

# Resting State fMRI

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fMRI Summer Course \* 2015

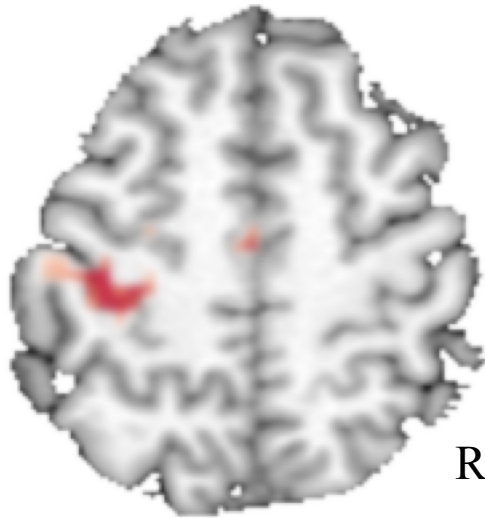
# Resting-state fMRI:

- What is it?
- How can we analyze the data?
- What are we measuring and how do we interpret it?
- Summary

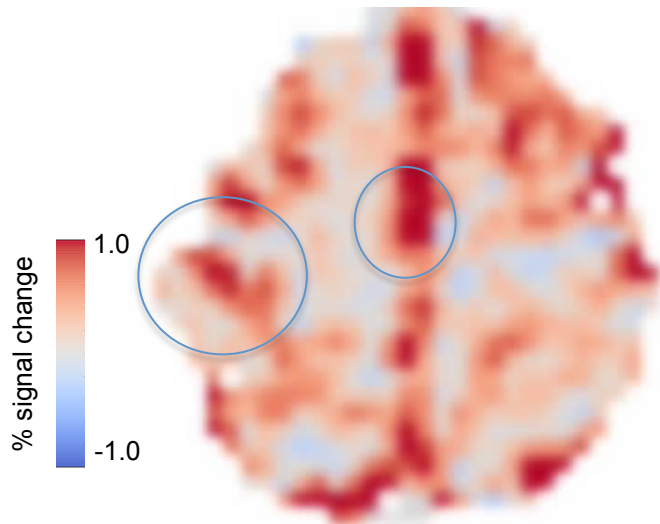
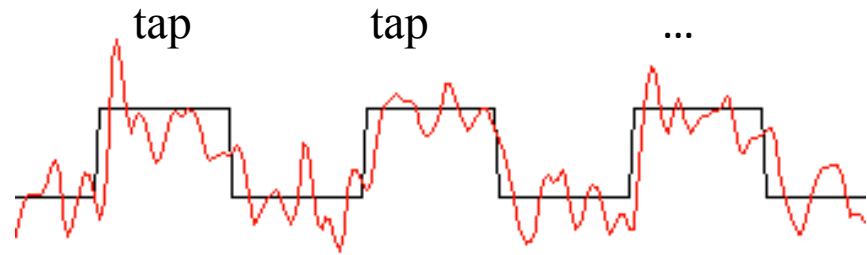
# Resting-state fMRI:

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# Task fMRI v. Resting State fMRI



## Right-hand fingertapping task

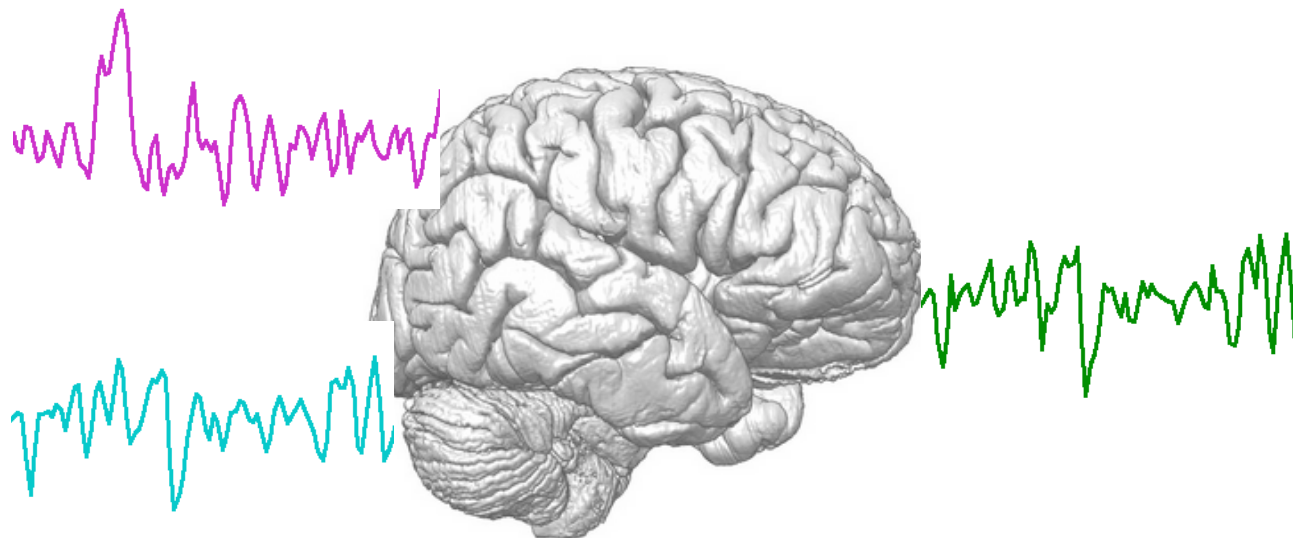
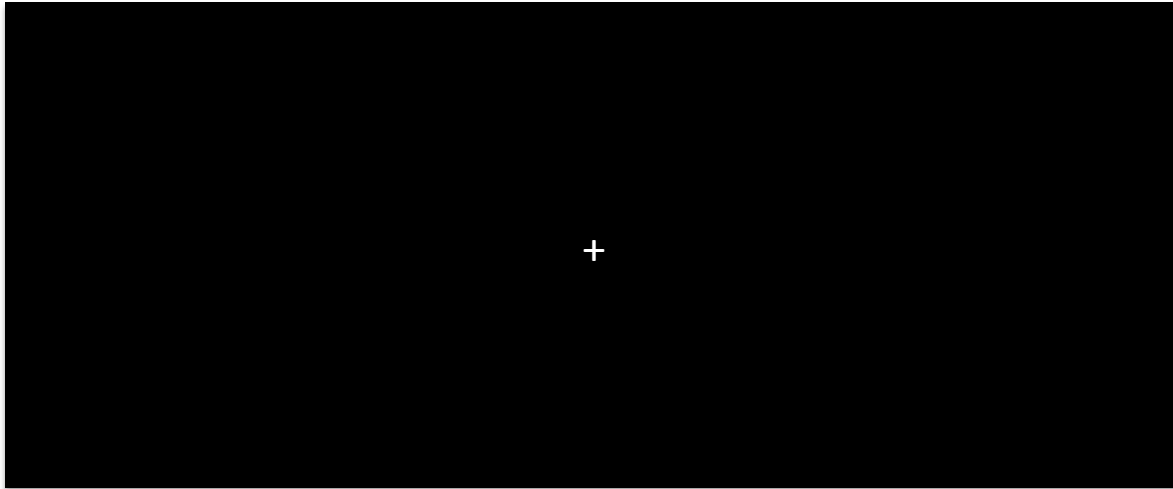


## Spontaneous activity

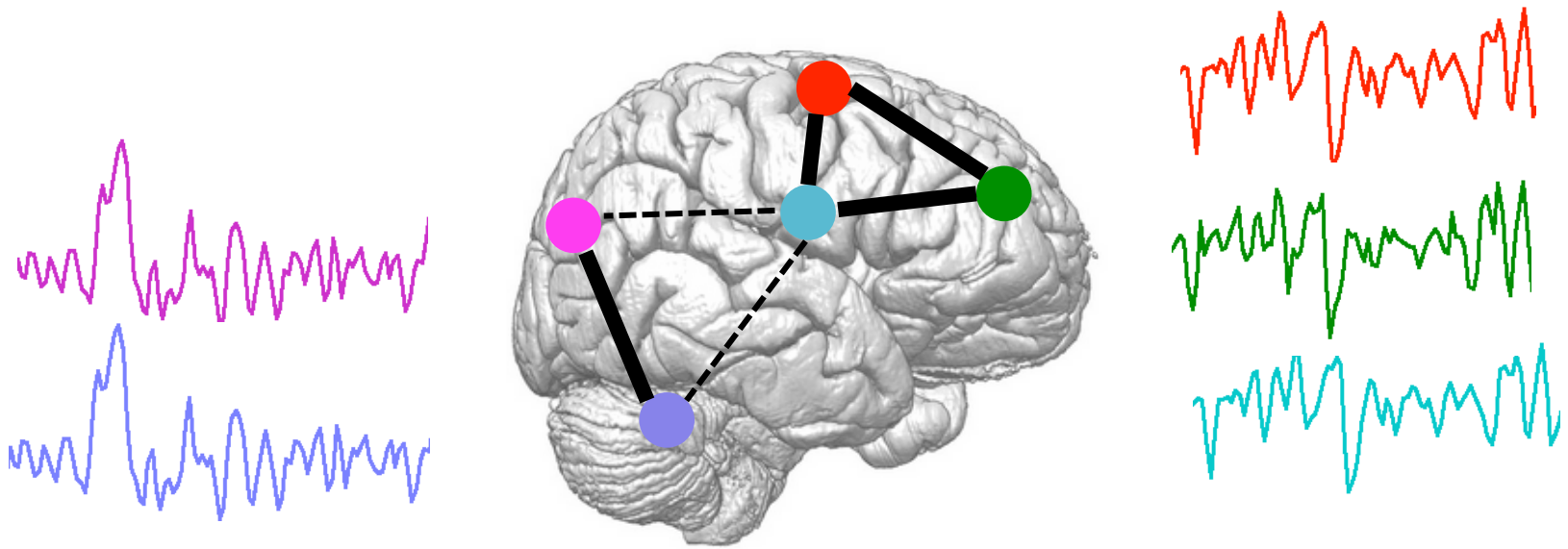
- accounts for most of the brain's energy consumption



