Resting-State fMRI: Principles and Basic Methods

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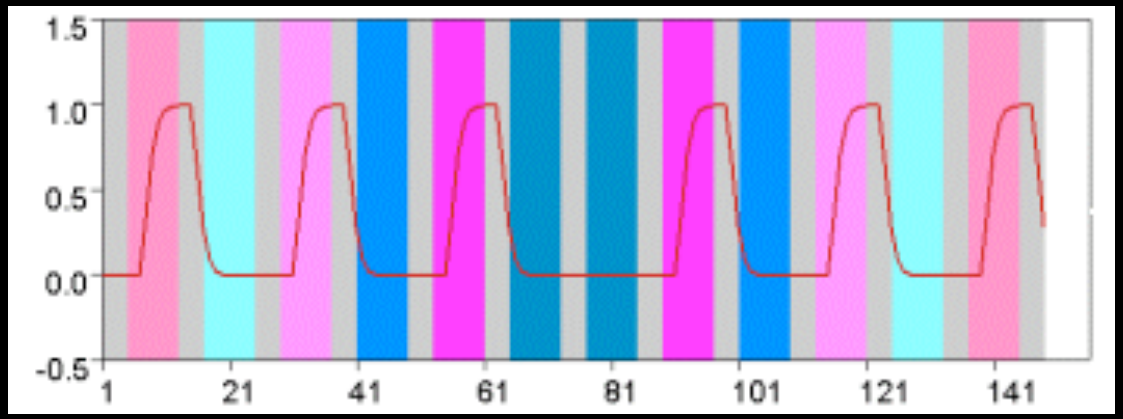
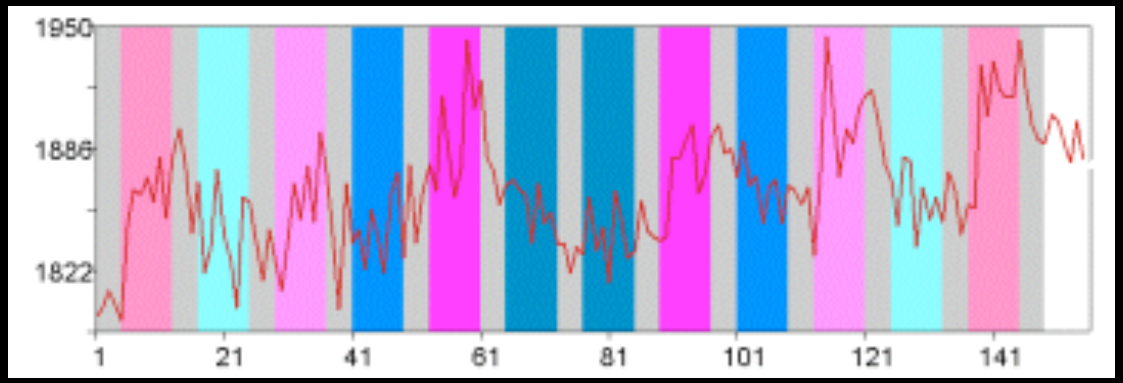
Overview

- Deactivation, the default mode and intrinsic connectivity networks
- Two approaches: ROI vs ICA
- Unbelievers and their reservations
- Converting the unbelievers
- The future (of resting-state fMRI)

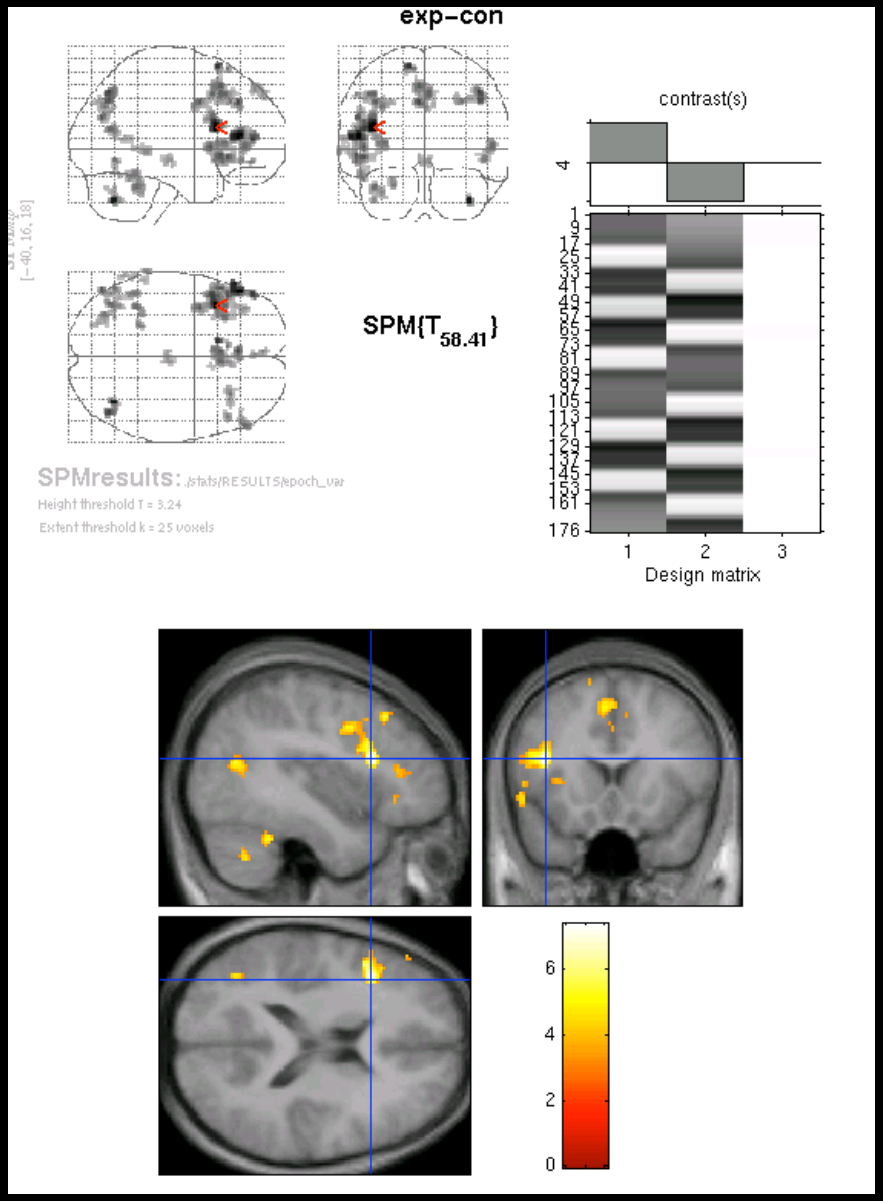
Task Waveform Used to Identify Activated (or Deactivated) Voxels



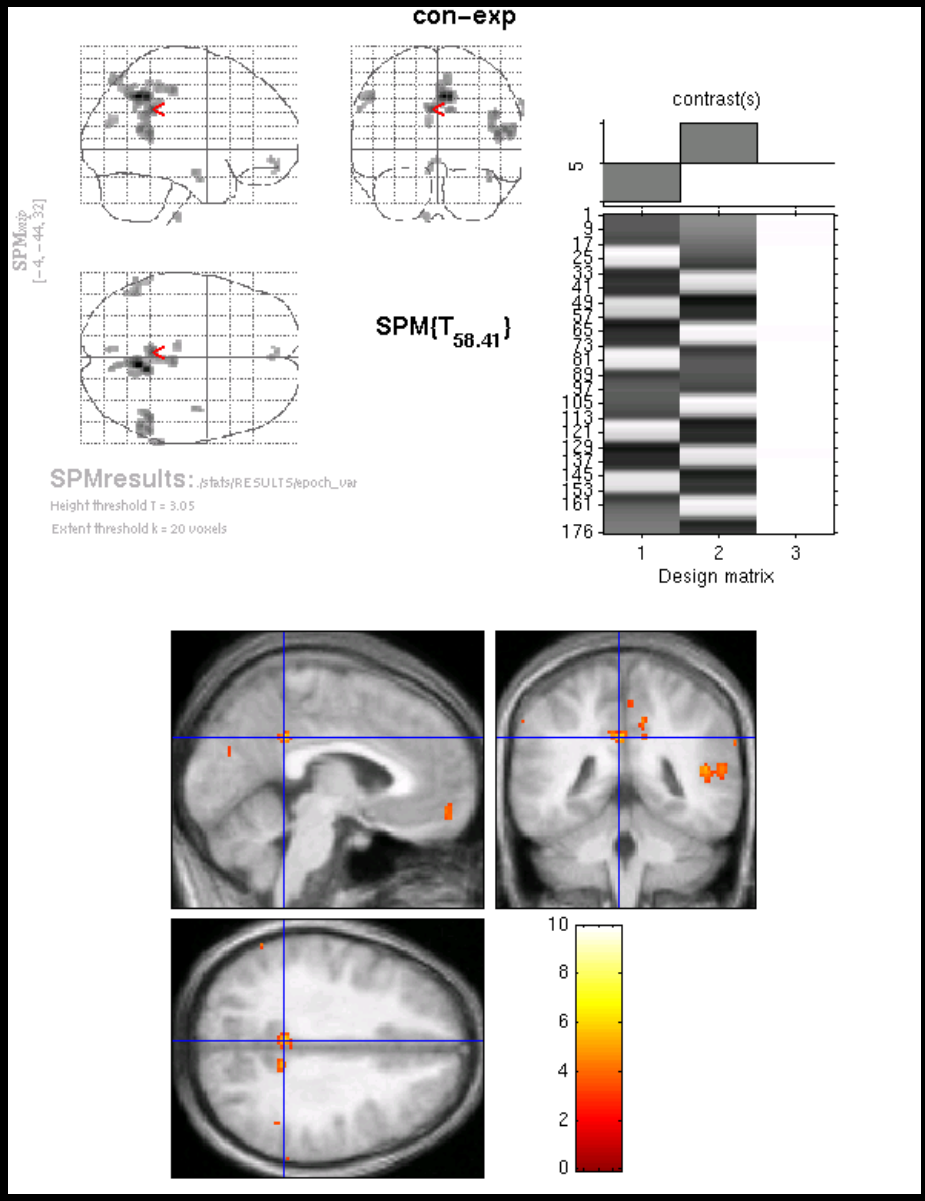


“active” voxel timecourse

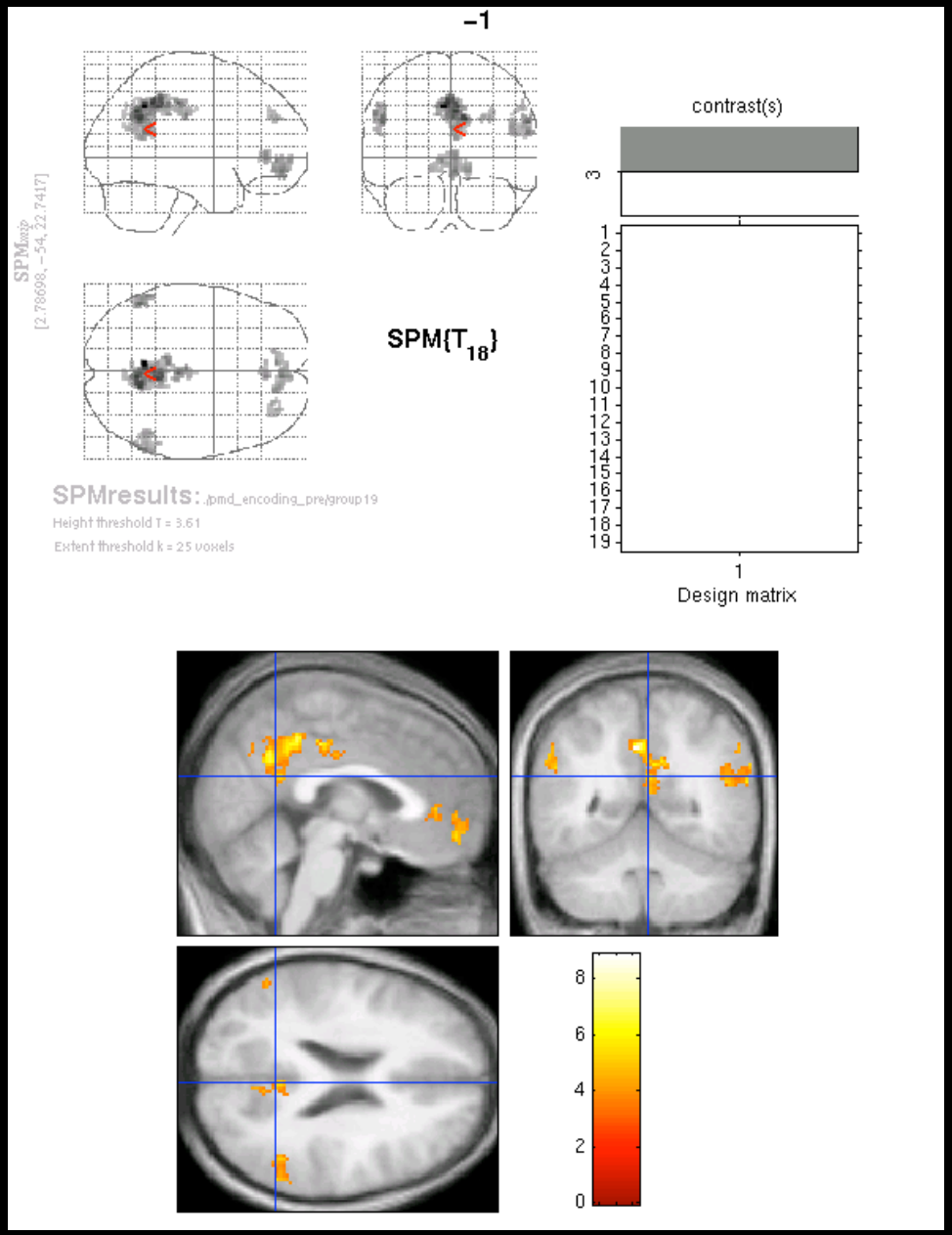
Activation



Deactivation

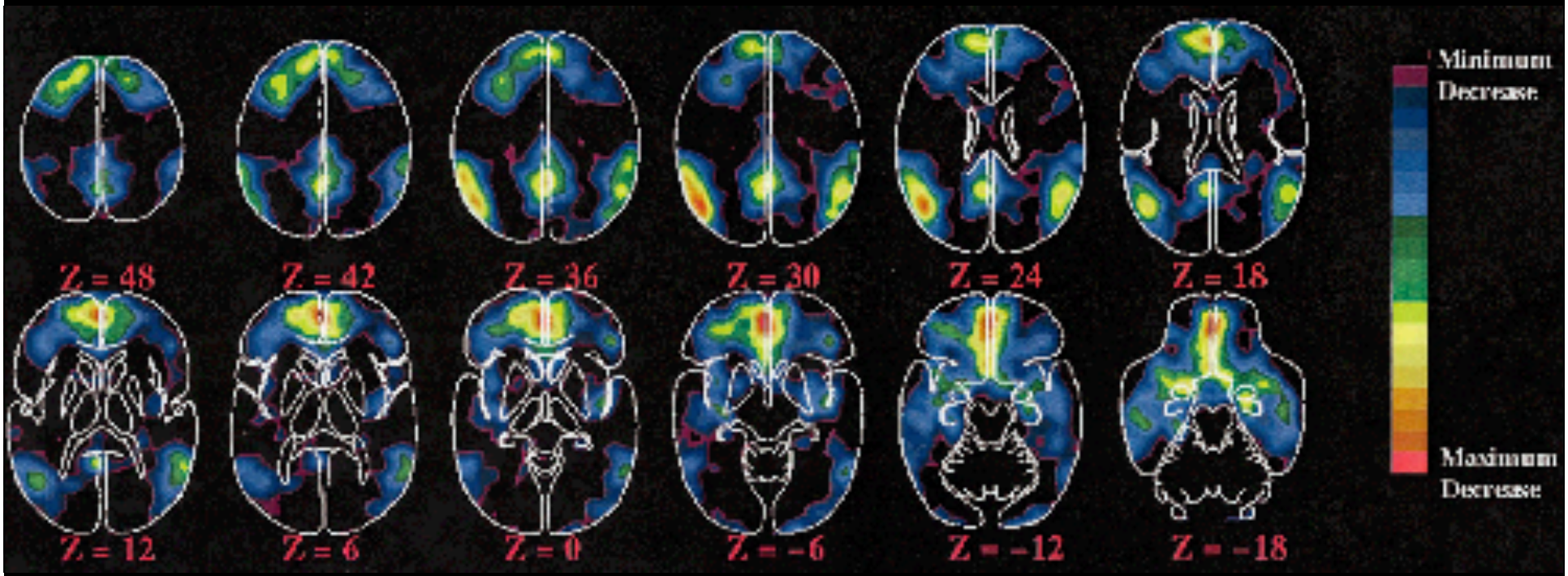


Deactivation Consistently Occurs in the Same Regions



Deactivation averaged across 19 subjects in a verbal encoding task

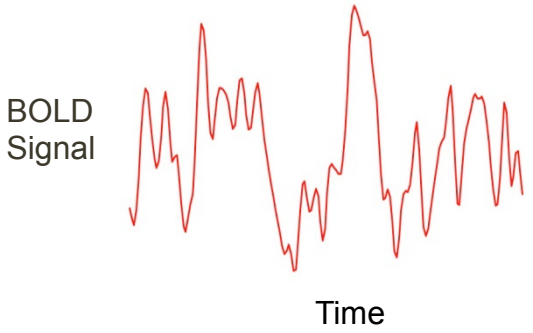
Deactivation and the Default Mode of Brain Activity



