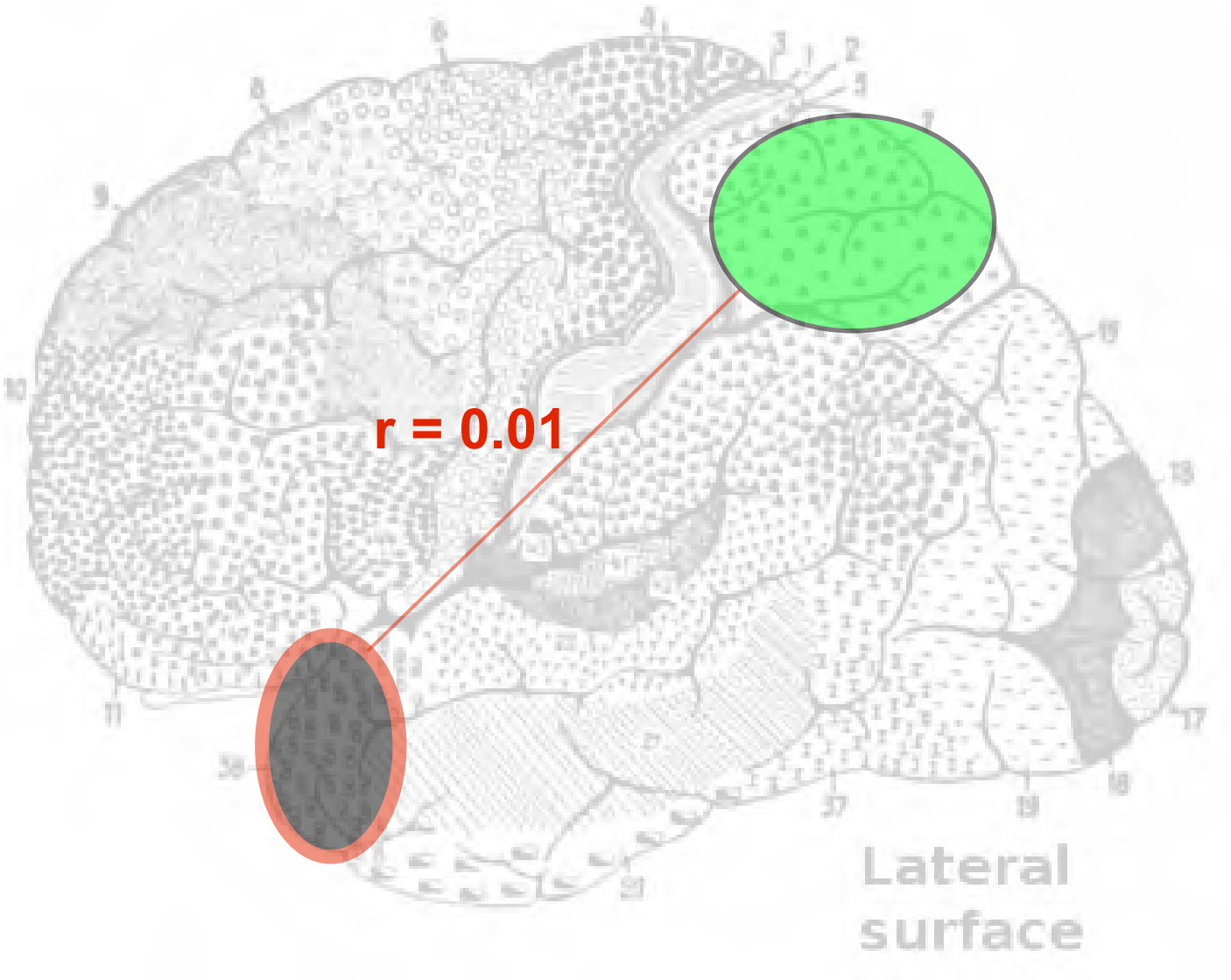

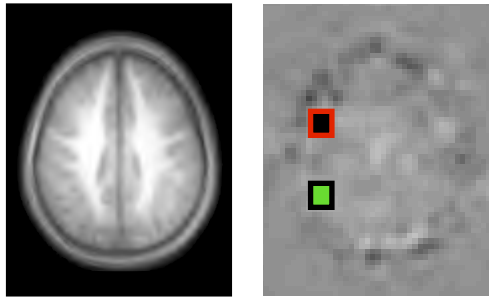

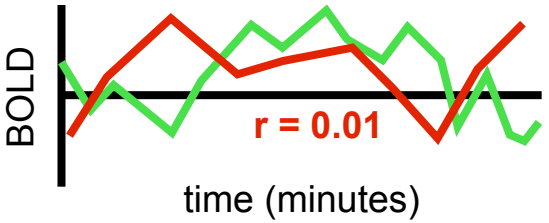

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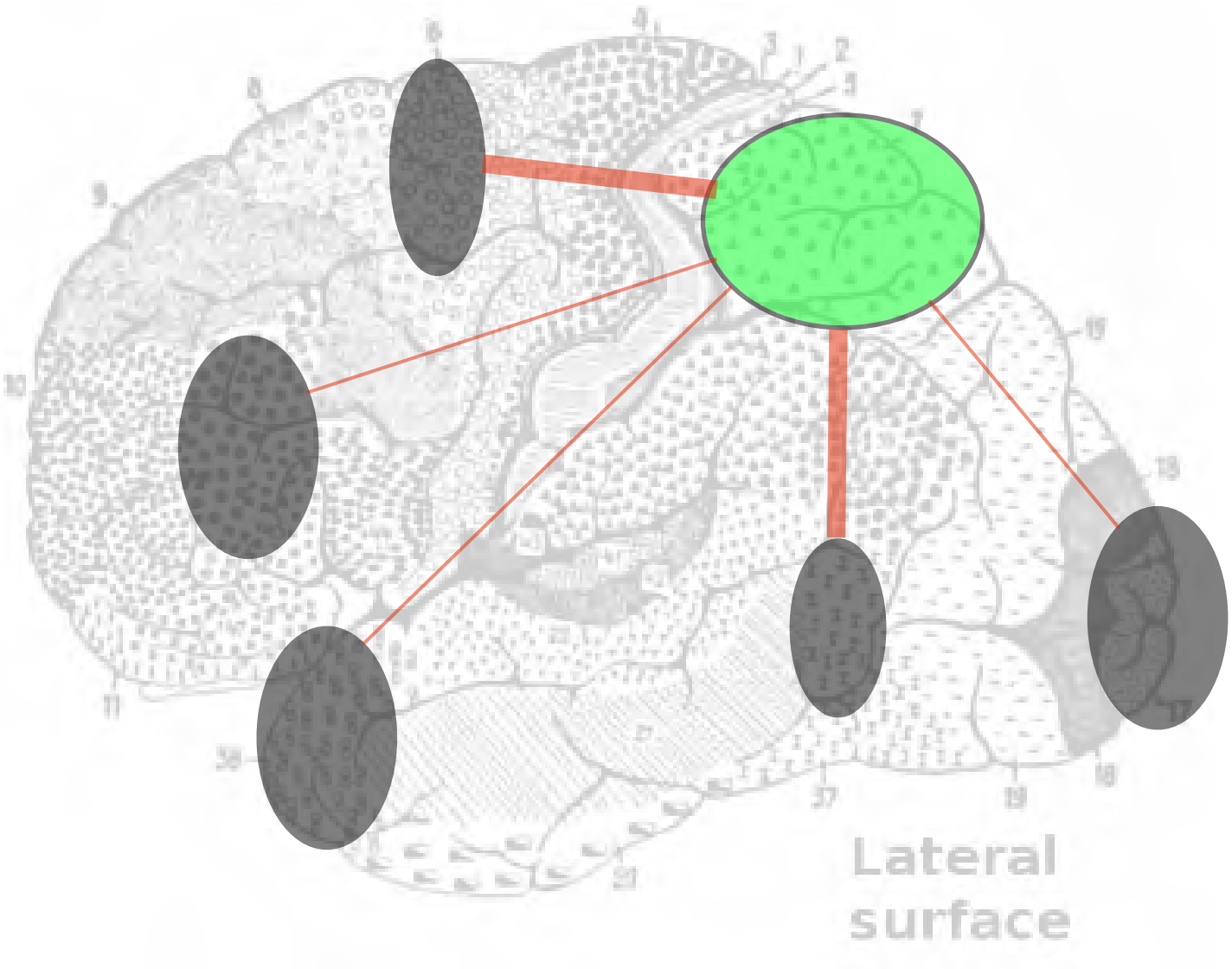

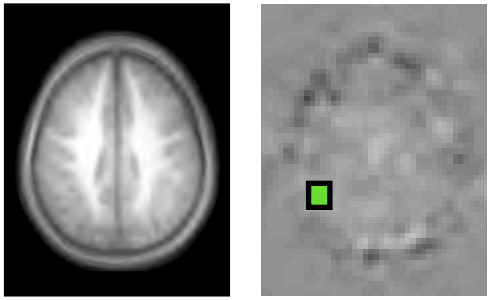

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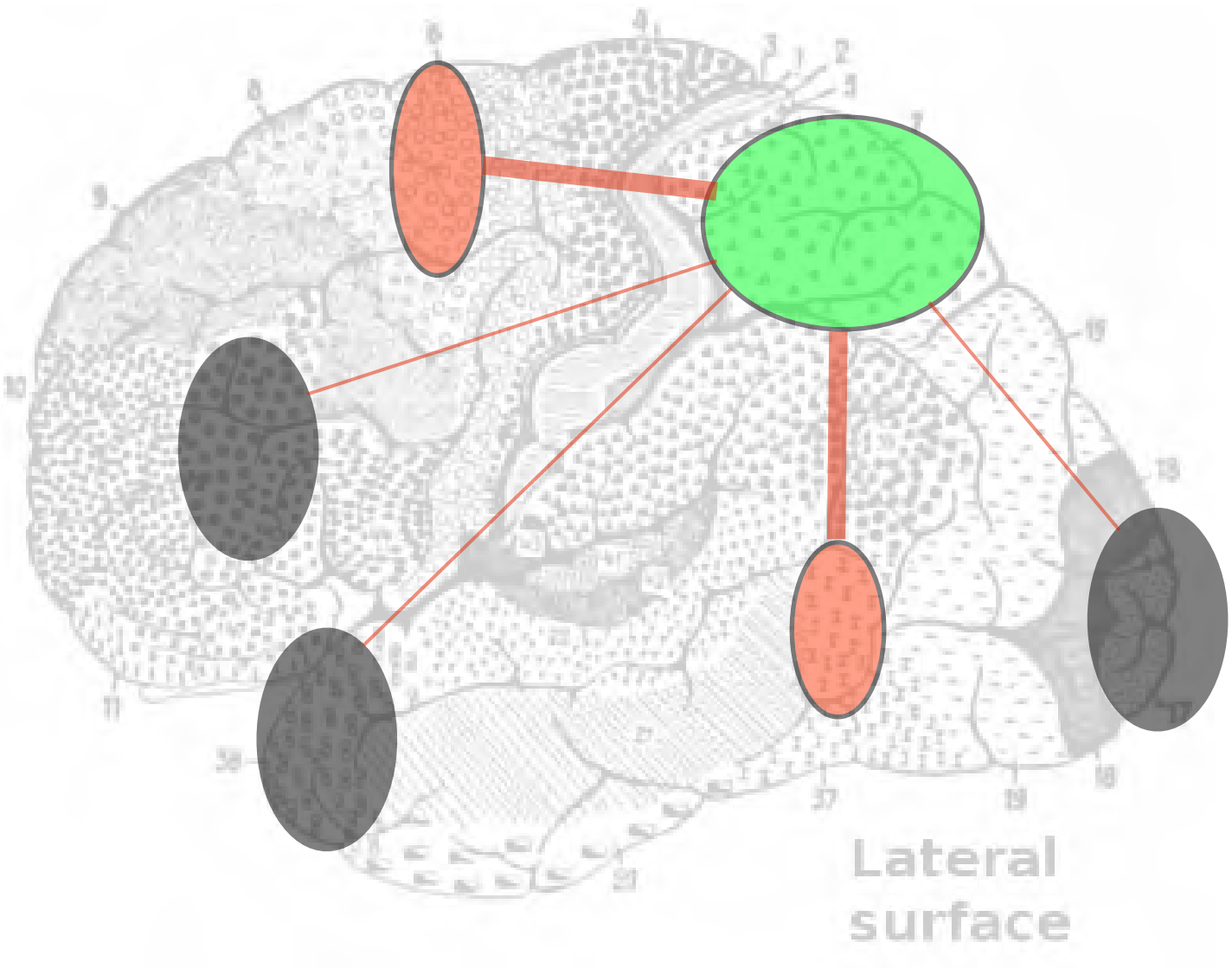
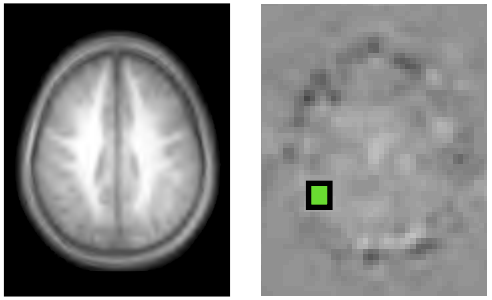
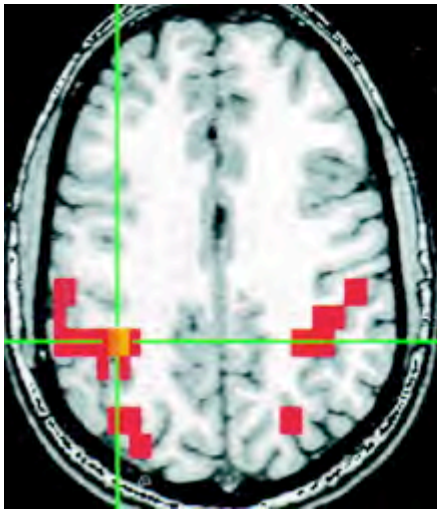
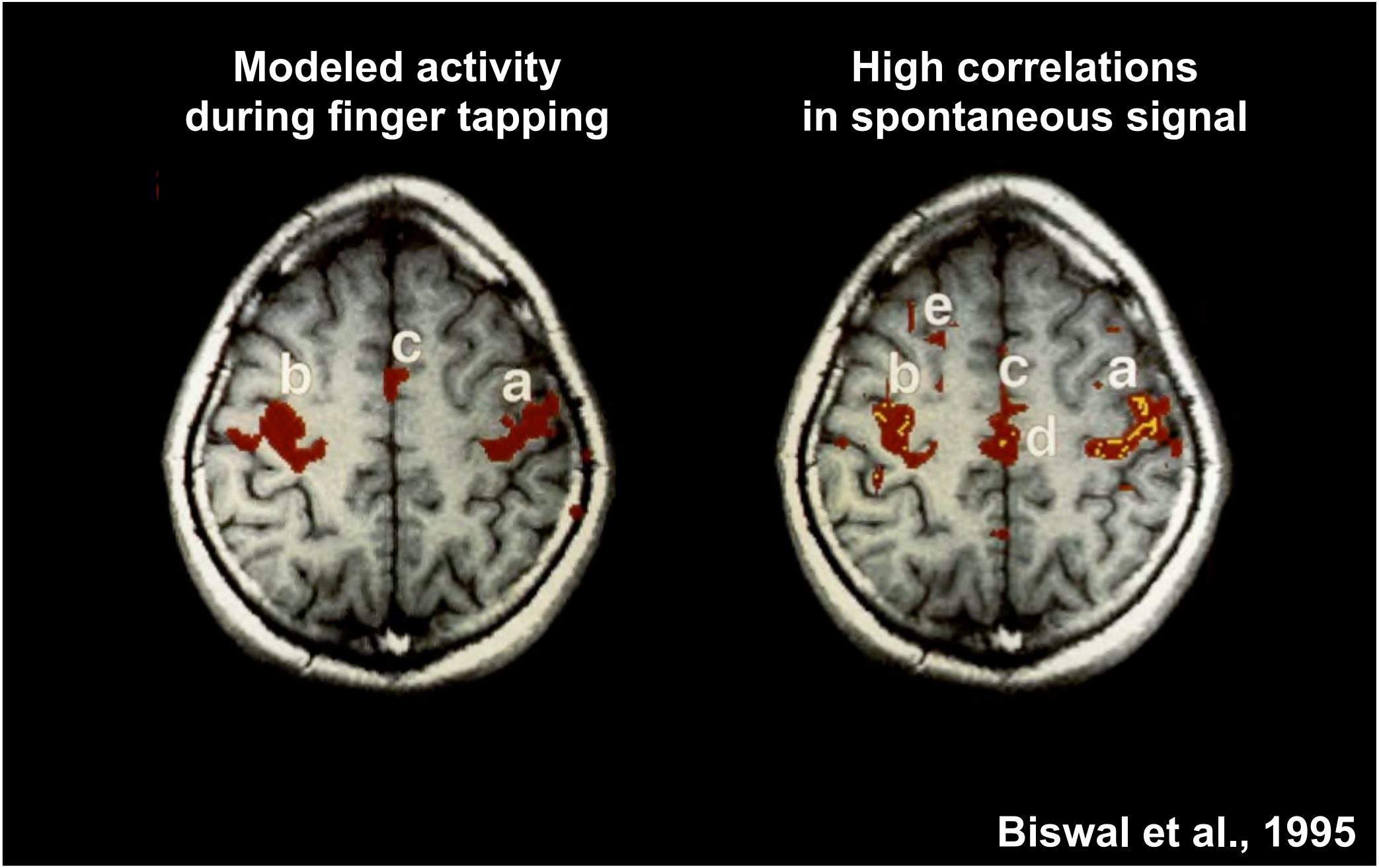






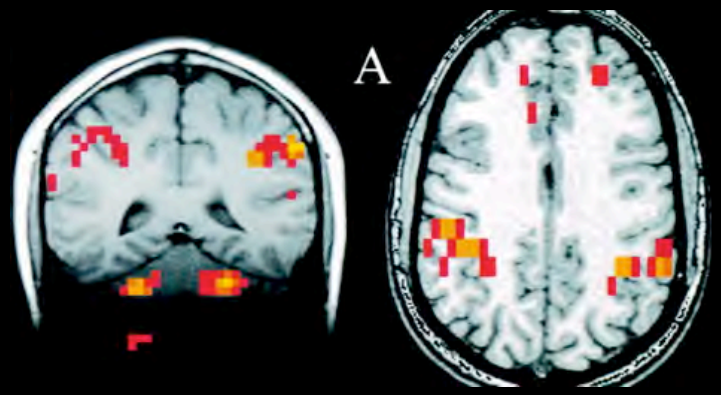
Resting state functional connectivity MRI



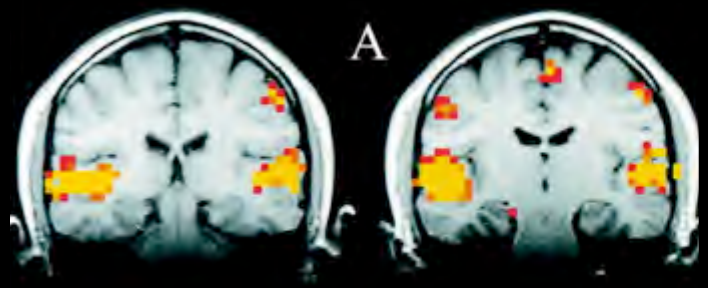
Resting state functional connectivity MRI

Task fMRI

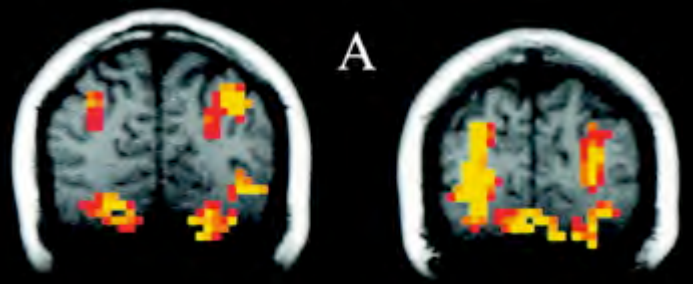
Push a button



Listen to story



Checkerboard



Lowe et al., 2000

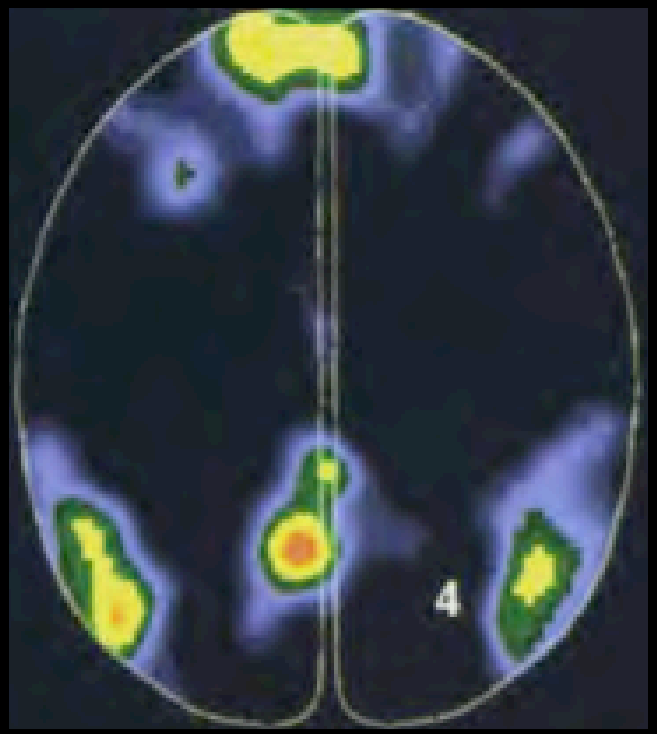
Resting state functional connectivity MRI

- These early studies established
  - Correlated signals present in many locations
    - Motor, visual, auditory, etc.
  - Unlikely due to artifact: cardiac, respiratory, etc.
  - Low frequencies (<0.08 Hz) contained most power
  - Spatial pattern of correlations recapitulated evoked activity

- Despite this, most neuroscientists were indifferent (at best)
  - “Rest” is uncontrolled, unspecified, unconstrained
  - fMRI signal seems likely to be dominated by noise

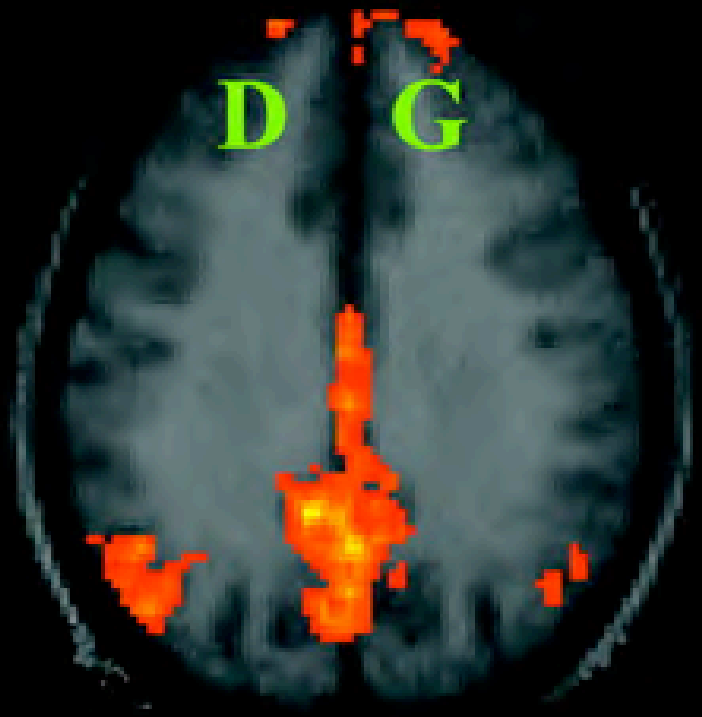
Resting state functional connectivity MRI

Task-induced deactivation in PET meta-analysis



Shulman et al., 1997

High correlations in spontaneous signal



Greicius et al., 2003

Resting state functional connectivity MRI

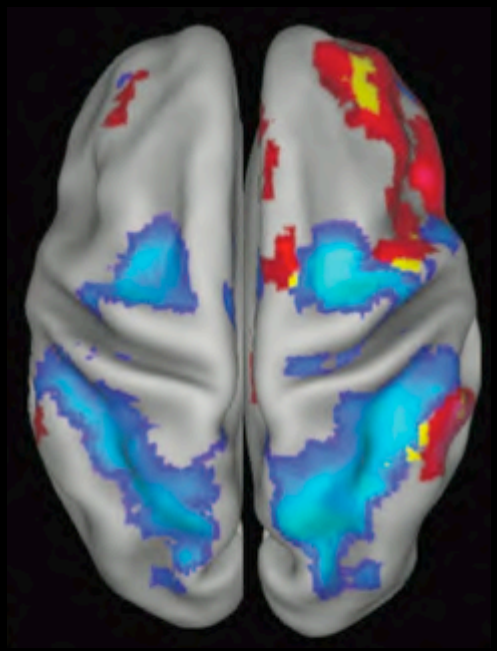
- This 2003 finding turned heads
- Followed by reports on correlations among
  - attention systems: Fox, 2006
  - executive control systems: Seeley, 2007; Dosenbach, 2007

- These reports recapitulated spatial patterns known from PET or task fMRI. They were essentially confirmatory, building confidence in the technique.

- Soon, though, fundamentally new knowledge emerged.