# Resting State fMRI



# Functional connectivity

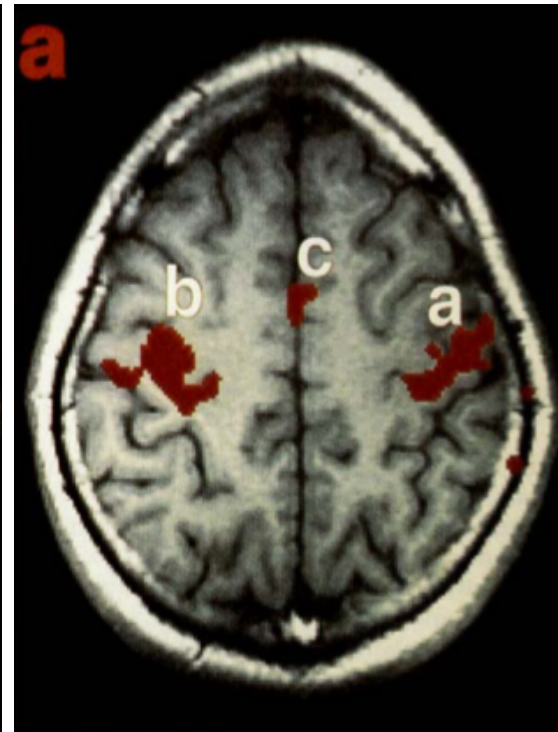
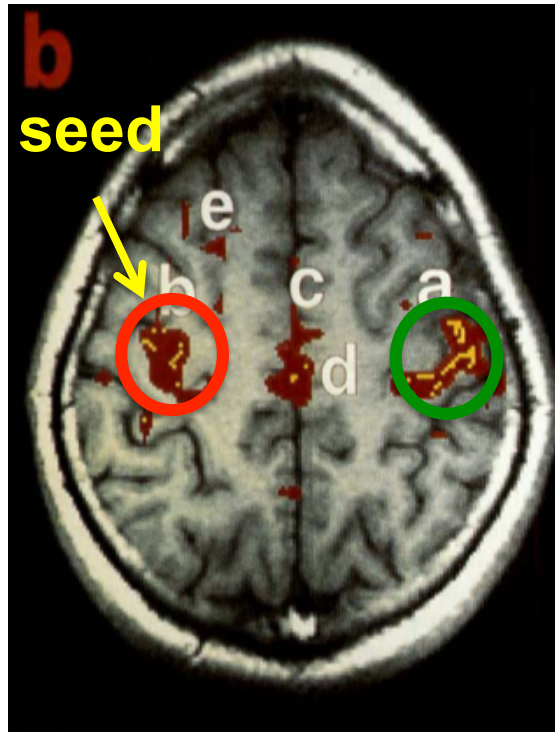


statistical dependence (e.g. correlation)  
between the activity of different brain regions

# Resting-state functional connectivity

no task

finger-tapping task



Correlation with seed

Correlation with task

Functional  
Connectivity

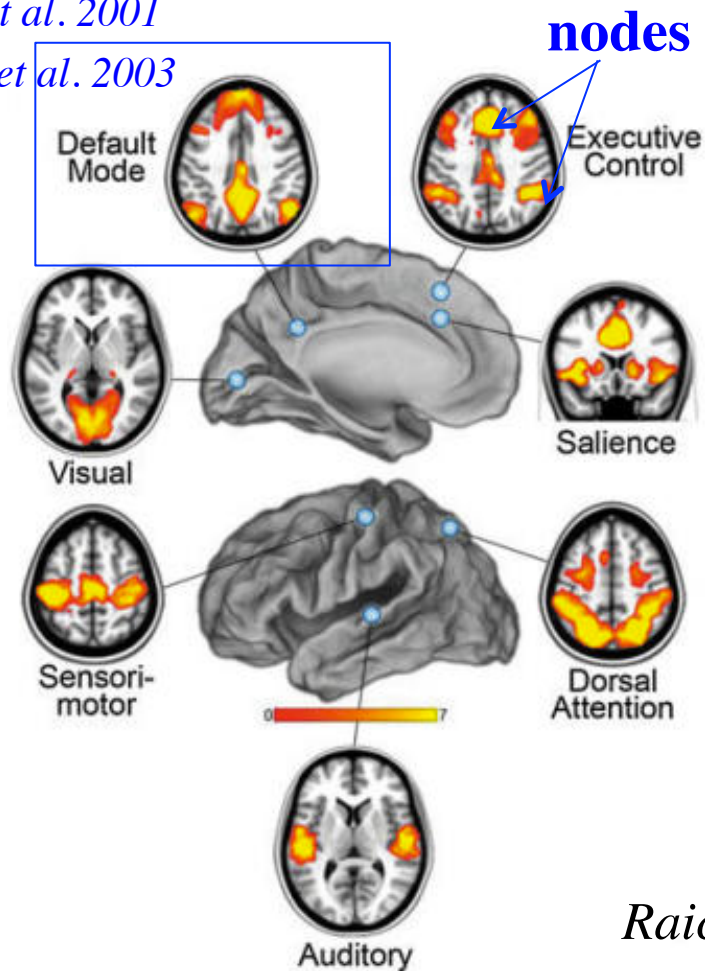
Activation

*Biswal et al., 1995*

# “Resting State Networks”

*Raichle et al. 2001*

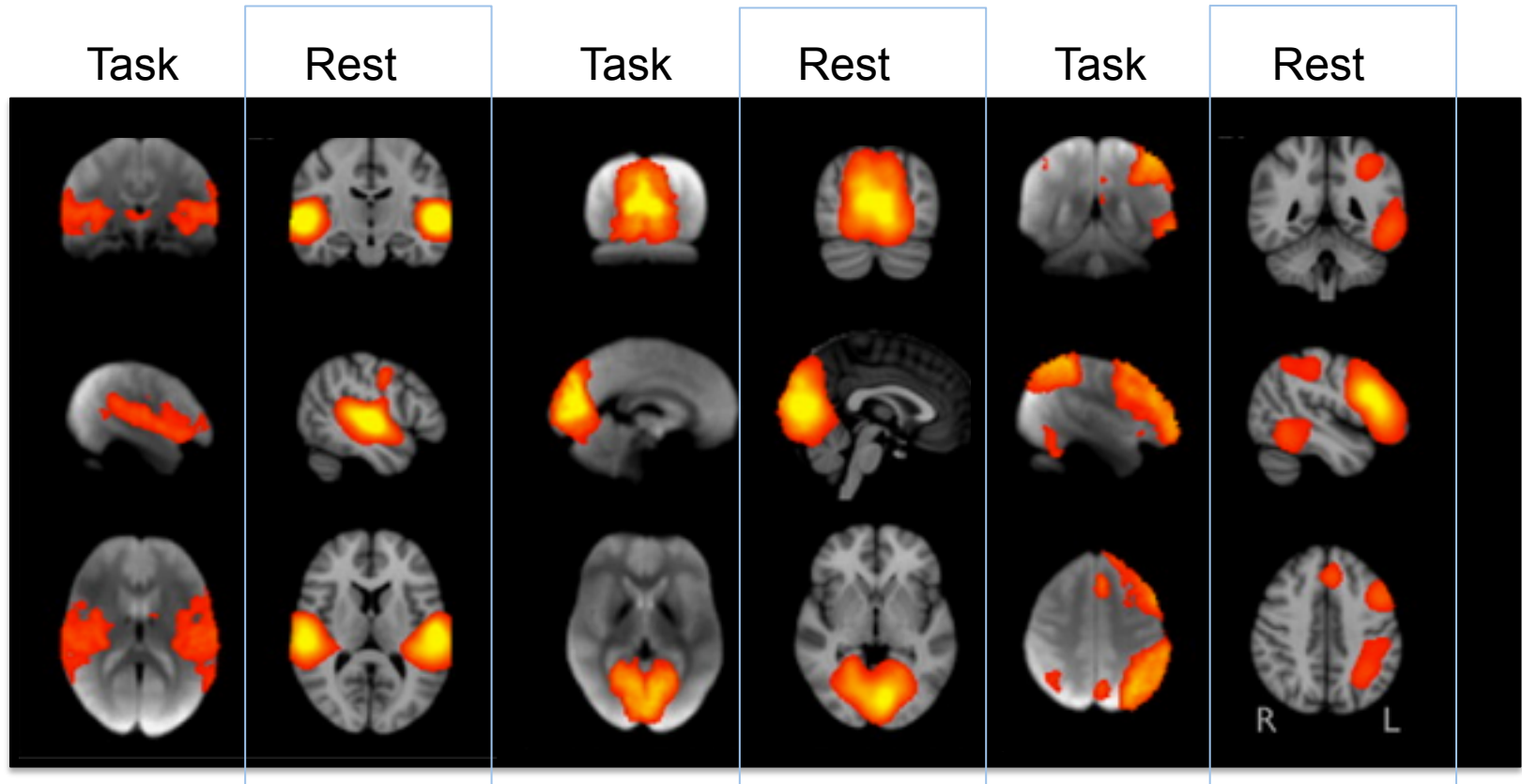
*Greicius et al. 2003*



Correlation between areas in resting state appears to provide information about functional organization