Raichle et al., *PNAS*, 2001

Resting-State Functional Connectivity (region-of-interest approach)

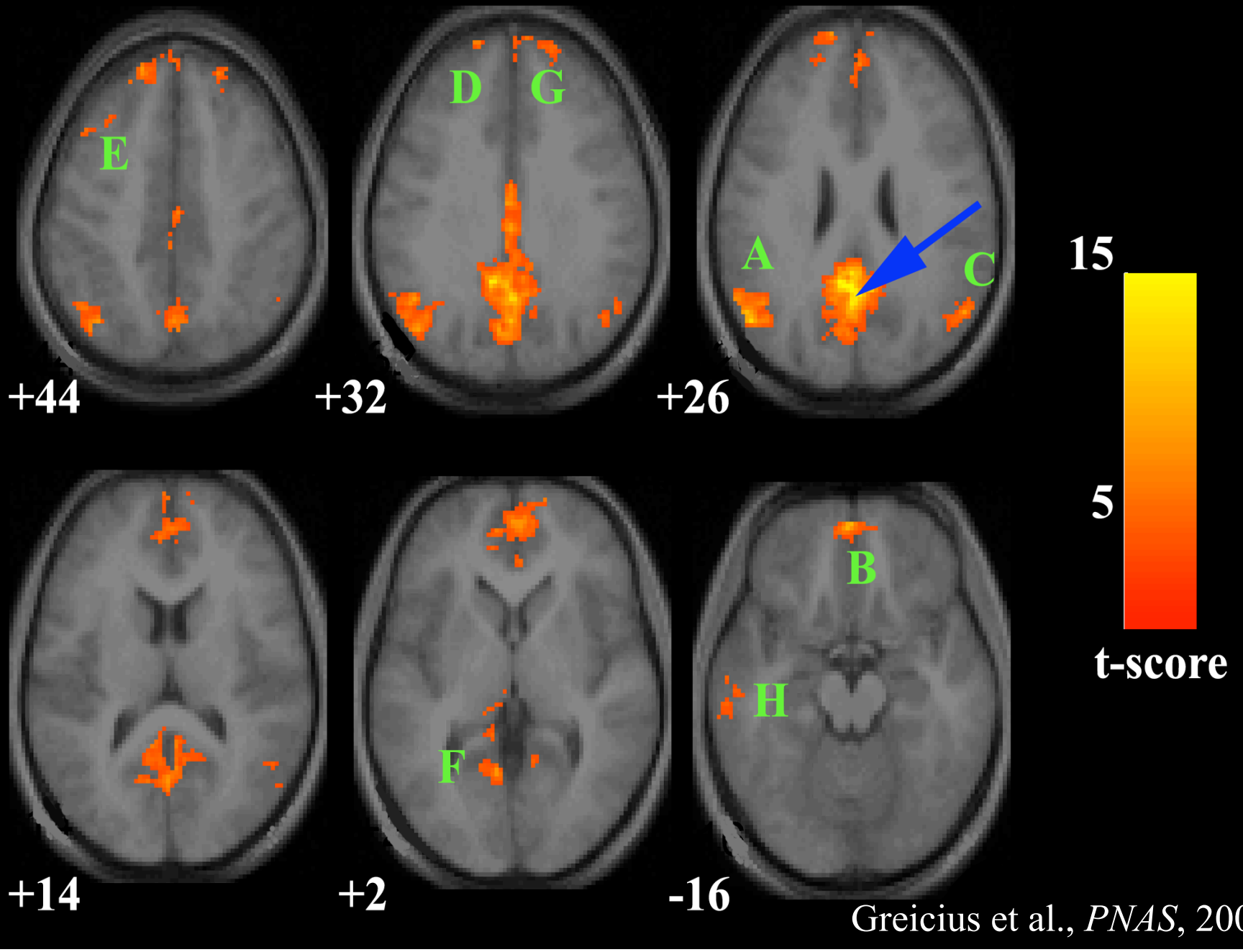
r = 0.80



r = 0.59

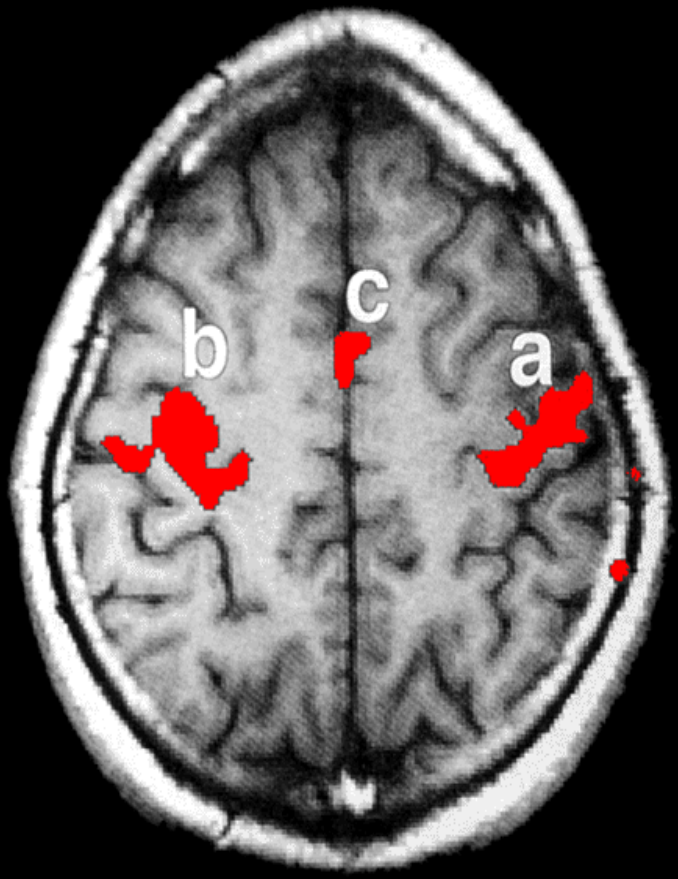
r = 0.75

Resting-State Default-Mode Network

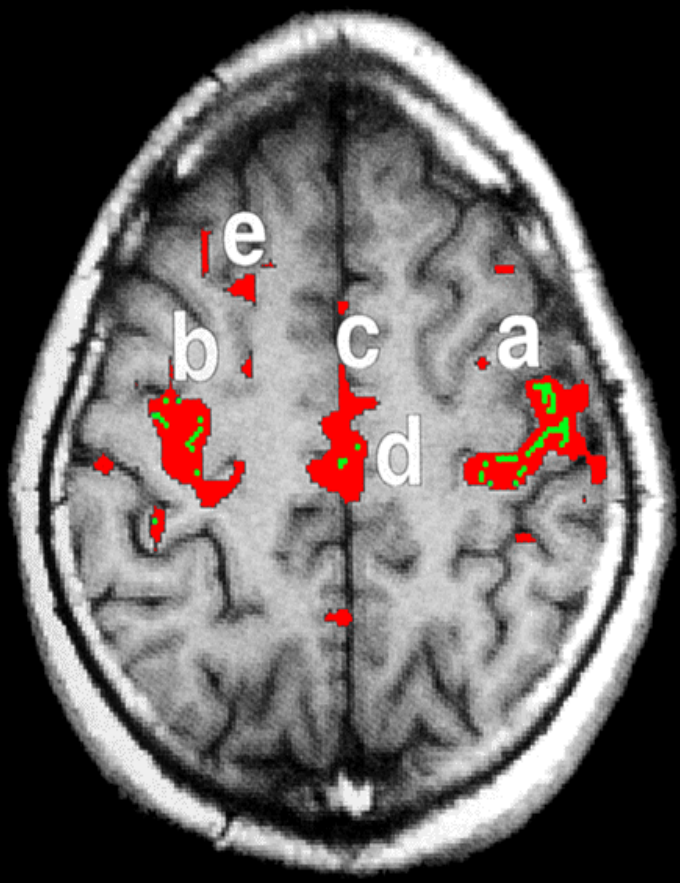


Greicius et al., *PNAS*, 2003

Resting Motor Cortex Connectivity



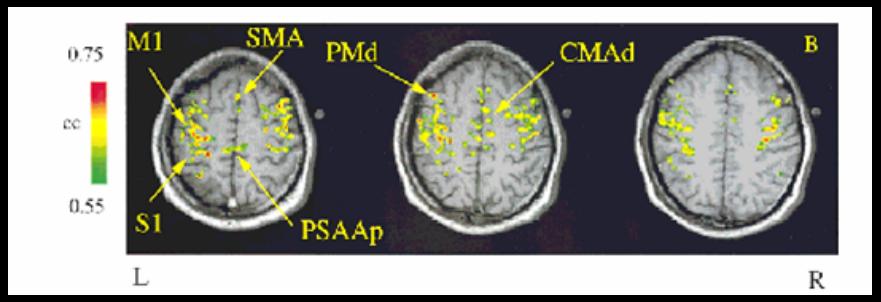
Motor cortex defined by task-activation *f*MRI



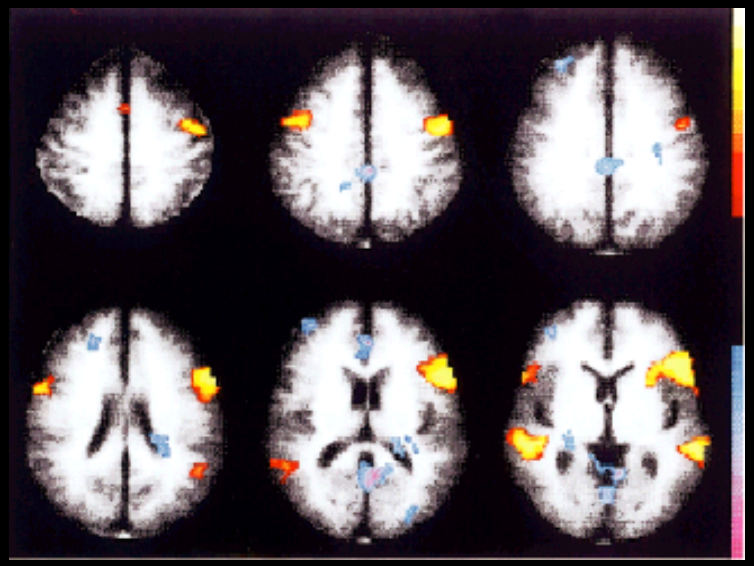
Spontaneous correlations with motor cortex

Biswal et al., *Magn Reson Med,* 1995

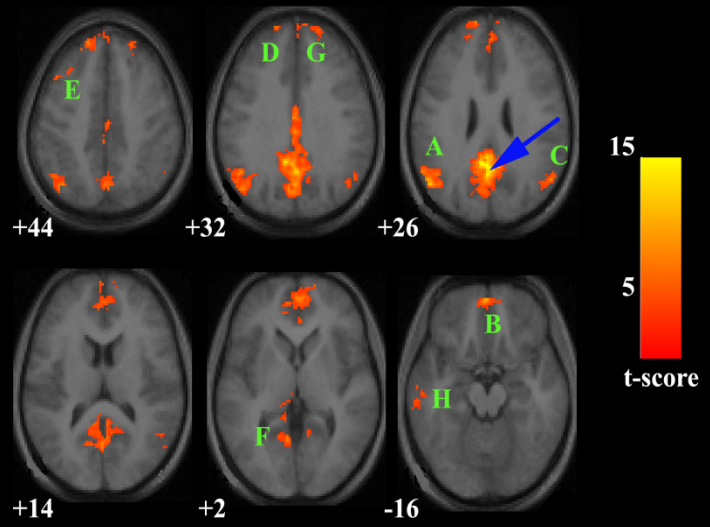
ROI-Based Approaches: Something for Everyone



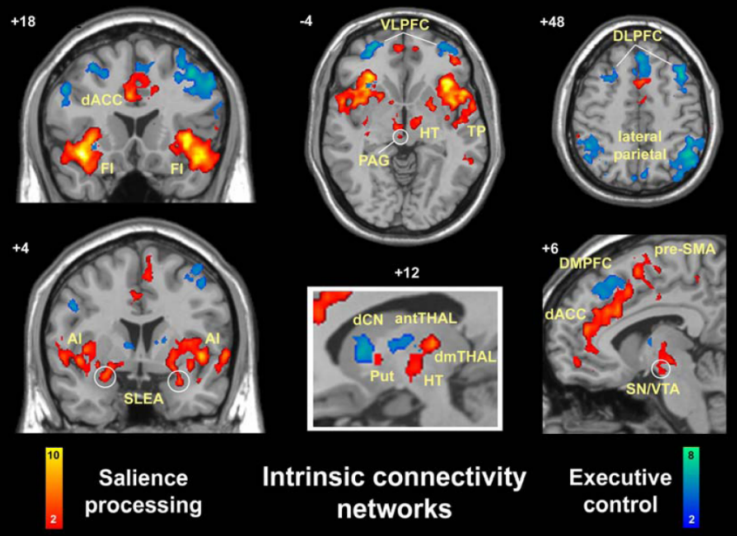
Motor: Biswal et al., 1995
Xiong et al., 1999



Language: Hampson et al., 2002

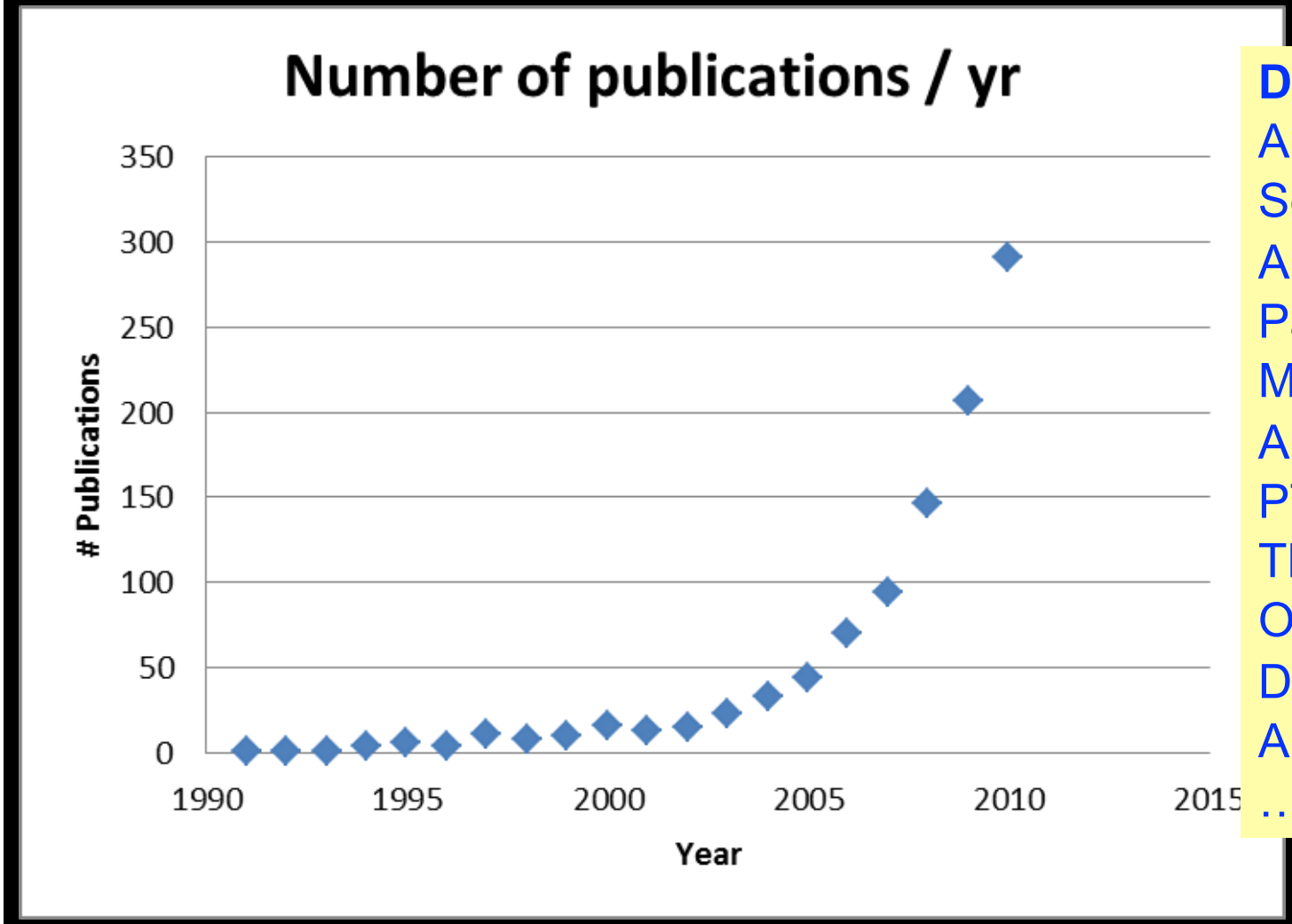


Default Mode: Greicius et al., 2003



Executive control and Salience: Seeley et al., 2007

Exponential Growth of Resting State fMRI Studies



Disorders Studied

Autism
Schizophrenia
Alzheimer's Disease
Parkinson's Disease
Multiple Sclerosis
ADHD
PTSD
TBI
OCD
Depression/Bipolar
Anxiety Disorder
…