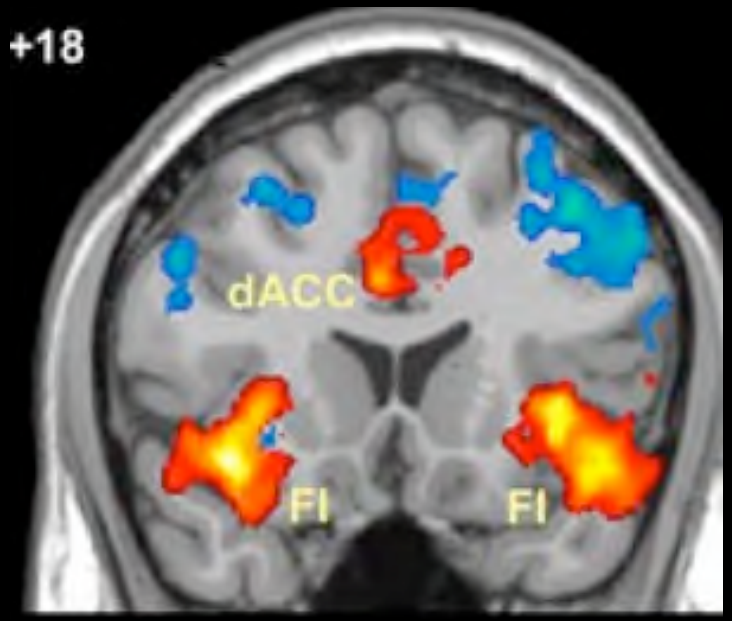
Resting state functional connectivity MRI

Dorsal attention system



Fox et al., 2006

Salience system



Seeley et al., 2007

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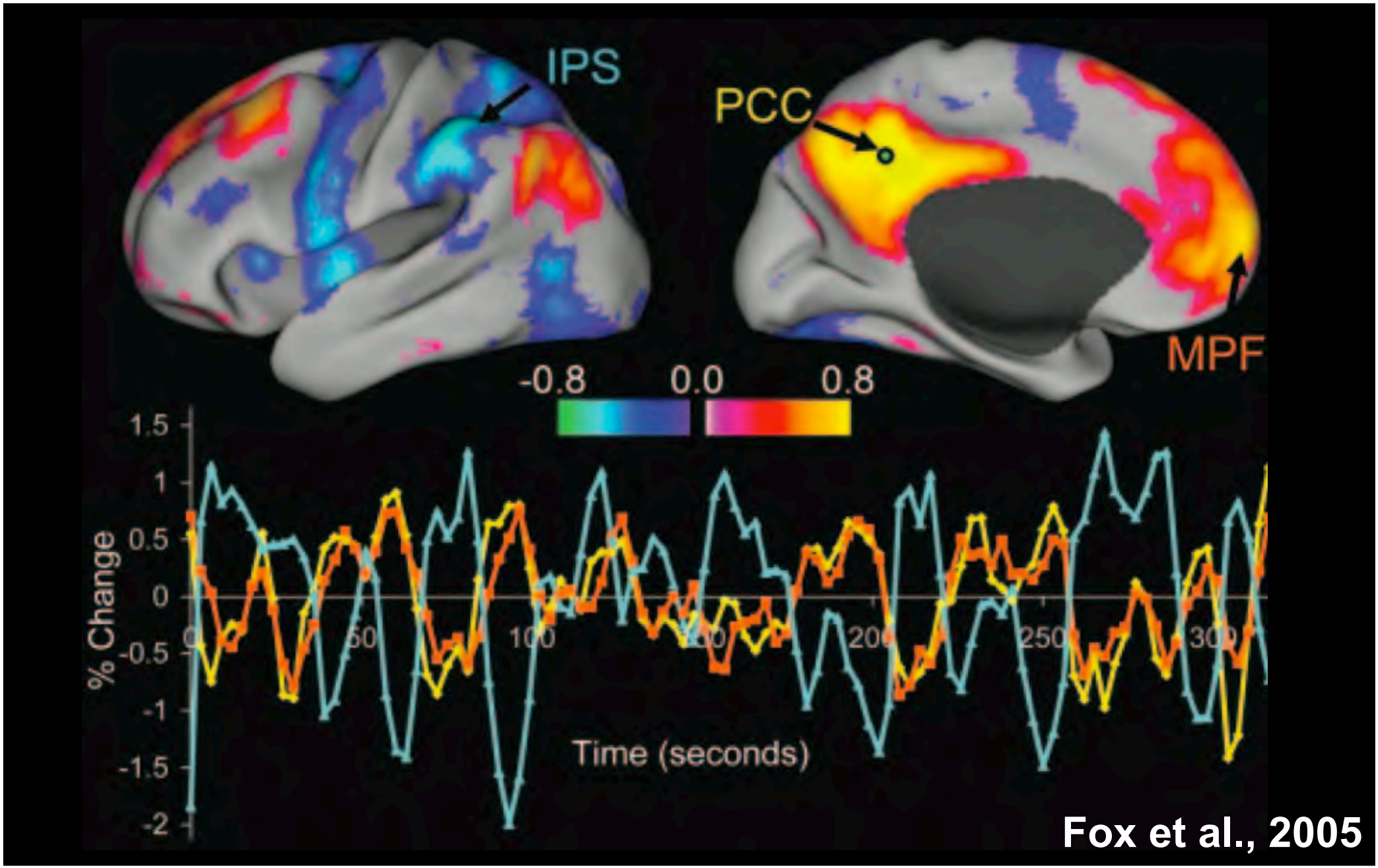


Fox et al., 2005

Resting state functional connectivity MRI

- Default regions deactivate during most tasks (known)
- Attention regions activate during most tasks (known)
- In the absence of tasks, ongoing signals in these two classes of brain region are anti-correlated (not known)

- RSFC began to move beyond confirmatory analyses.

Resting state functional connectivity MRI

- Does RSFC reflect experience? Individual characteristics?
- How does RSFC relate to ongoing behavior?
- What neural processes are reflected in RSFC?
- Can RSFC discriminate pathology?
- How does RSFC relate to anatomical connectivity?
- Can RSFC be used in ways analagous to tracers?
- We have gone from known systems to finding correlations between those regions. Can we go in reverse? Learn new functional systems from the patterns in RSFC?

Resting state functional connectivity MRI

- RSFC now studied in macaques, mice, rats, pigeons
- RSFC patterns are similar in light sleep, and light anesthesia
- RSFC patterns are recapitulated by ECoG and LFPs
  - high gamma frequencies in particular
- RSFC modulated by experience, scales with behavior
  - perceptual learning, motor learning, cognitive training
- RSFC patterns persist during task performance
- RSFC reflects mono- *and poly-synaptic* connectivity
  - e.g., cerebellar RSFC, eccentric V1 bilaterality in macaques

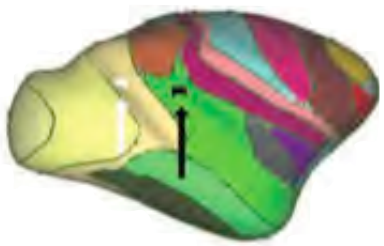
Resting state functional connectivity MRI

- RSFC
  - appears to be evolutionarily conserved
  - not strongly reflective of conscious thought
  - is energetically costly
  - has amplitudes similar/greater than evoked activity
  - reflects anatomy and function

- “Default mode” patterns reported in macaques, mice...

Resting state functional connectivity MRI

Brodman 1905
macaque, 28 areas/hemi



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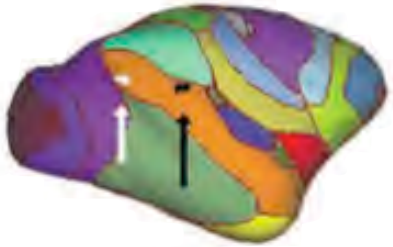

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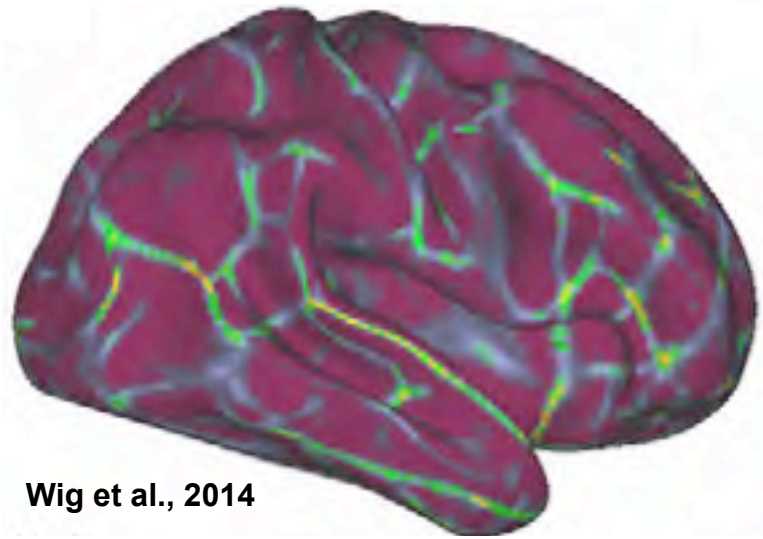
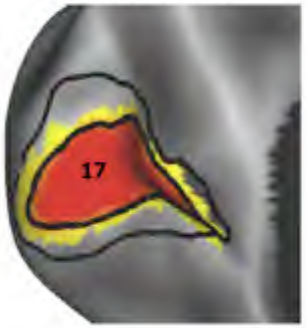


Wig et al., 2014

Area 17 – Cytoarchitecture (Probabilistic)



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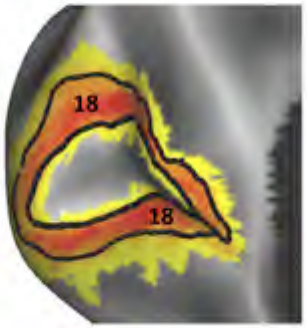
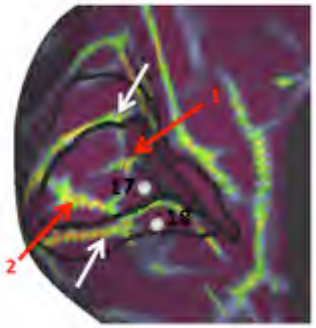


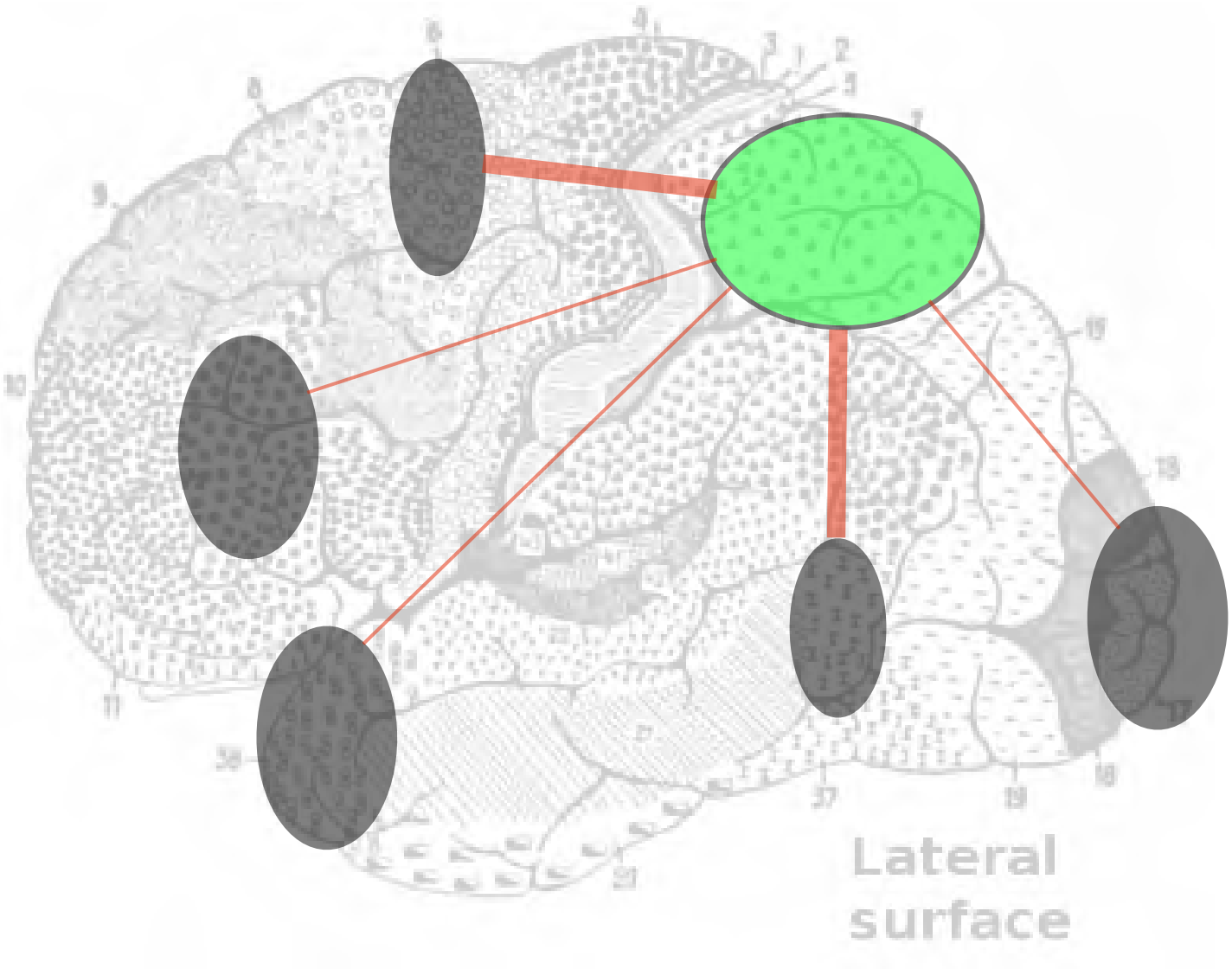
RSFC Boundaries

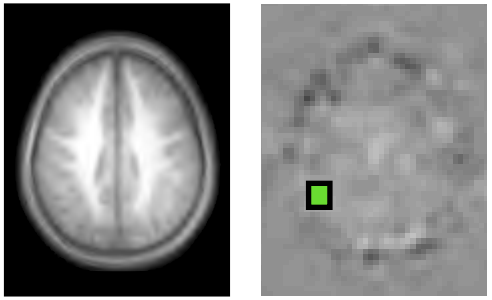


A specific set of RSFC analyses

- Now, we will follow a specific line of results... my own
- Building network representations of the healthy adult brain
- Deriving properties of brain locations
- Making predictions about the effects of lesions
- Testing those predictions

Resting state functional connectivity MRI





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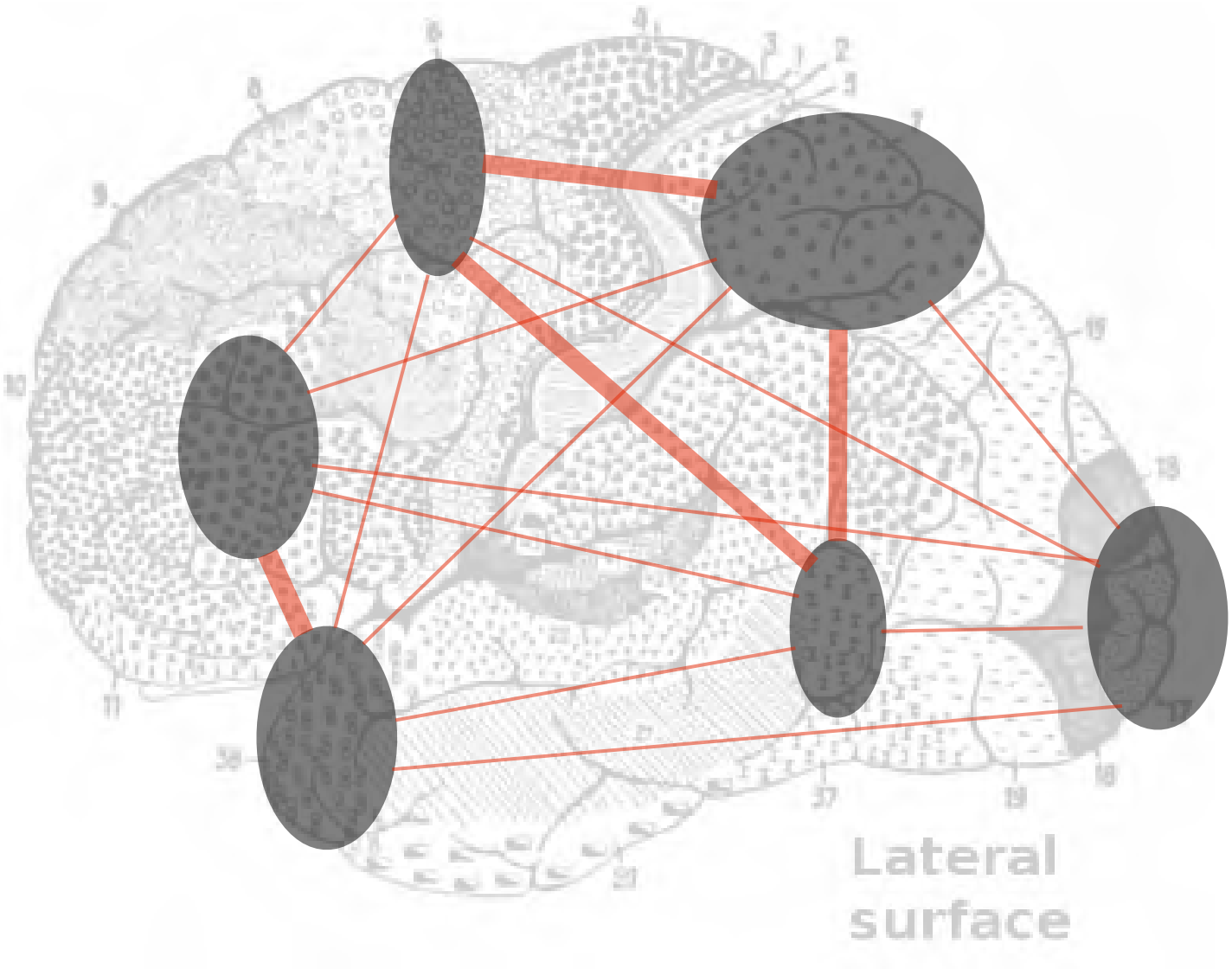
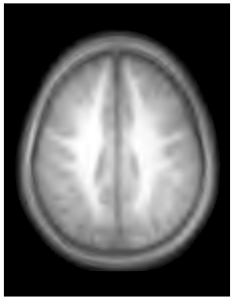
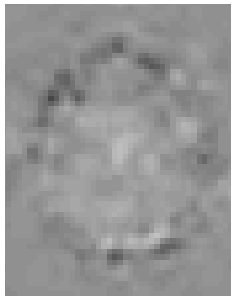
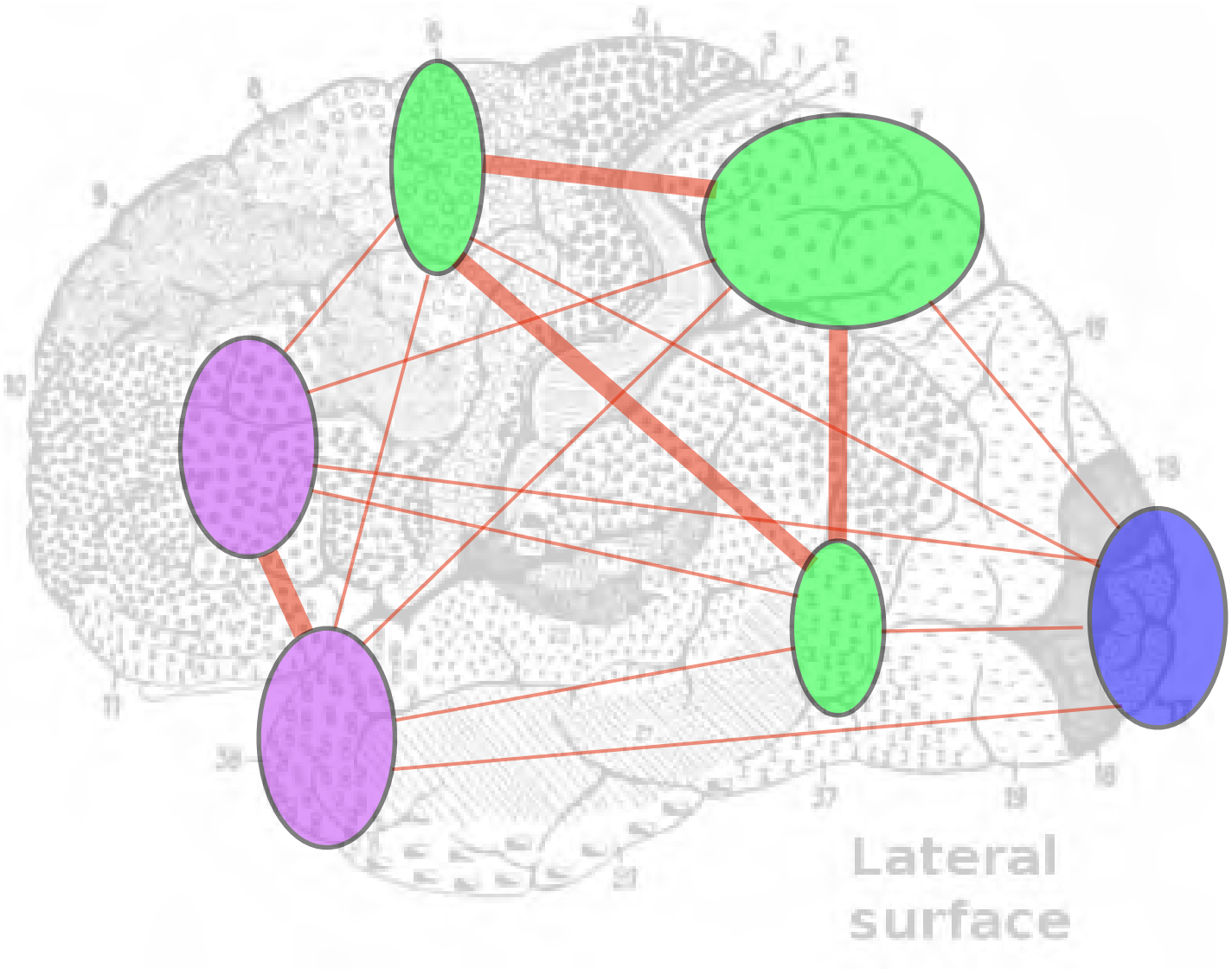
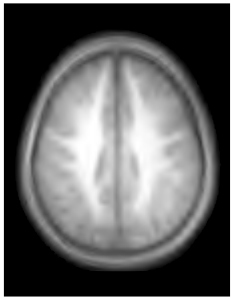


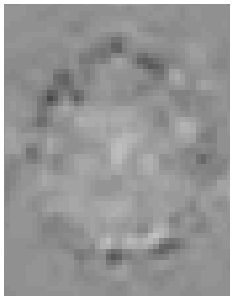




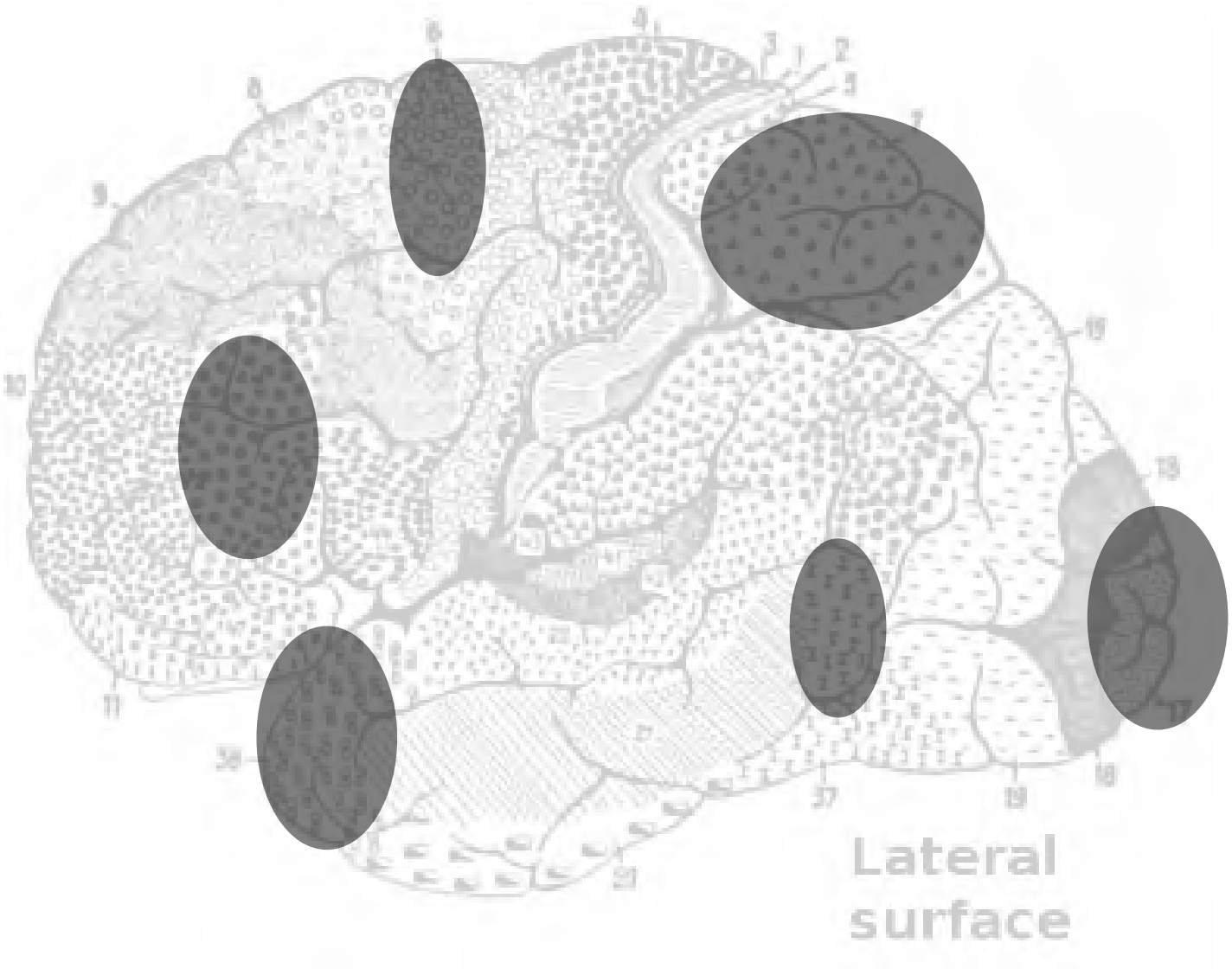
Resting state functional connectivity MRI

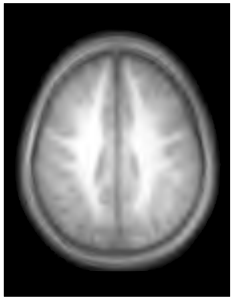


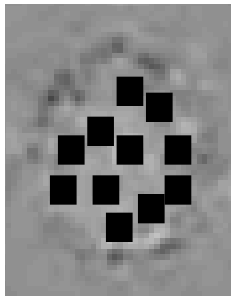




Resting state functional connectivity MRI







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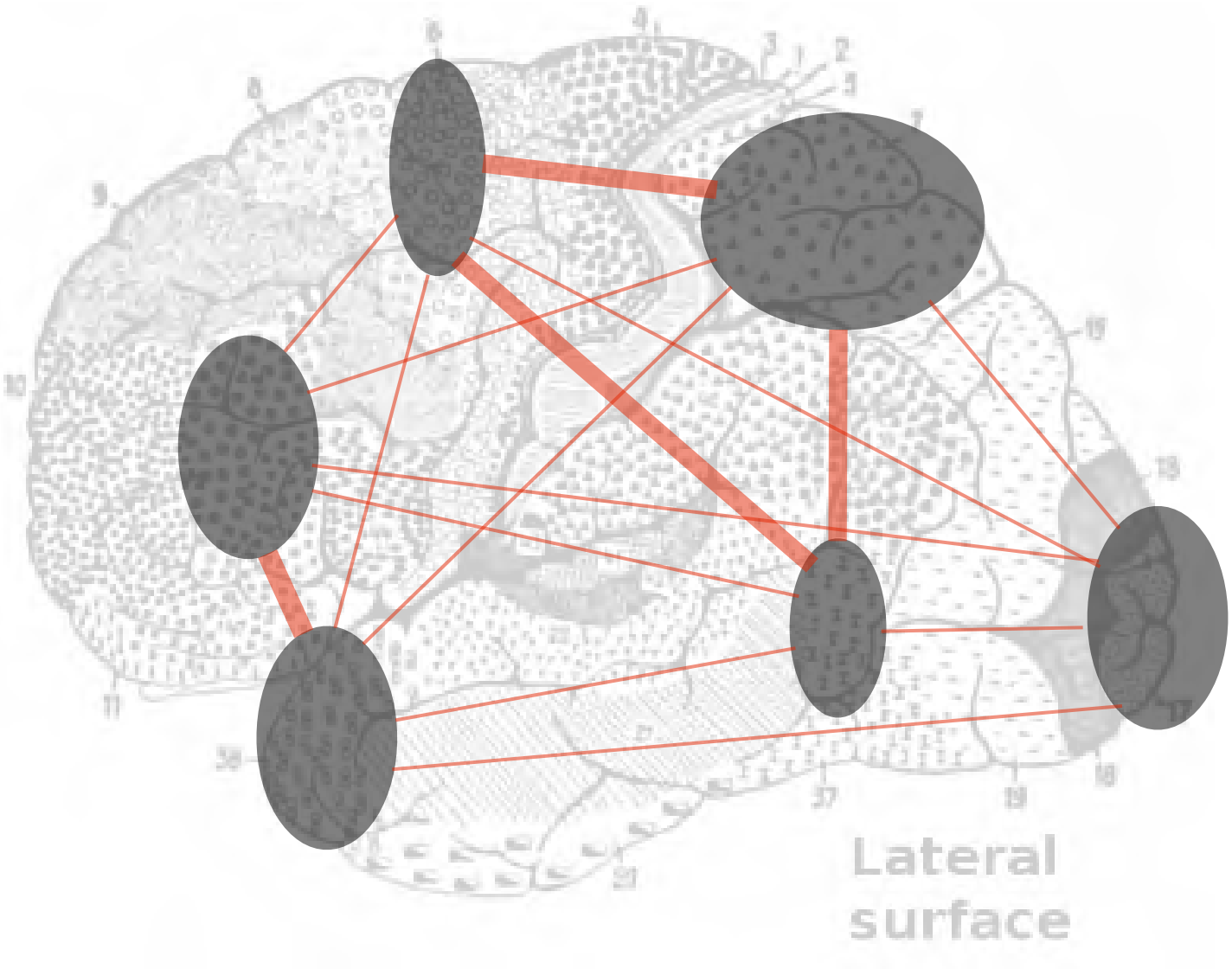