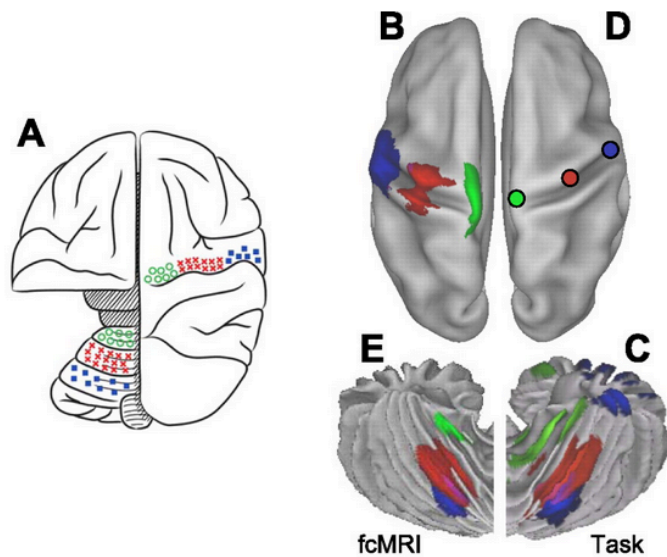
*Raichle, 2011*

# Correspondence with task activation

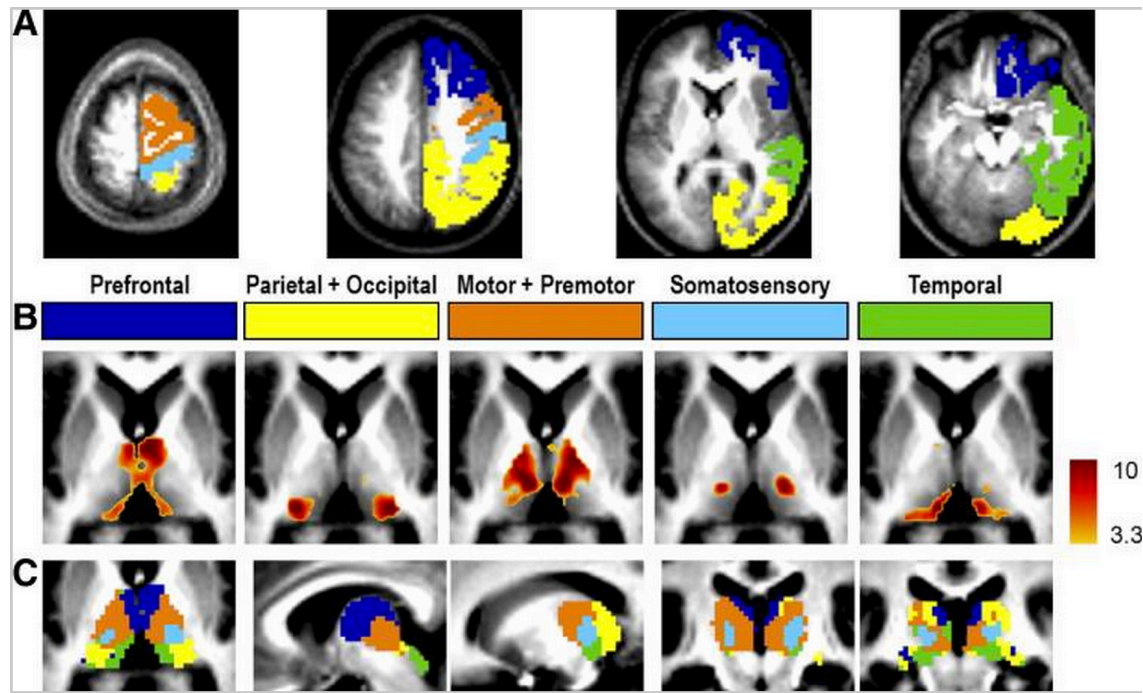


*Smith et al. 2009*

# Correspondence with known anatomic/ functional organization



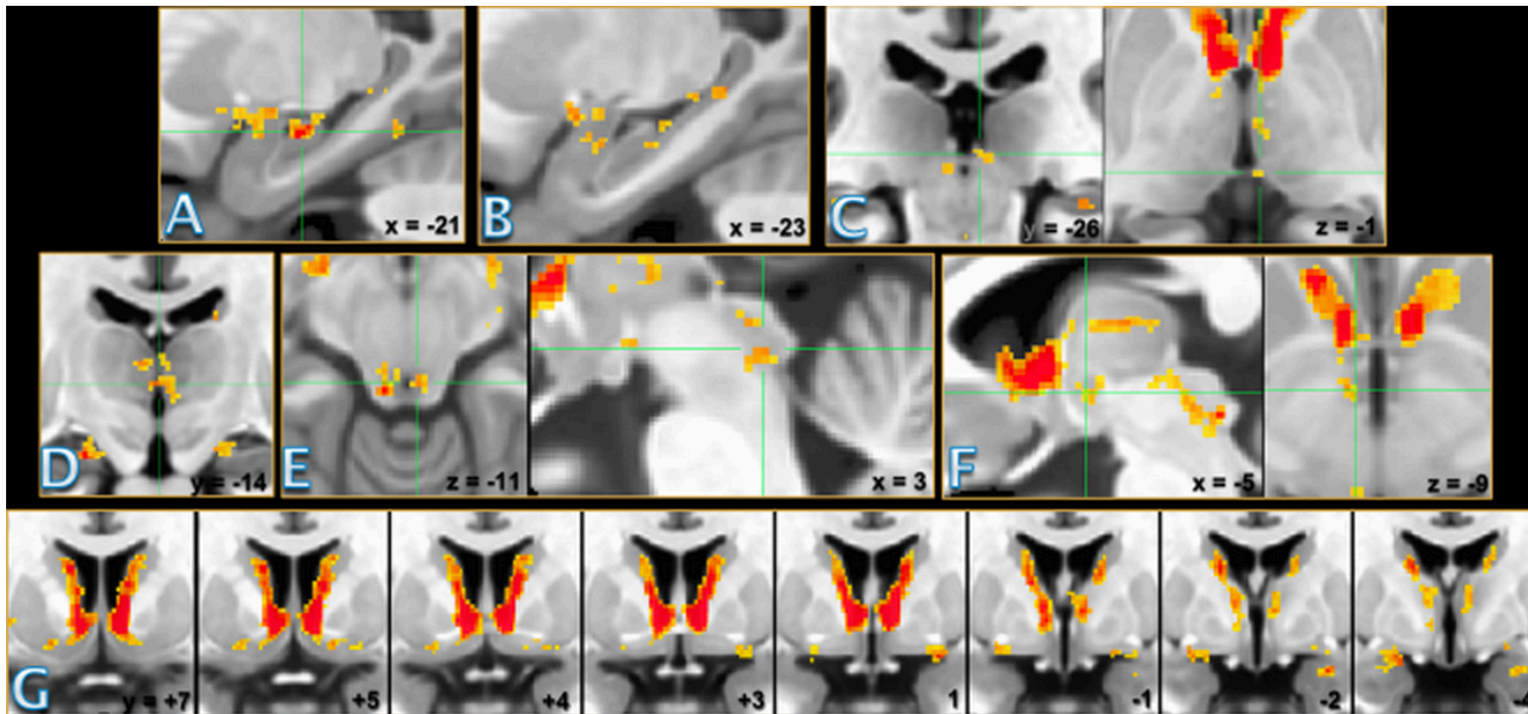
*Buckner et al. 2011*



*Zhang et al. 2008*



# Correspondence with known anatomic/ functional organization

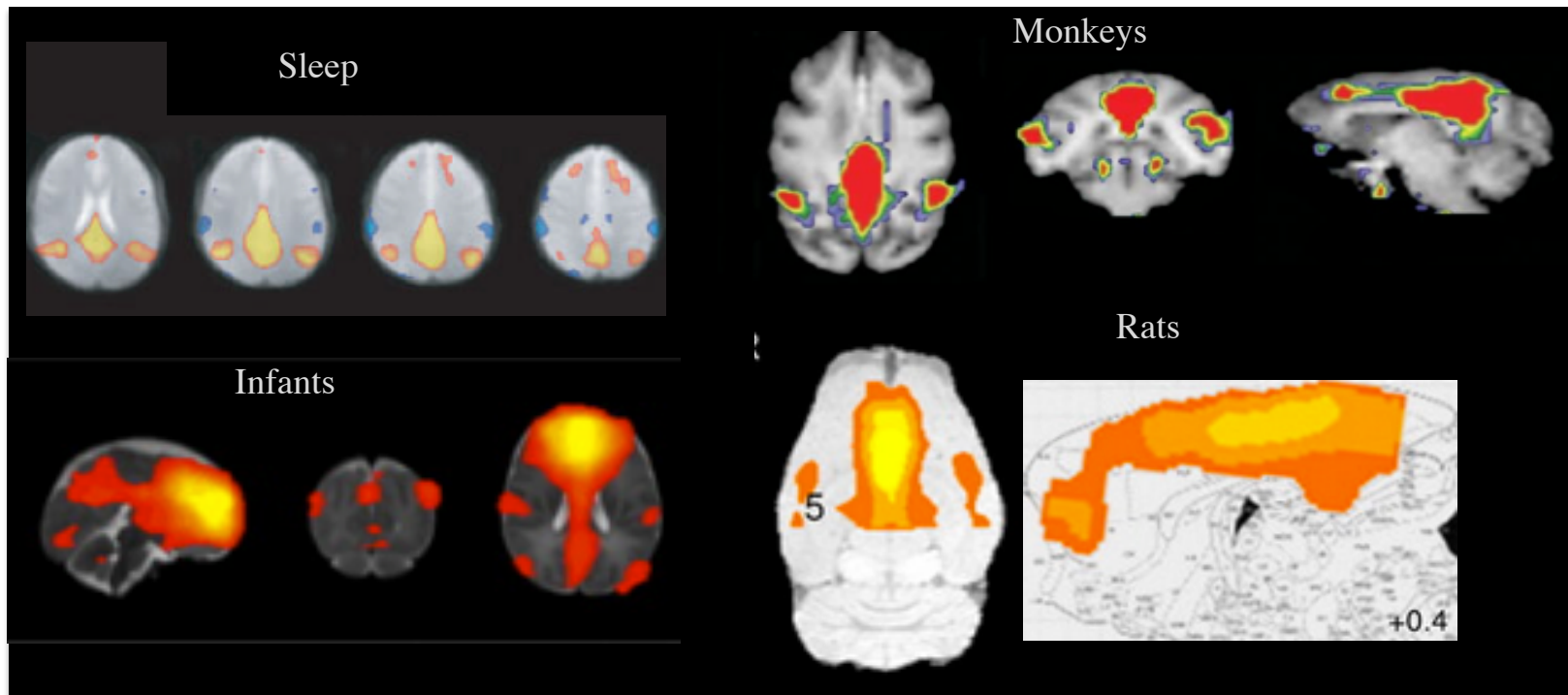
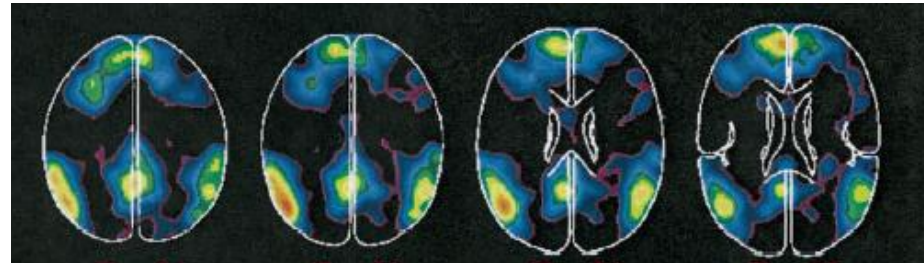


FC with BNST (bed nucleus of the stria terminalis)