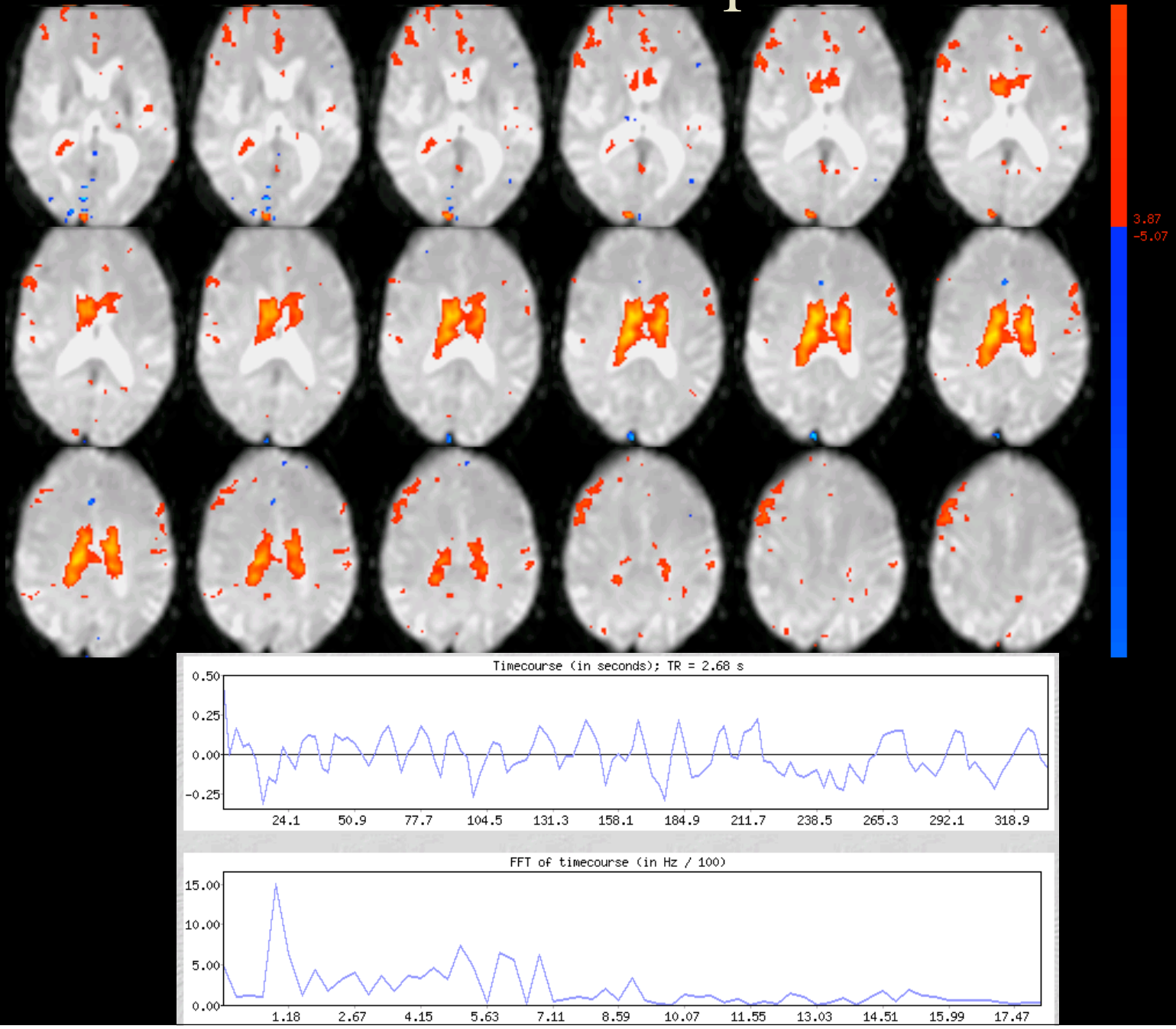
Slide and scopus search courtesy of Rasmus Birn, University of Wisconsin

If you don’t believe Scopus

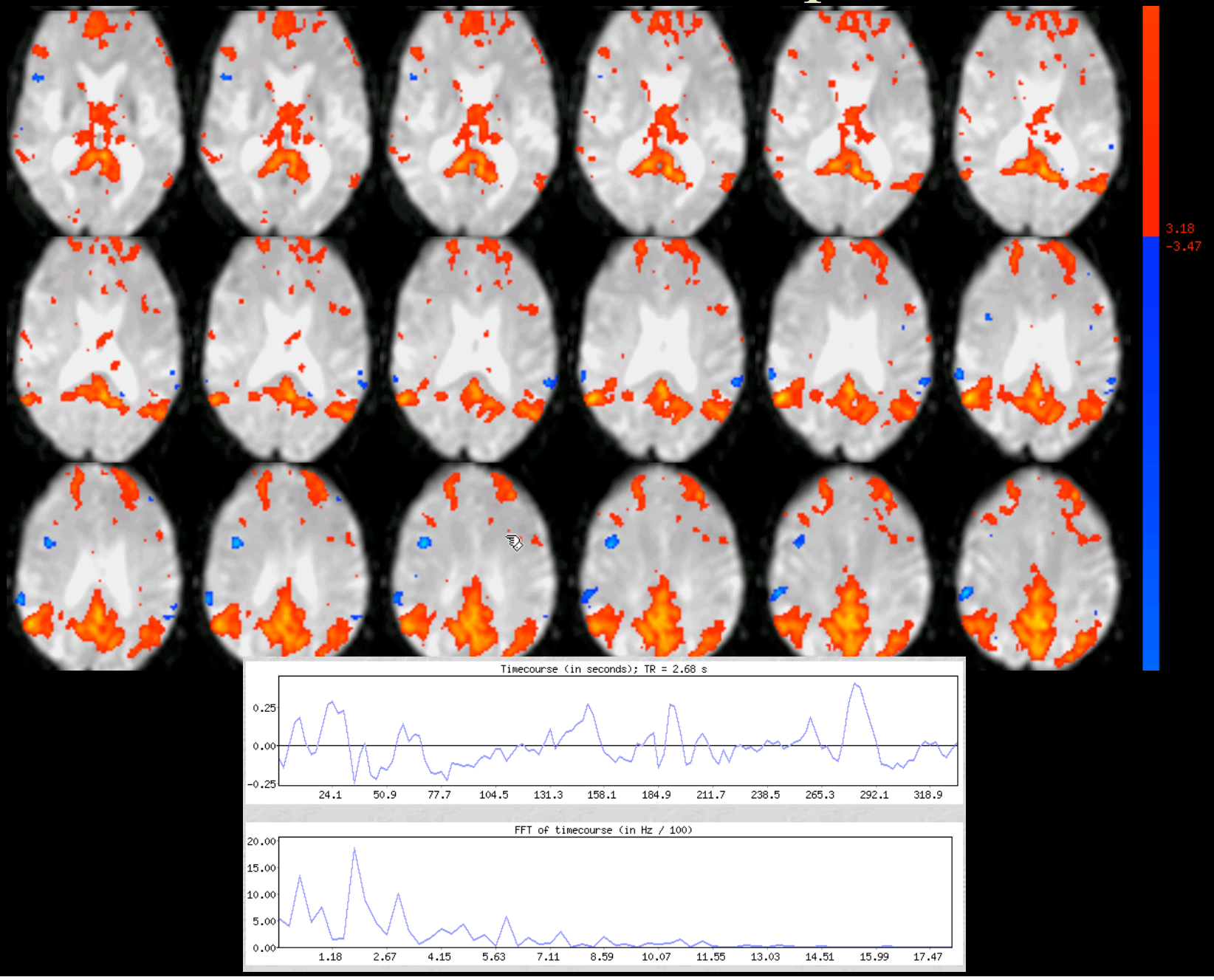
Independent Component Analysis in the Detection of Intrinsic Connectivity Networks

- ICA separates the fMRI signal into (largely) non-overlapping spatiotemporal components
- Data-driven but can also be hypothesis-driven
- Allows for better removal of noisy components (motion, scanner drift, etc).
- Reliably extracts default-mode network (and others) en bloc

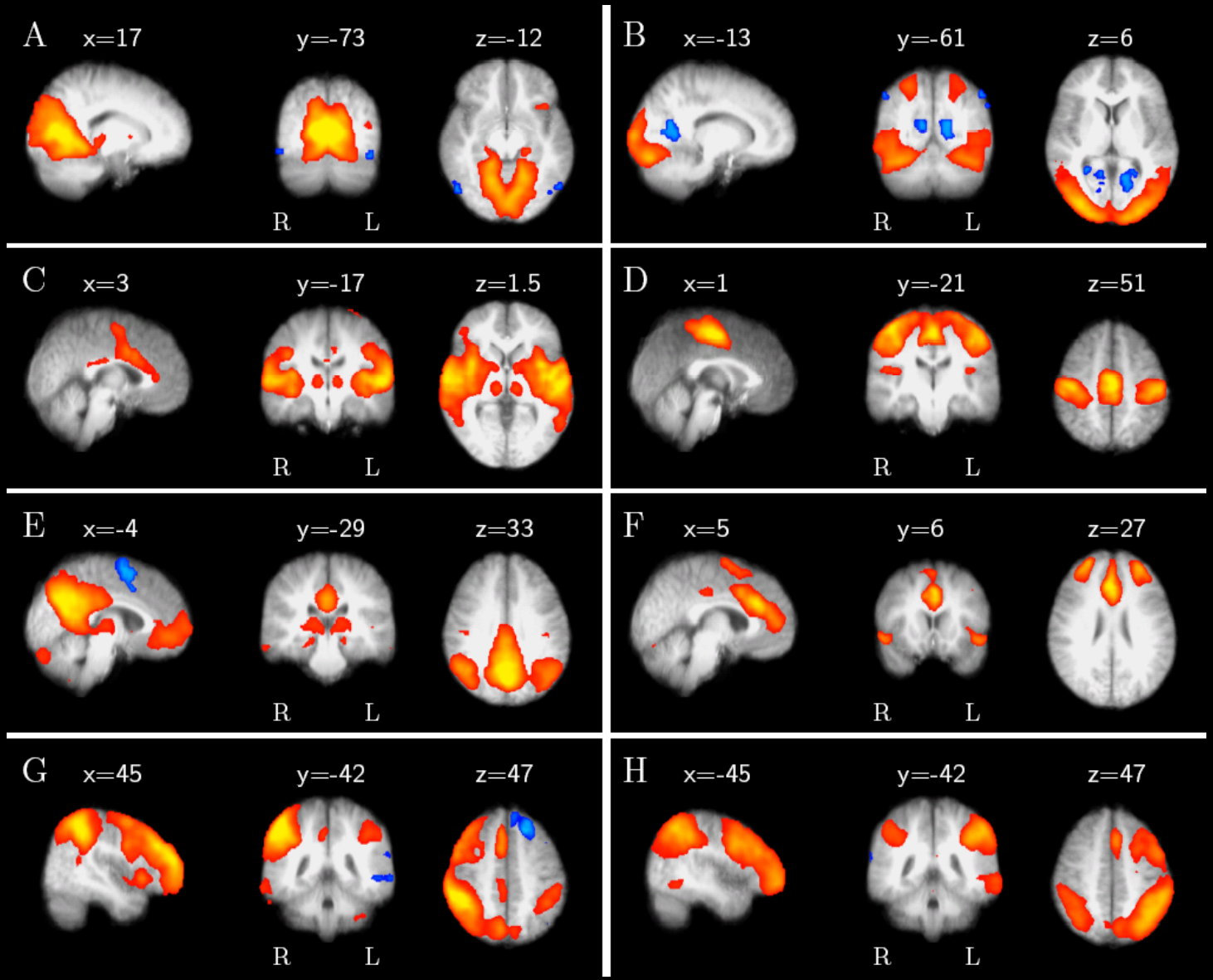
“Bad” ICA Component



“Good” ICA Component



ICA: A Network for Every Function



Beckmann et al., *Philos Trans R Soc Lond*, 2005

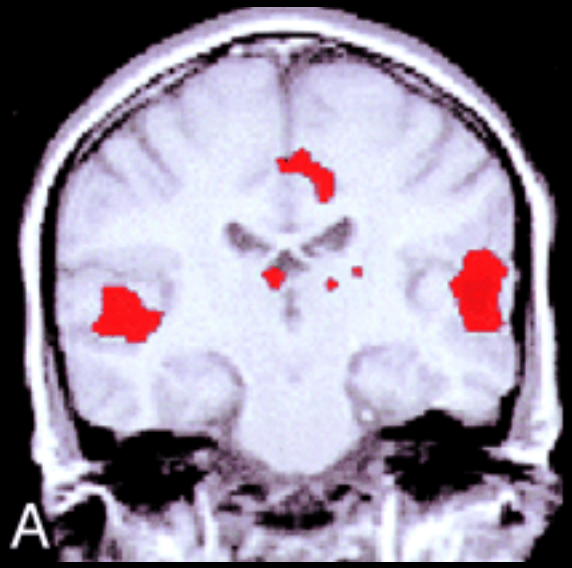
Healthy Skepticism

"For example, is this merely an effect of mechanical symmetry between the hemispheres in response to cardiac and CSF pulsations? Can the response be explained by vasomotor oscillations …? Is this response modulated by levels of consciousness? Are crossing white matter pathways truly necessary …?"

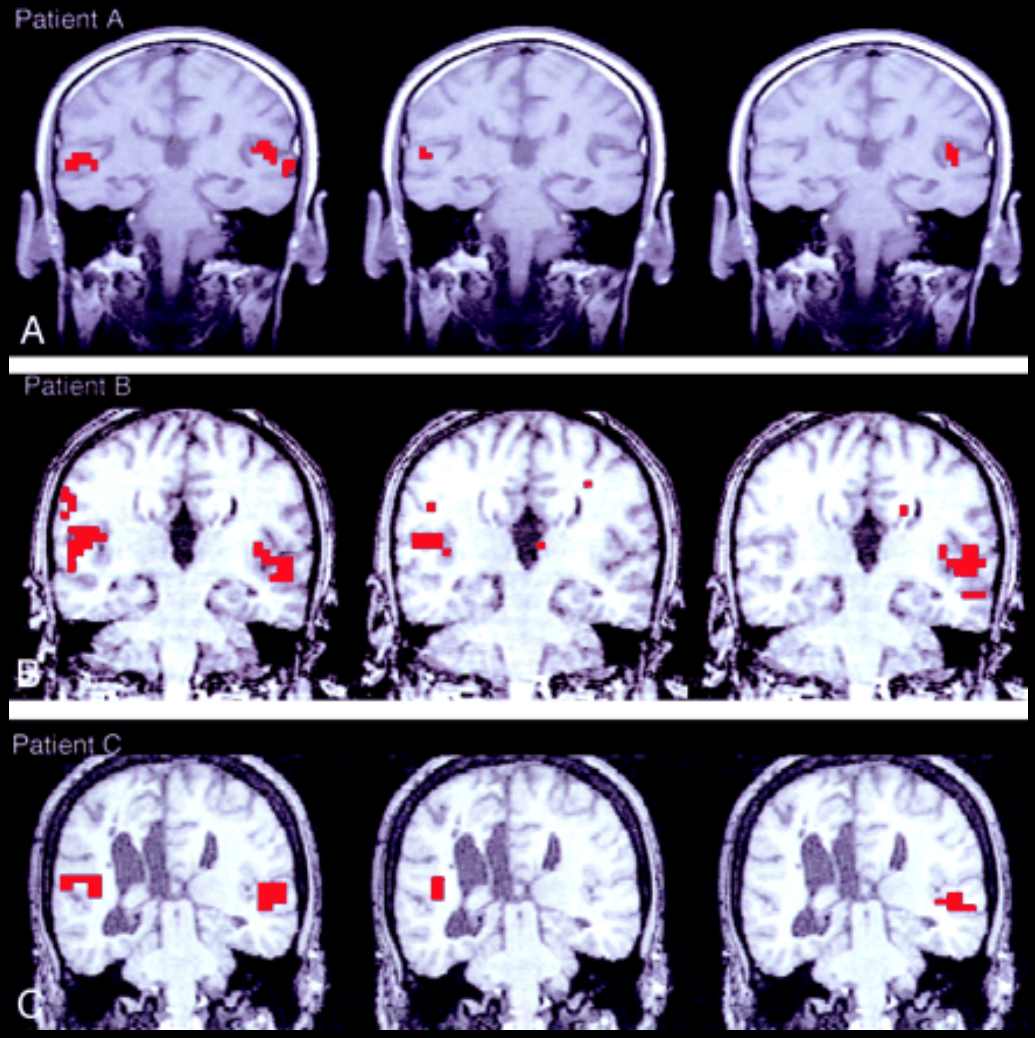
---Functional connectivity MR imaging: fact or artifact?