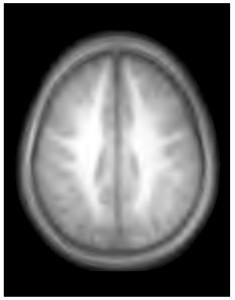

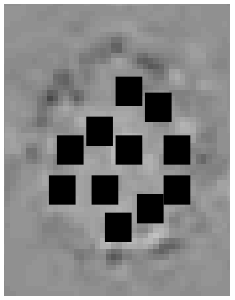

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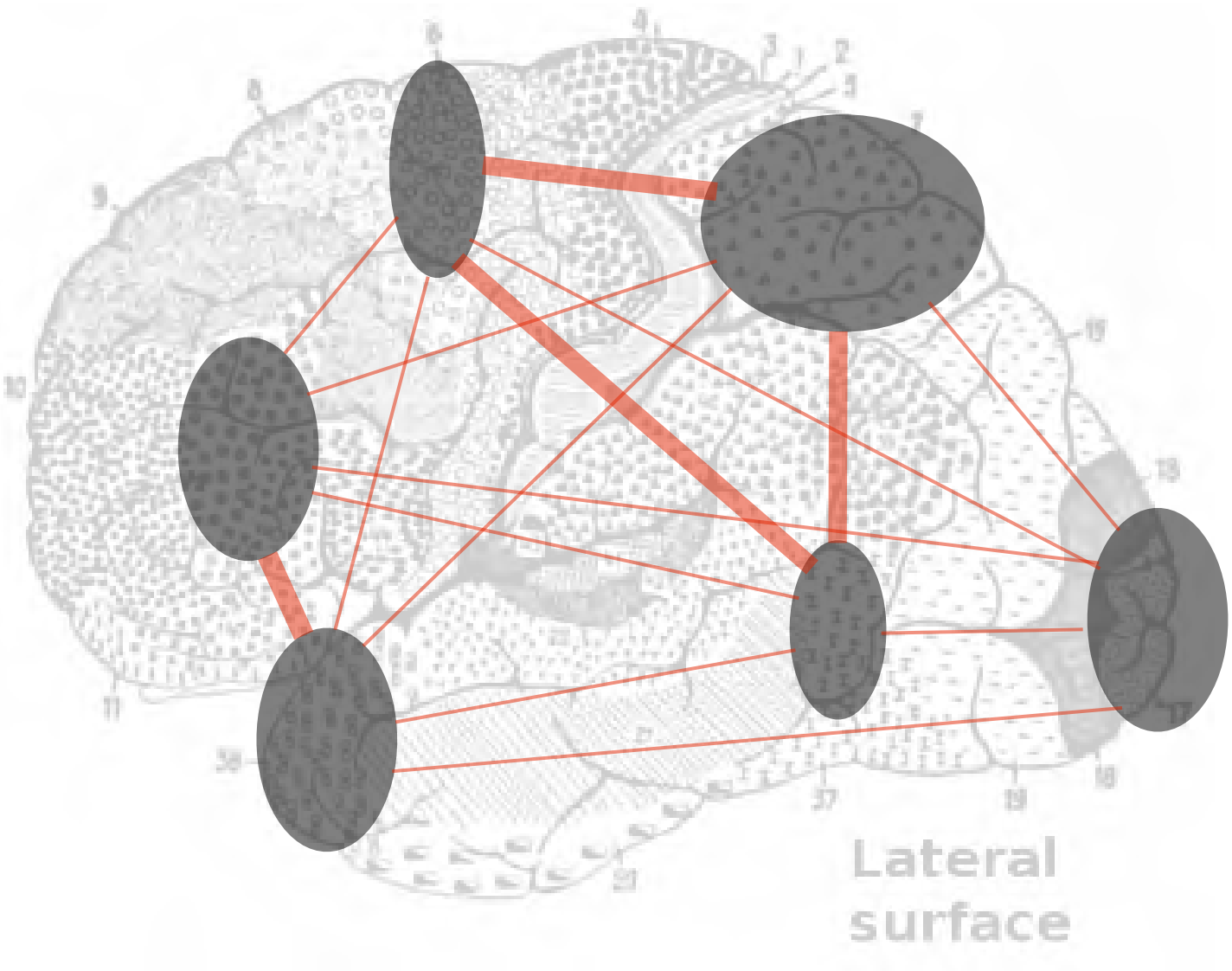

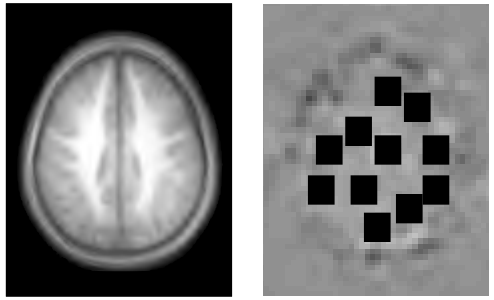

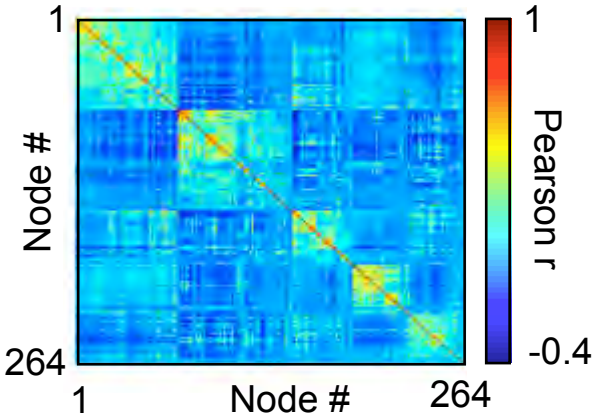

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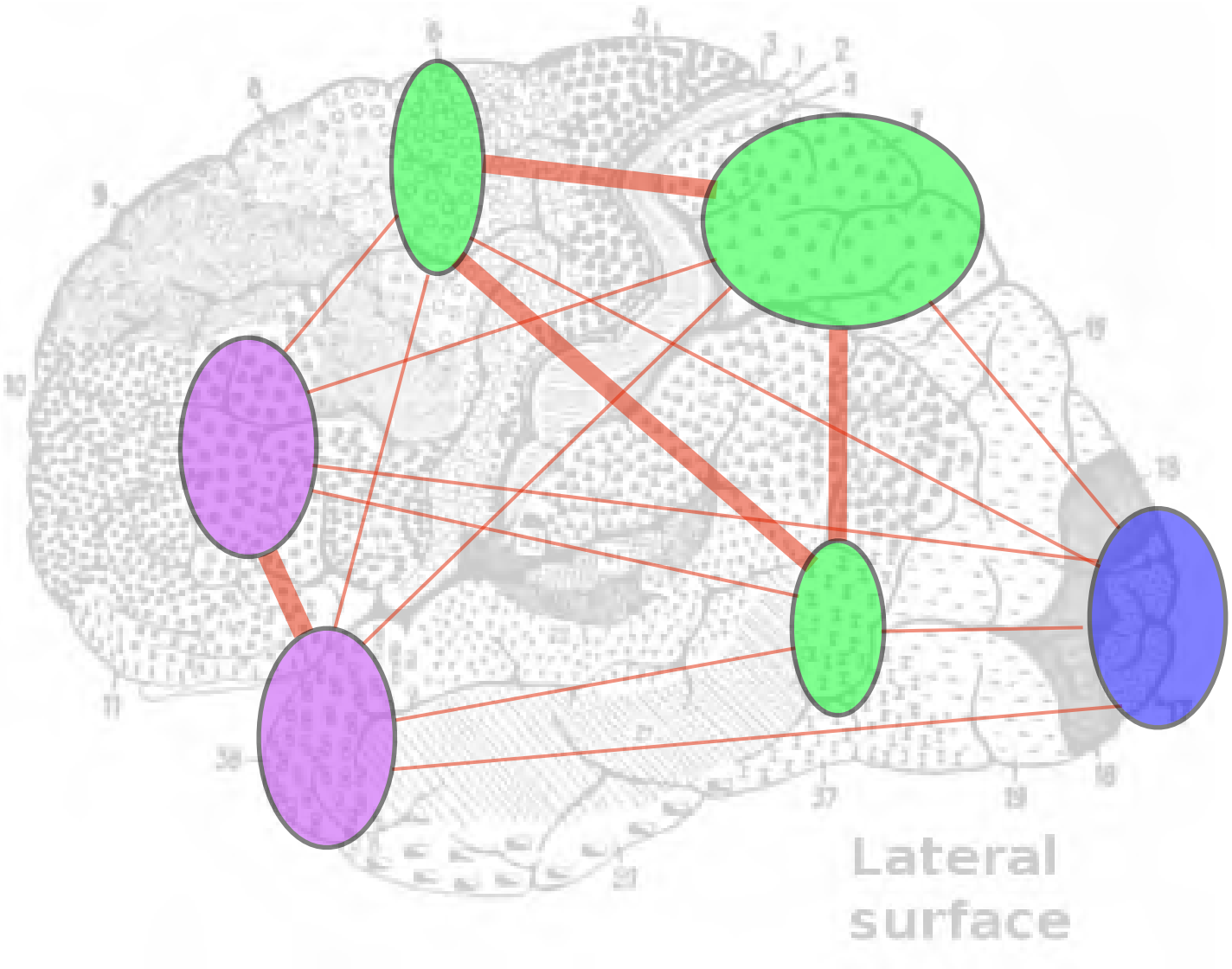

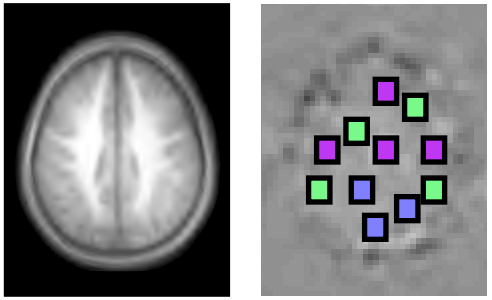

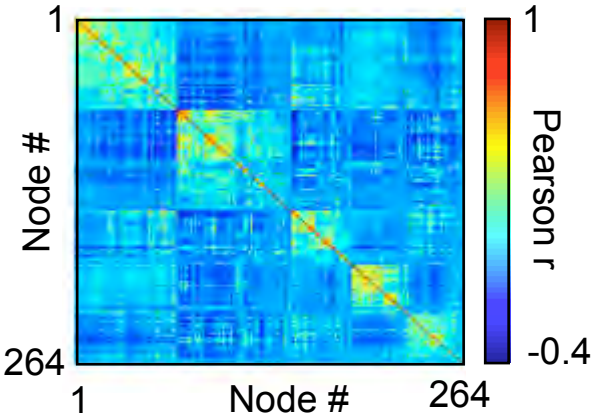

A theoretical challenge: defining networks

- Network analyses are just math
- A network is just nodes and edges (between nodes)
- Network definition <u>strongly</u> influences network properties
- If your network is well-defined
  - The math will work
  - Network properties hopefully represent the system
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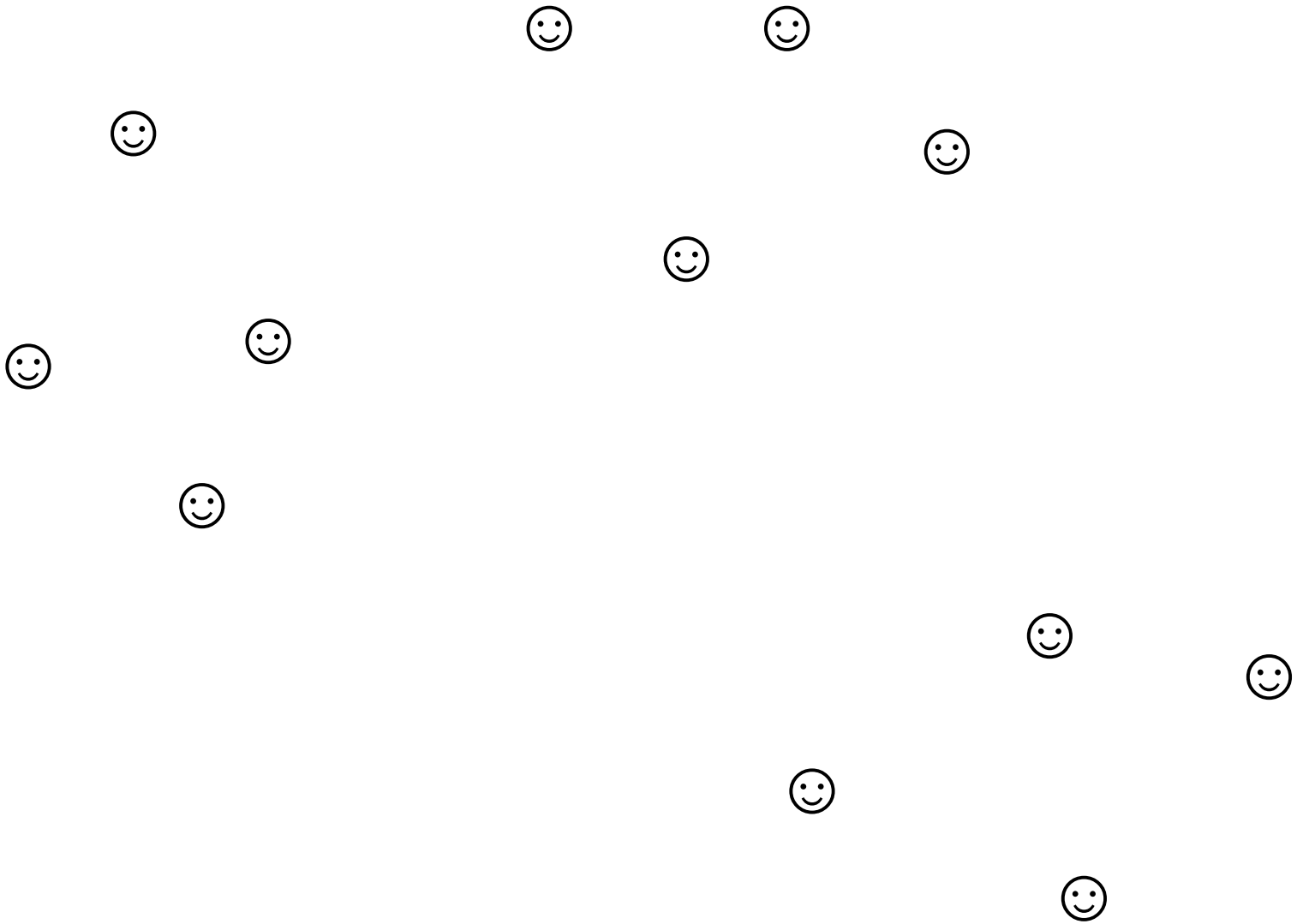
A theoretical challenge: defining networks



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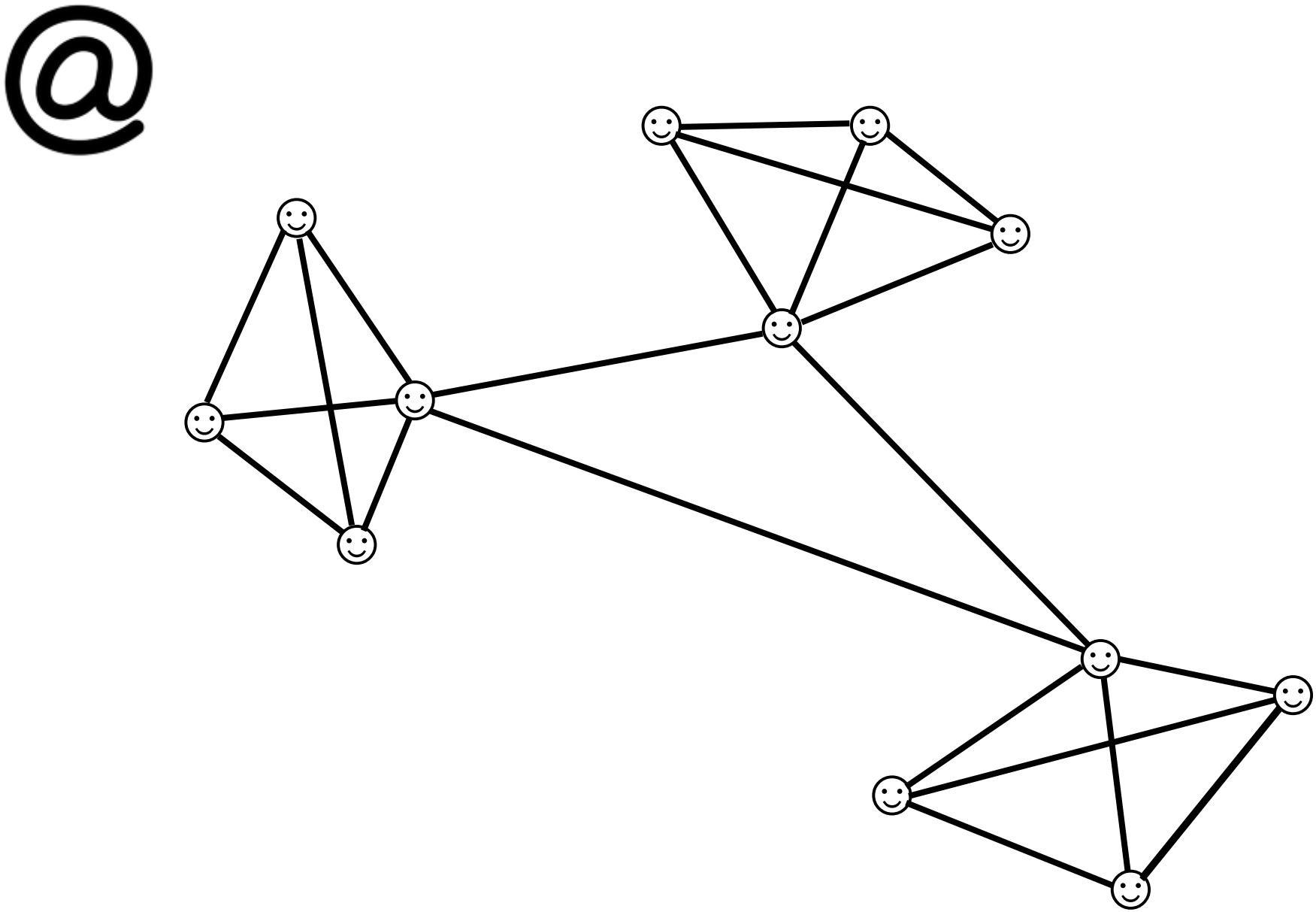

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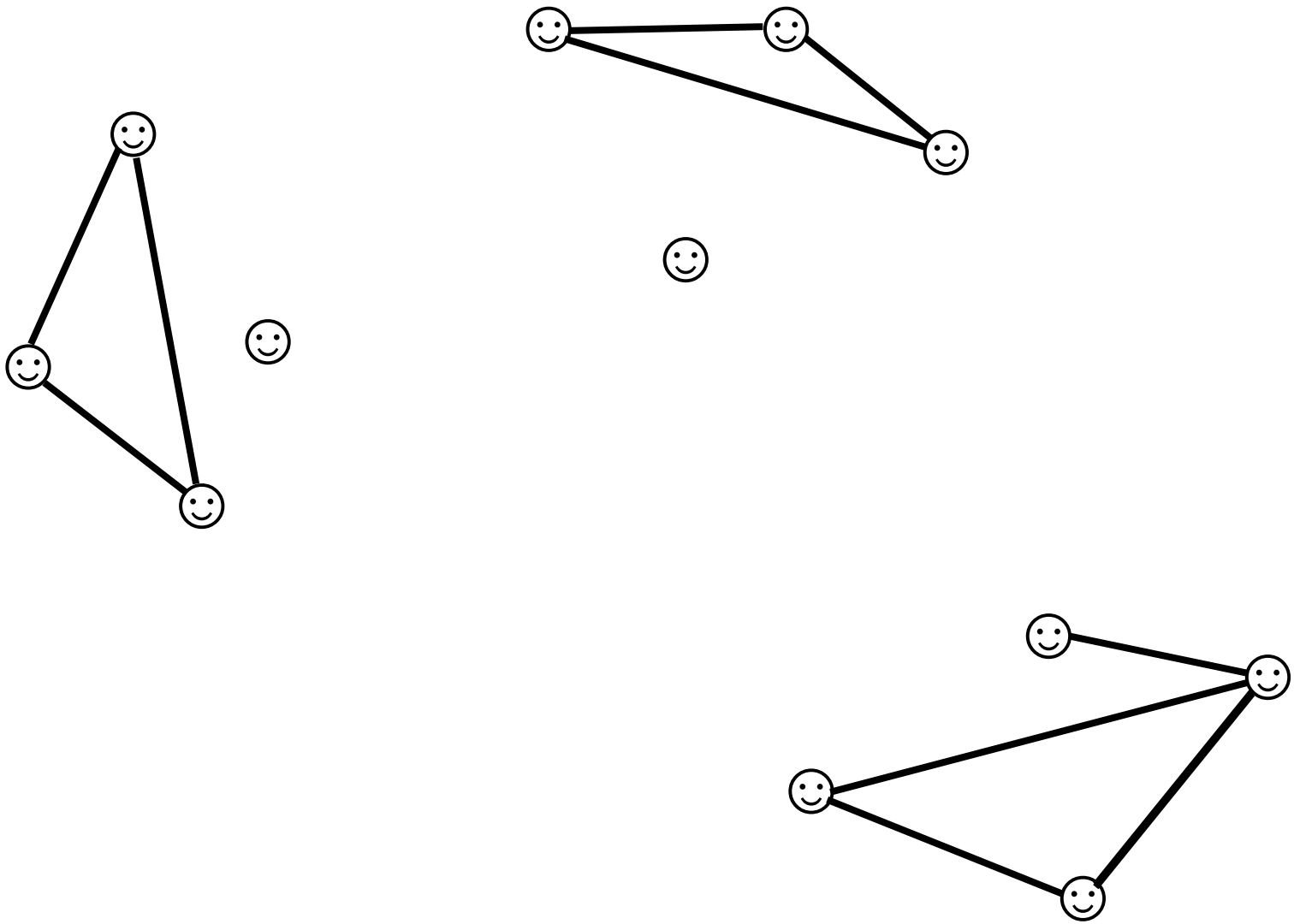

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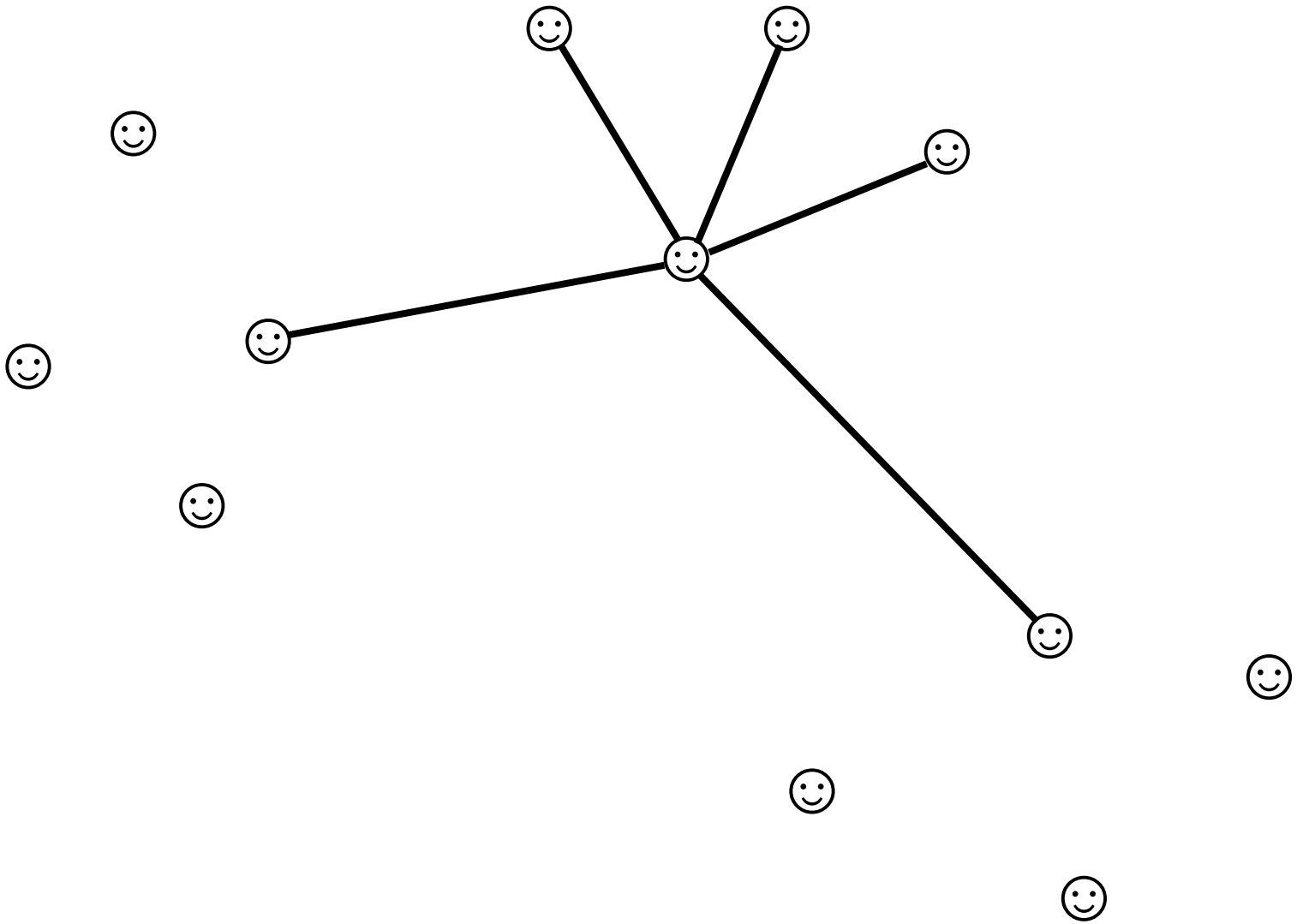

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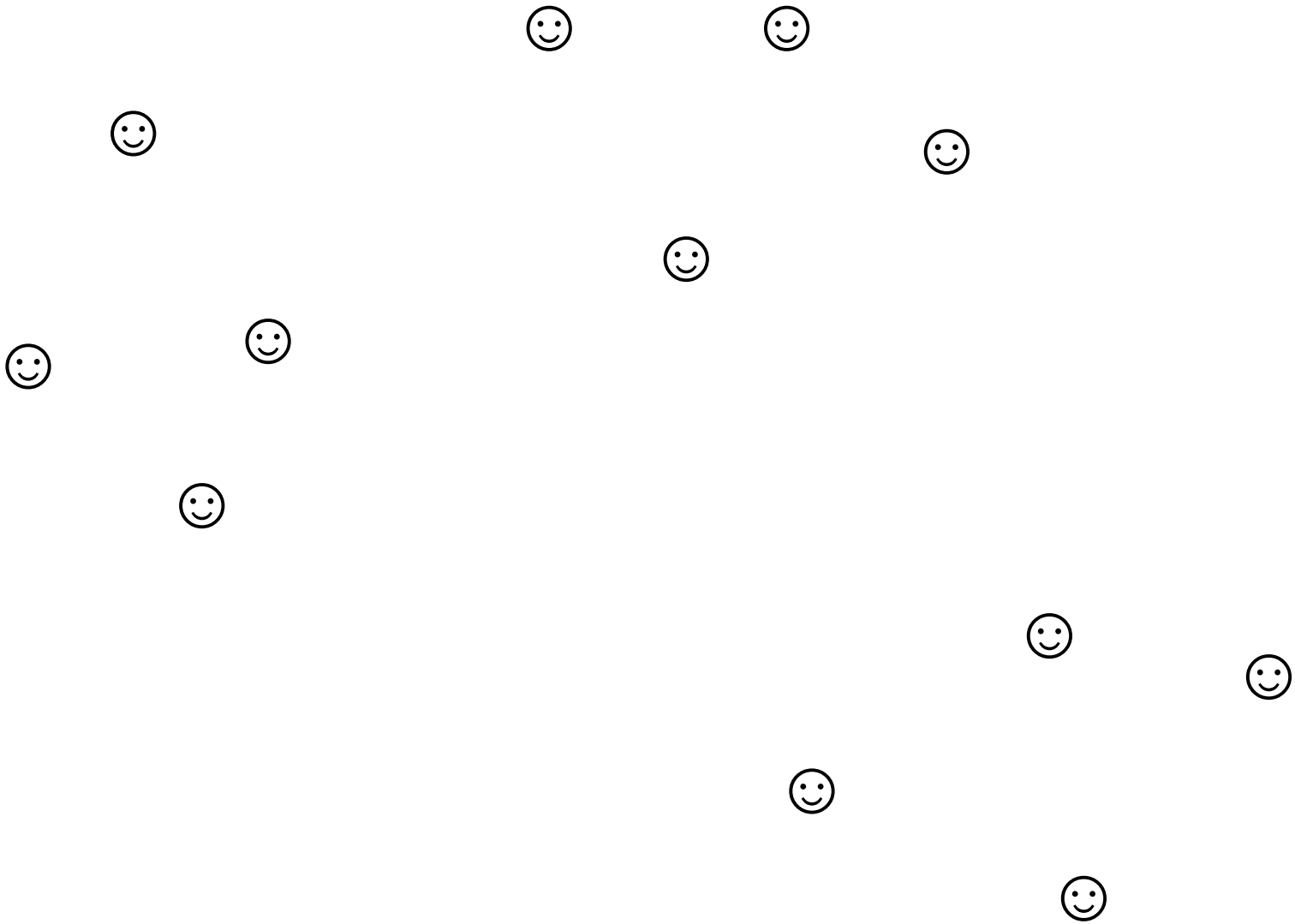