# Stability across brain states, species

## Default-mode network

*Raichle et al., 2001 (PET imaging)*

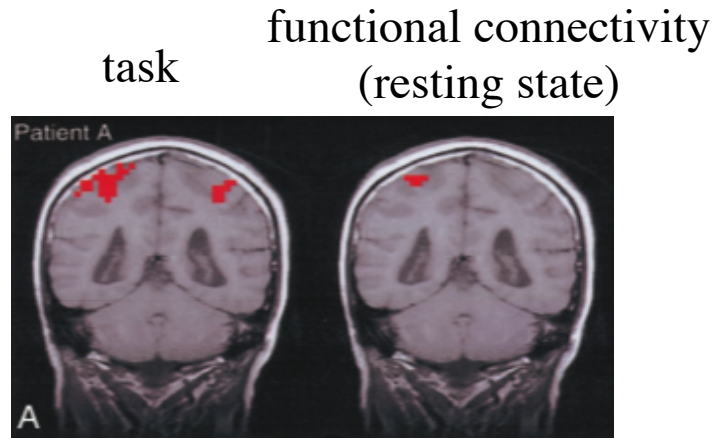


*Horovitz et al. 2008; Doria et al. 2010; Vincent et al. 2007; Lu et al. 2007*

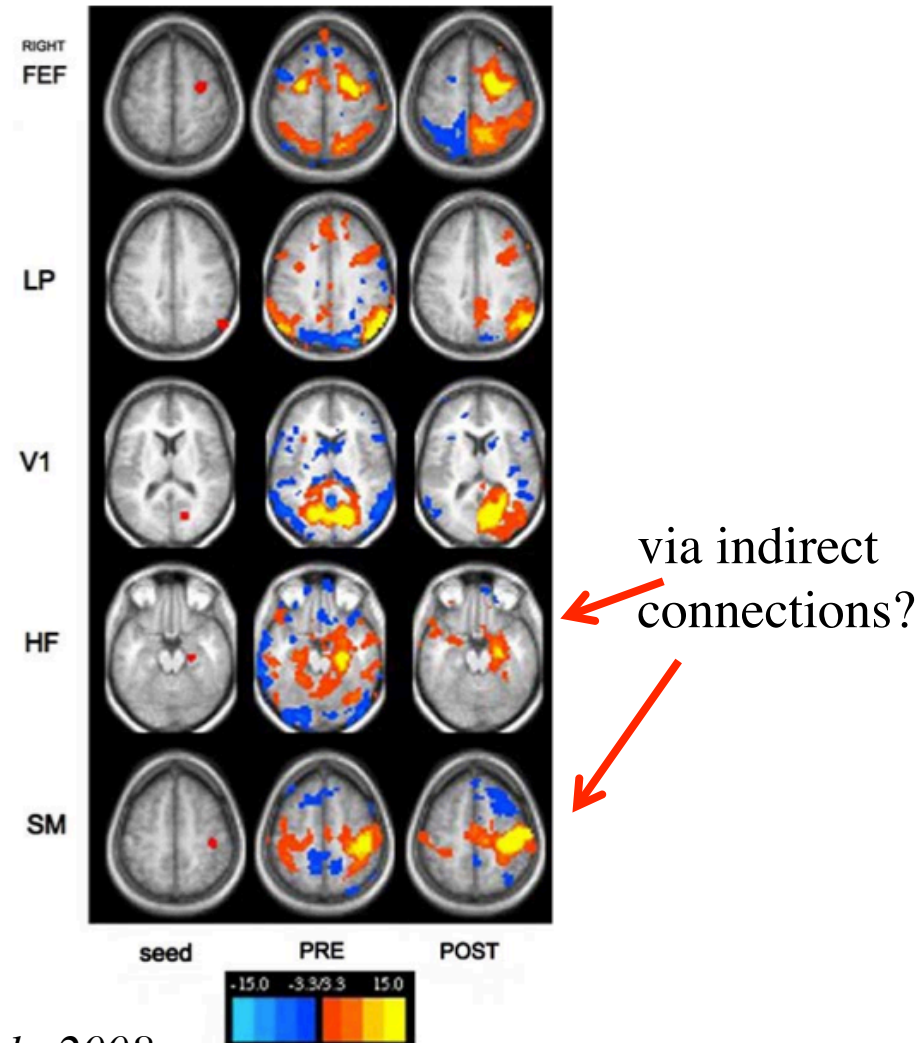


# Structural connectivity shapes functional connectivity

## Agenesis of the Corpus Callosum

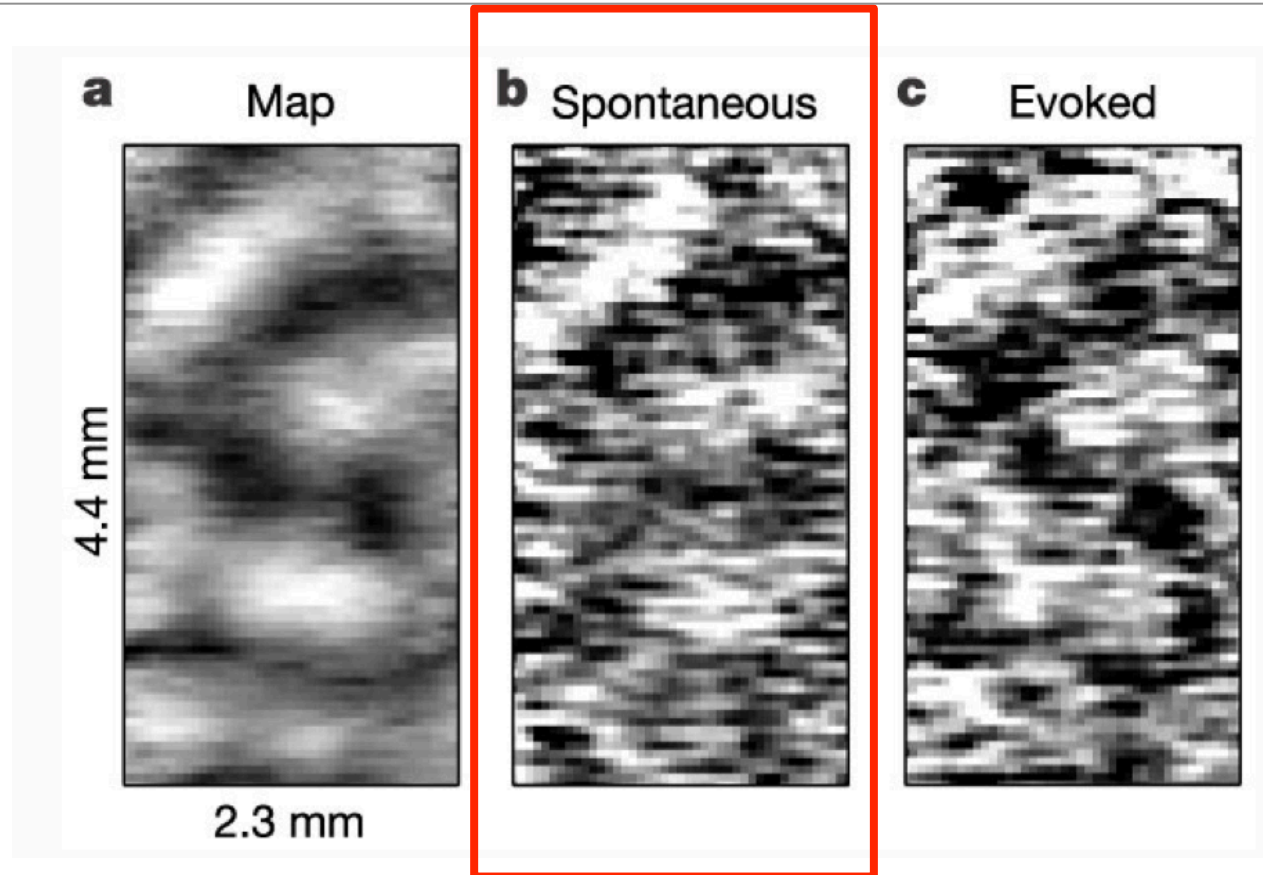


*Quigley et al., 2003*



*Johnston et al., 2008*

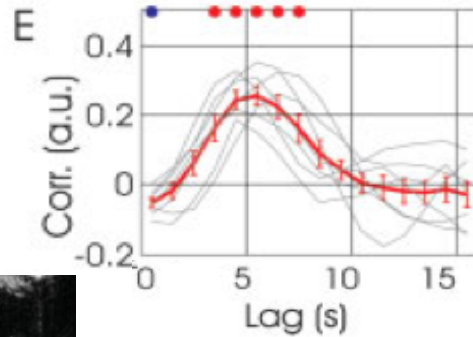
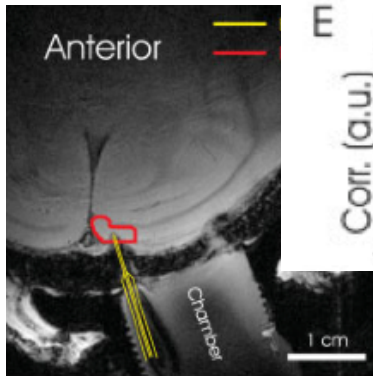
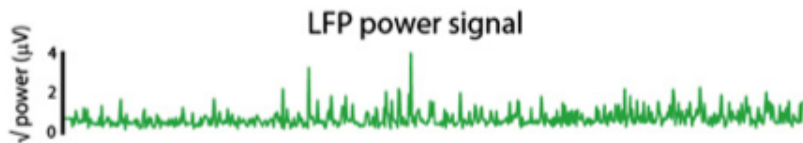
# Coherence in spontaneous electrophysiological signals



spontaneous fluctuations in membrane voltage resemble orientation columns & evoked activity

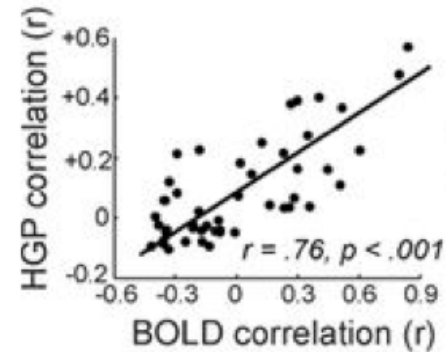
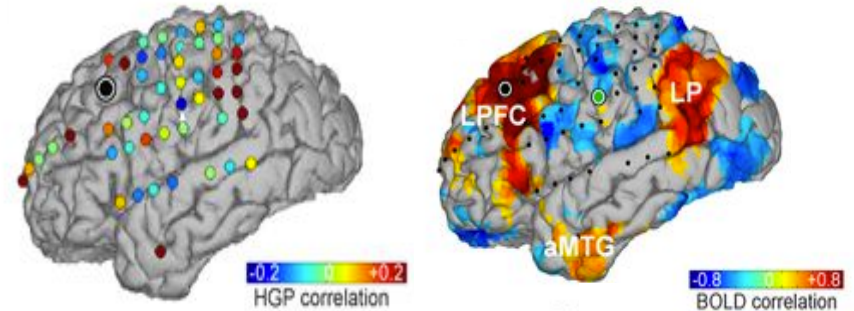
# Electrophysiological correlates

gamma power fluctuations in local field potential (LFP) correlate with fMRI signal



*Shmuel & Leopold, 2008*

*Logothetis et al 2001*



*Keller et al. 2013*

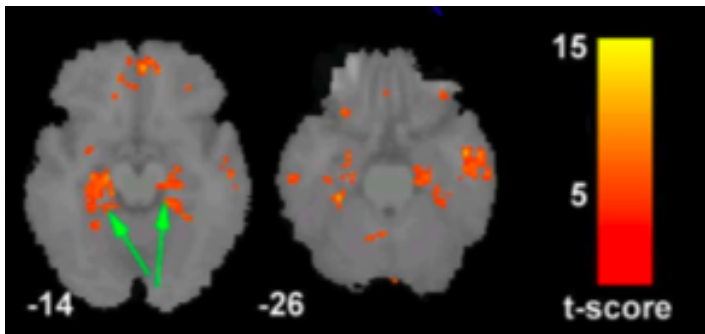
- slow cortical potential (He et al, 2010)
- broadband (Liu et al. 2014)