Maldjian, JA *AJNR*, 2001

Absent Contralateral Connectivity in Agenesis of the Corpus Callosum



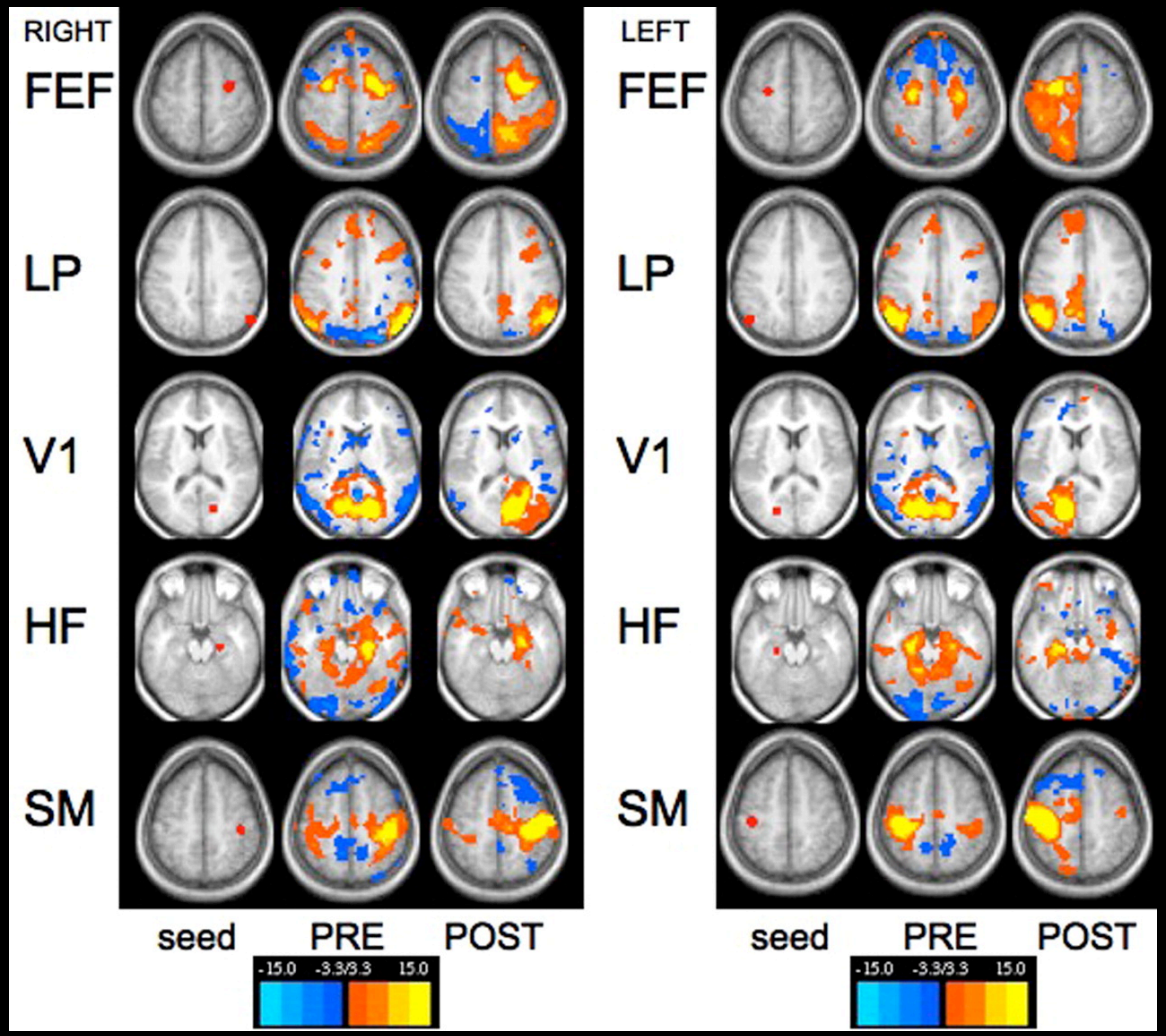
Healthy control



3 subjects with agenesis of the corpus callosum

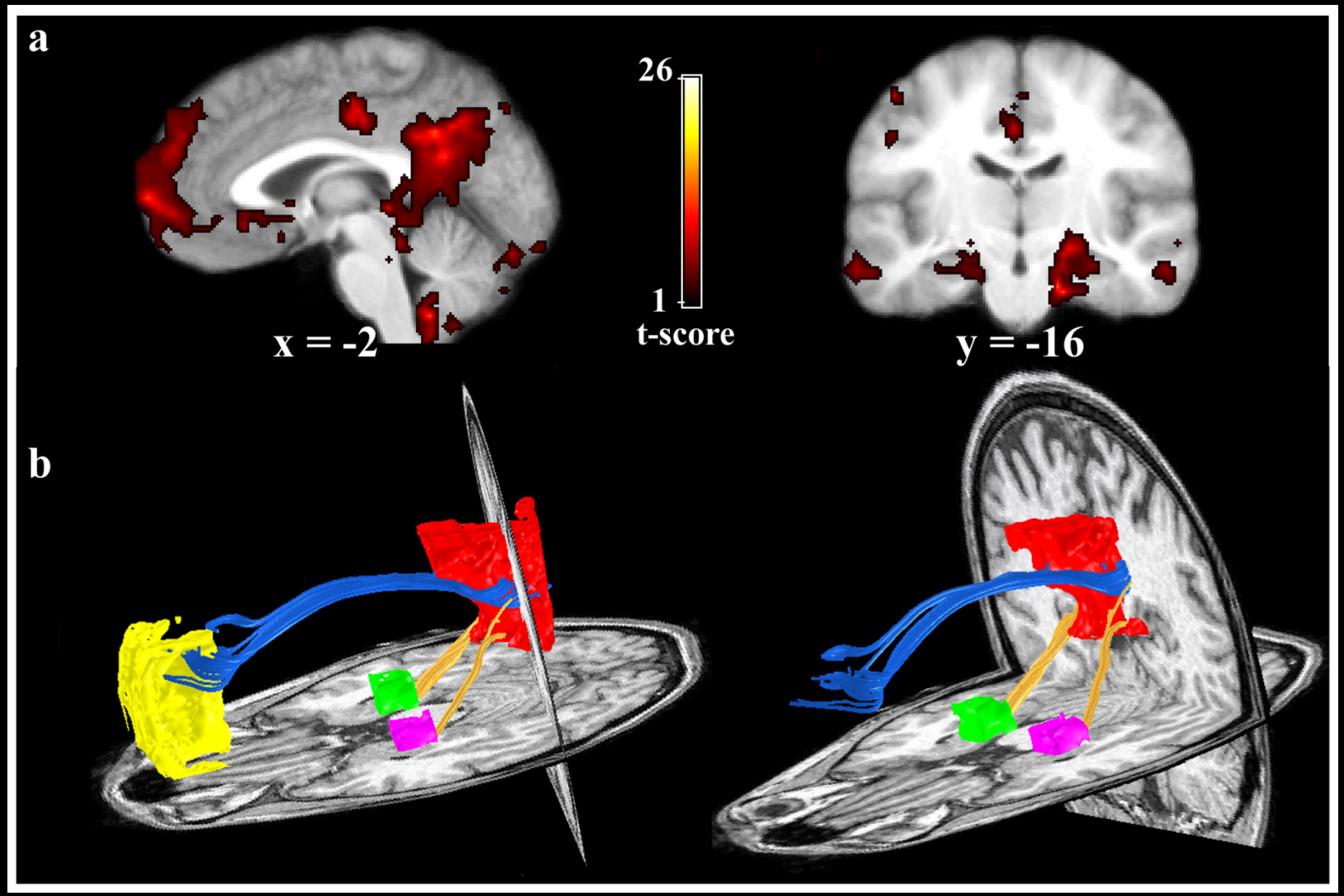
Quigley et al., *AJNR*, 2003

Callosotomy



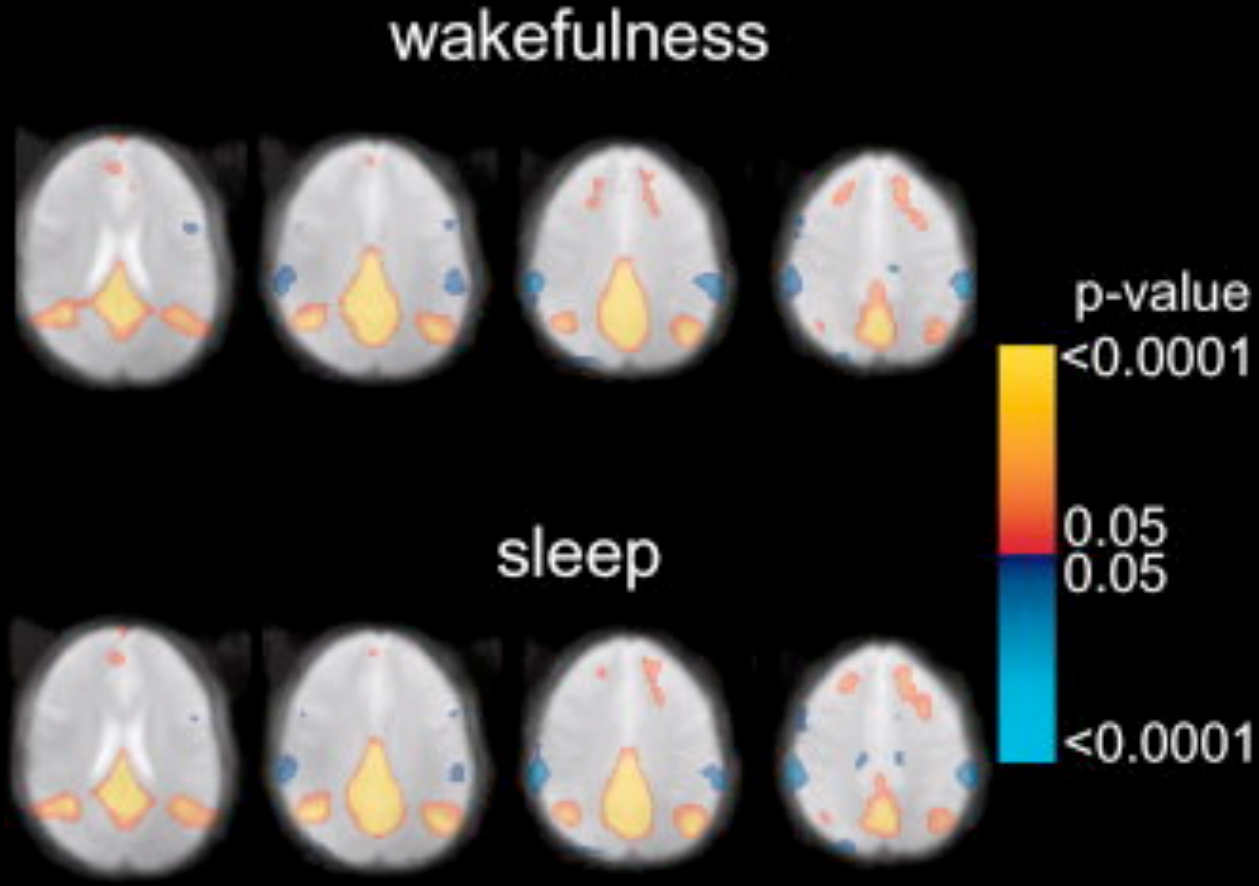
Johnston et al., *J Neurosci*, 2008

Functional Connectivity Reflects Structural Connectivity



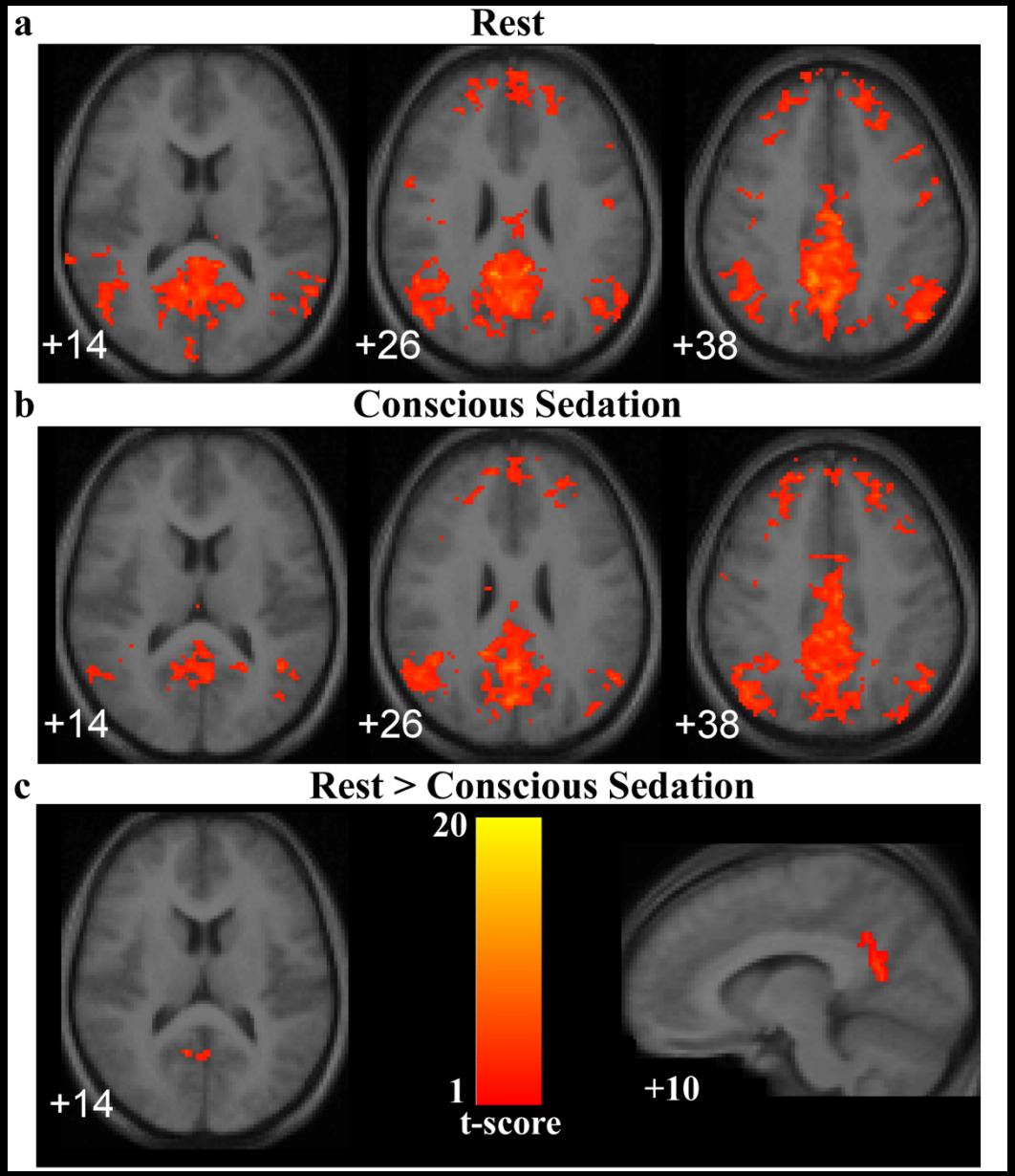
Greicius et al., *Cer Cortex*, 2008

Light Sleep



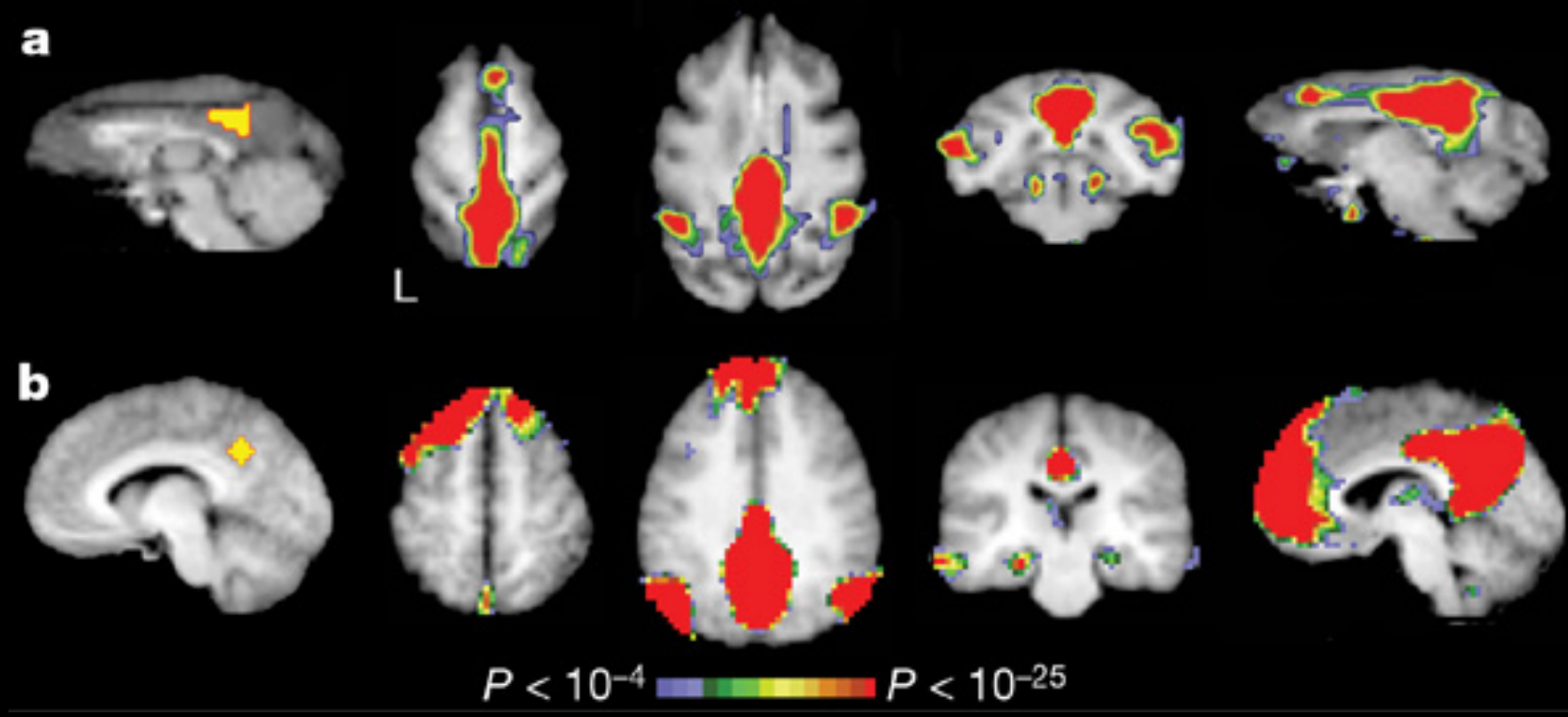
Horovitz et al., *Hum Brain Mapp*, 2008

Decreased but Detectable DMN under Conscious Sedation



Greicius et al., *Hum Brain Mapp*, 2008