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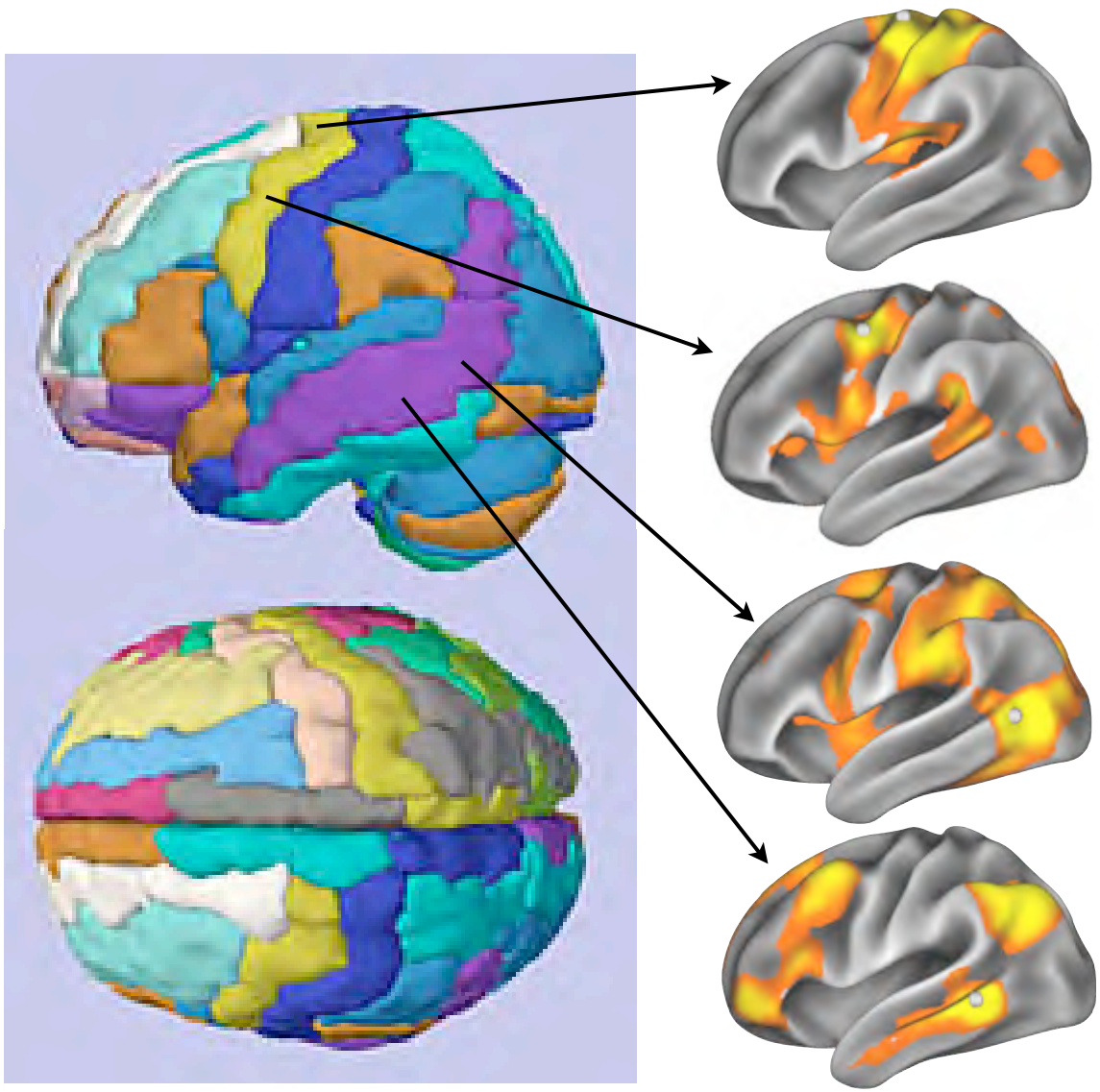
A theoretical challenge: defining networks

AAL atlas **Seed maps**

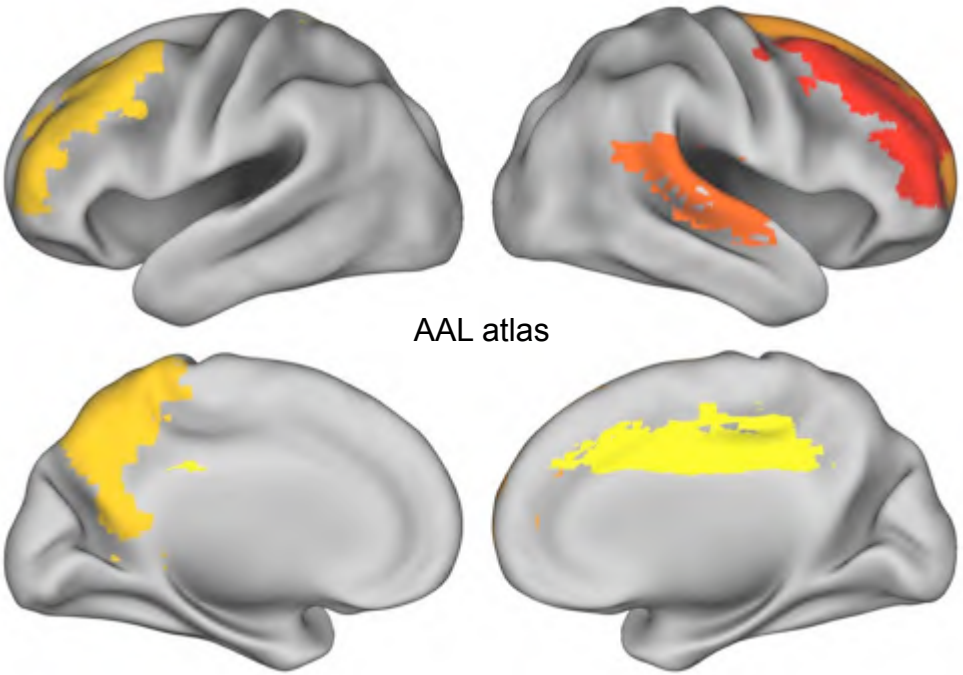


"The most striking result [of our study] was that the use of functionally inaccurate ROIs (when defining the network nodes and extracting their associated timeseries) is extremely damaging to network estimation; hence, results derived from inappropriate ROI definition (such as via structural atlases) should be regarded with great caution."

-Stephen Smith et al., 2011

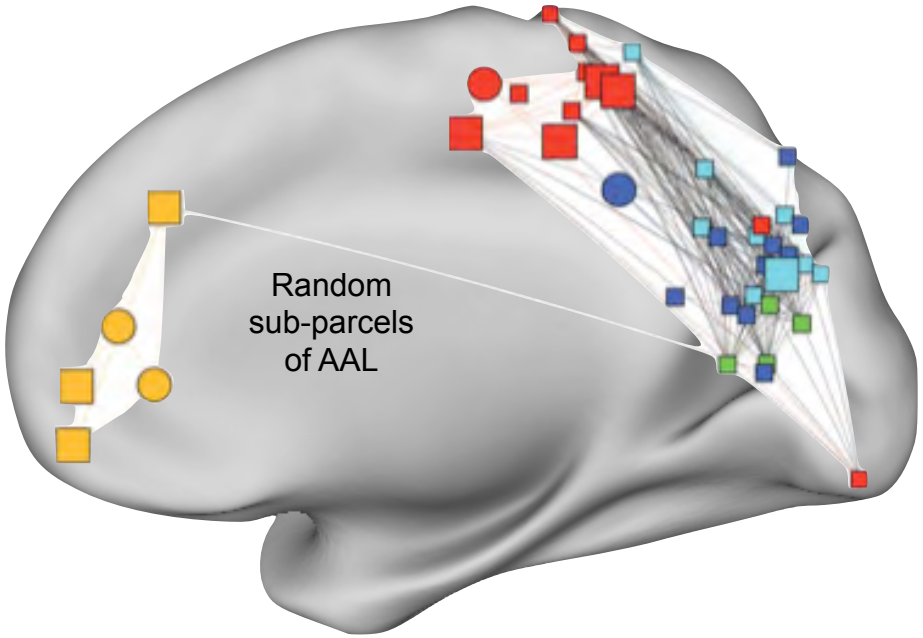
A theoretical challenge: defining networks

Meunier et al., 2009, NI



5/90 ROIs “connector” hubs by high within-module degree and high PC

Meunier et al., 2010 Front. Neurosci.



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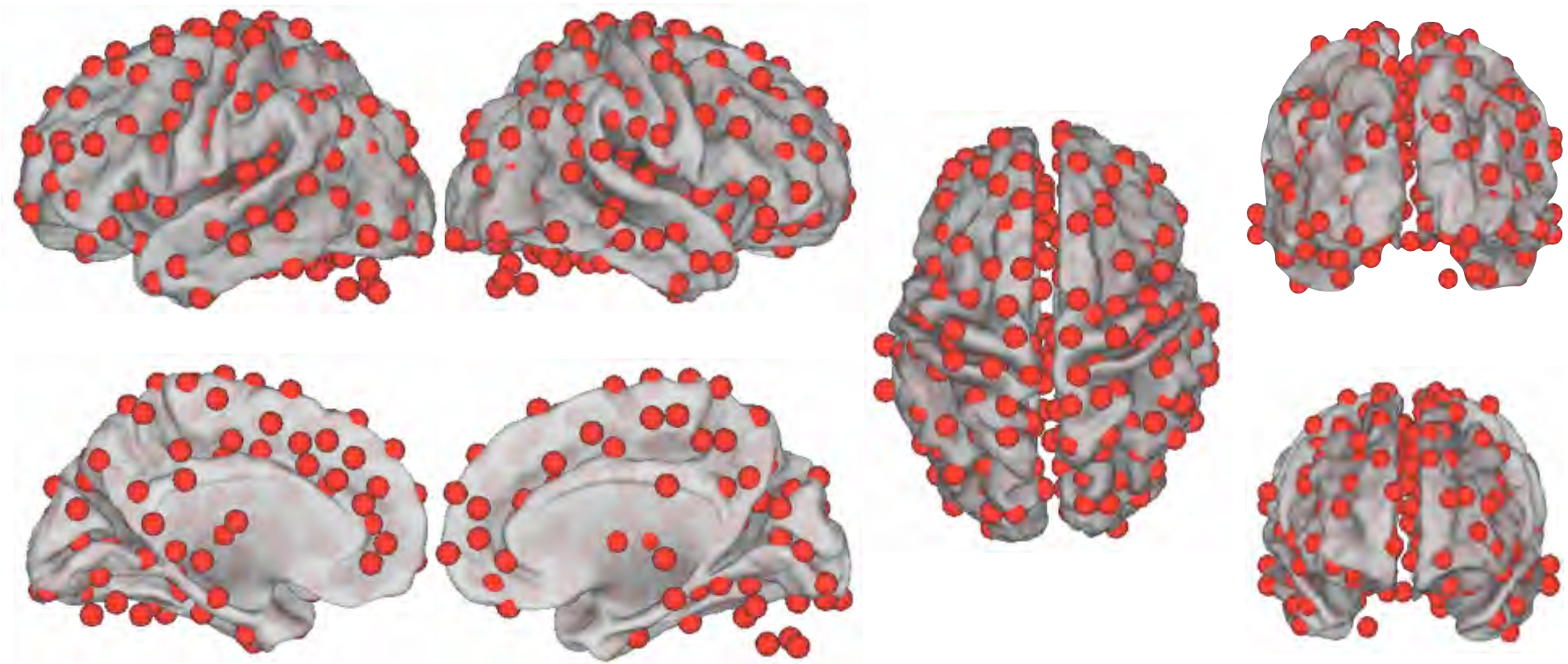
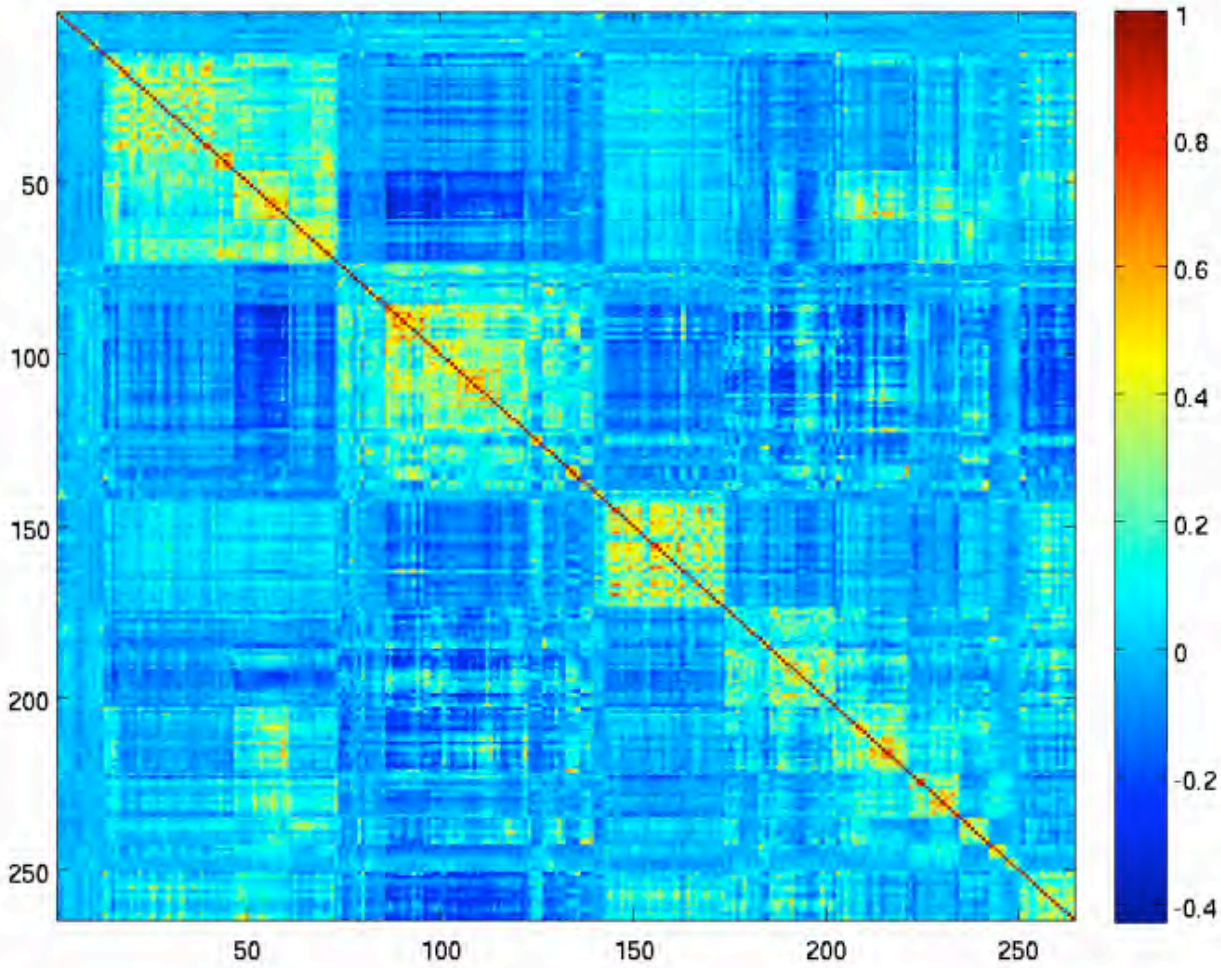
A theoretical challenge: defining networks

264 ROIs, our best guess for area/nucleus coordinates
(from task fMRI, also from fc-Mapping)



Network modules

Pearson correlation, 52 healthy young adults



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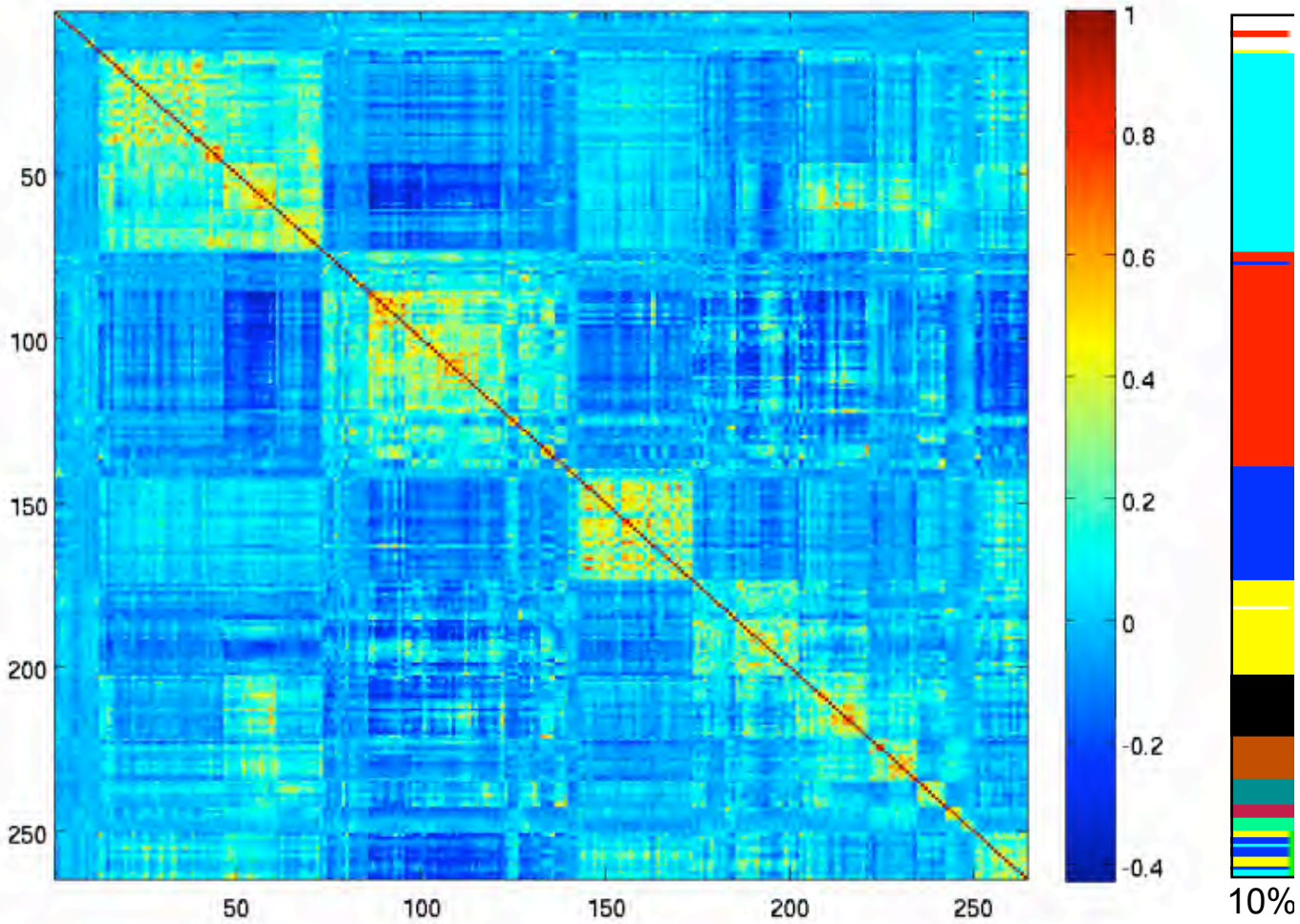
Infomap algorithm



Edge density

Network modules

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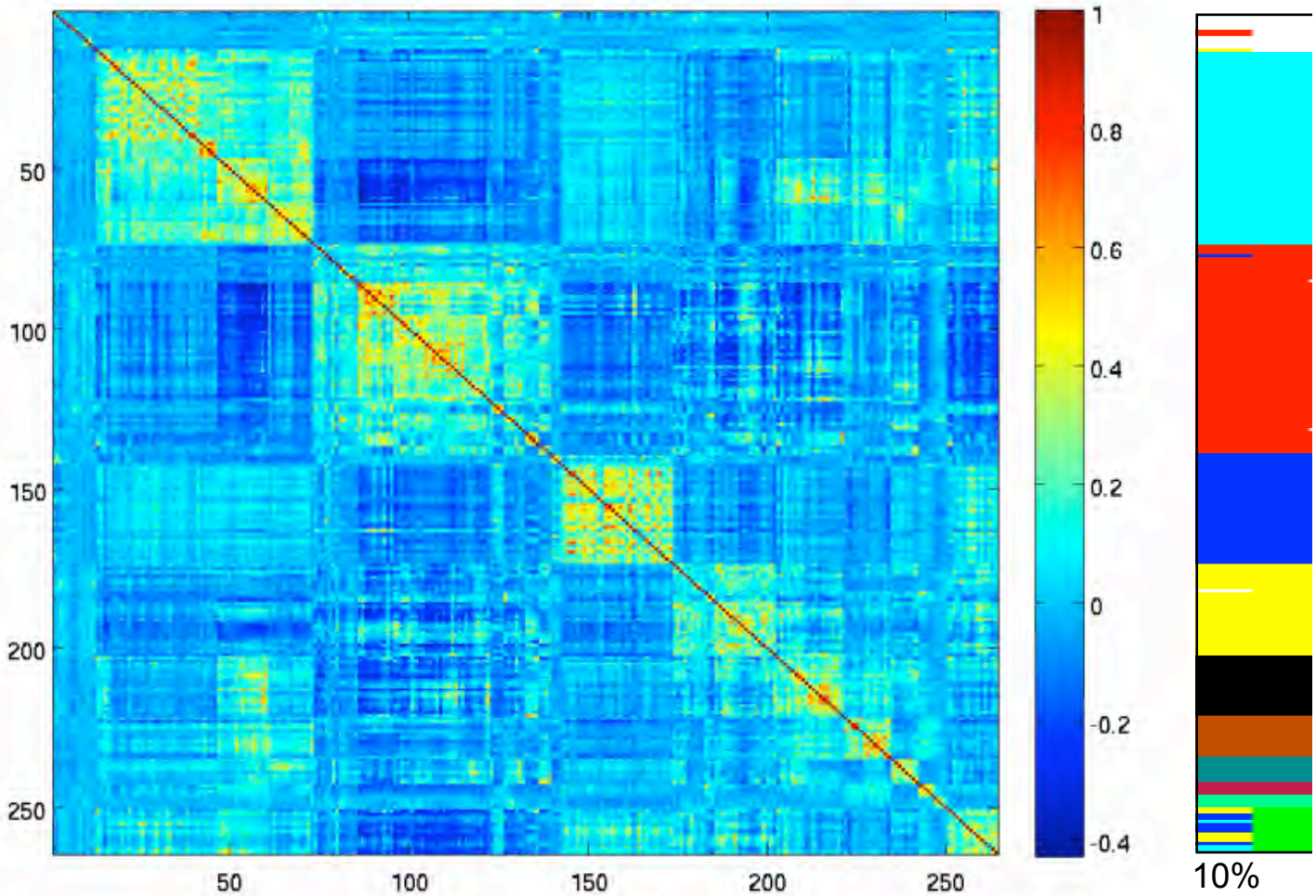

10%

Edge density

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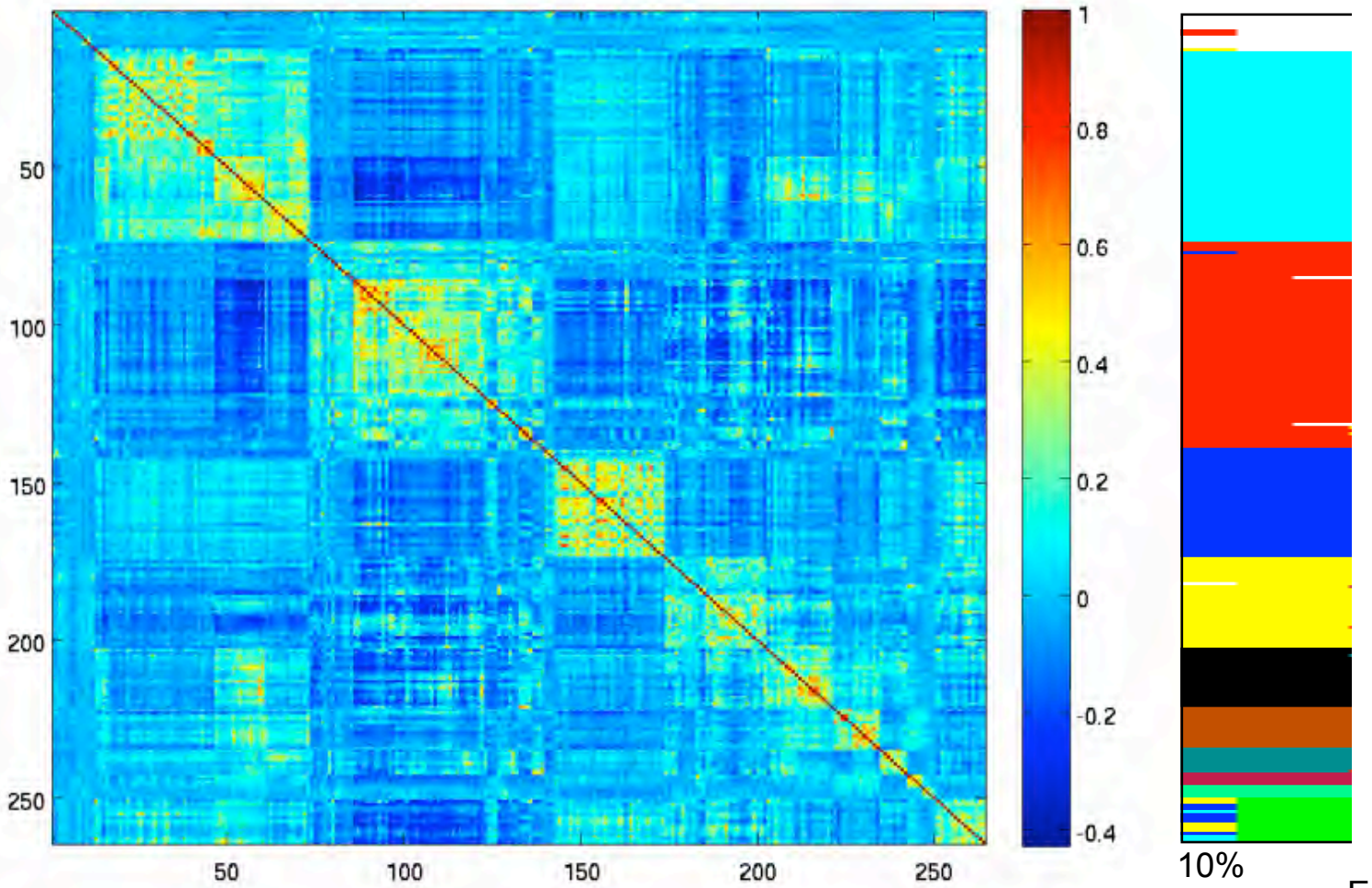