# Recap

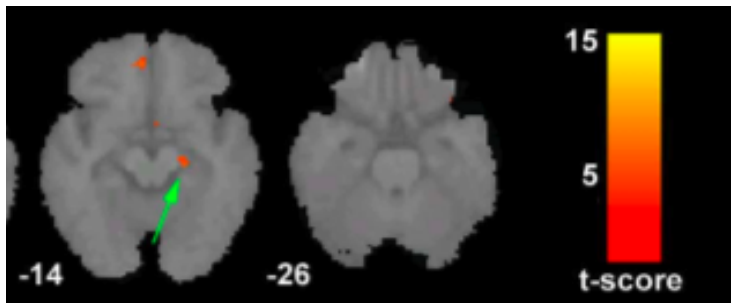
- Resting state: study “intrinsic” brain activity
  - usually no task or stimuli
- Correlation between regions appears to reflect functional/structural organization of the brain
- Promising implications:
  - + can derive many networks with the same data
  - + no task needed, so applicable to infants, sleep, coma, ...
  - + tool for studying disease-related differences in functional organization

# Clinical applications

Healthy control

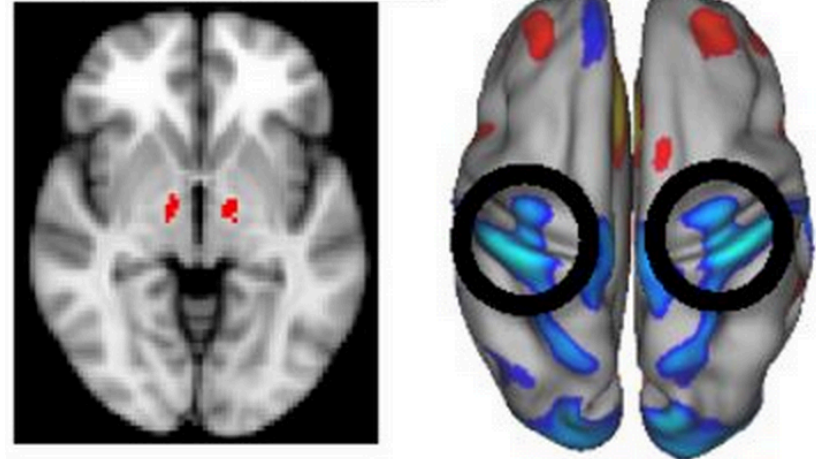


Alzheimer's



*Greicius et al. 2004*

**Parkinson's**



*Fox et al. 2014*

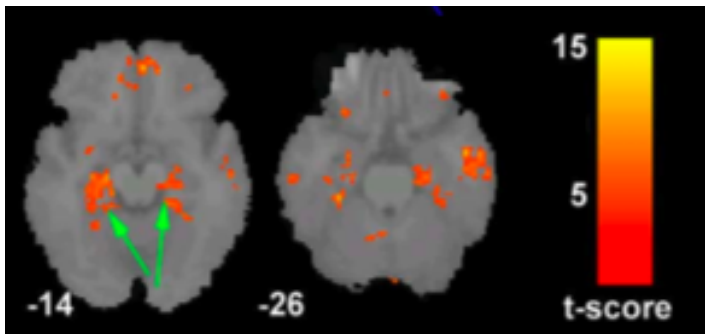
**Table 1. Number of publications in which iFC or resting state approaches have been used to study a variety of disorders and conditions (PubMed search on 25 January 2012)**

<b>Disorder/Condition</b>	<b># studies</b>
Schizophrenia	45
Alzheimer's Disease	44
Depression	42
Mild Cognitive Impairment (MCI)	33
Aging	39
Epilepsy	29
Substance Dependence	28
ADHD	16
Multiple Sclerosis	13
Autism	12
Parkinson's Disease	11
Pain	10
Anxiety Disorders	8
Sleep	2
Miscellaneous Neurological Disorders	10
Stroke	7
Obsessive Compulsive Disorder (OCD)	8
Posttraumatic Stress Disorder (PTSD)	8
Amnesia	4
Brain Lesions	7
Dementia	2
Seizure	3
Trauma	4
Bipolar Disorder	3
Personality Disorders	2
Cerebral Palsy	2
Fetal Alcohol Syndrome	2
Migraine	2
Psychopathy	2
Learning Disabilities	1
Tourette Syndrome	1

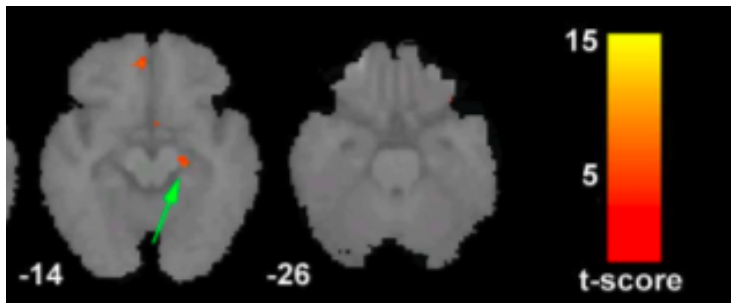
*Kelly et al. 2012*

# Clinical applications

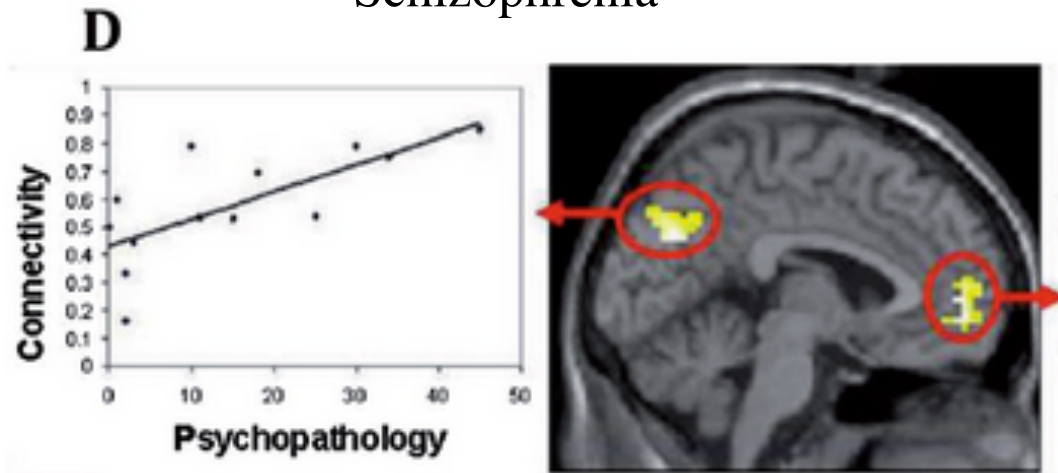
Healthy control



Alzheimer's



Schizophrenia



*Whitfield-Gabrieli et al. 2009*

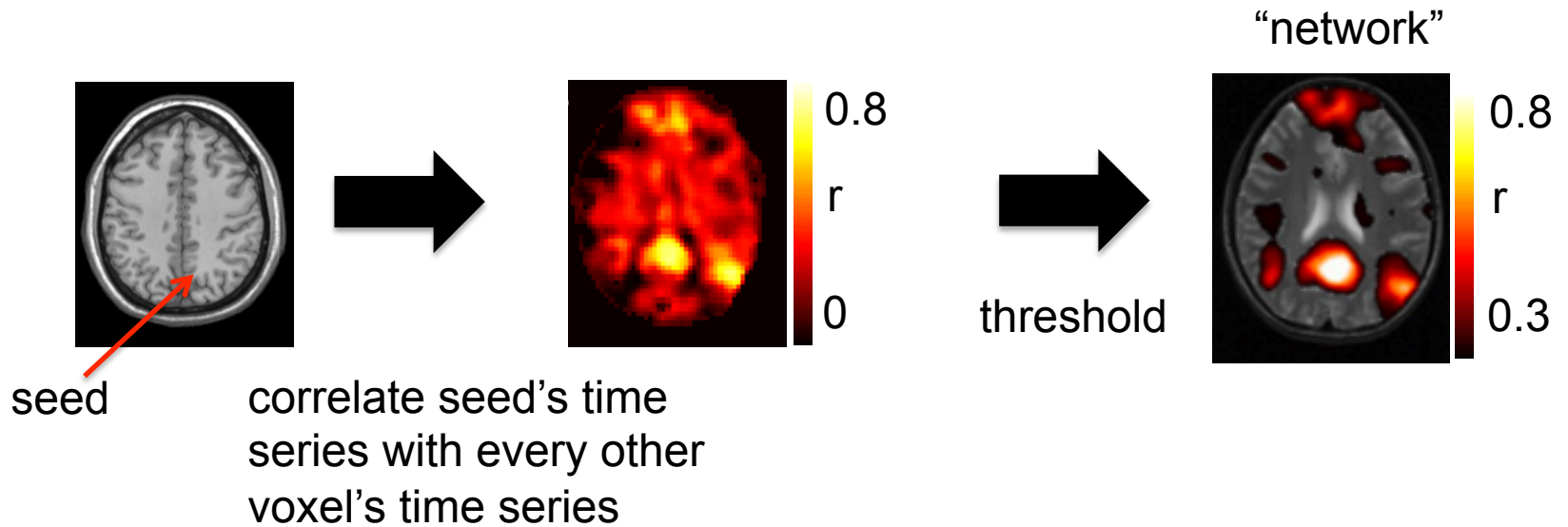
*Greicius et al. 2004*

# Outline

- What is it?
- **How can we analyze the data?**
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# Seed-based correlation



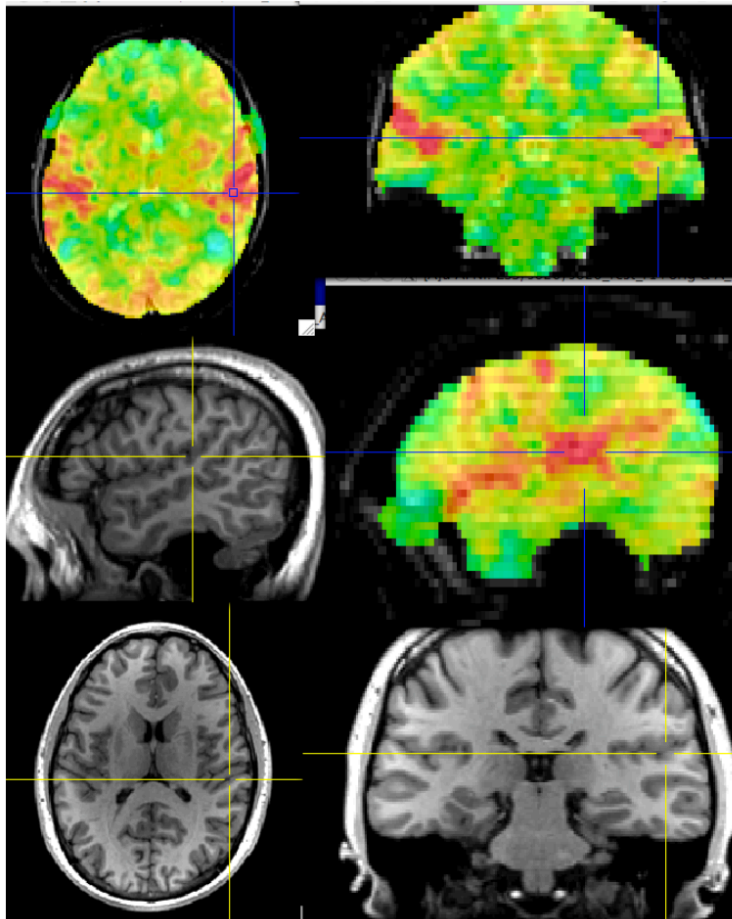
# Seed-based correlation

-1-

**AFNI!** InstaCorr

All data herein  
from Alex Martin,  
*et al.* [NIMH IRP]