DMN in Sedated Macaques



Vincent et al., *Nature,* 2007

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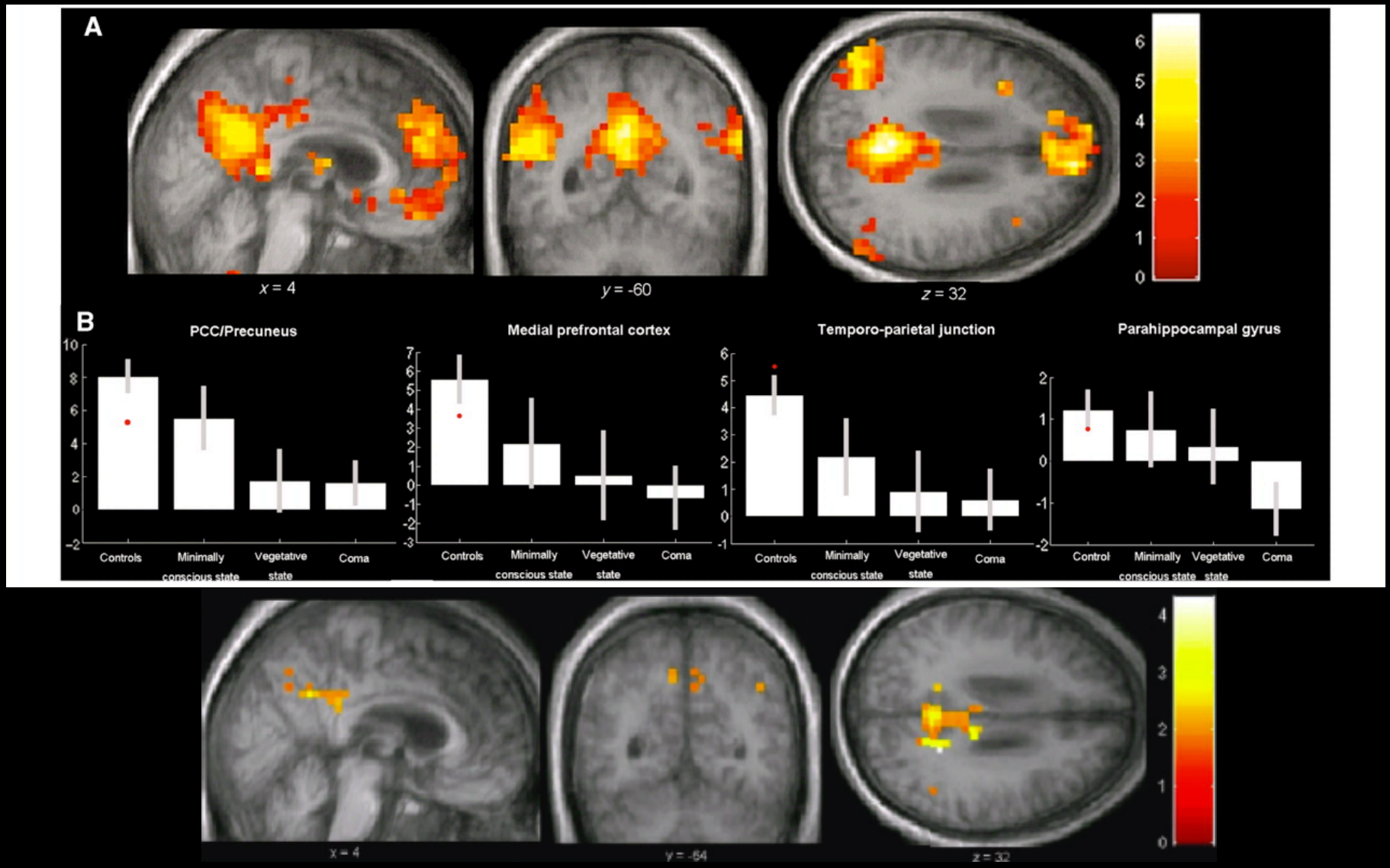
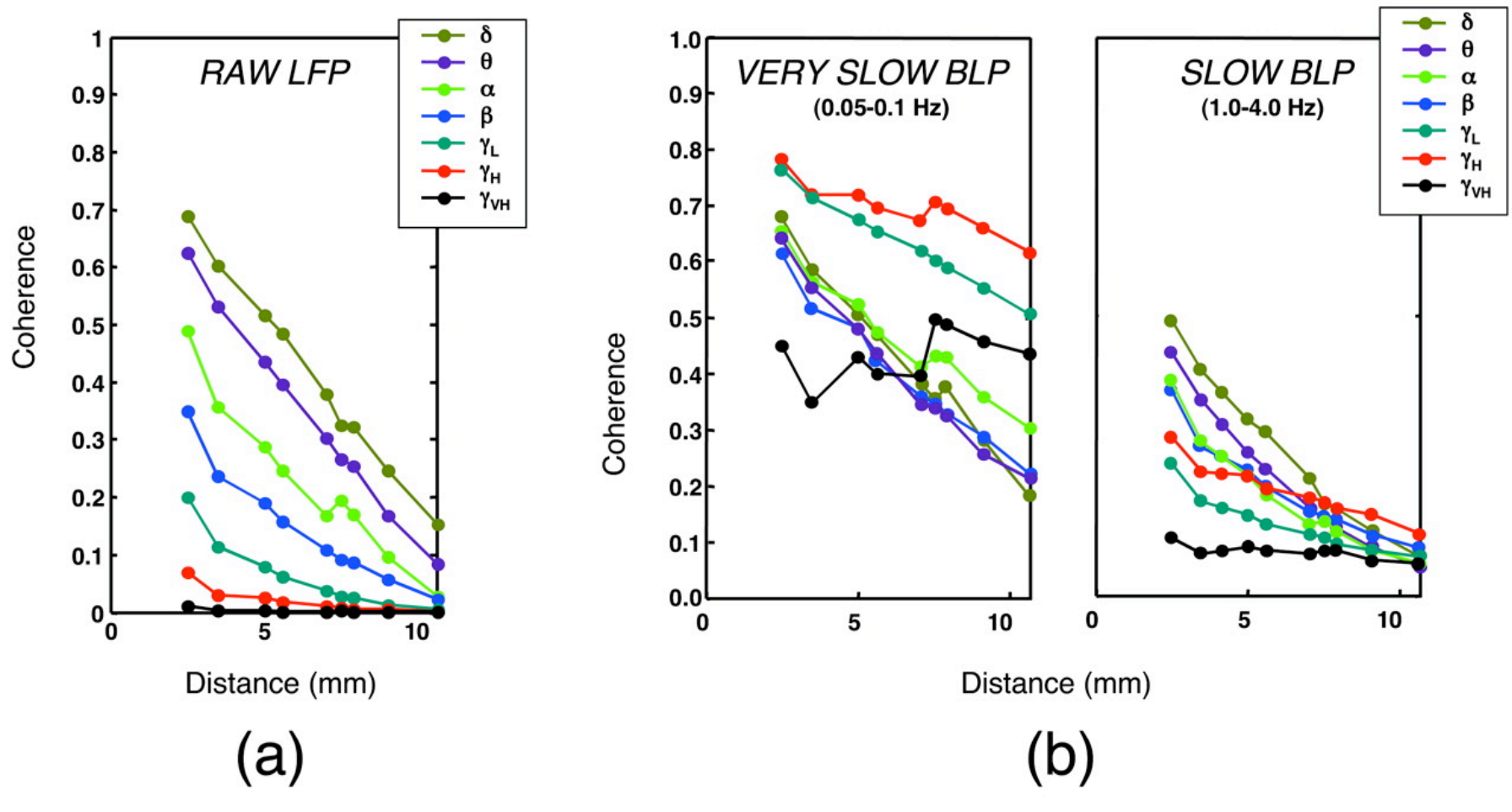


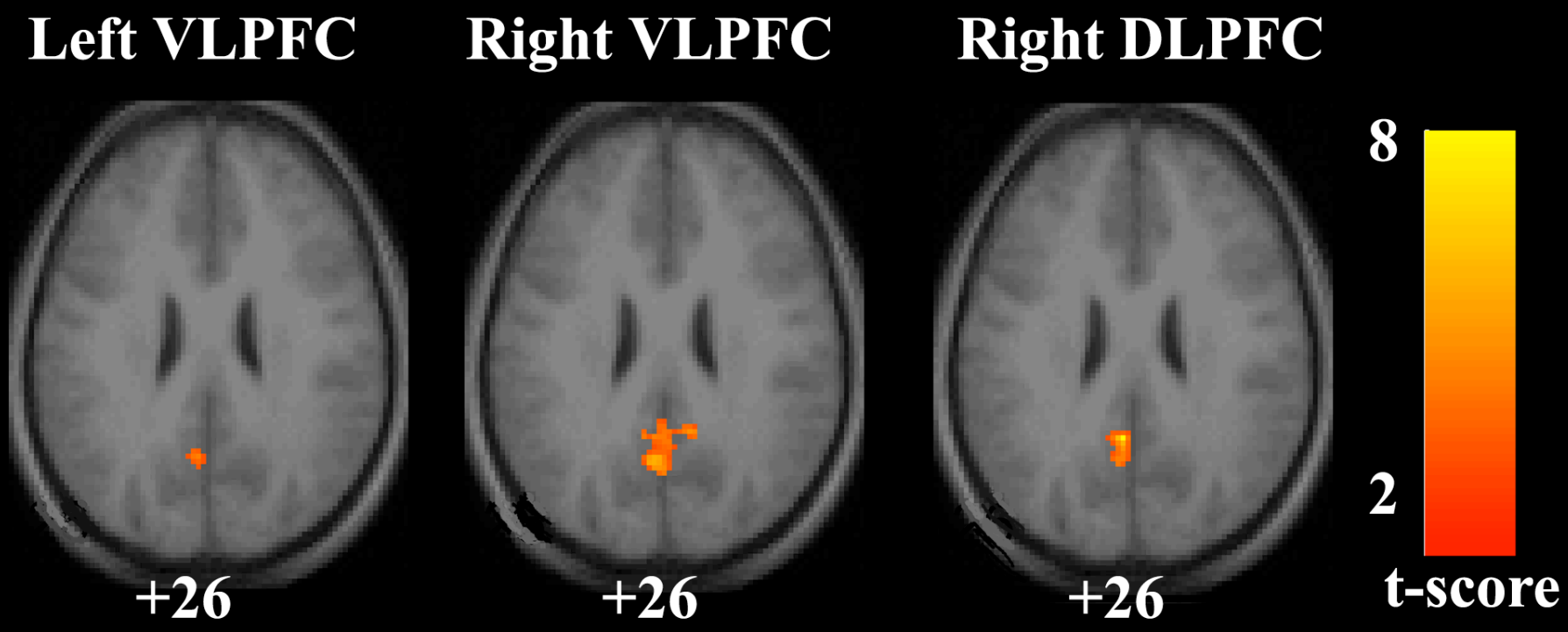
Vanhaudenhuyse et al., *Brain*, 2010

Low-Frequency Oscillations in Gamma Power Are Correlated Across Distant Electrodes



Leopold et al., *Cereb Cortex*, 2003

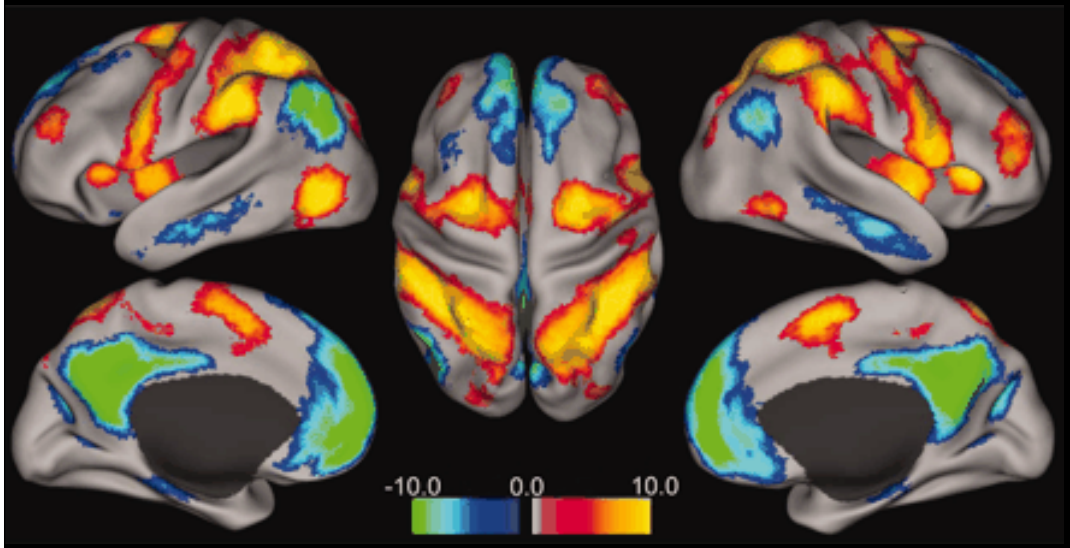
Inter-Network Interactions



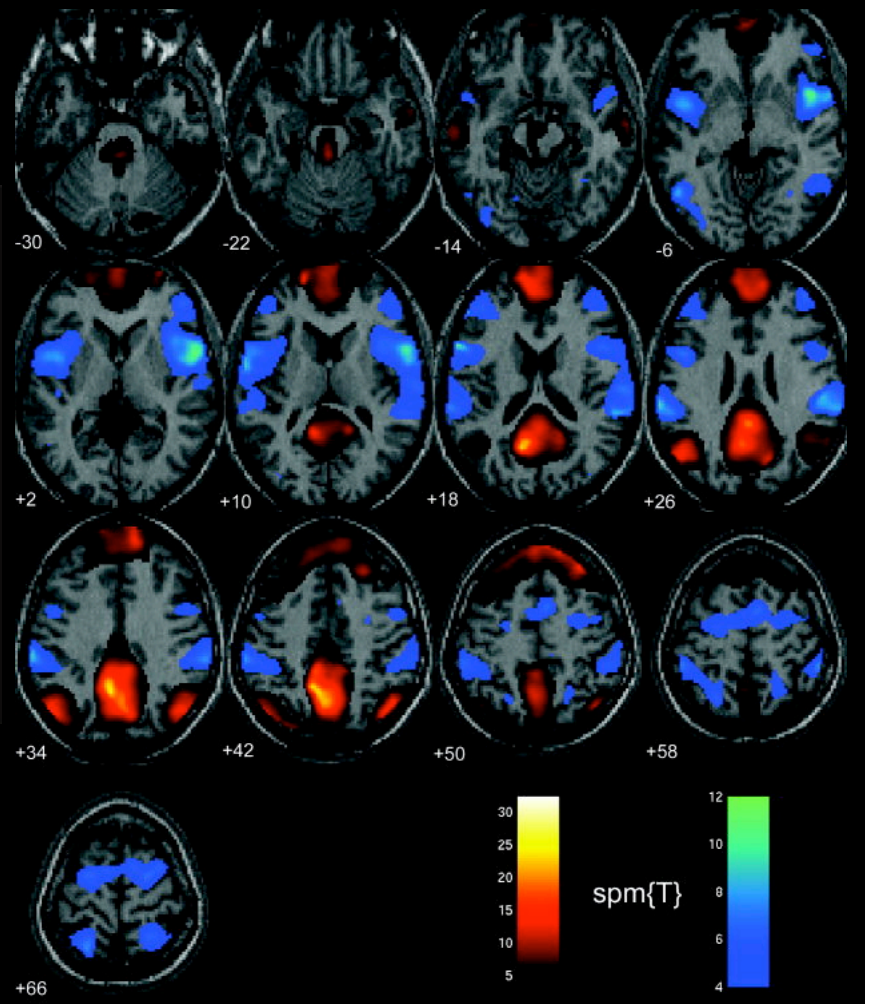
The default mode network "is maintained in a dynamic equilibrium with lateral prefrontal regions that commonly show task-related increases in activity."