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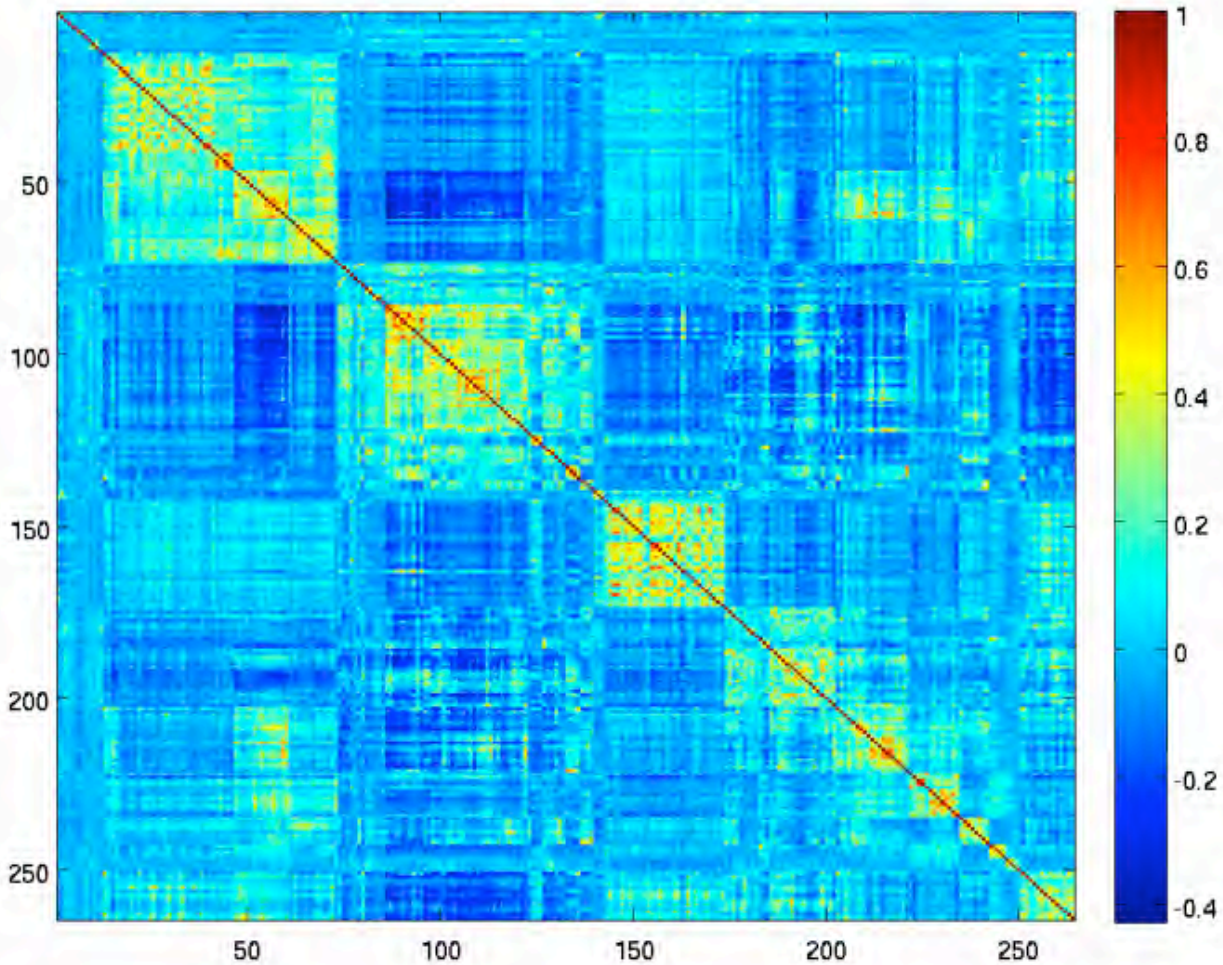
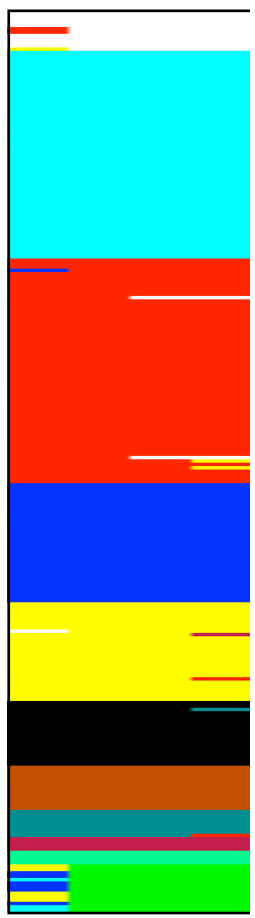


Infomap algorithm



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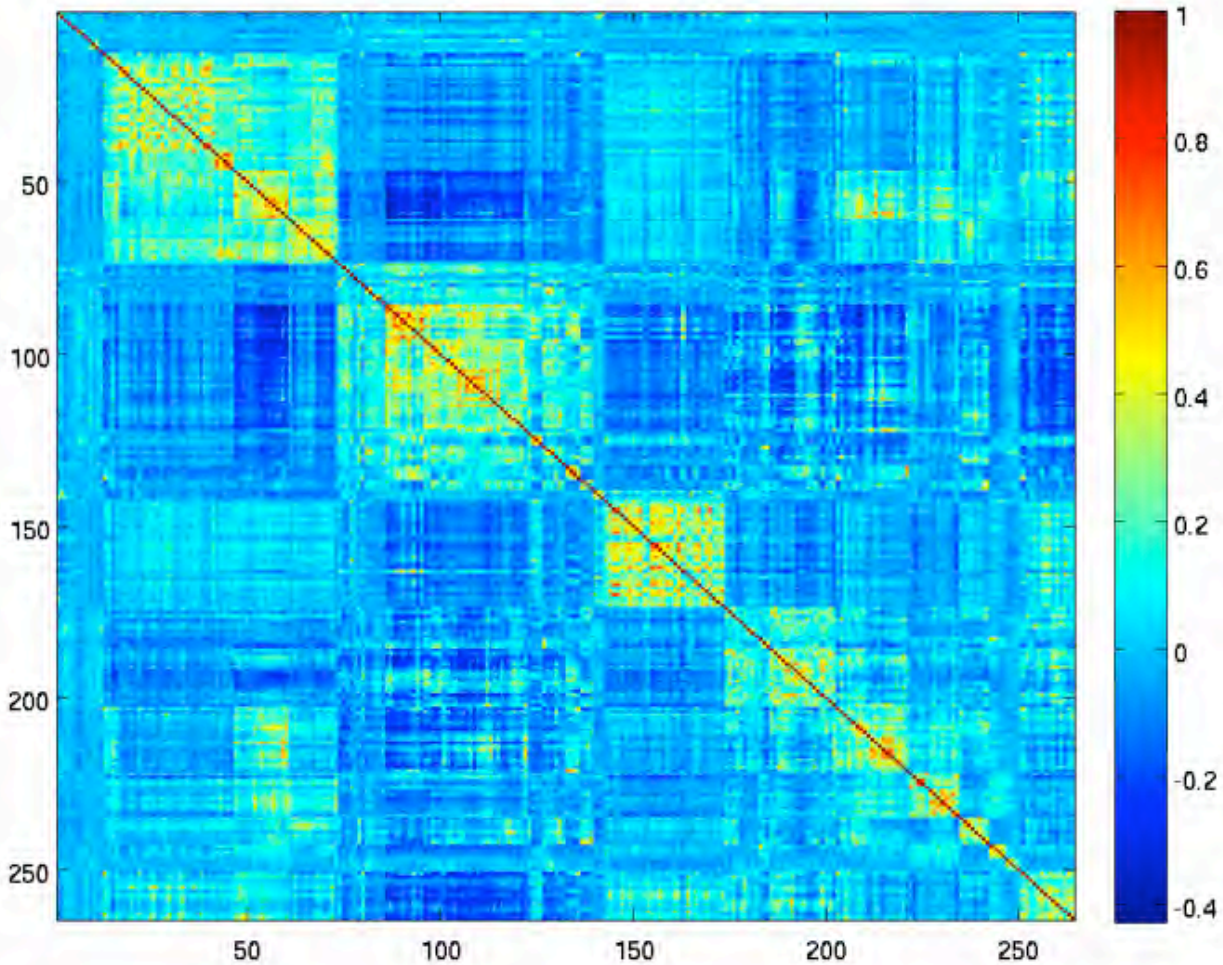

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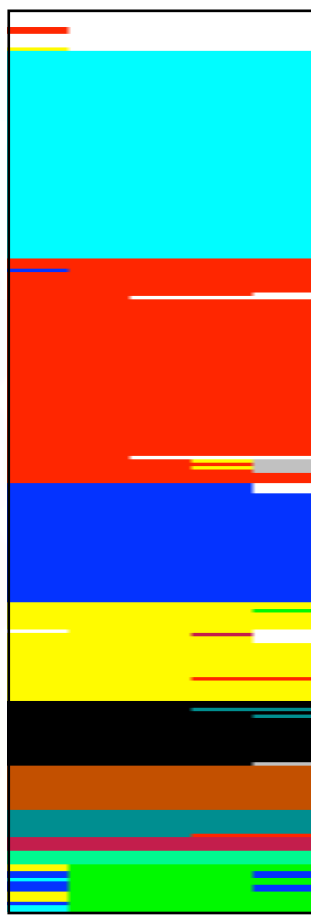

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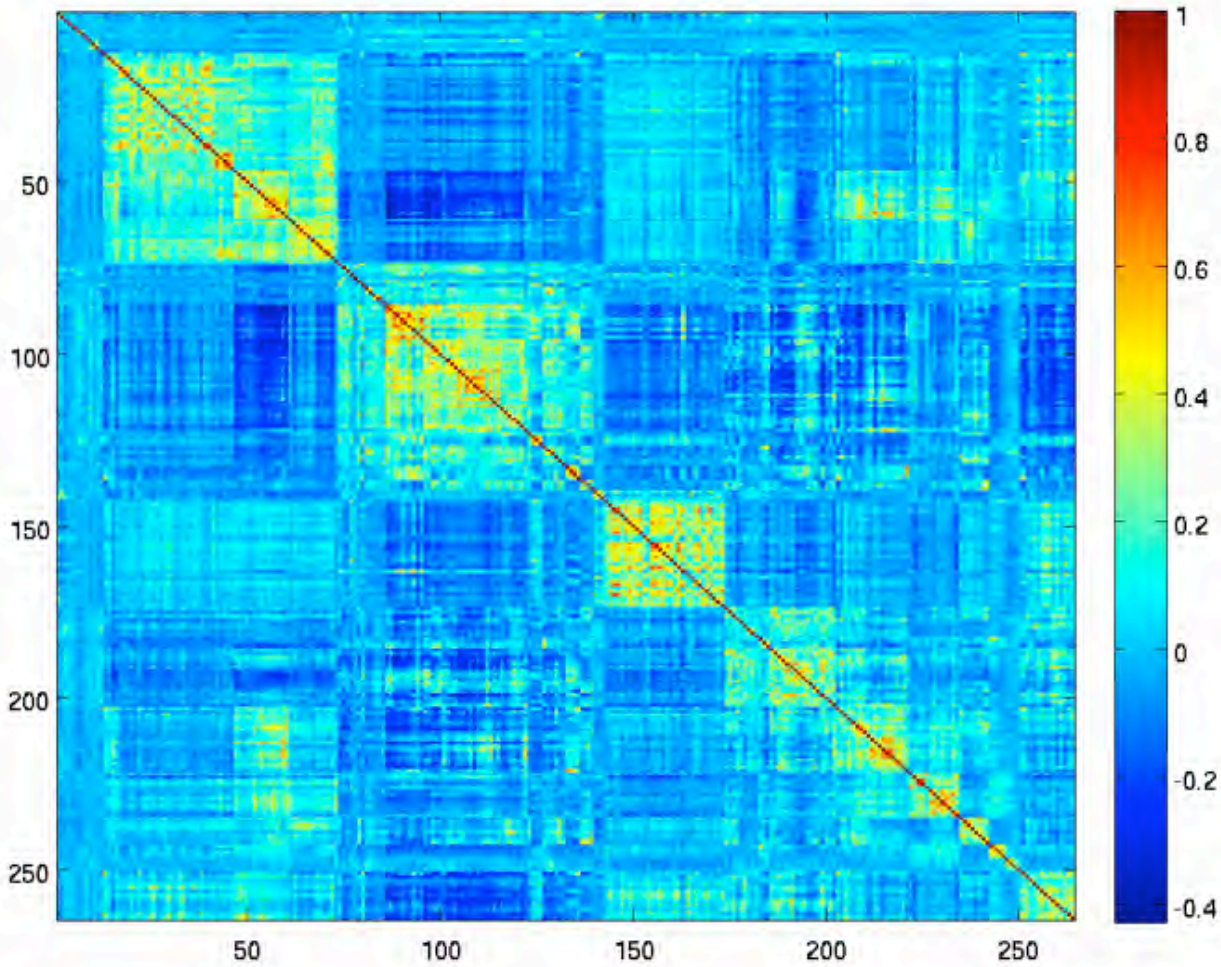

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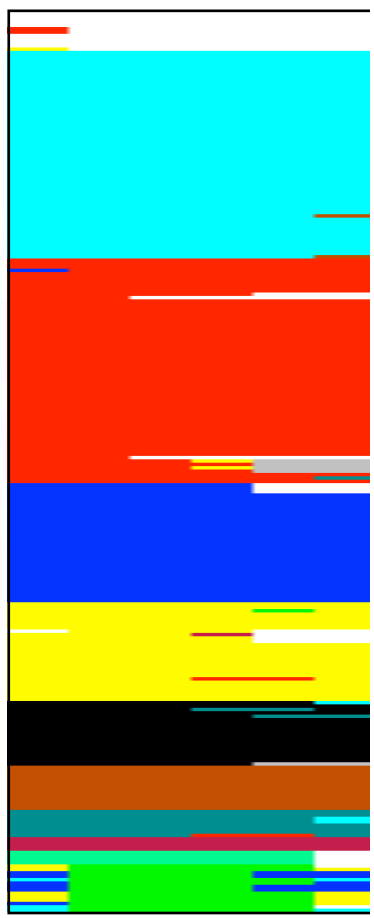

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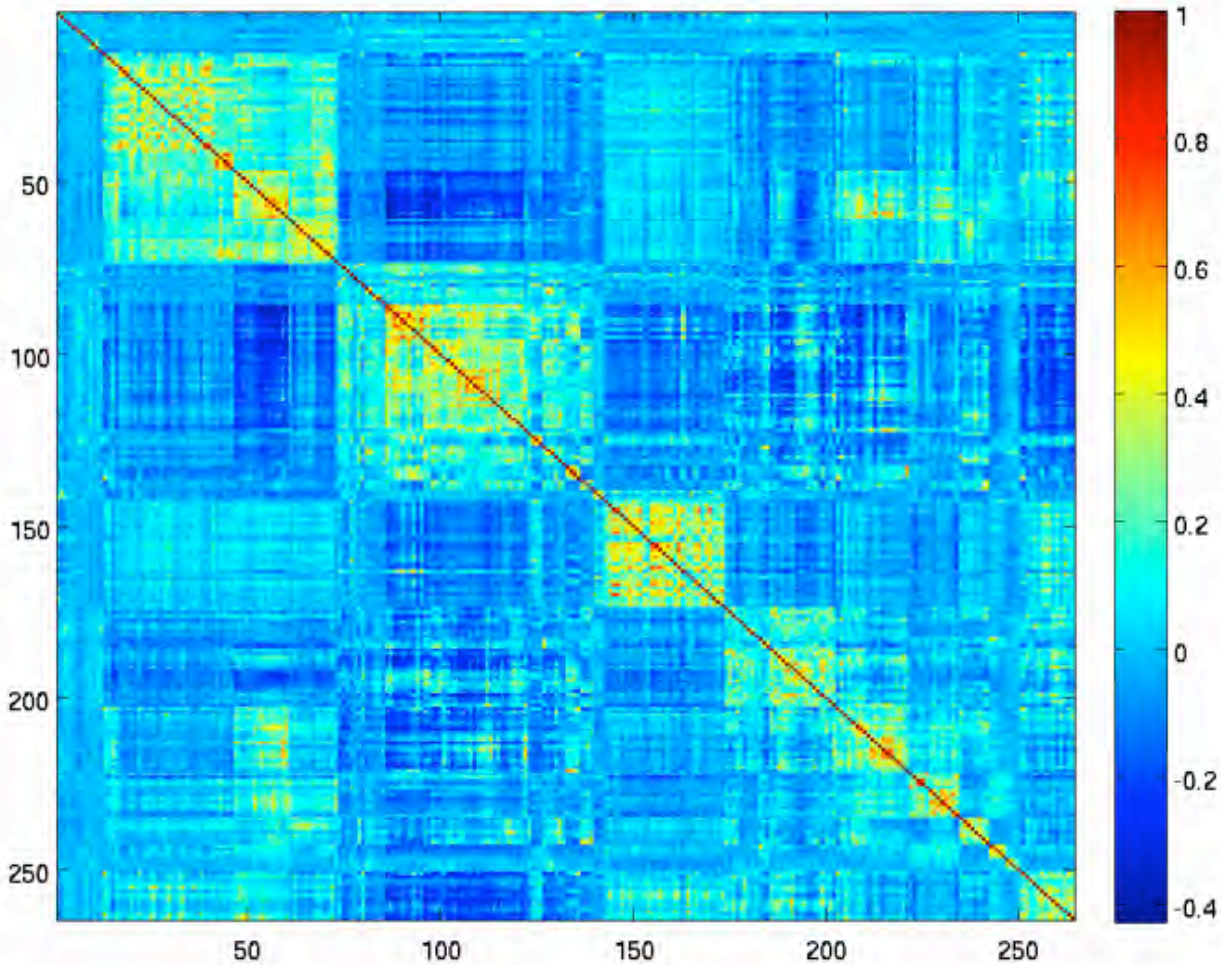

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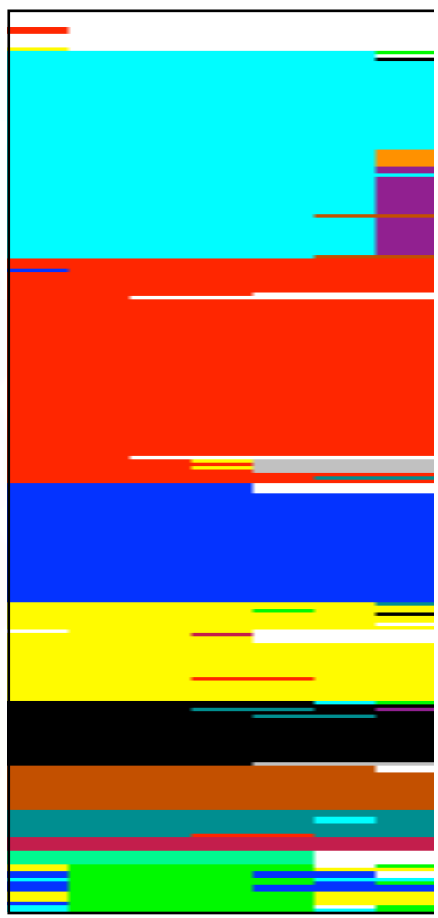

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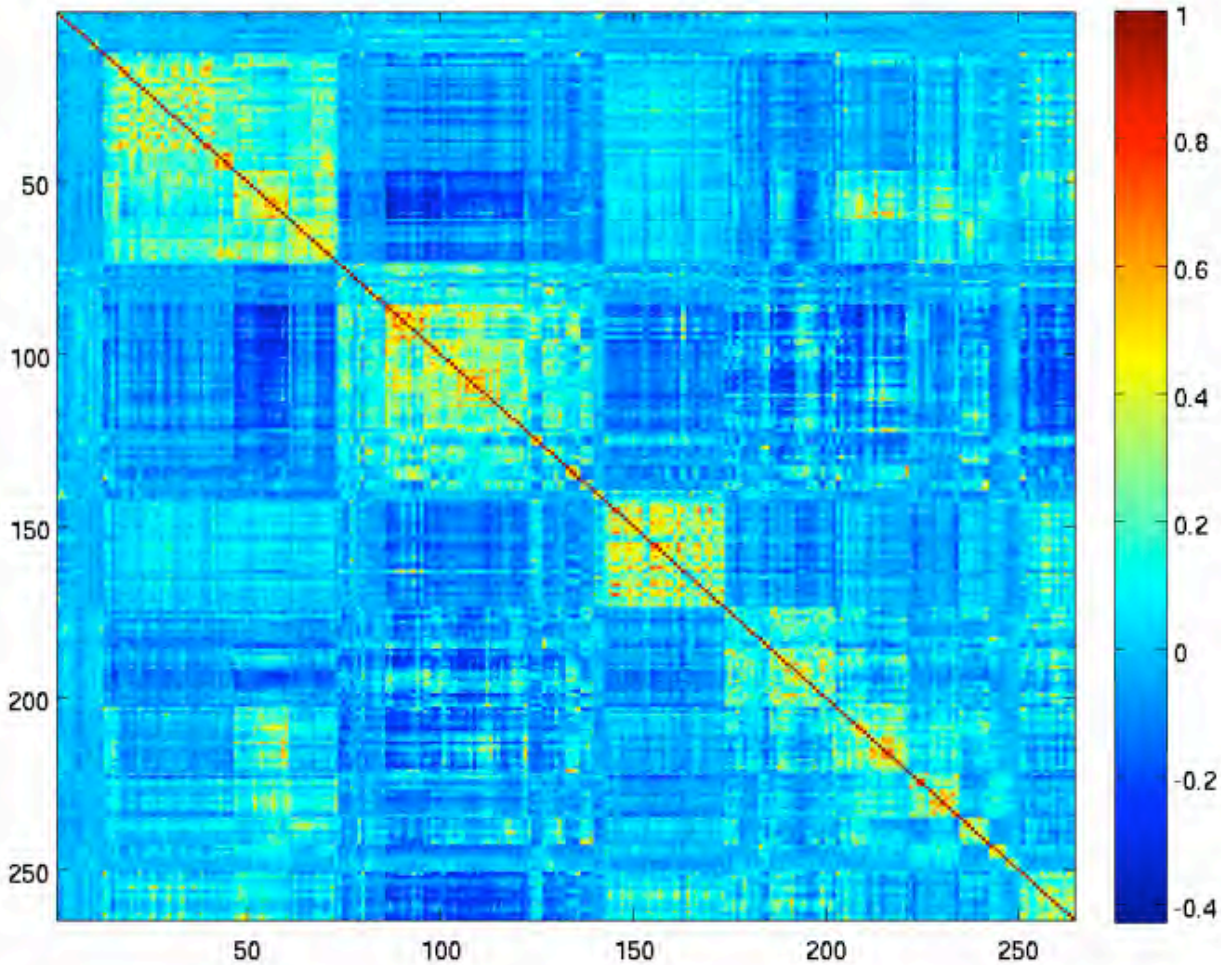

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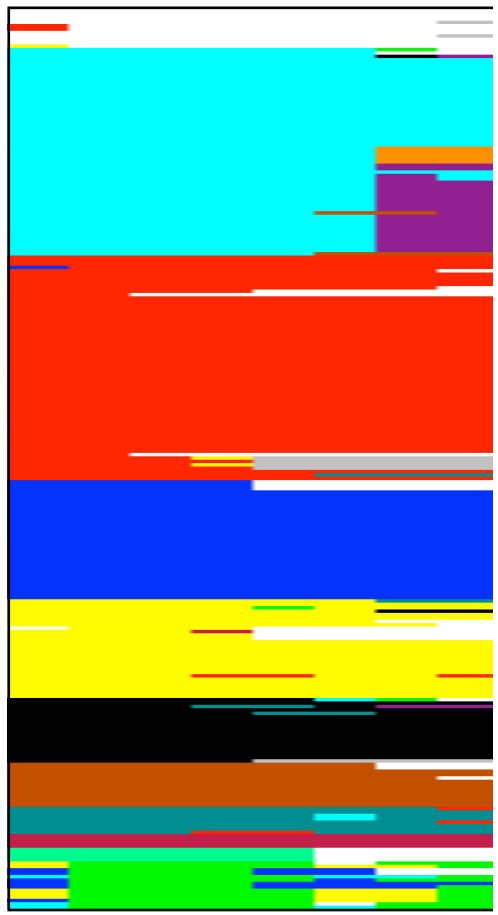

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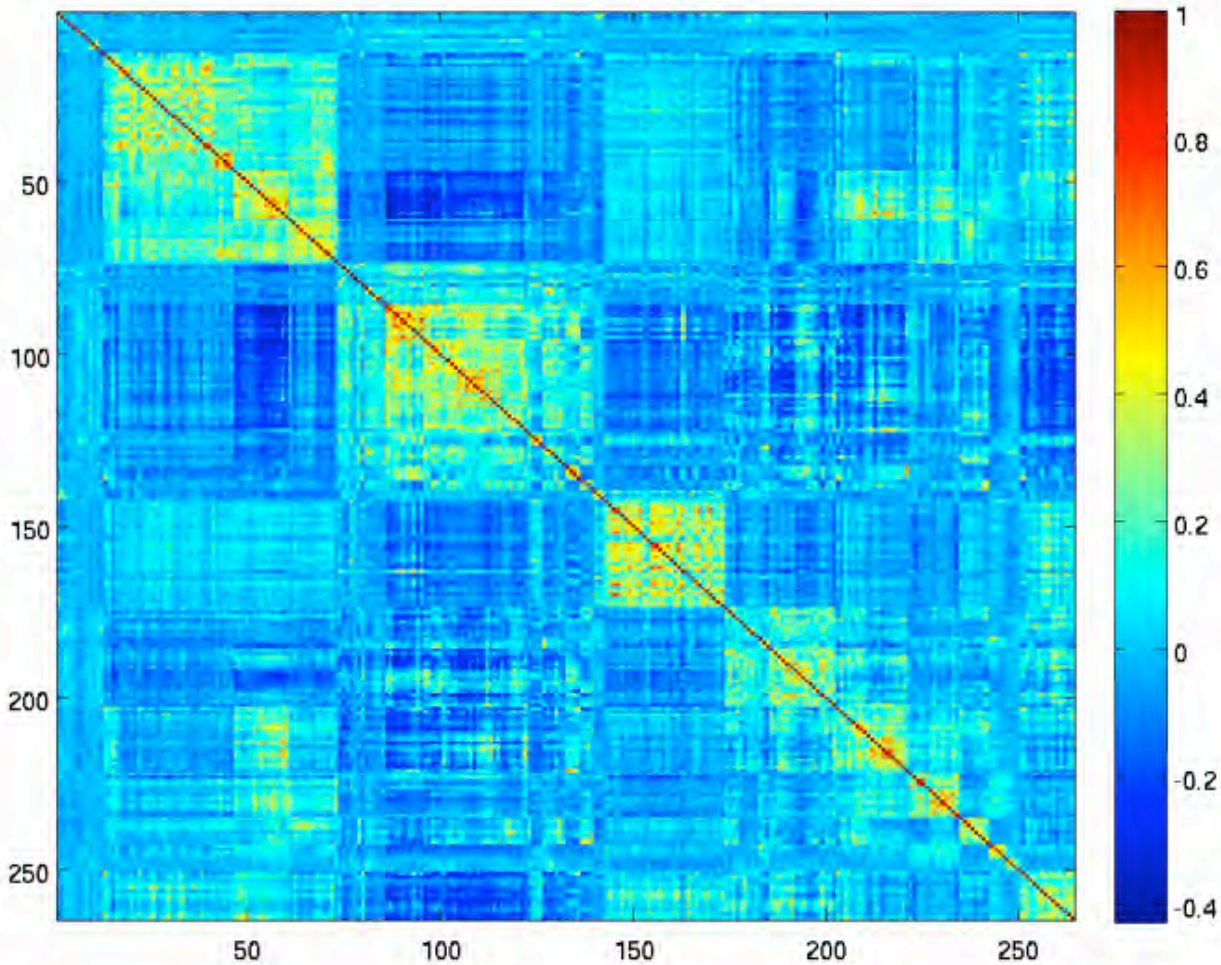