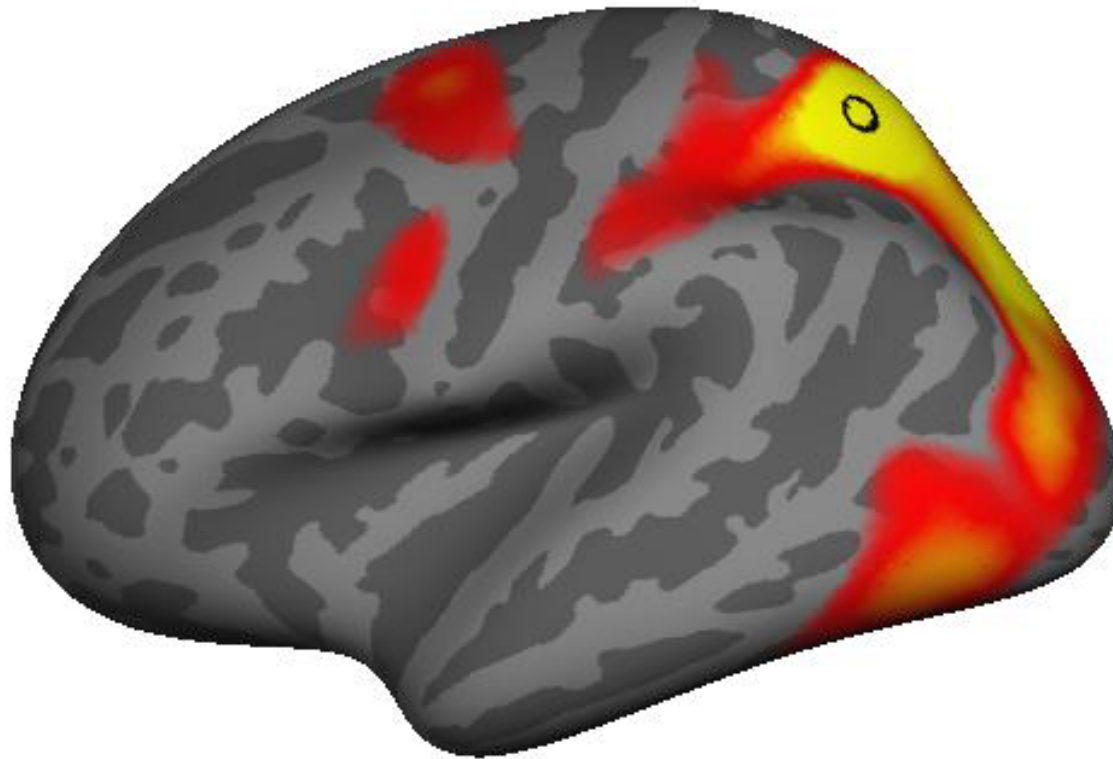
<http://afni.nimh.nih.gov/pub/dist/doc/misc/instacorr.pdf>



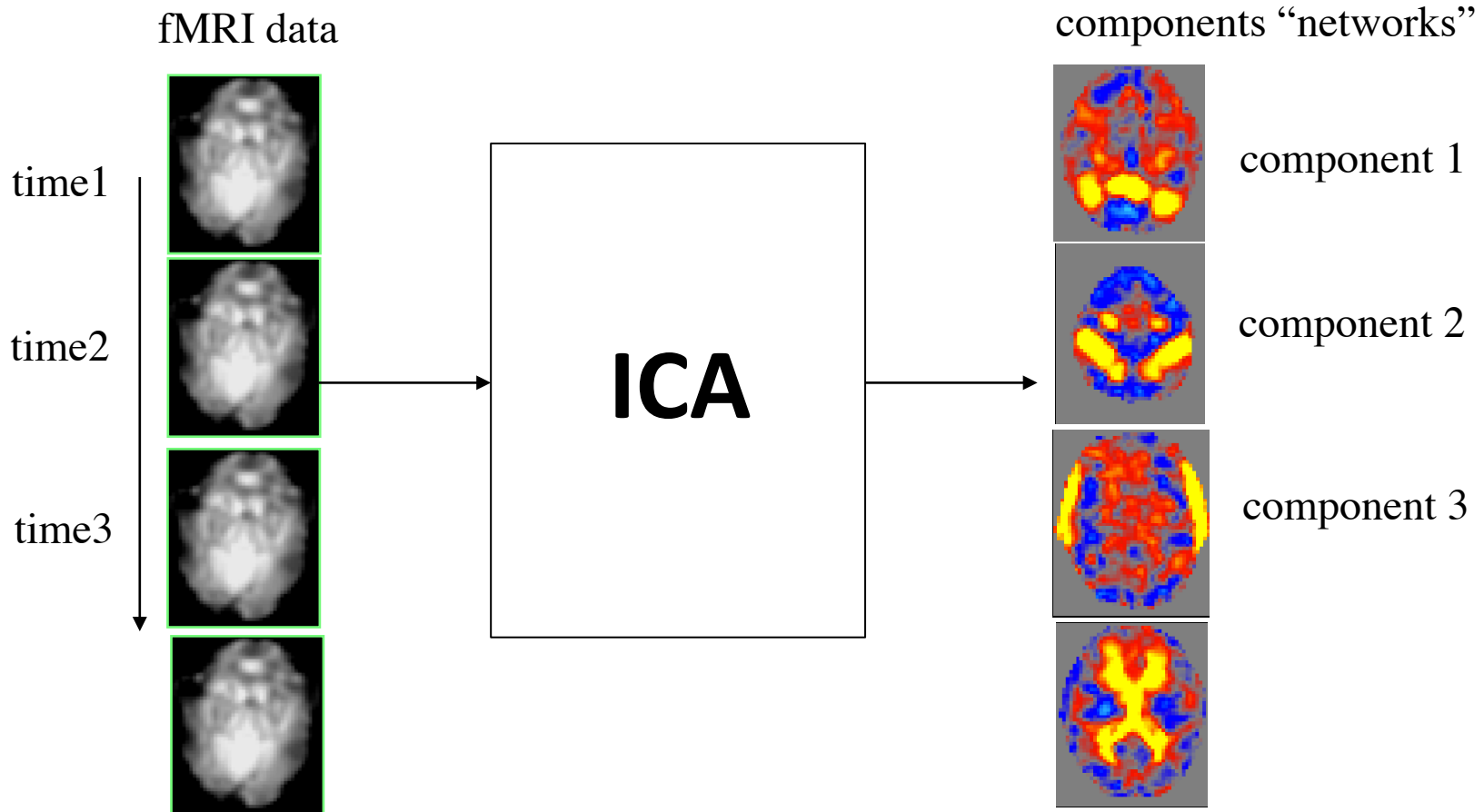
- On-the-fly instantaneous correlation map of resting state data with interactively selected seed voxel
- **Setup phase:** prepares data for correlations (several-to-10+ seconds)
- **Correlation phase:** you select seed voxel, correlation map appears by *magic*