Greicius et al., *PNAS*, 2003

Inter-Network Interactions

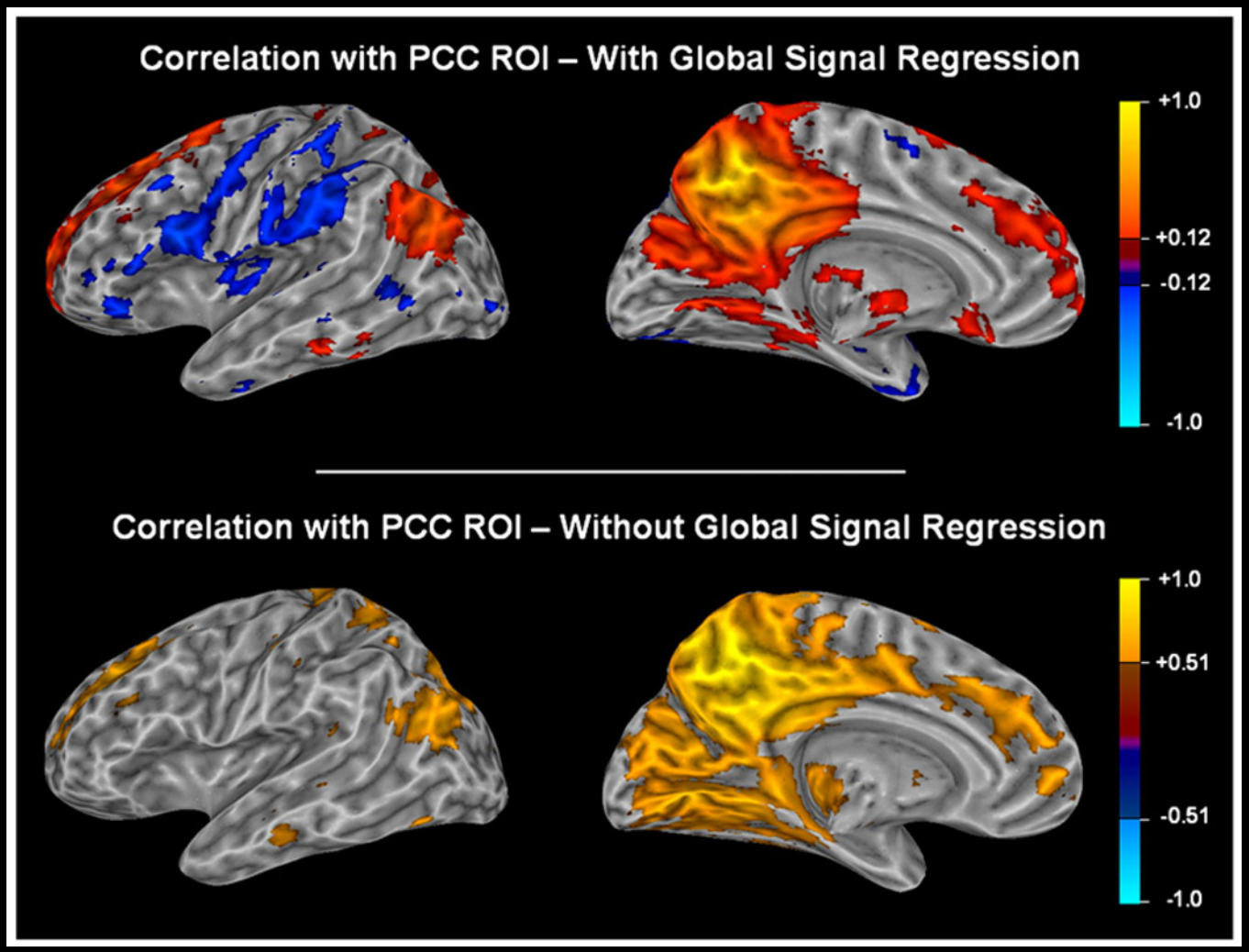


Fox et al., *PNAS*, 2005



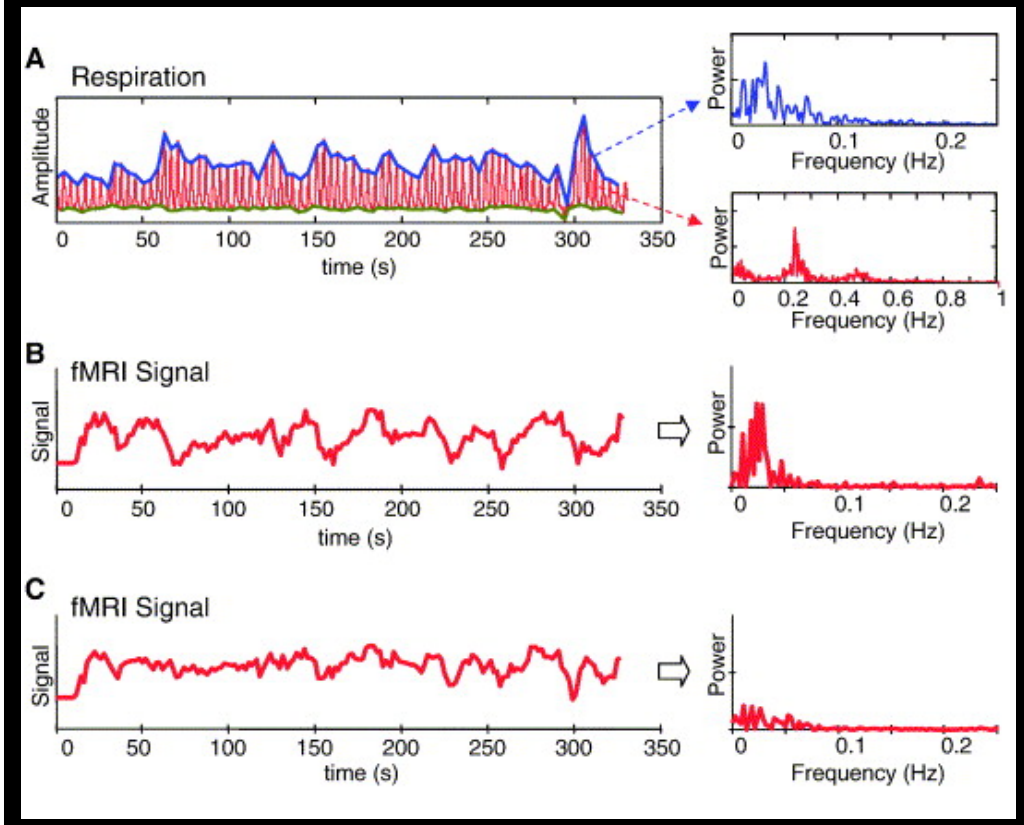
Fransson, *Hum Brain Mappp*, 2005

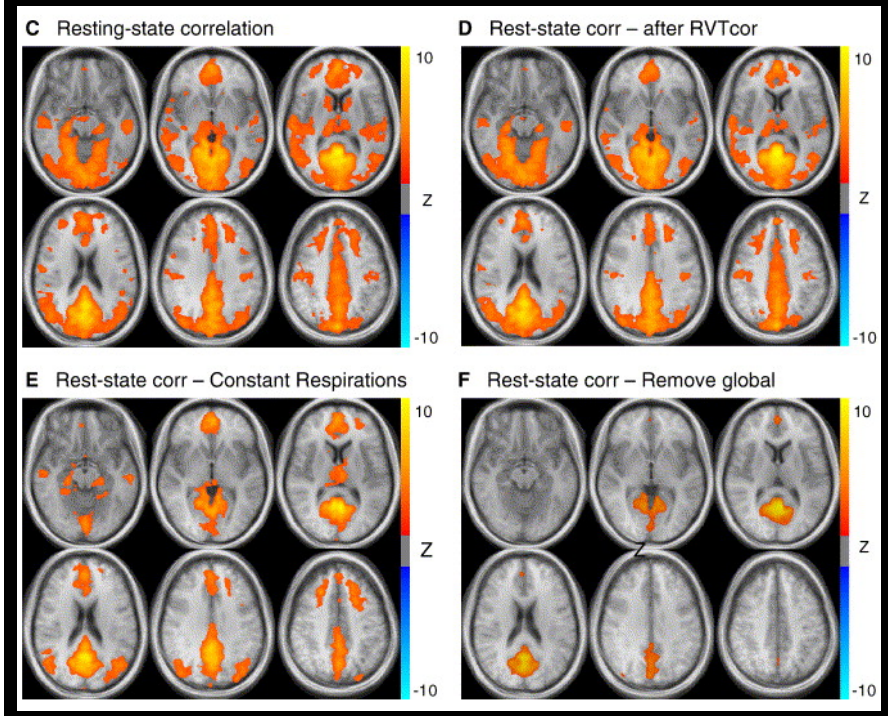
The Global Signal Skirmishes



Murphy et al., *Neuroimage*, 2009

Low-Frequency Respiratory Cycle Noise

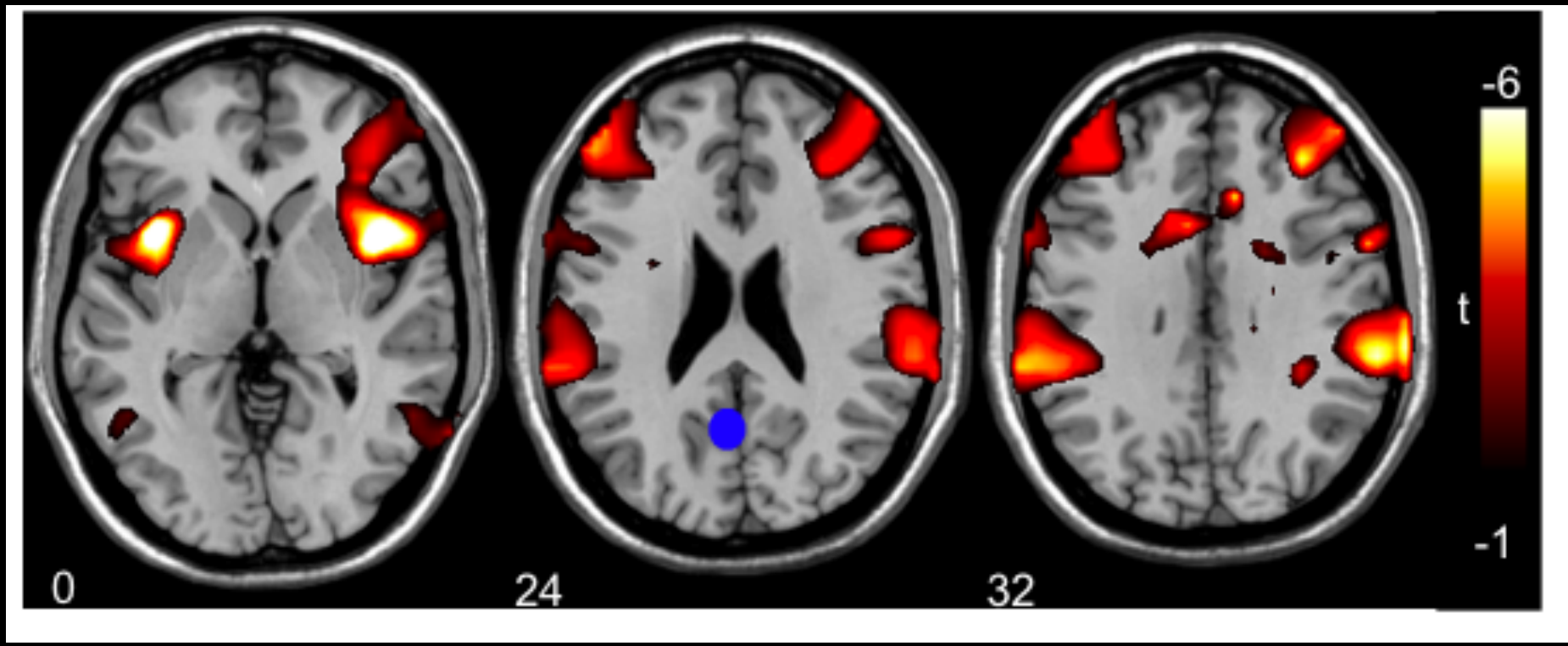




Birn et al., *Neuroimage*, 2006

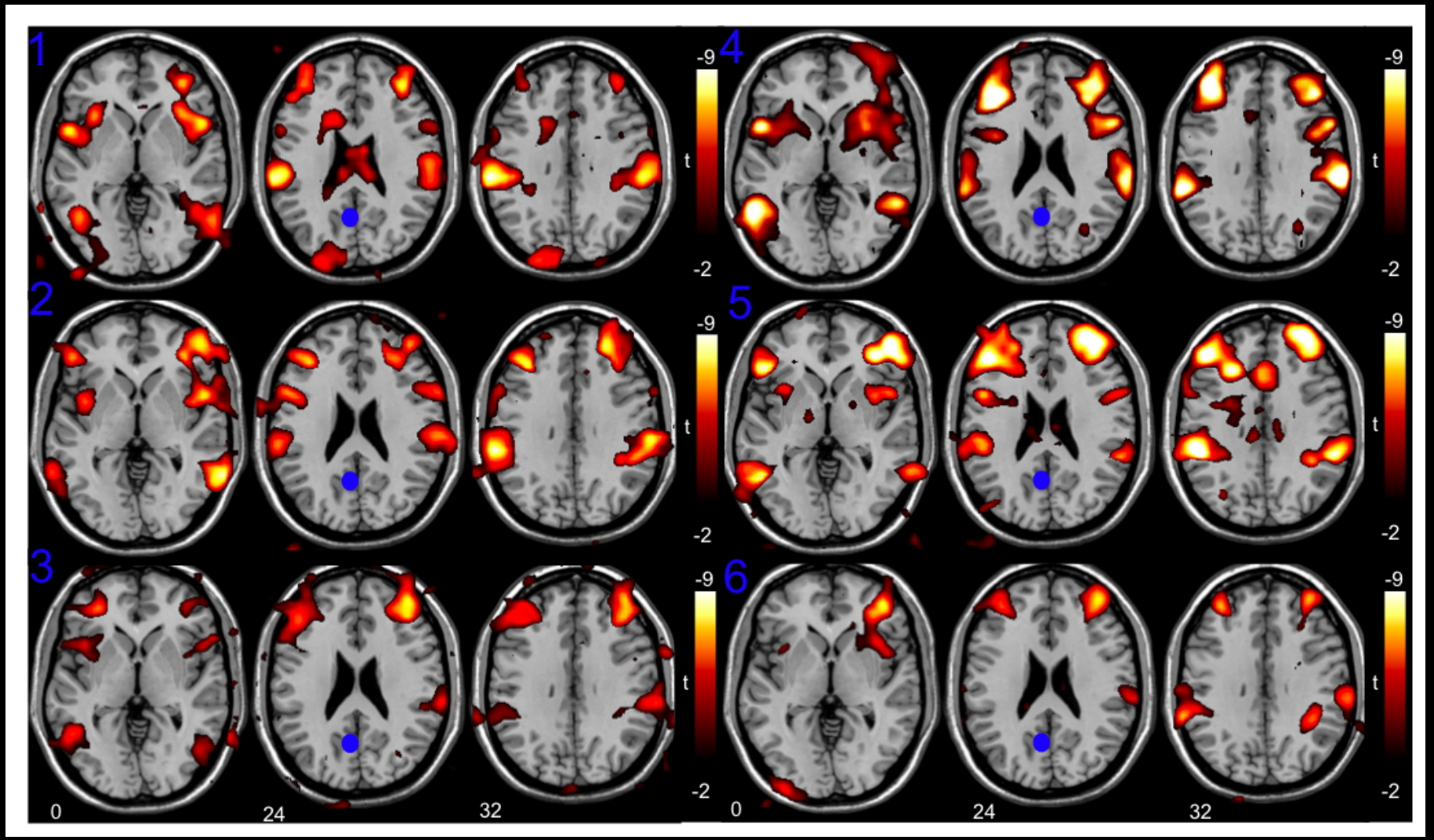
Collect cardiac and respiratory signal and regress it out or
Use seeds in the ventricles and white matter as nuisance covariates

Anti-Correlations without Global Scaling (Group Level)