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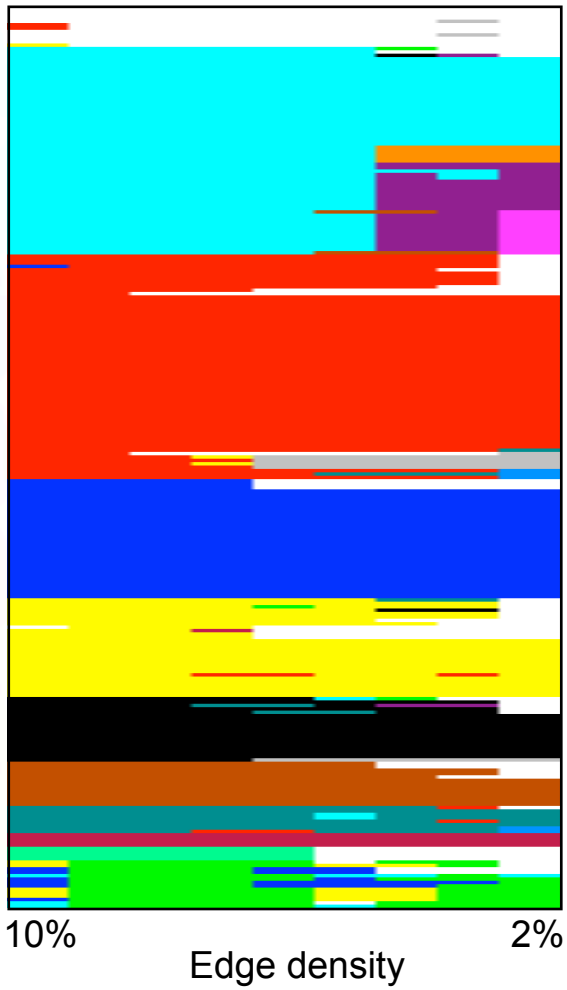

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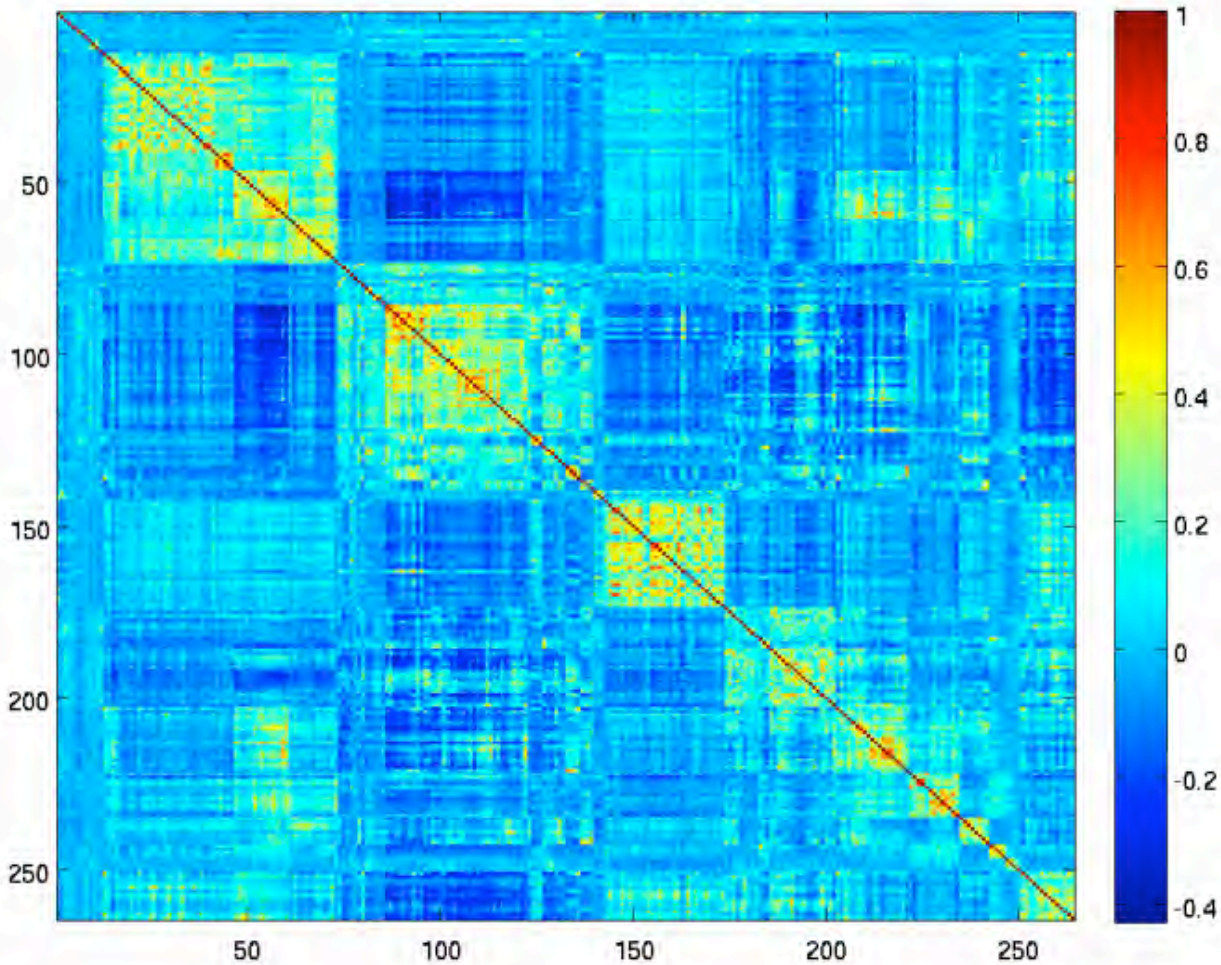

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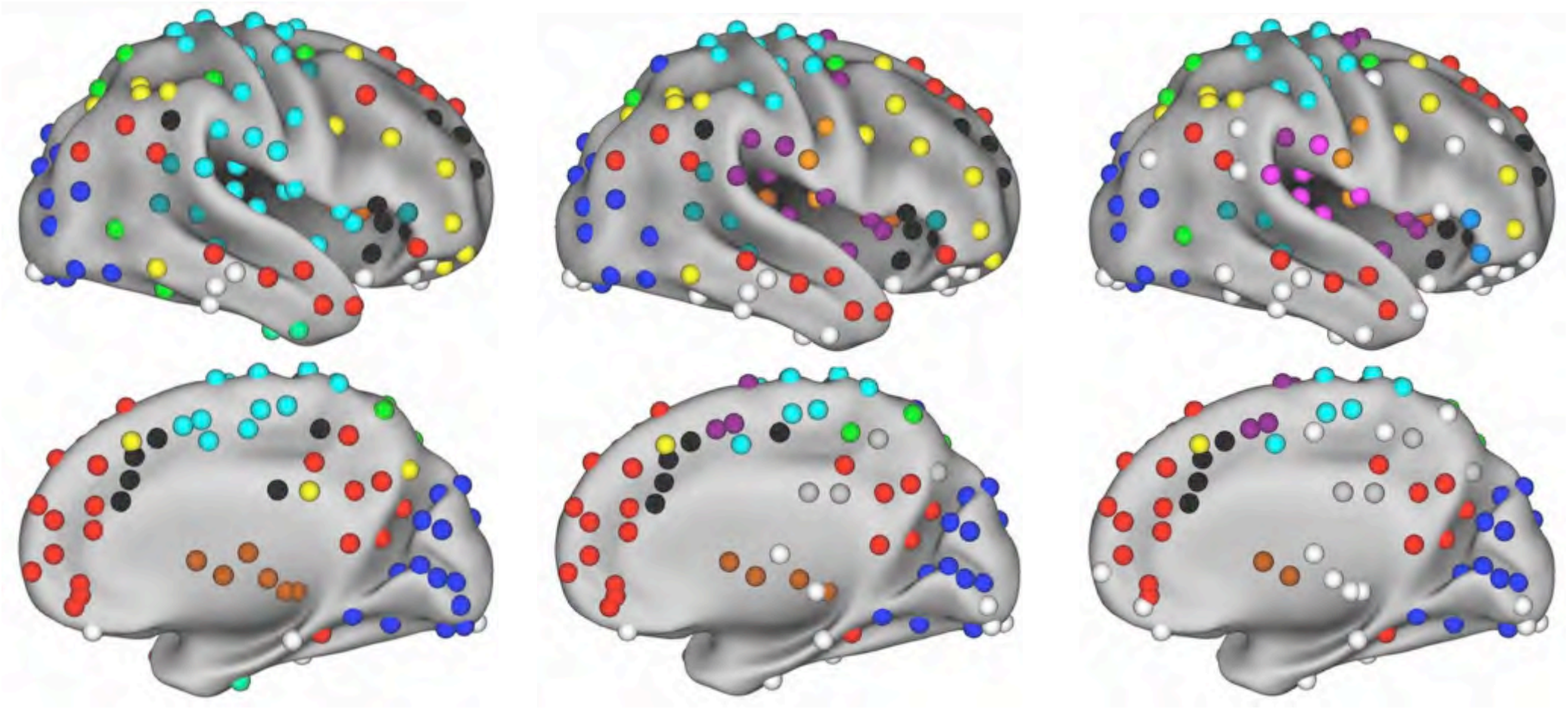
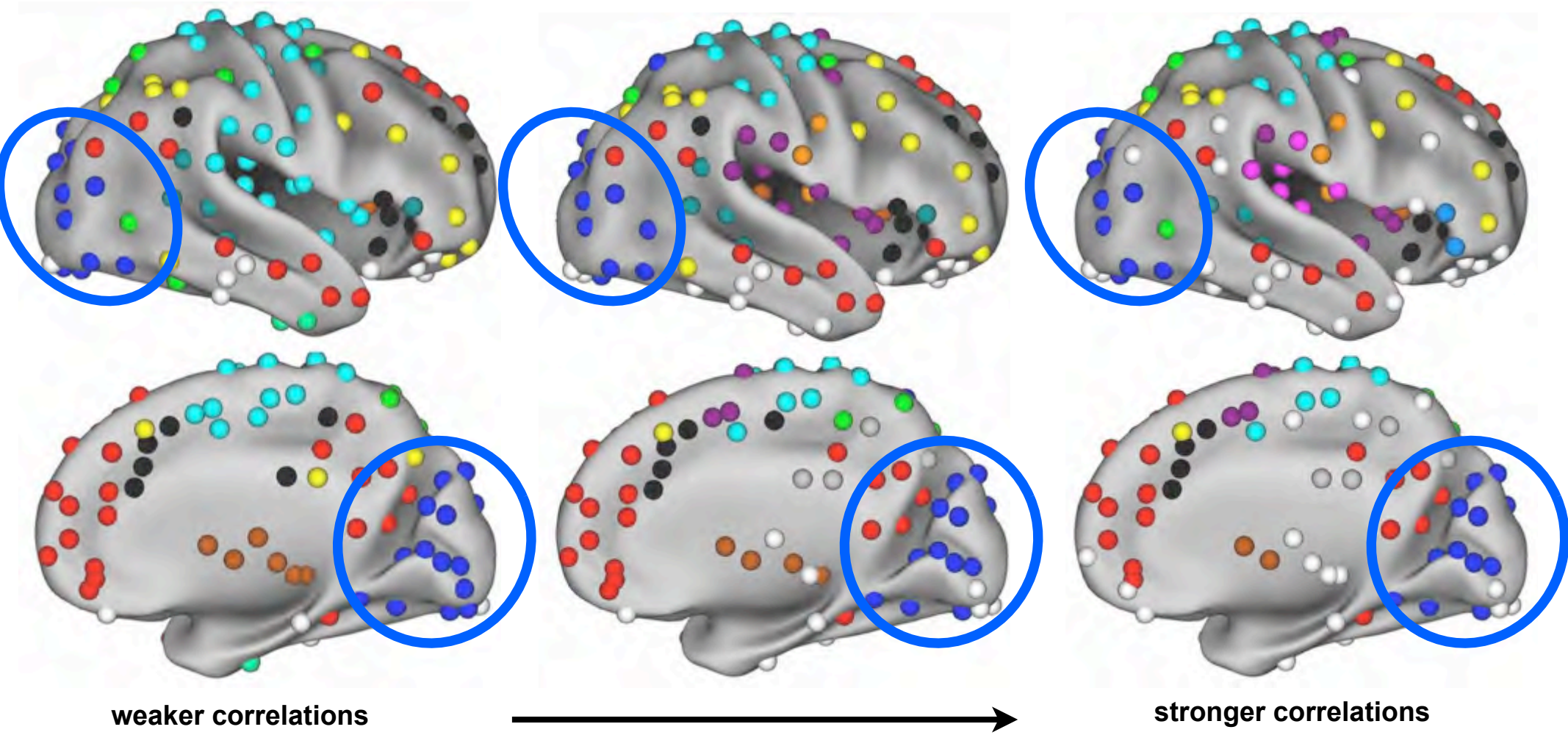


weaker correlations → stronger correlations

Network modules



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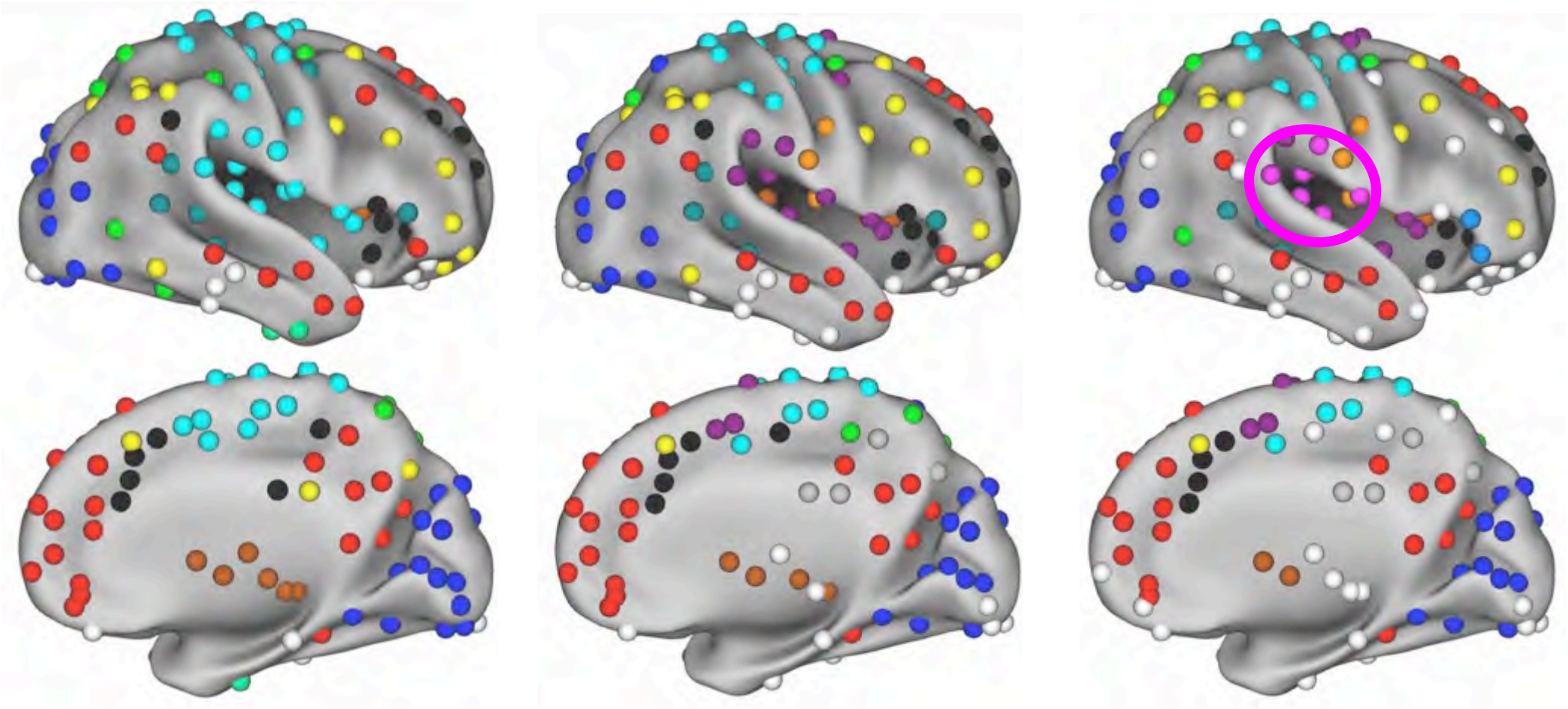

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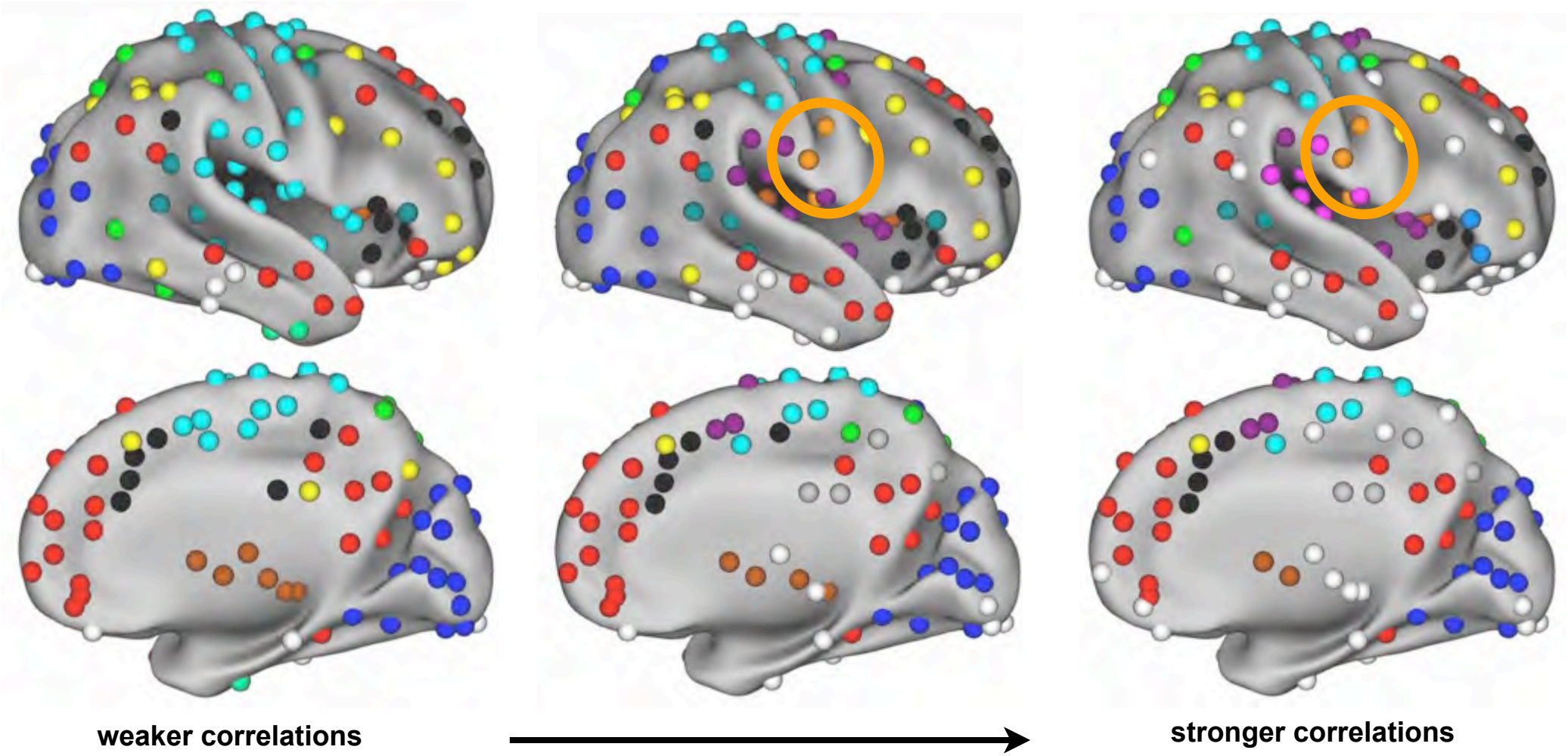

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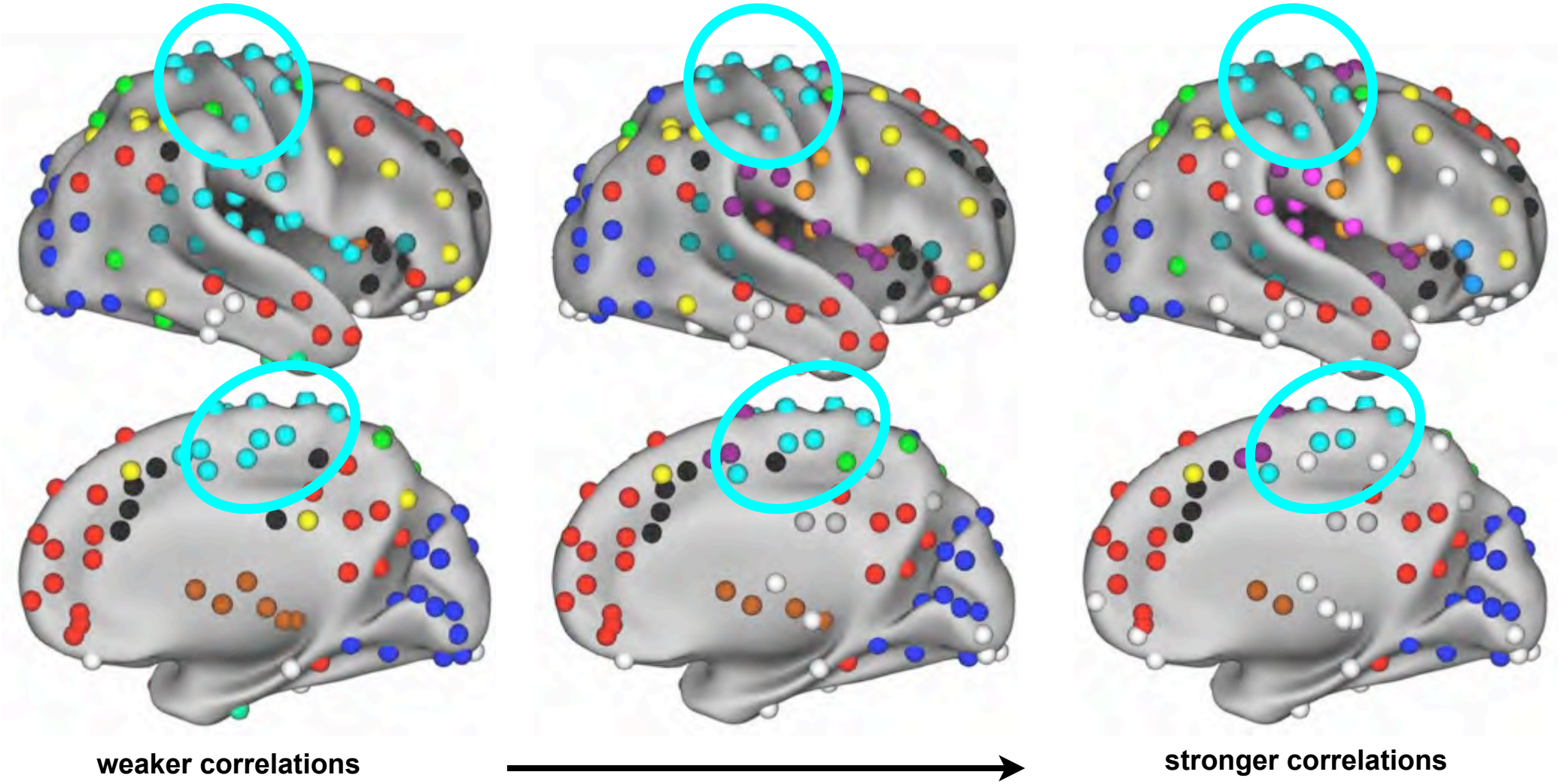

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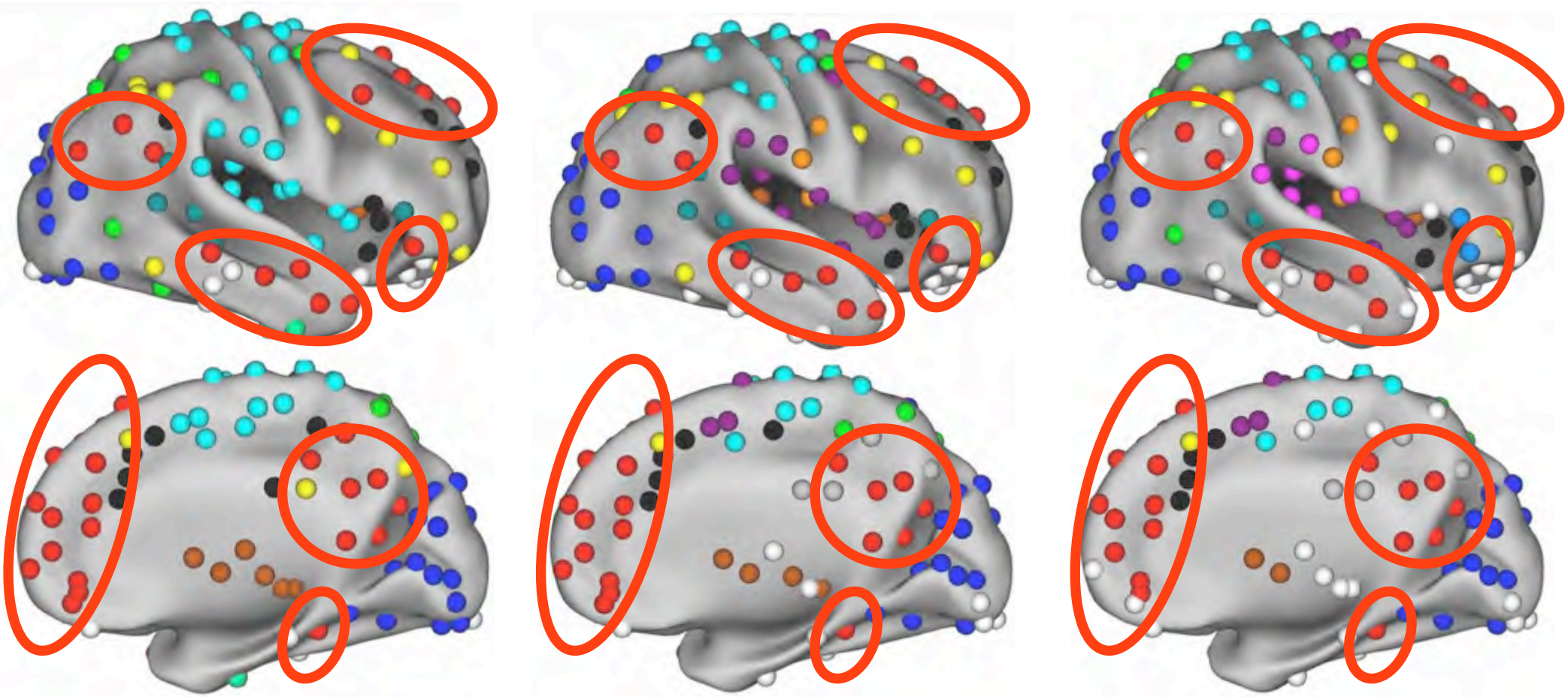

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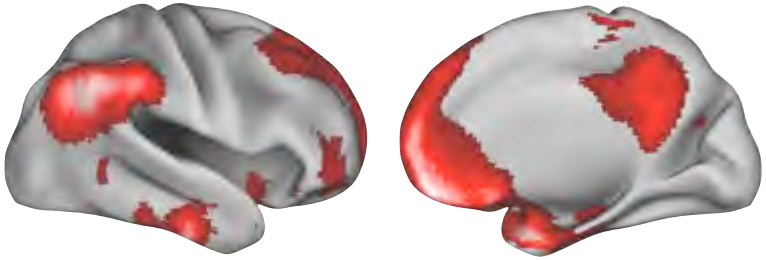