# Seed-based correlation

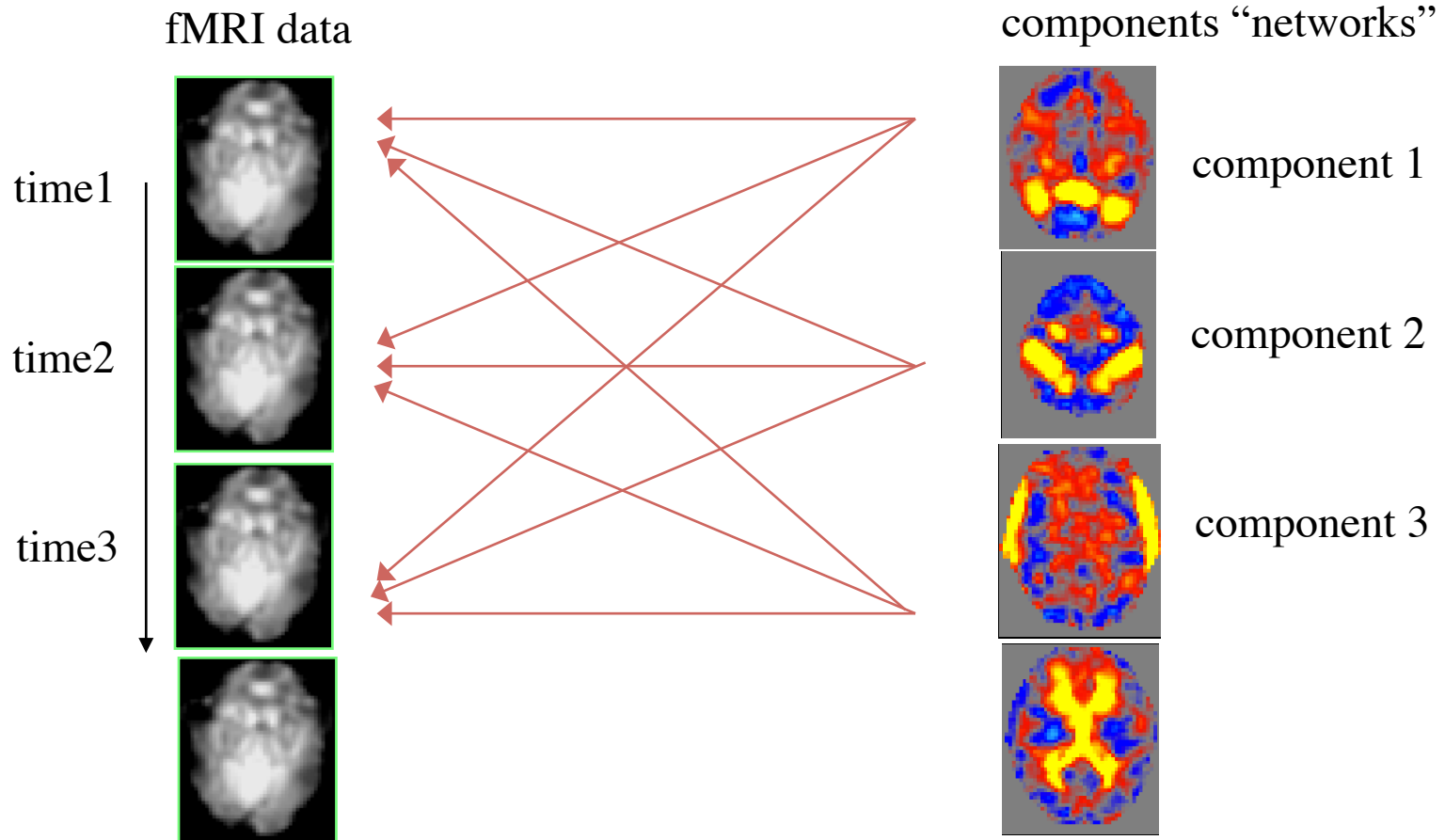
*Buckner et al. 2013*



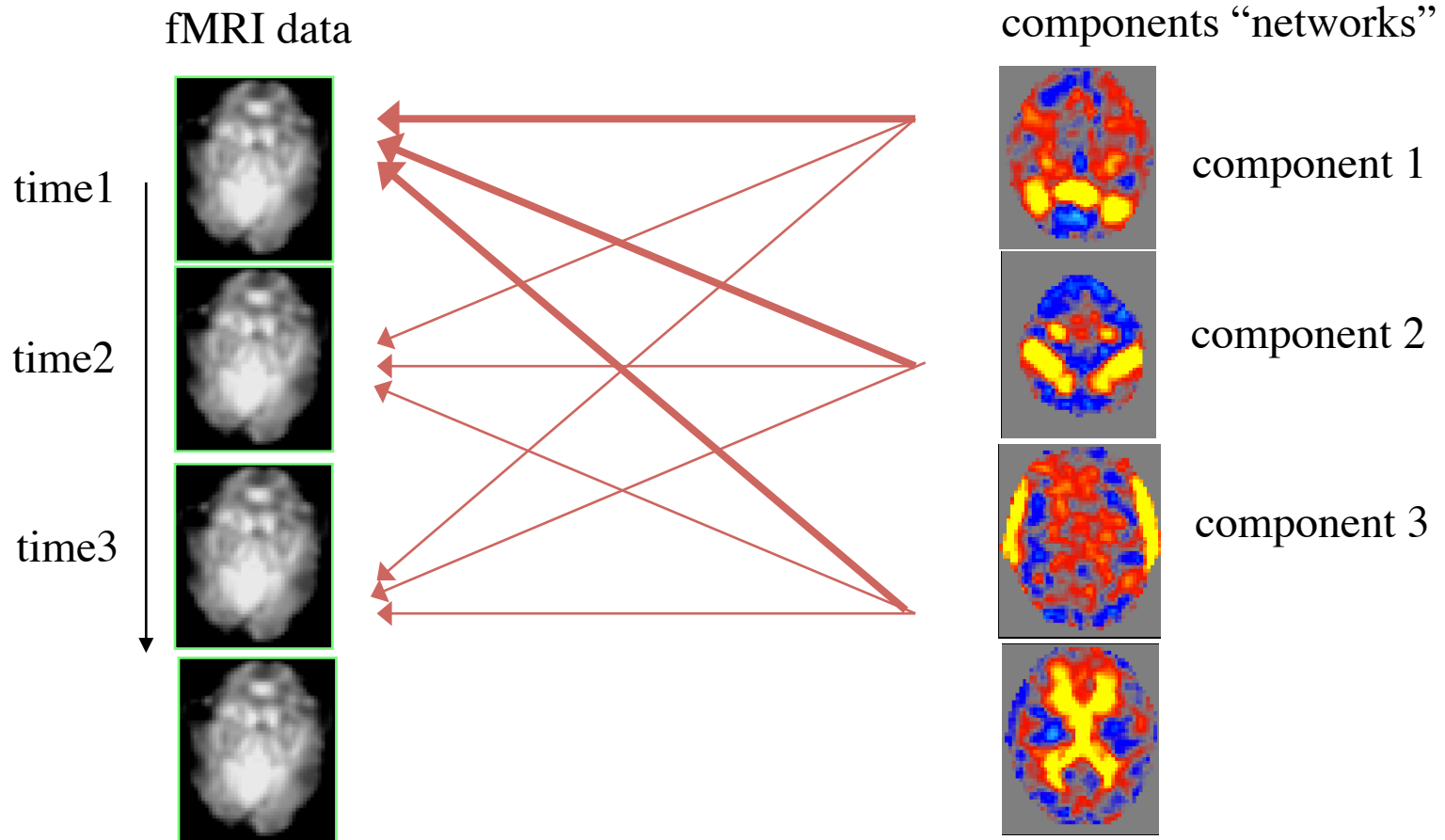
# Independent Component Analysis (ICA)



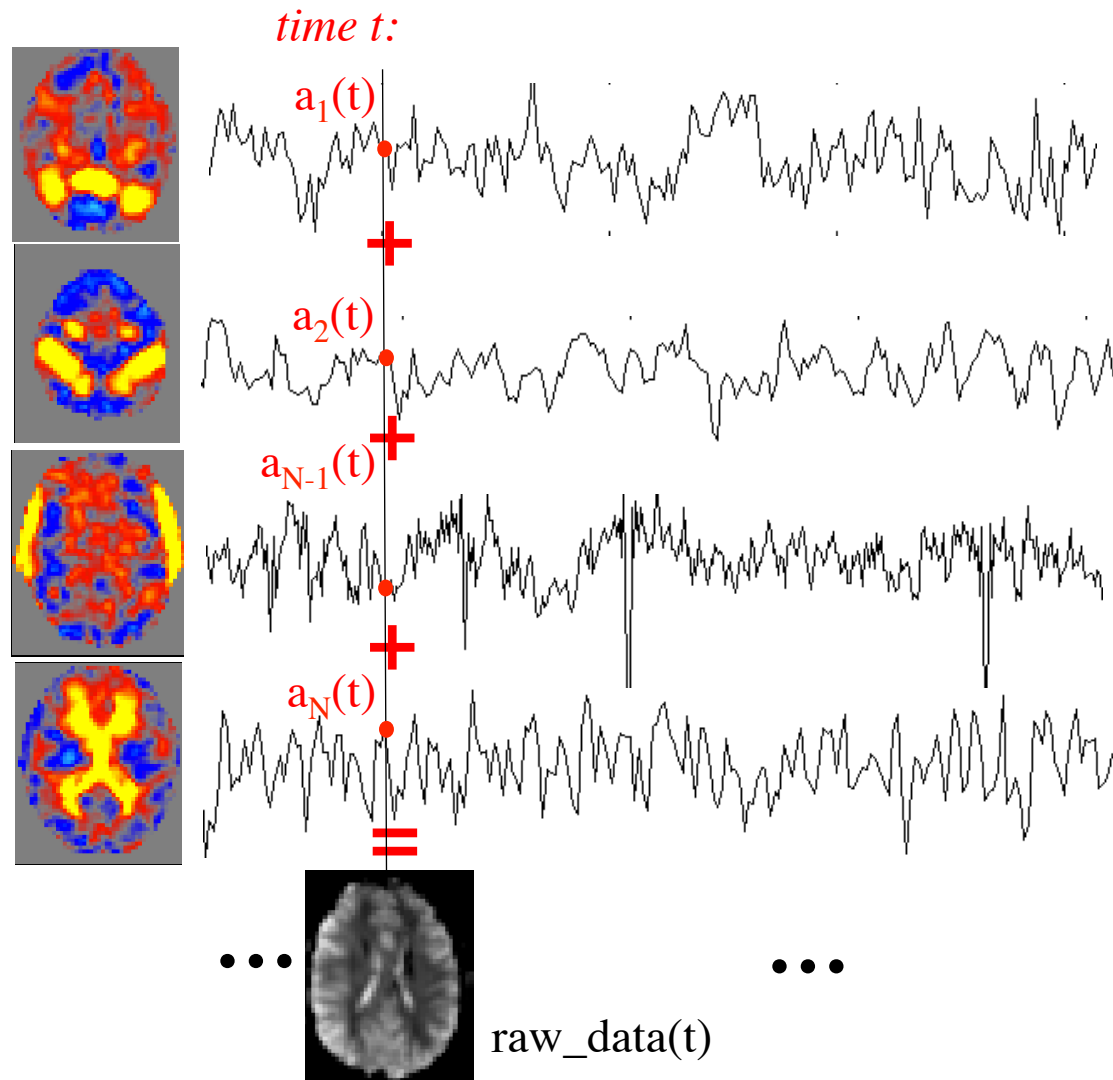
# Independent Component Analysis (ICA)



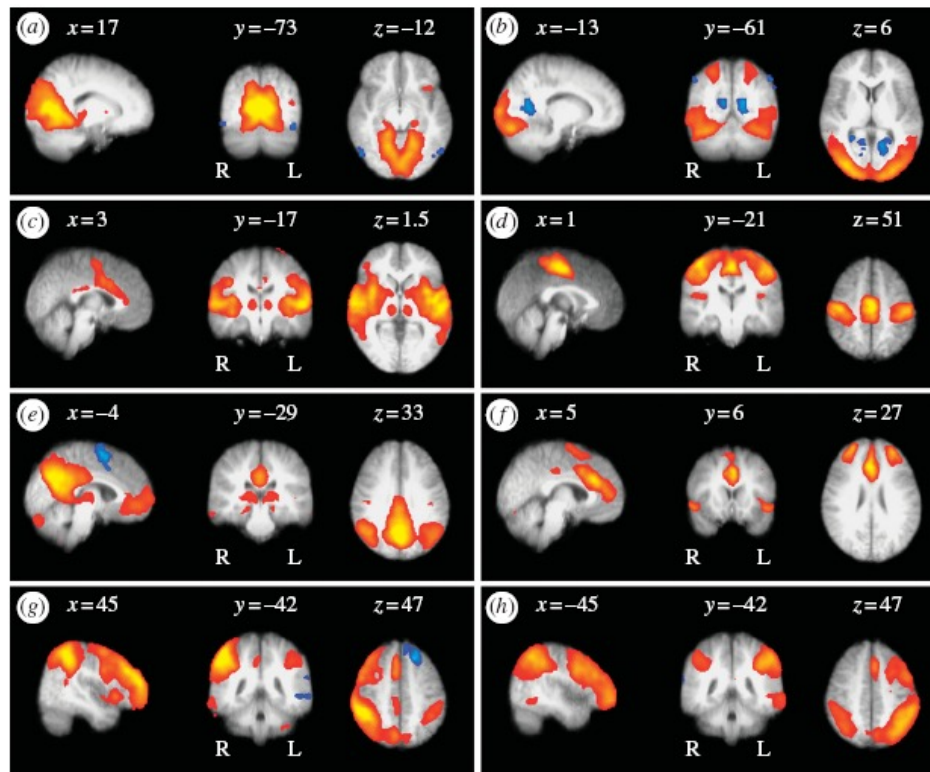
# Independent Component Analysis (ICA)