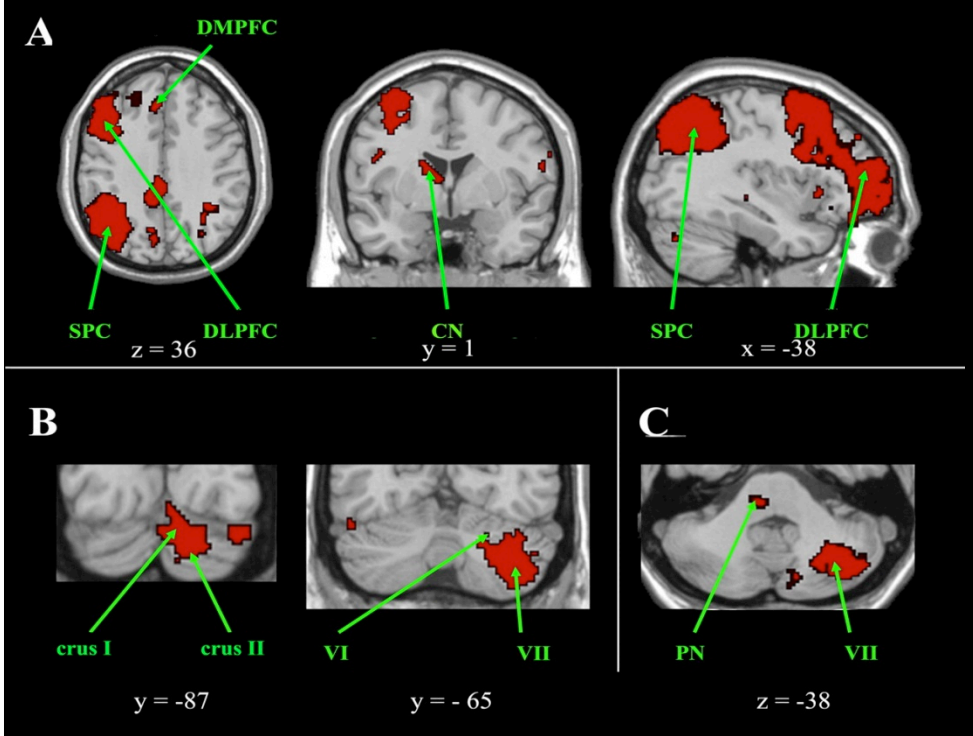
Chang and Glover, Neuroimage 2010

Anti-Correlations without Global Scaling (Single-Subject Level)

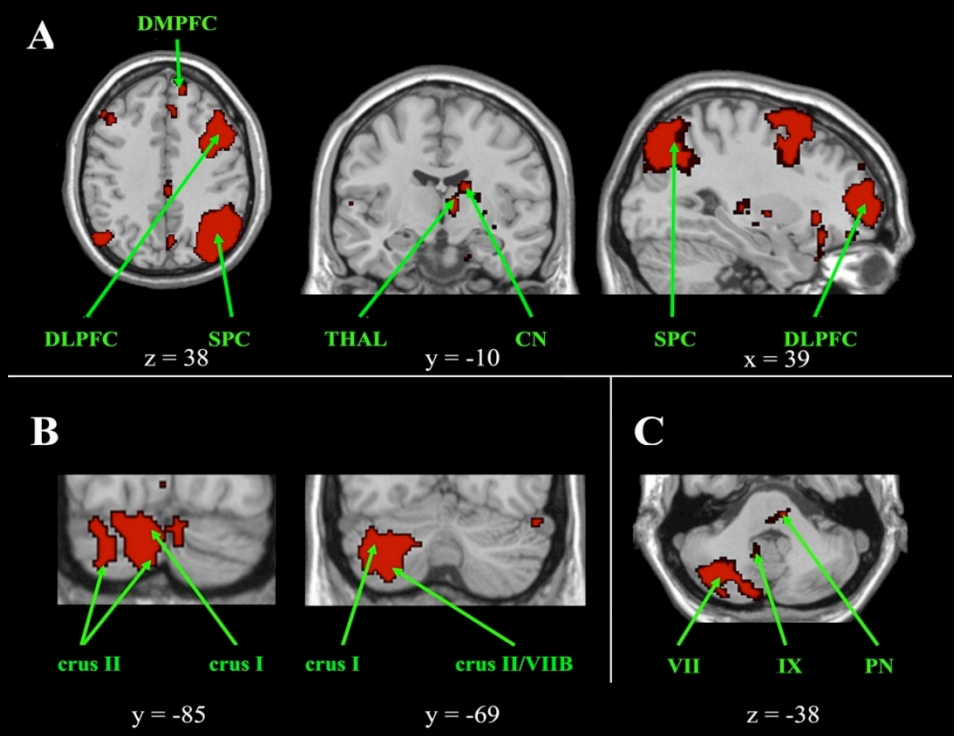


Chang and Glover, Neuroimage 2010

Distinct Cerebellar Contributions to ICNs



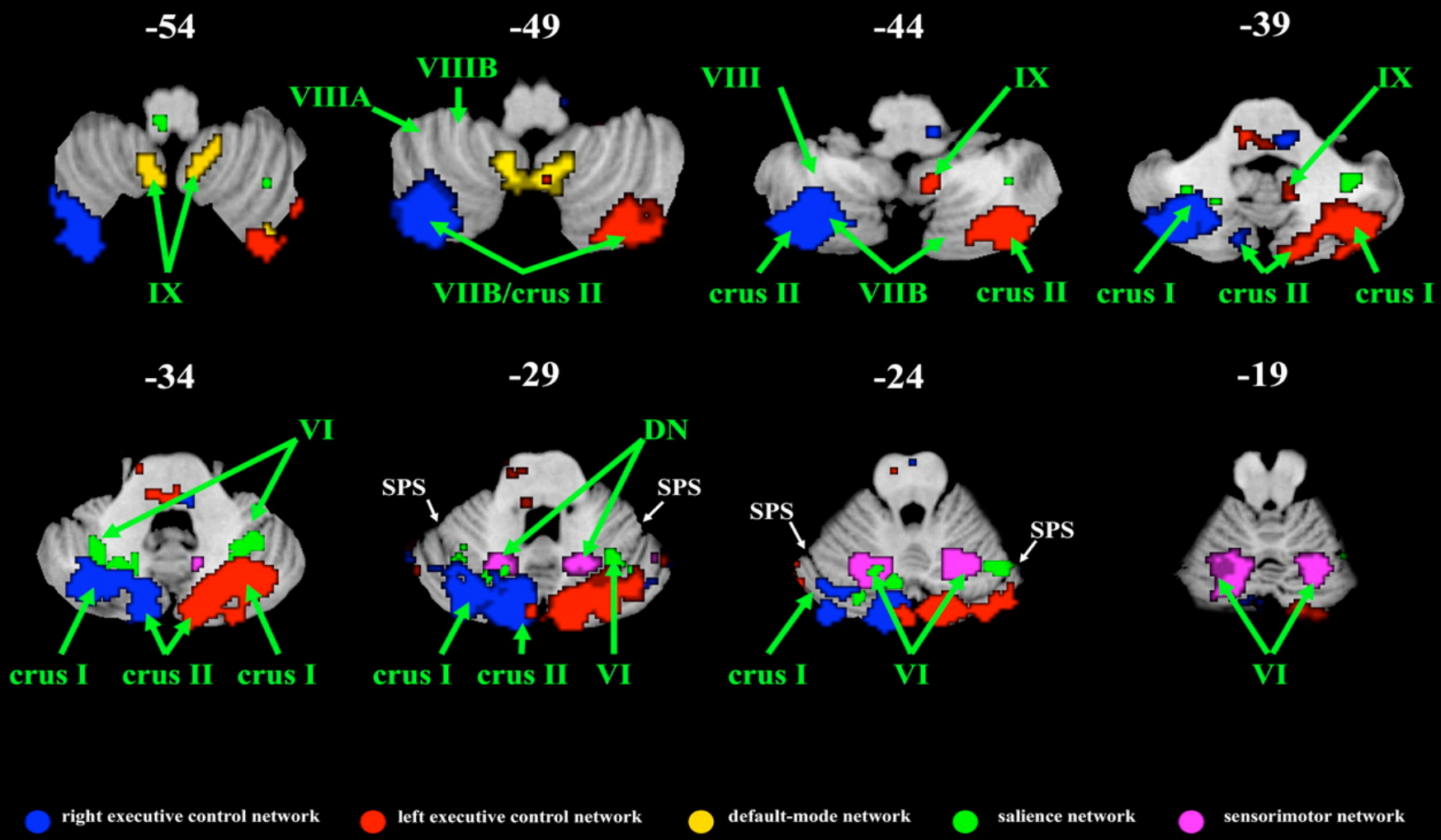
left executive control network



right executive control network

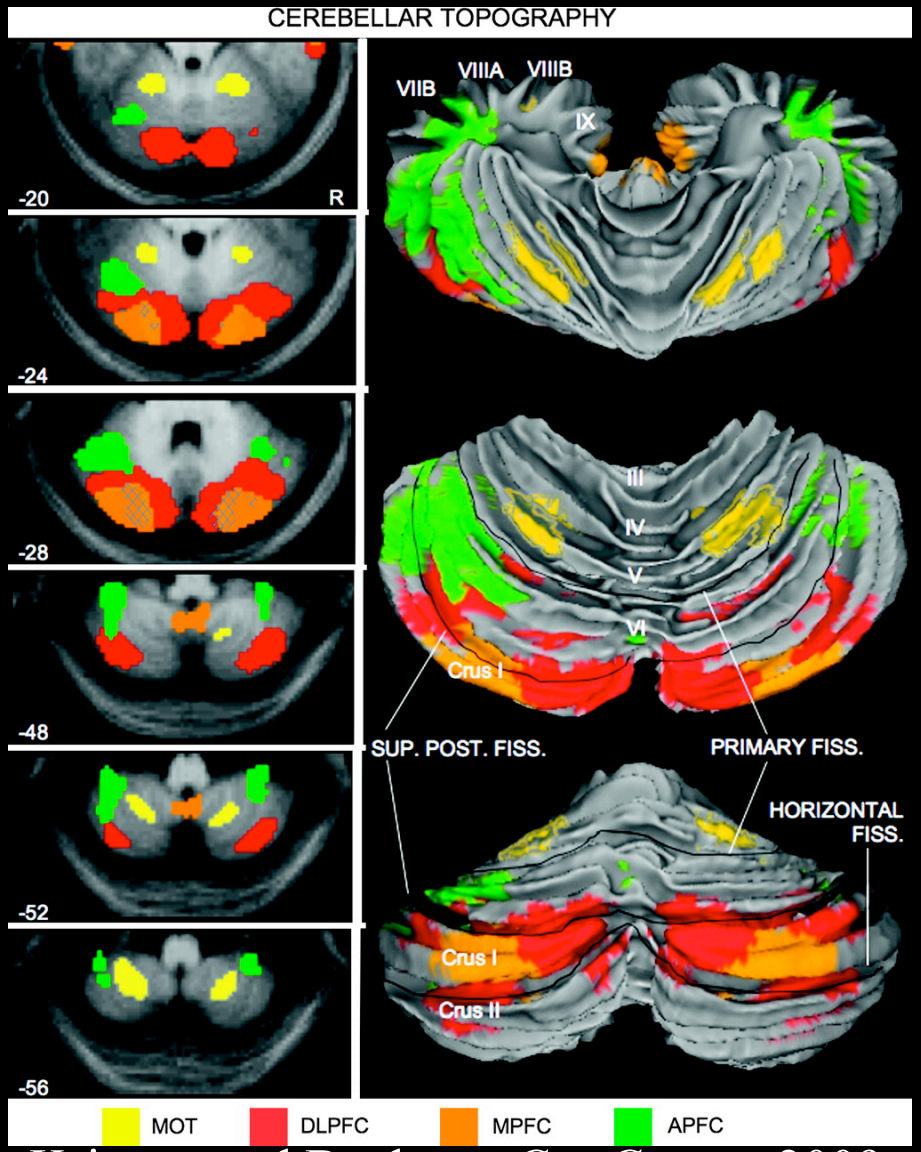
Habas et al., *J Neurosci* 2009

Distinct Cerebellar Contributions to ICNs

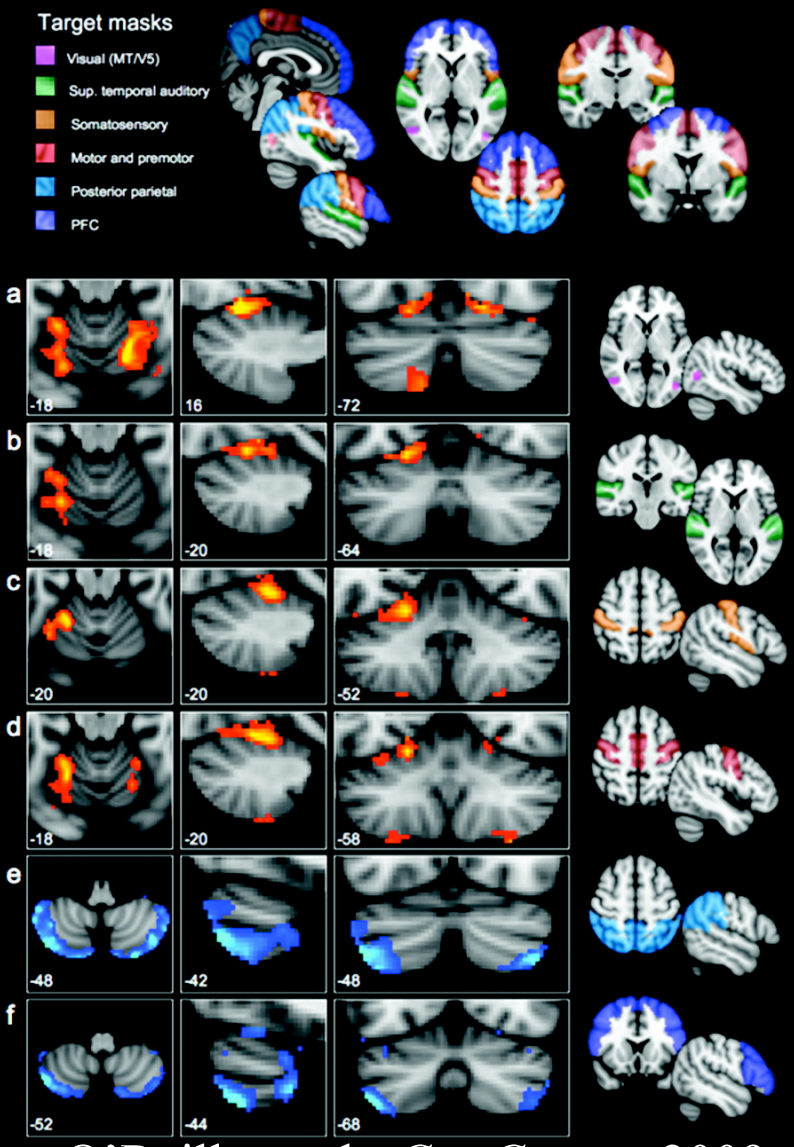


Habas et al., *J Neurosci* 2009

Distinct Cerebellar Contributions to ICNs Twice-Replicated (in a 4-Week Span)