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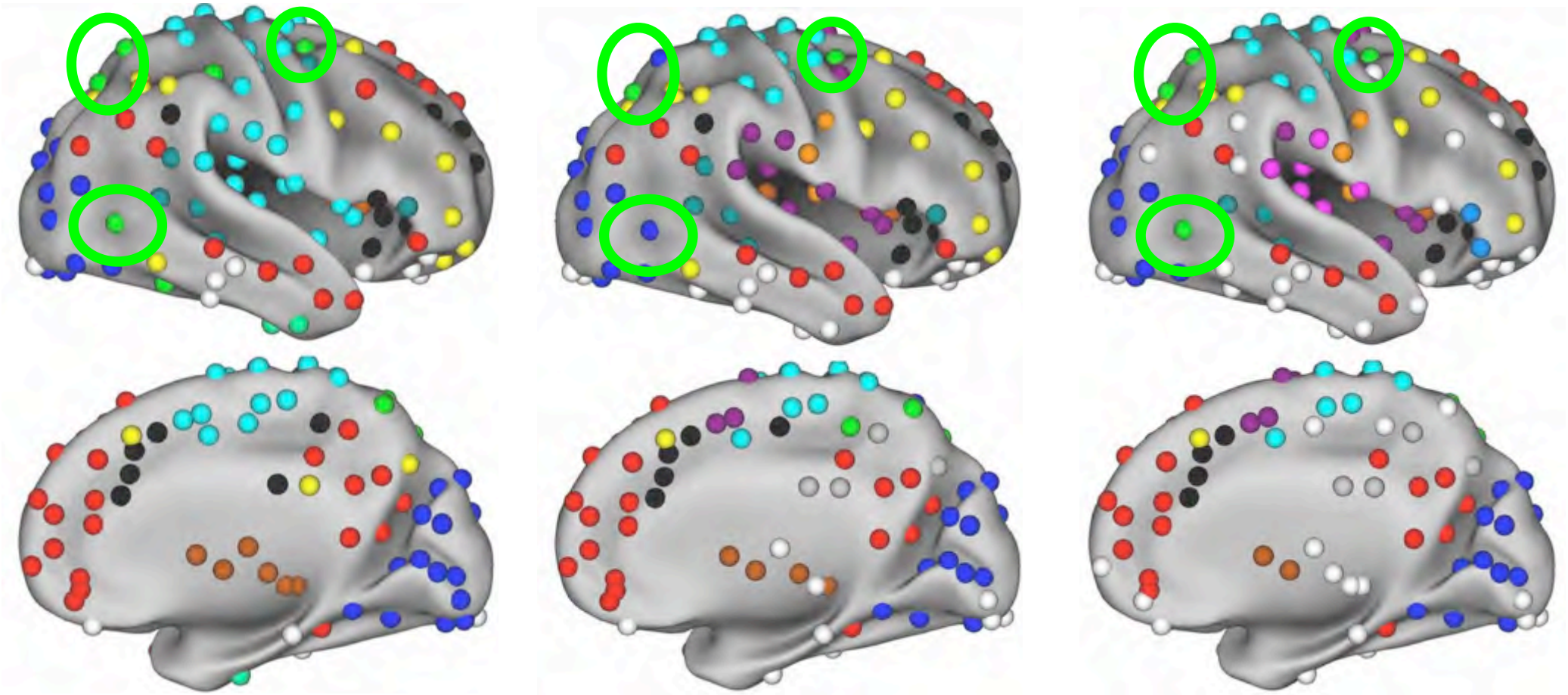

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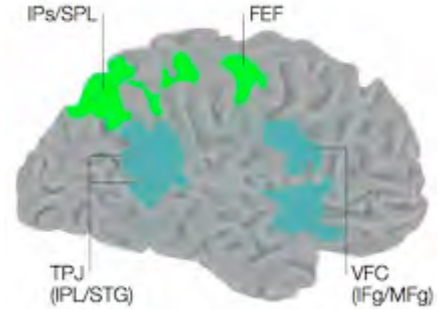

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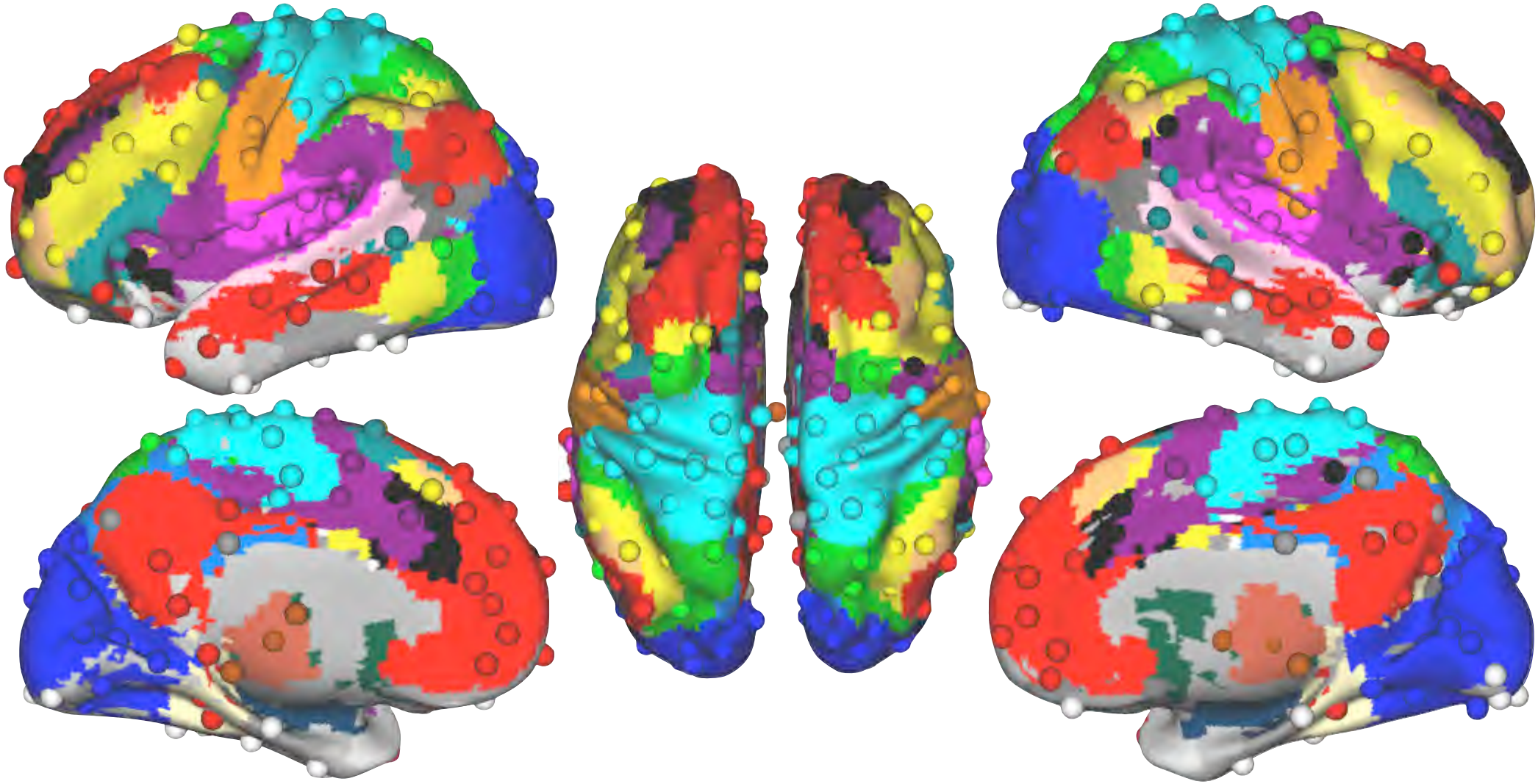

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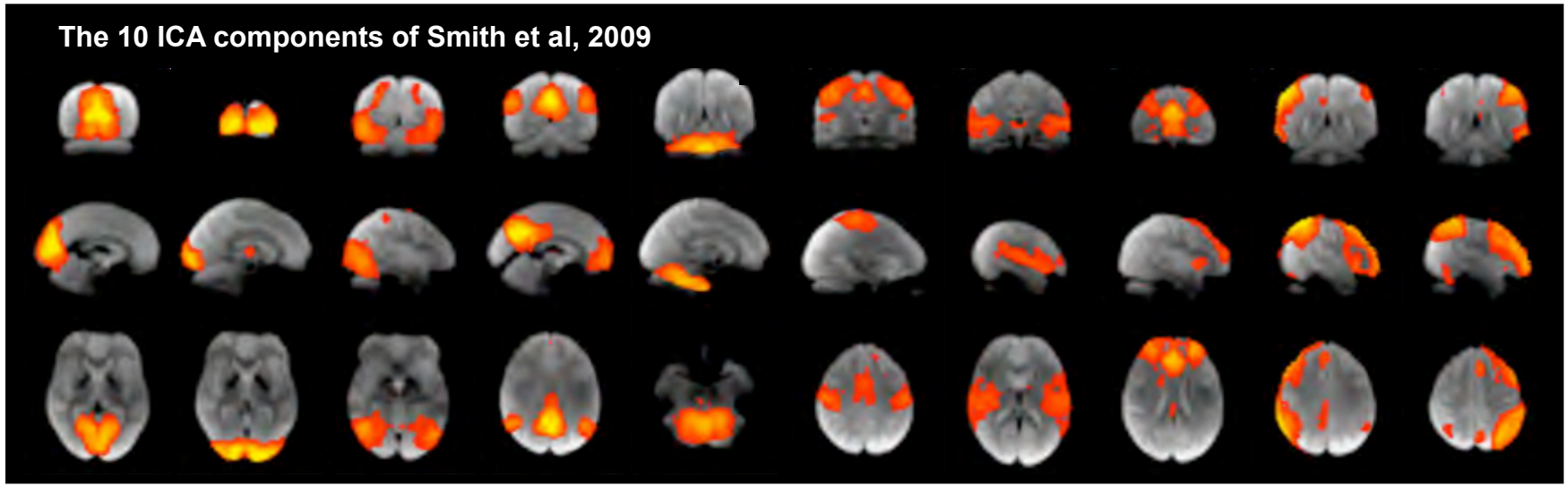
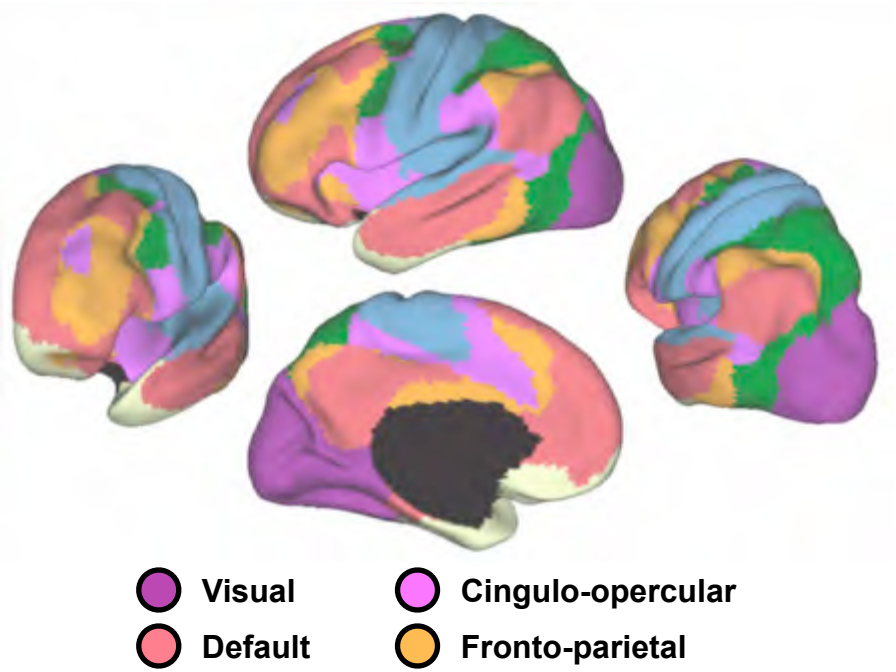
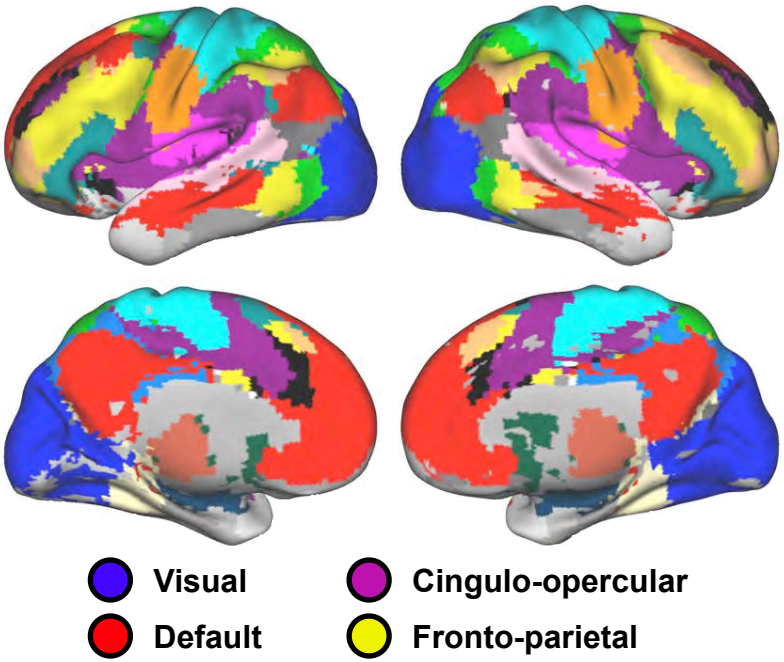


Resting state clusters of Yeo et al., 2011



Resting state clusters of Power et al., 2011

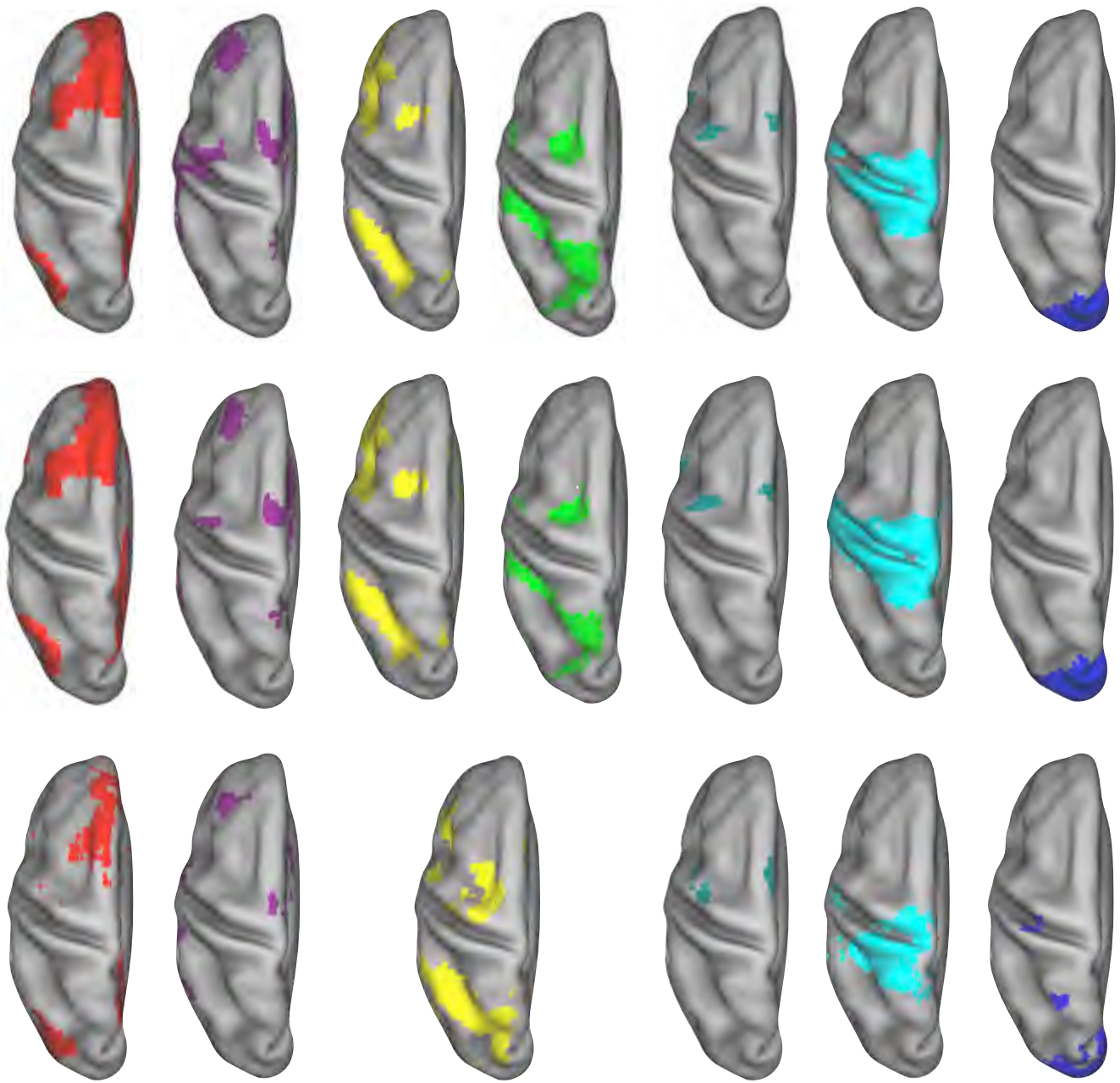


Network modules

Main cohort

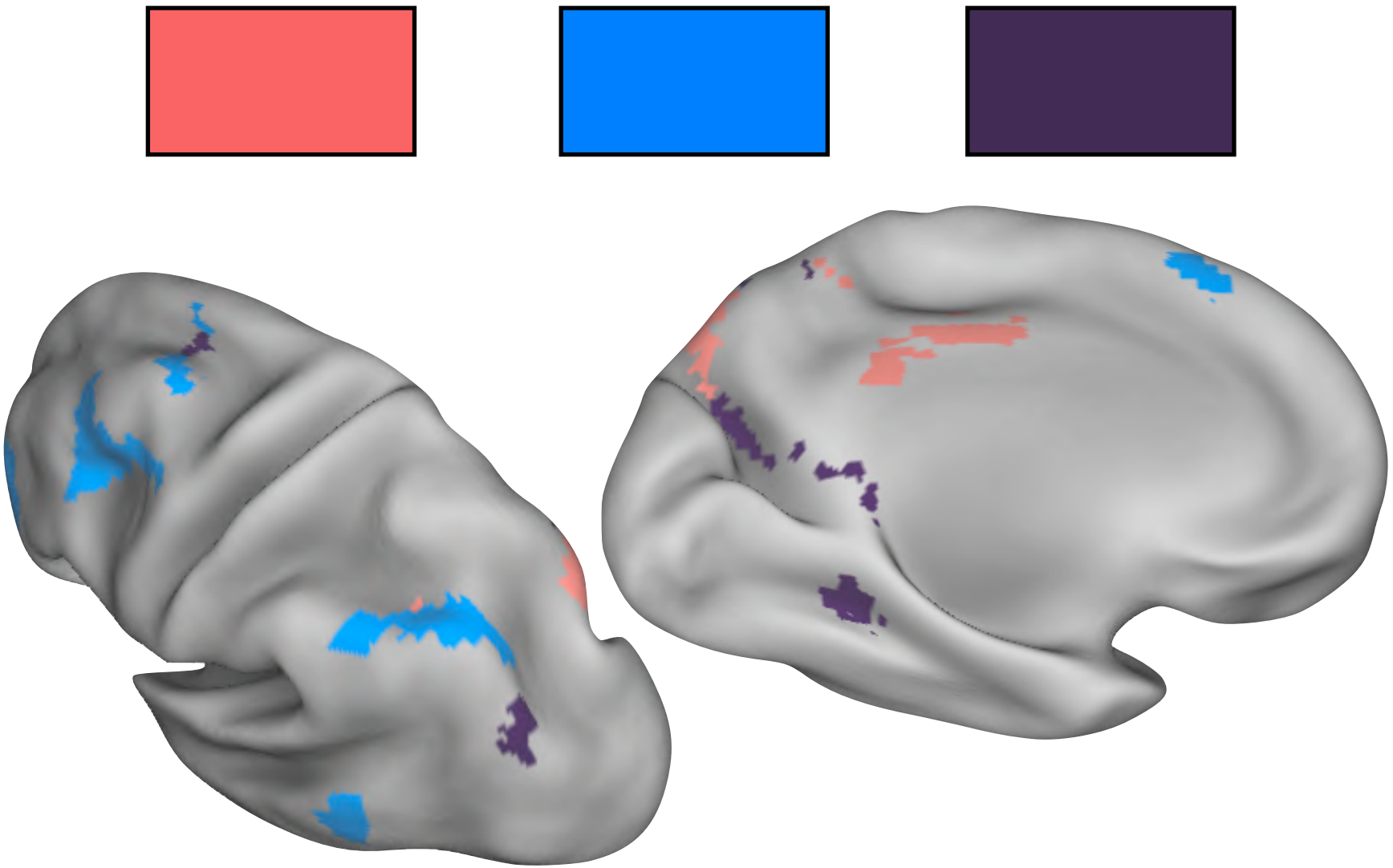
Replication cohort

Single subject



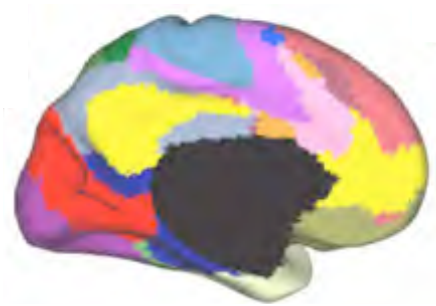
Network modules

Unfamiliar communities: under-recognized systems?



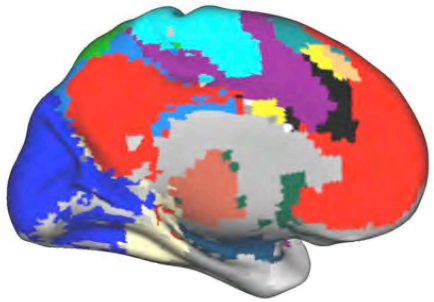
Network modules

Resting state clusters



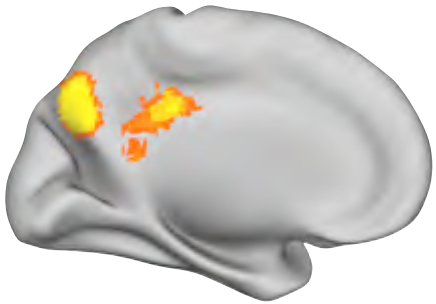
Yeo et al., 2011

Resting state clusters



Power et al., 2011

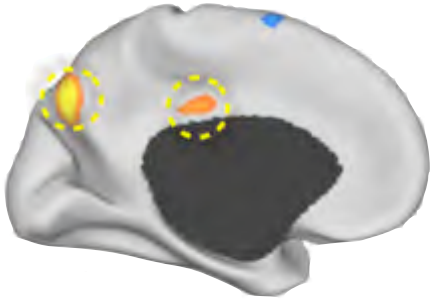
Task fMRI activation



Power et al., 2011

Memory retrieval meta-analysis

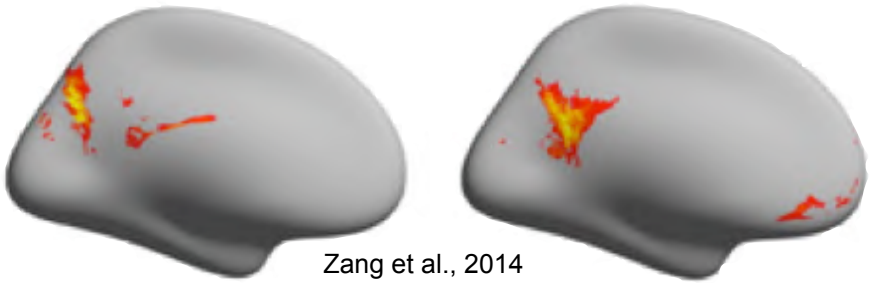
Task fMRI activation



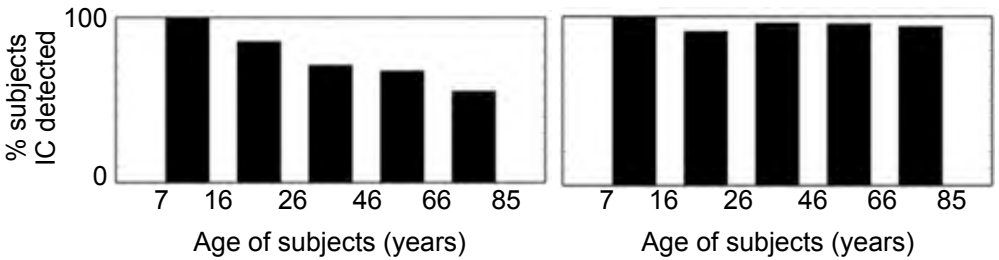
Nelson et al., 2013

Restudy vs initial study of a word pair

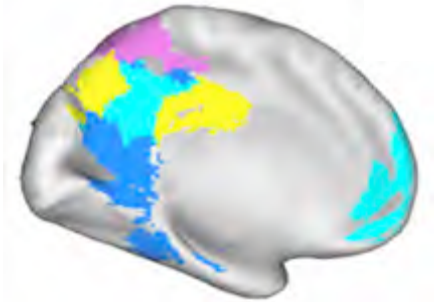
Resting state ICA components



Zang et al., 2014

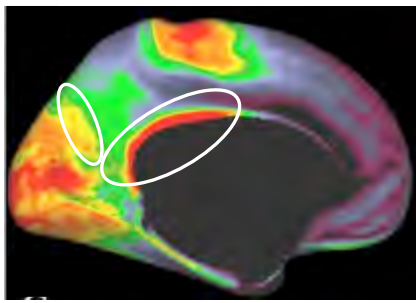


Resting state ICA components



Doucet et al., 2011

"Myelin mapping"

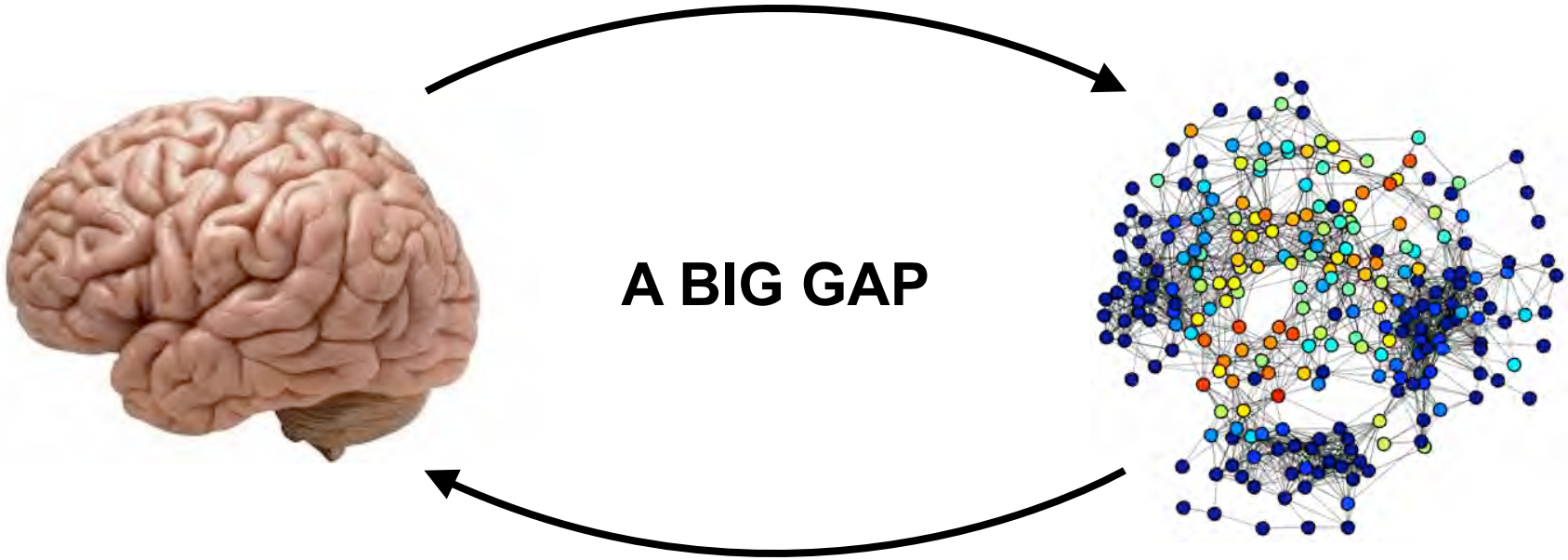


Glasser et al., 2011

T1/T2 intensity ratio

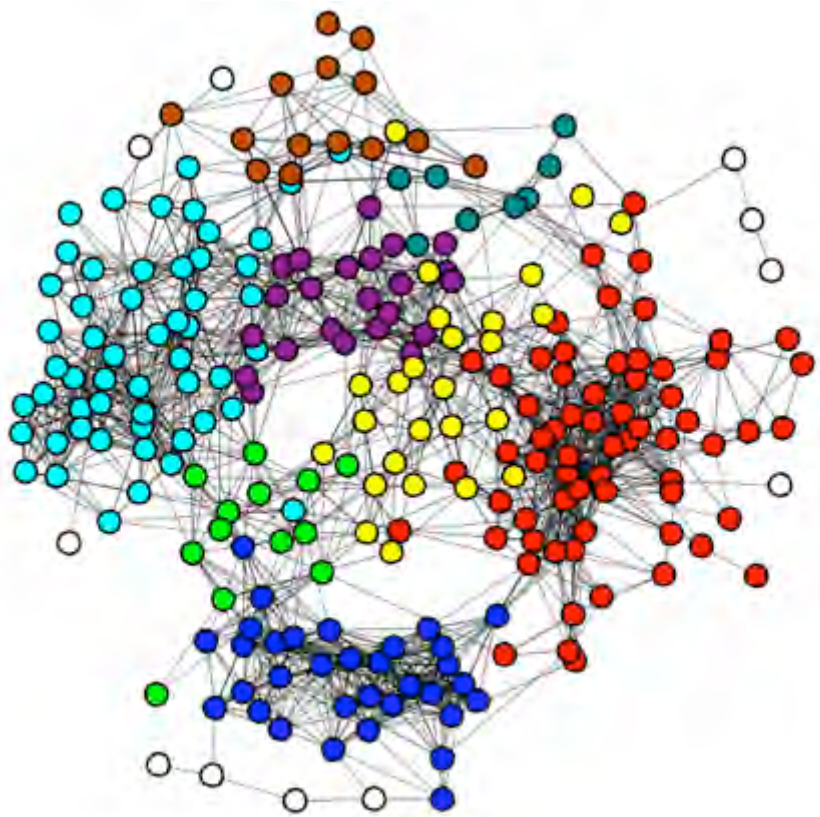
Translating model properties into brain properties

Creating a model of the brain

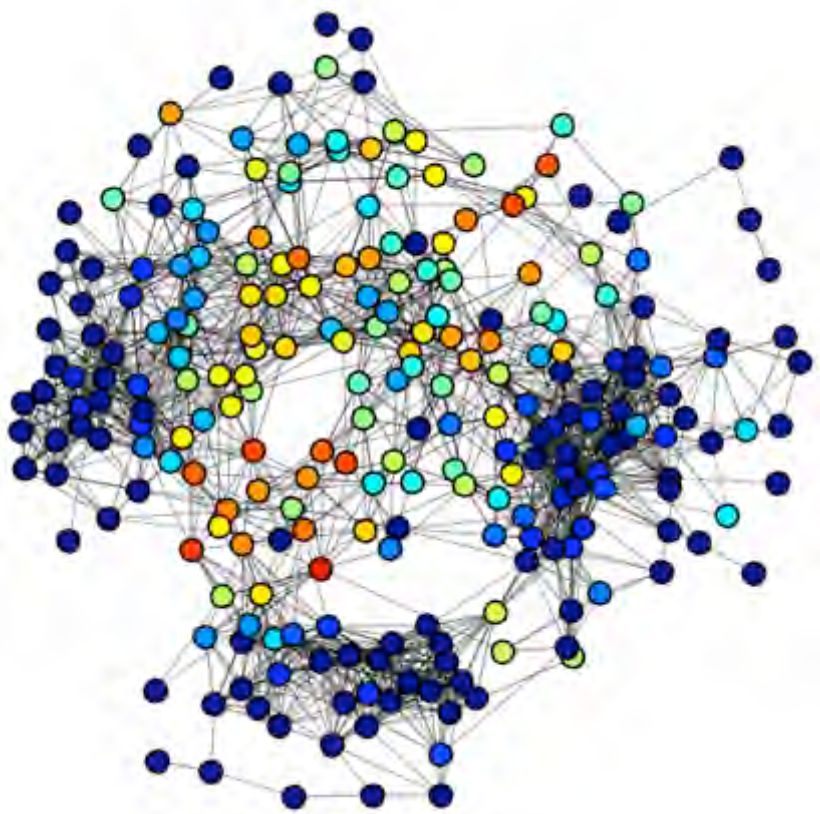


Translating model properties into brain properties

Translating model properties into brain properties



Modules



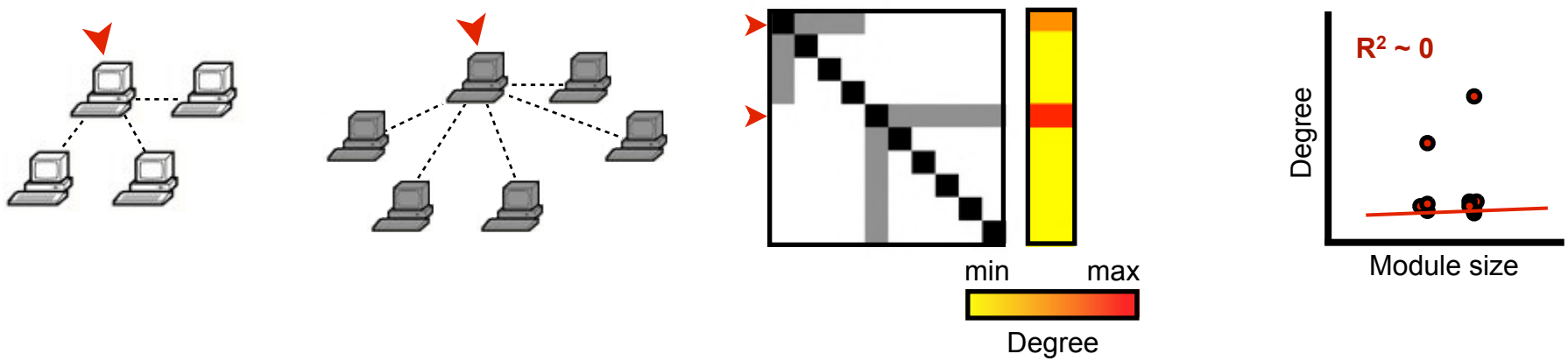
Participation coefficient

Translating model properties into brain properties

Are there especially important nodes?

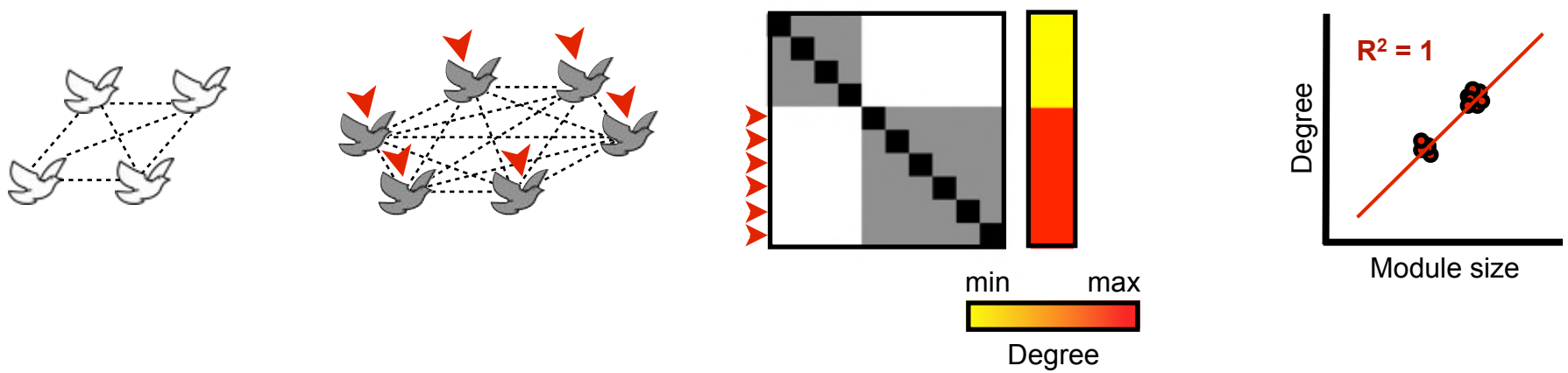
Translating model properties into brain properties

Degree ~ importance

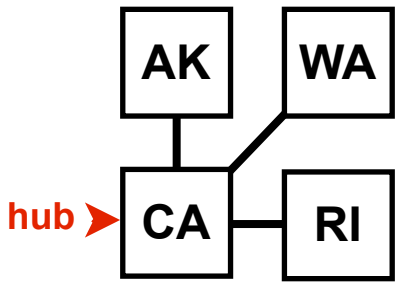


Degree ~ largest modules

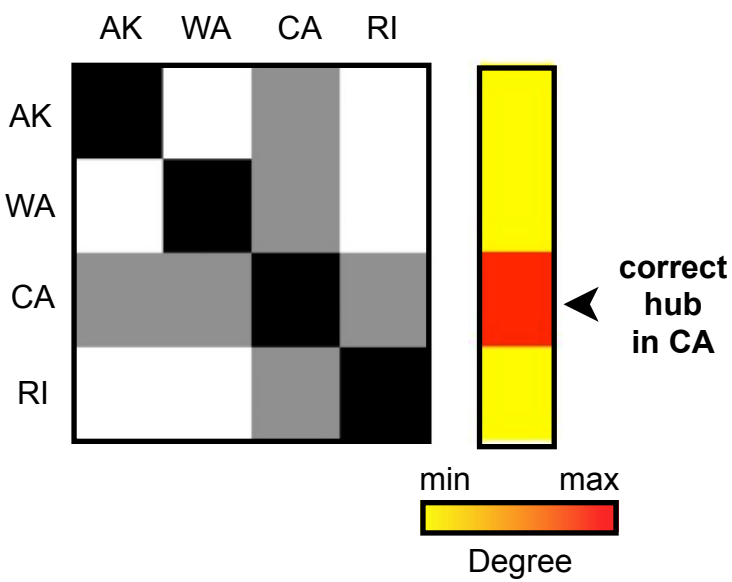
Strong relationship



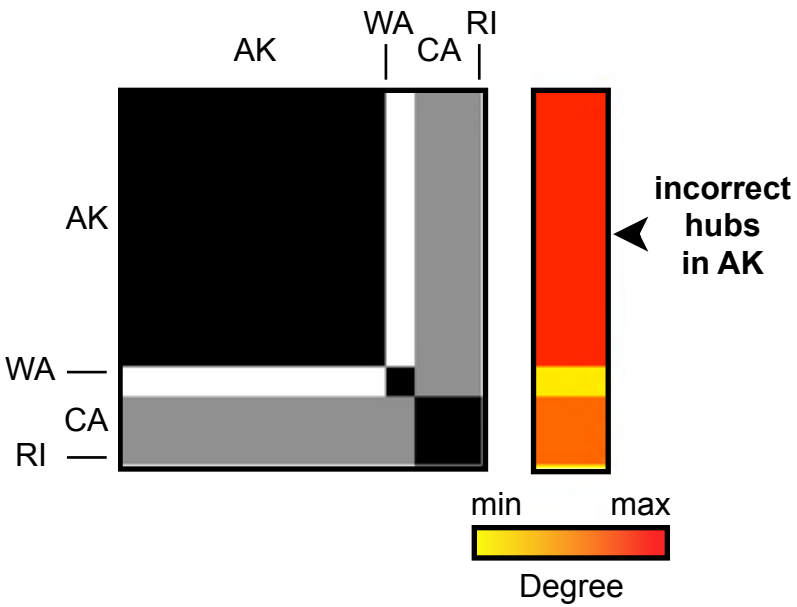
Translating model properties into brain properties



State-based model



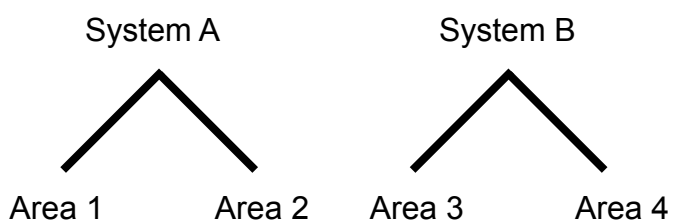
Acreage-based model



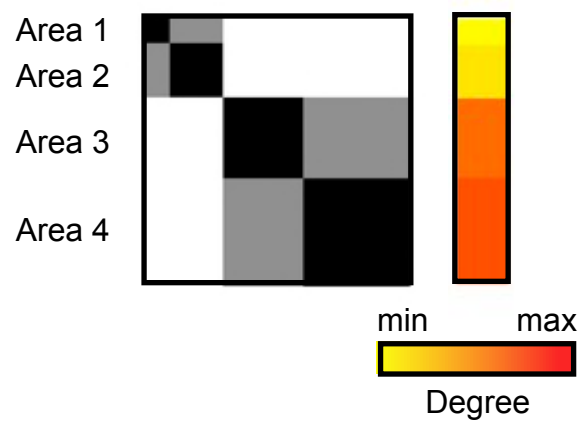
Translating model properties into brain properties

An interpretation of RSFC degree in voxel-based models

A hierarchical system

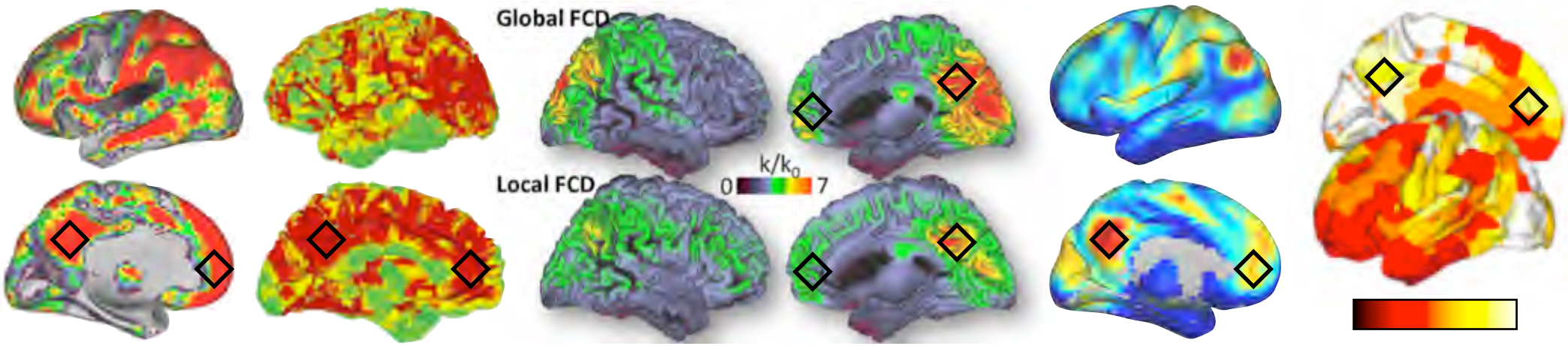


Volumetric model



Translating model properties into brain properties

Studies illustrating node degree centrality (or versions of strength centrality)



Buckner et al., J. Neurosci. 2009

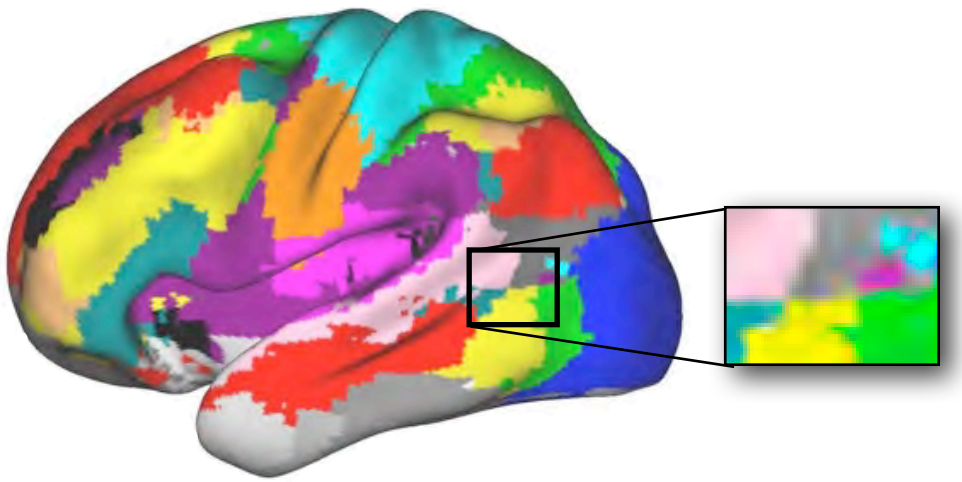
Cole et al., Neuroimage 2010

Tomasi & Volkow, Neuroimage 2011

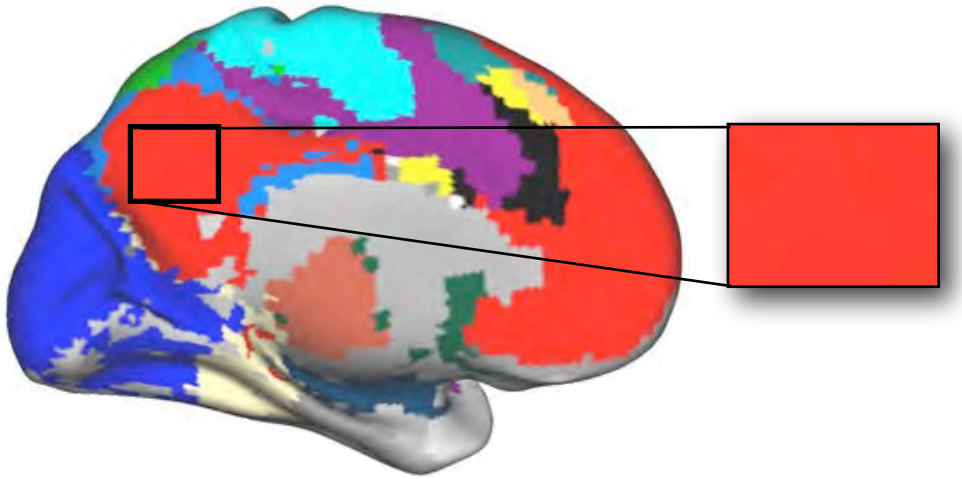
Power et al., Neuron 2013

Achard et al., PNAS 2012

Translating model properties into brain properties

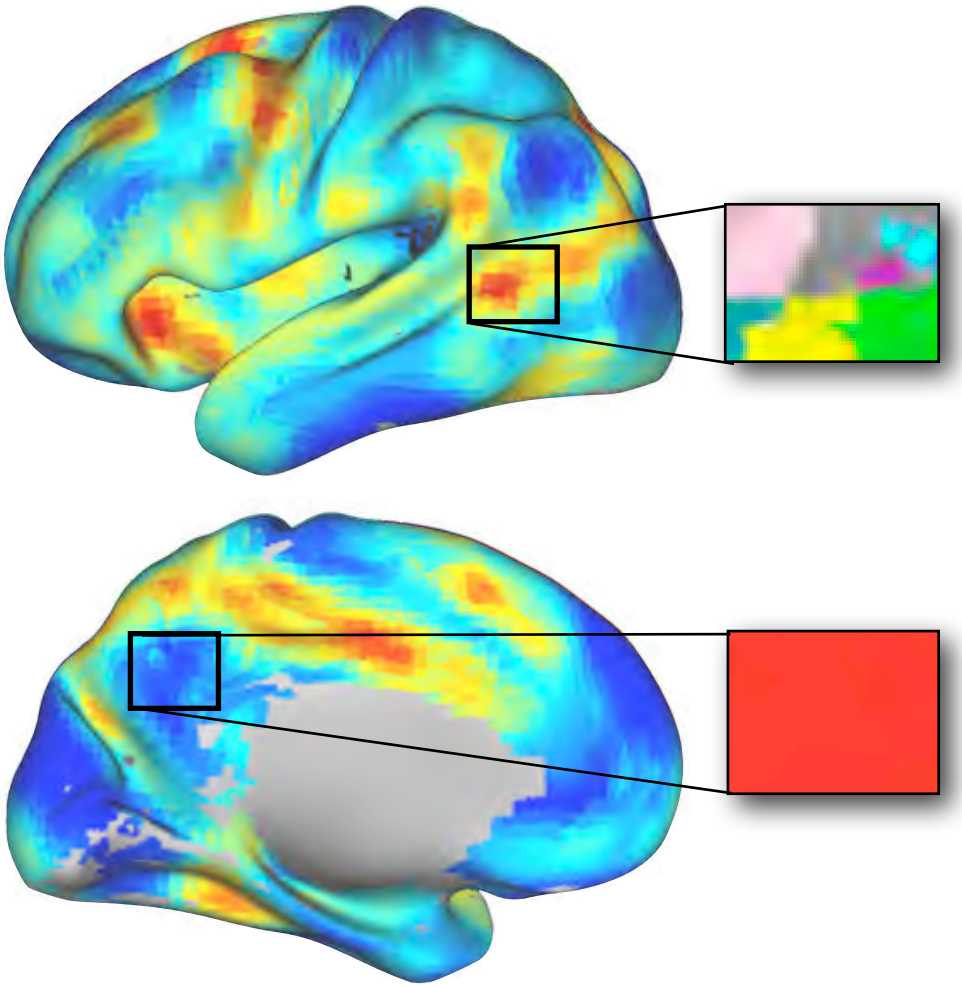


Multi-system deficits

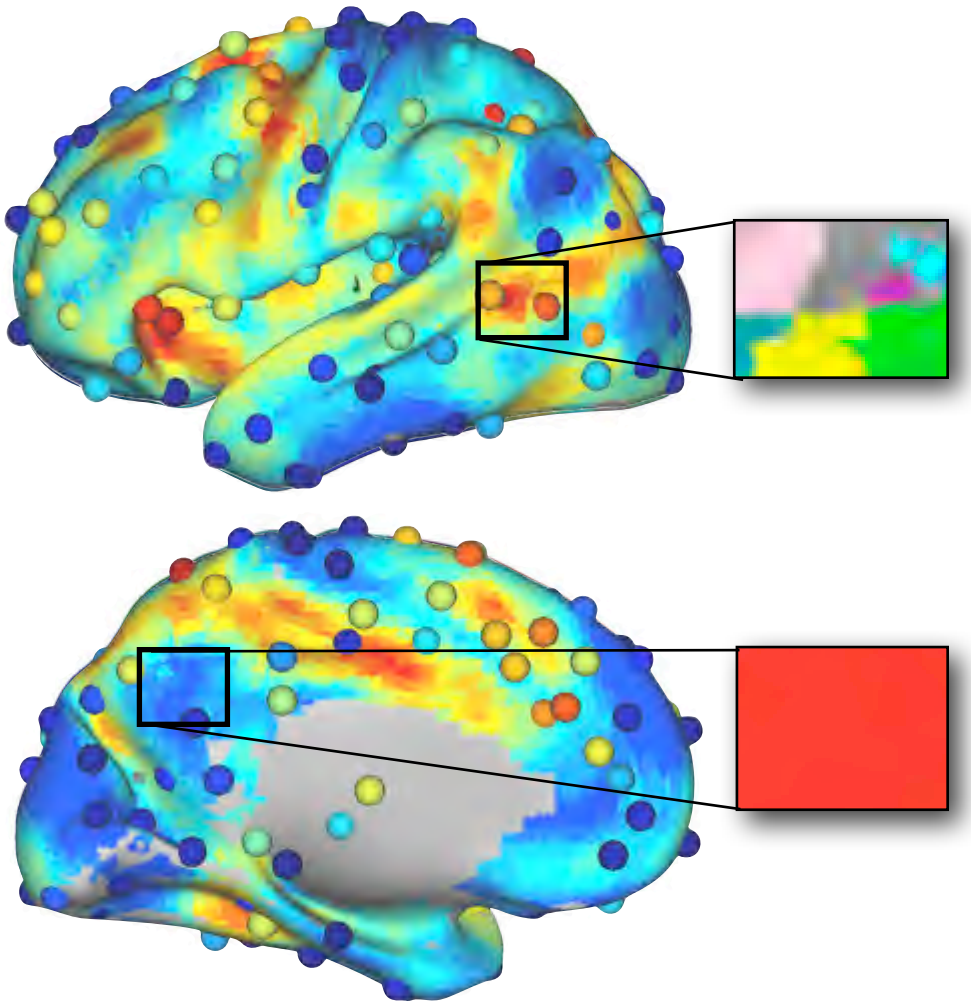


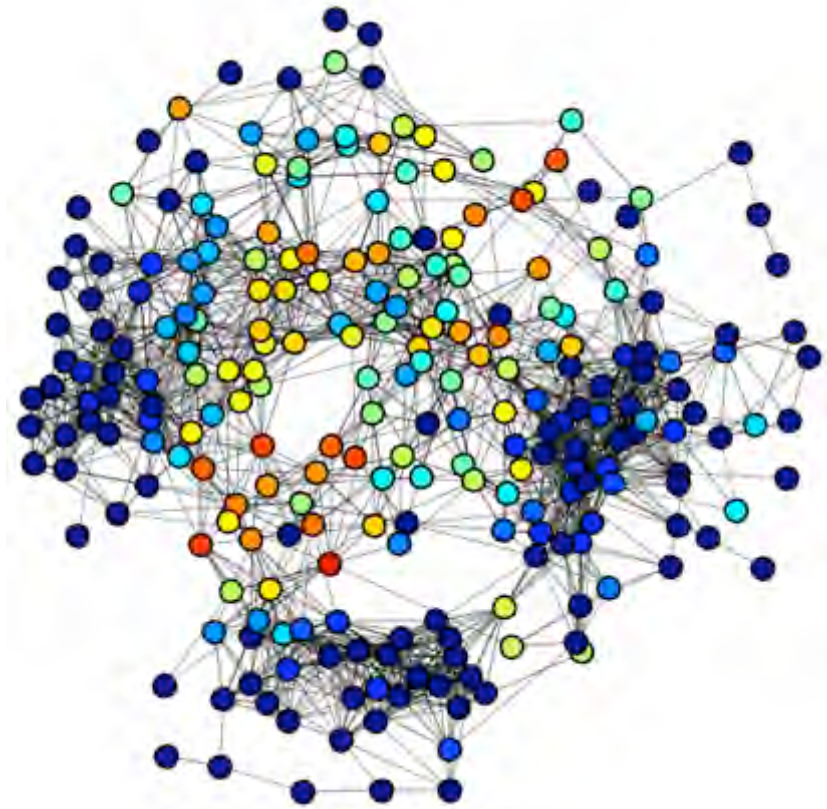
Single-system deficits

Translating model properties into brain properties



Translating model properties into brain properties





Participation coefficient

Main Conclusions

- RSFC
  - is growing in popularity
  - reflects aspects of brain organization
  - has relevance to traits, ongoing behavior, and disease

  - is poorly understood
    - what processes contribute?
    - what function(s)?

  - helps make simple models of a complex thing

Main Conclusions

- Some reviews on resting state:
  - Raichle, 2010. Two views of brain function. TICS.
  - Buckner et al., 2013. Opportunities and limitations of intrinsic connectivity MRI. Nature Neuroscience.
  - Bullmore & Sporns, 2012. The economy of brain network organization. Nature Reviews Neuroscience.