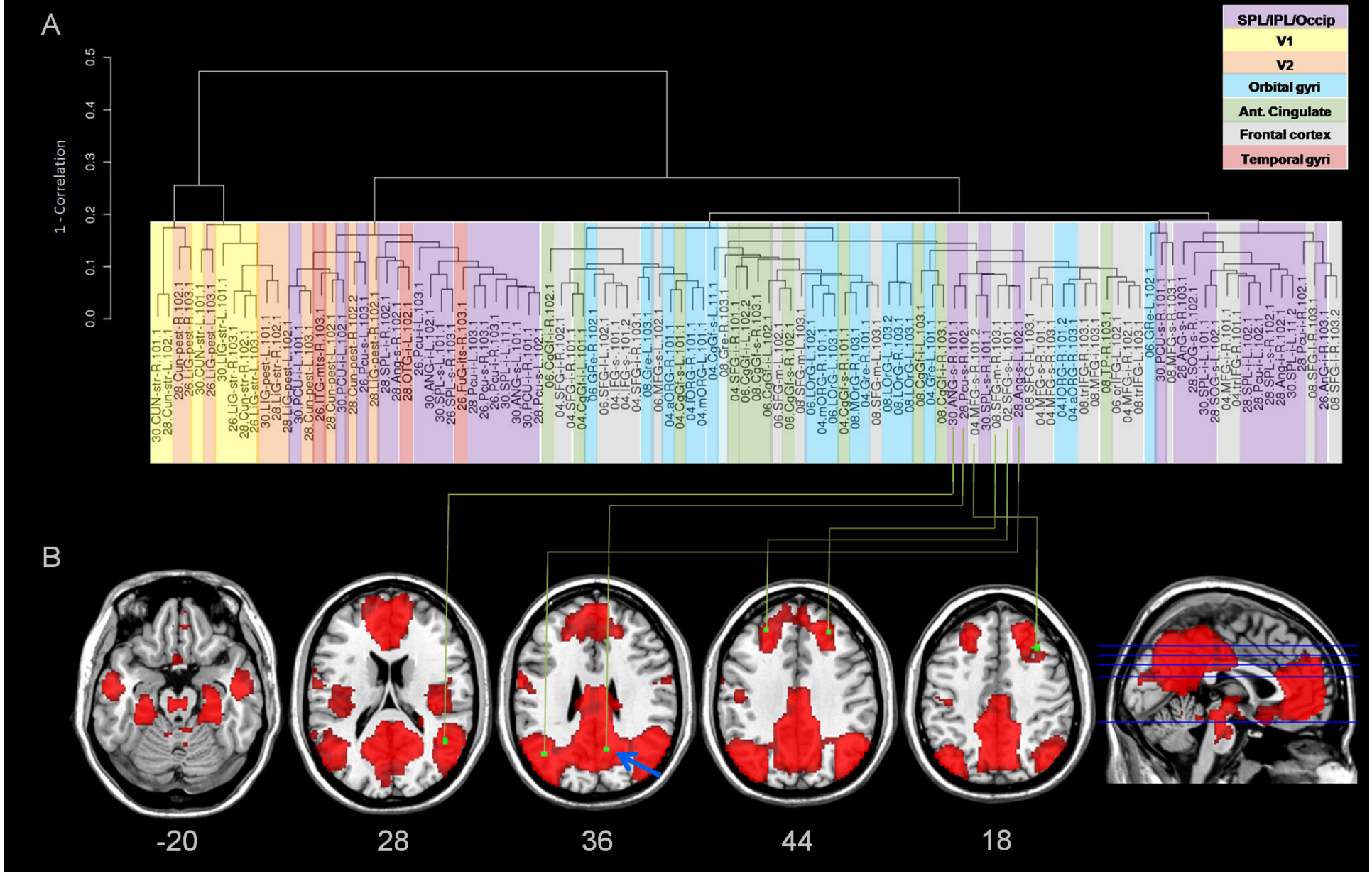


Krienen and Buckner, *Cer Cortex*, 2009



O'Reilly et al., *Cer Cortex*, 2009

Gene Expression Networks Recapitulate Intrinsic Connectivity Networks



Resting-State fMRI and ICNs

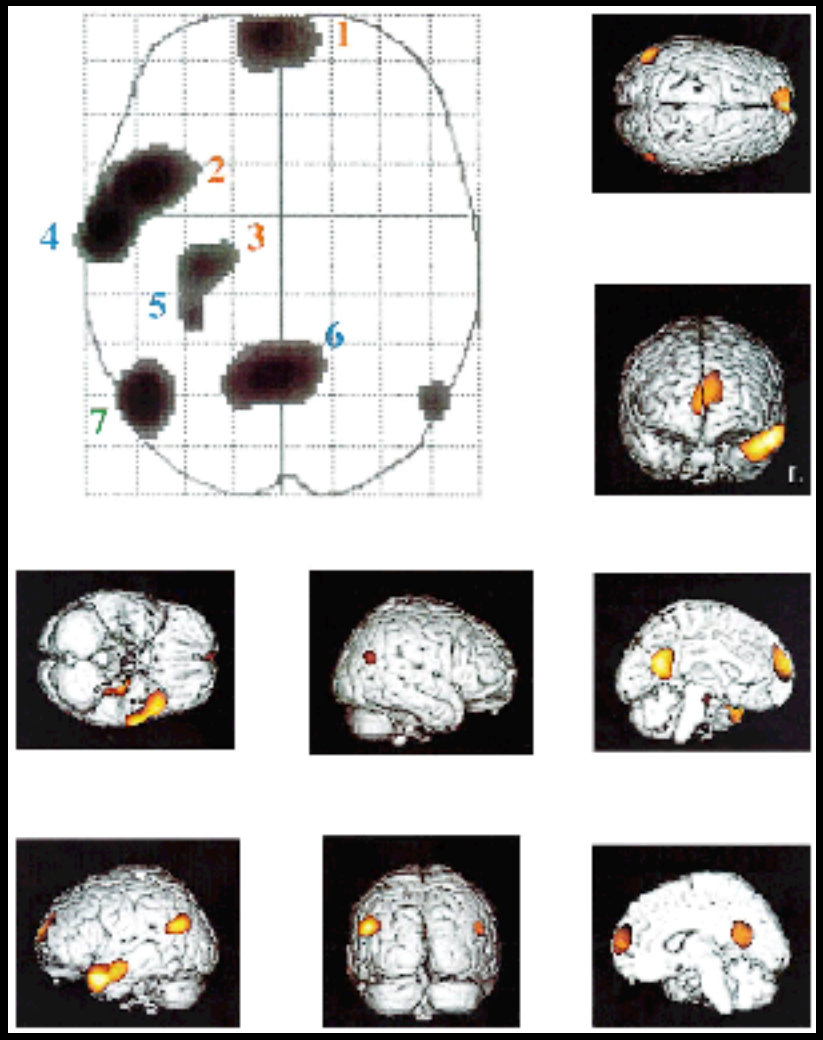
- Spontaneous, low-frequency BOLD fluctuations reveal canonical networks (of which the DMN is only one of 15-20)
- ROI and ICA-based approaches are complementary
- Yes, there is noise mixed in with the signal
- Beneath the noise is an elegantly structured, mysterious, but reliable, neuronal phenomenon of unclear etiology and limitless functional relevance

What Role Does the Default-Mode Network Play?

- Function is hard, by definition, to assess directly with behavioral paradigms

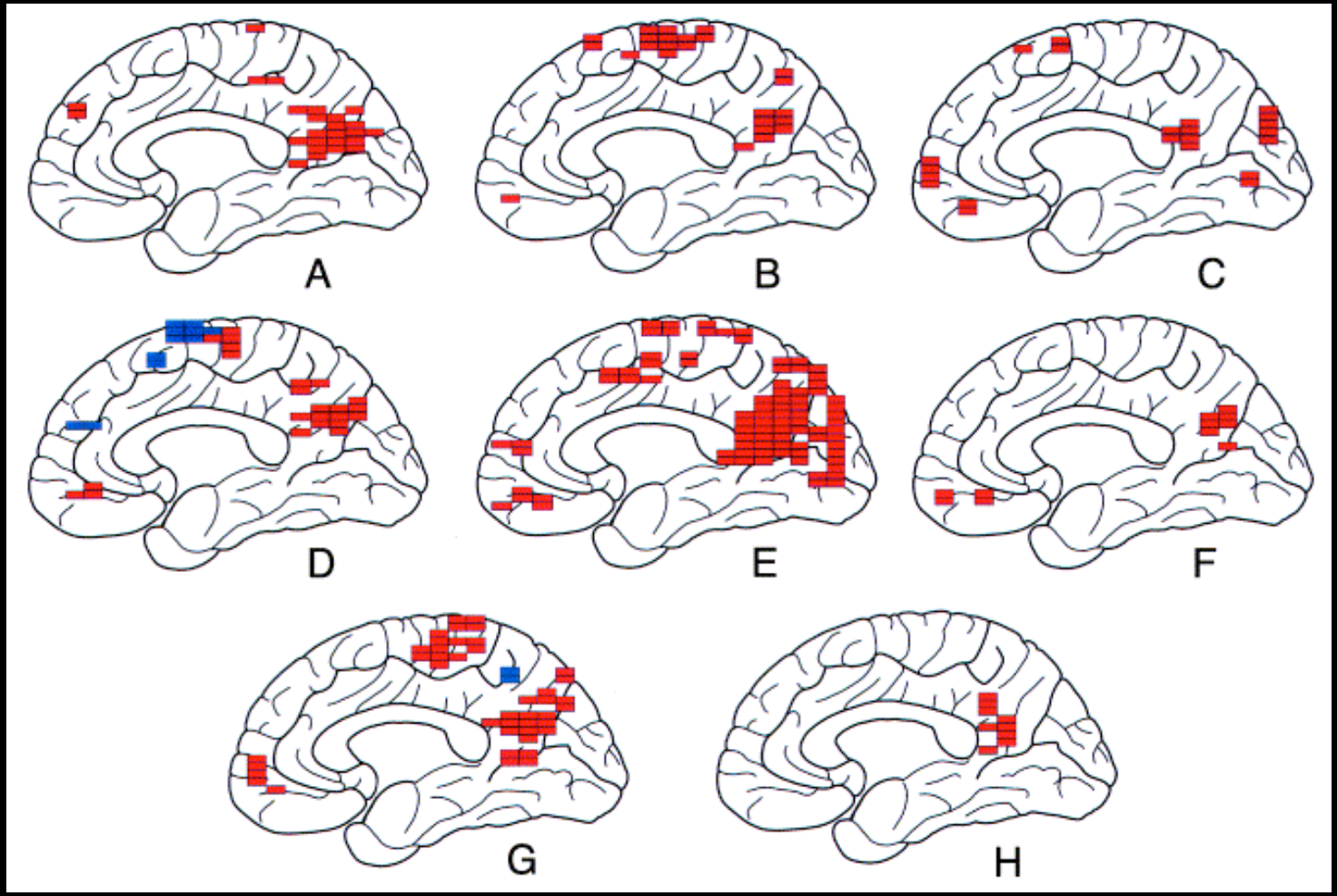
- Rely instead on
  - lesion studies or lack thereof
  - rare task activation paradigms with default-modish activation maps
  - comparisons of network activity between two groups or states differing in some fundamental attribute
  - interactions within network and between the default mode and other networks

Episodic Memory Retrieval



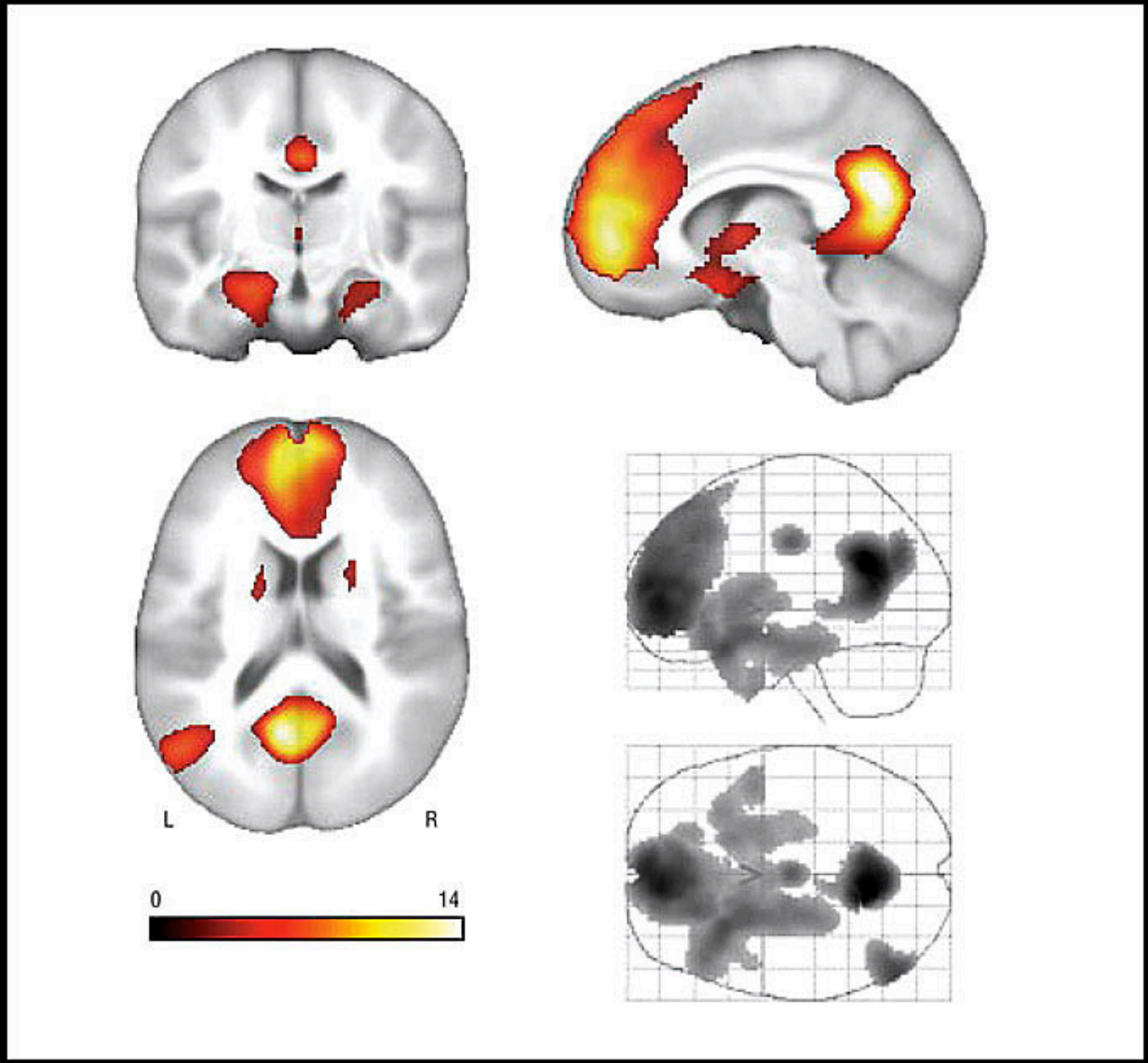
Maguire and Mummery, *Hippocampus*, 1999

Posterior Cingulate and Autobiographical Memory



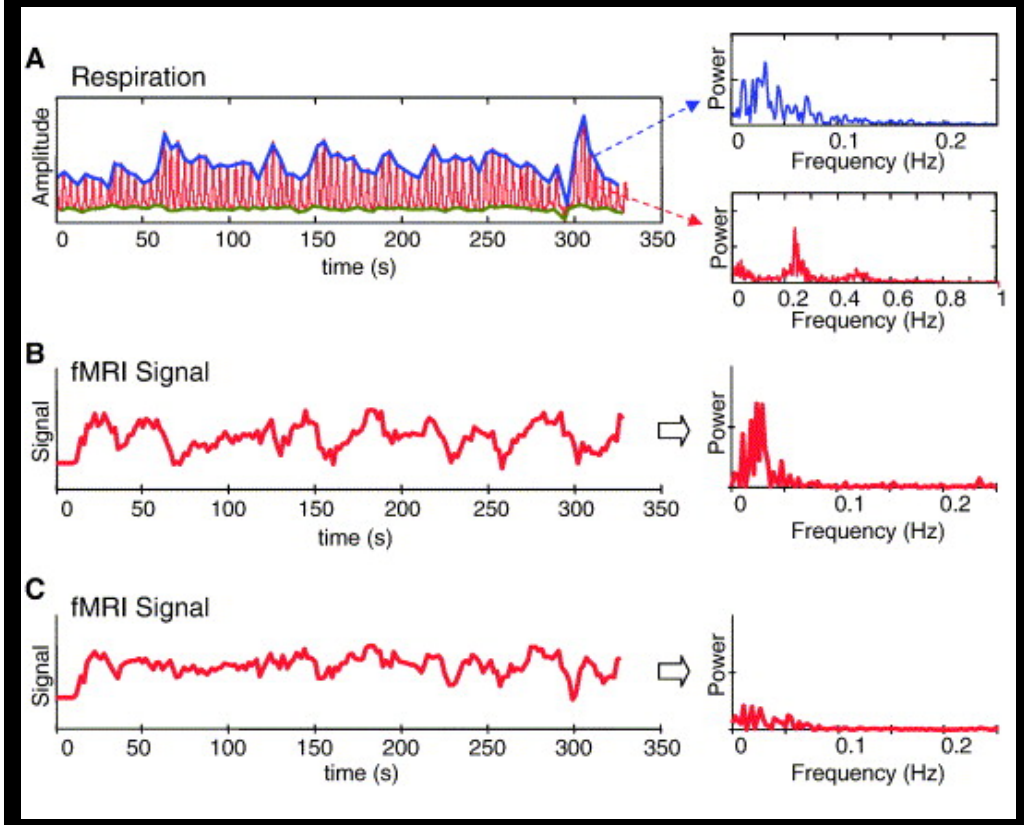
Maddock, Garrett, Buonocore, *Neuroscience*, 2001

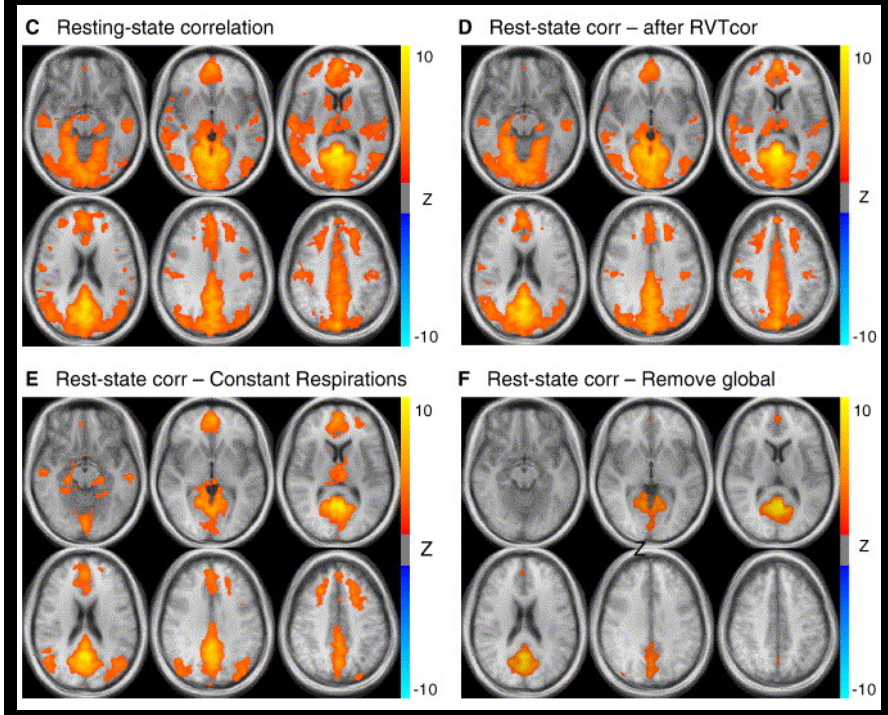
Self-Reflection (110 subjects!)



Johnson et al., *Arch Gen Psychiatry*, 2007

Low-Frequency Respiratory Cycle Noise





Birn et al., *Neuroimage*, 2006