# Independent Components



# RSNs from ICA



*Damoiseaux et al. 2006*

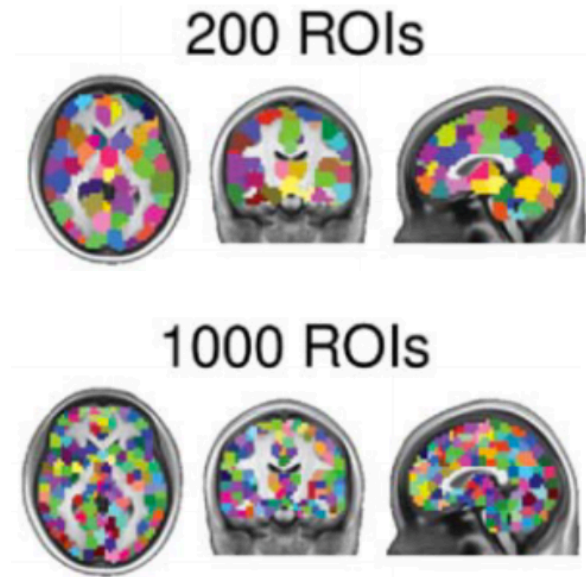




# Complex network analysis



*Meunier et al. 2011*



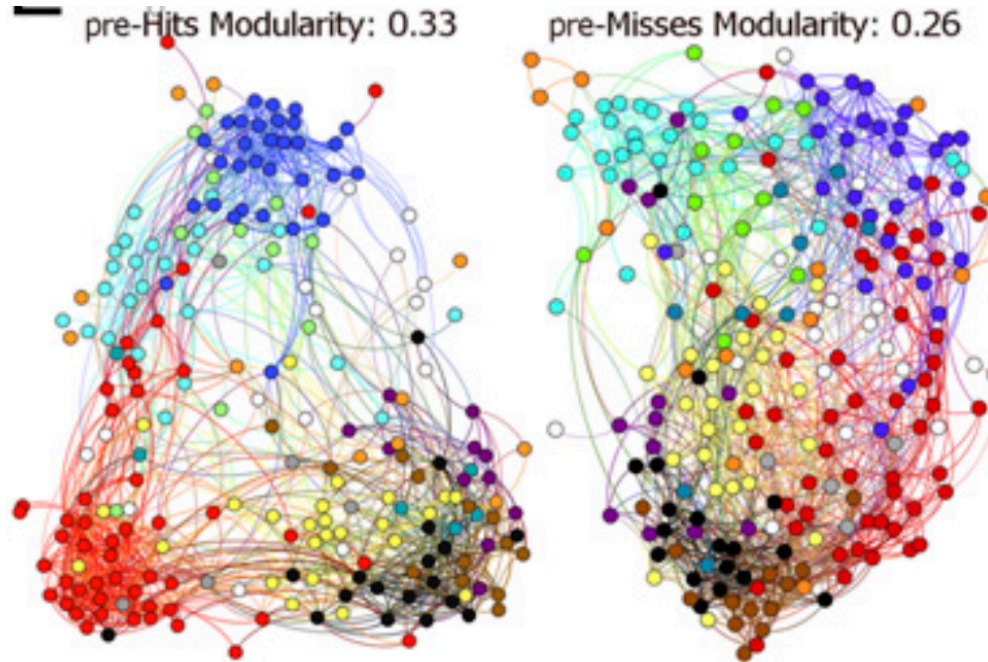
*Craddock et al. 2012*

Reviews:

Rubinov & Sporns, 2010

Bullmore & Sporns, 2009

# Complex network analysis



Modular structure predicted perception of near-threshold auditory stimulus

# Outline

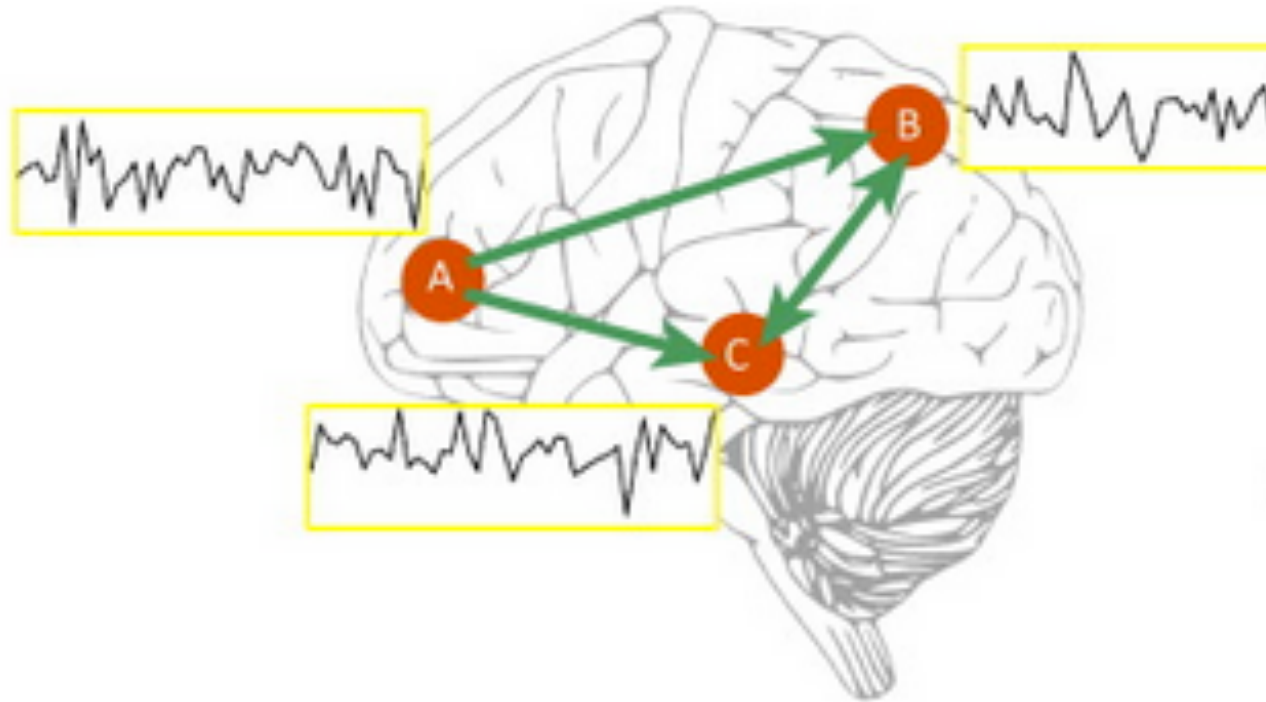
- What is it?
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# What are we measuring?

*Functional connectivity is a powerful  
but ambiguous mapping tool*

(Buckner et al. 2013 Nat. Rev. Neuro)

# What are we measuring?

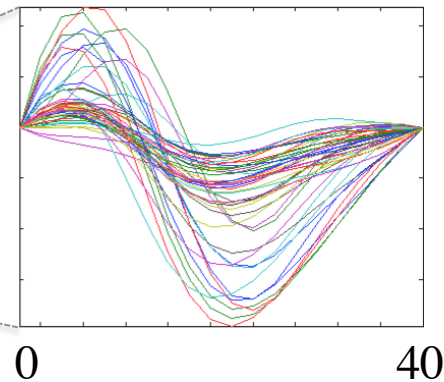
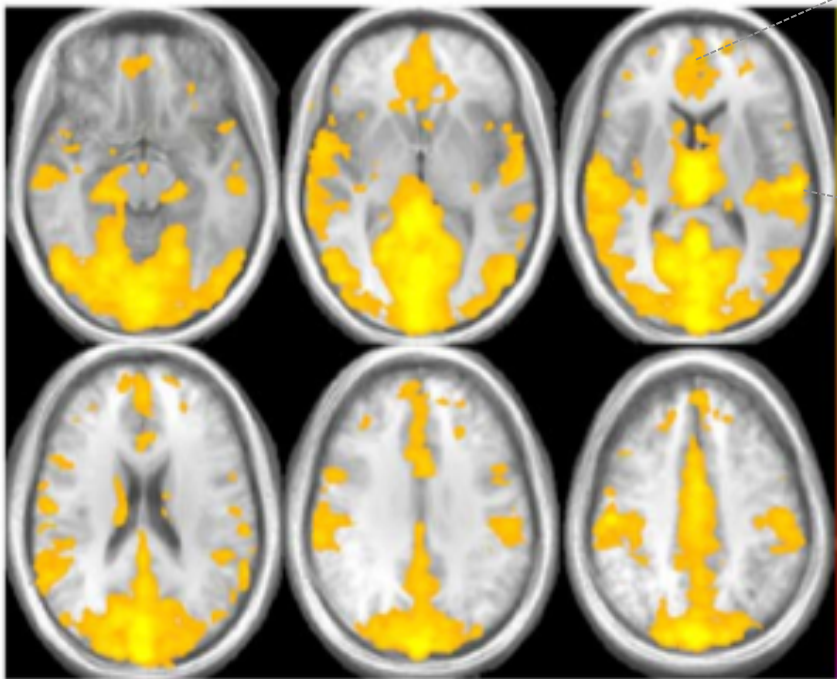


*Smith et al. 2011*

# Physiological noise

- Any non-neural fluctuations shared in common across regions will create the appearance of “functional connectivity”

**B** BOLD signal correlated with RVT

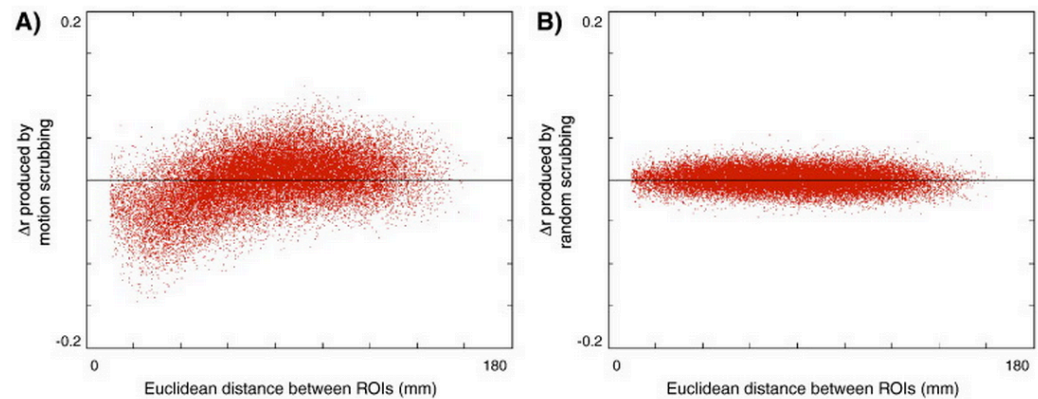
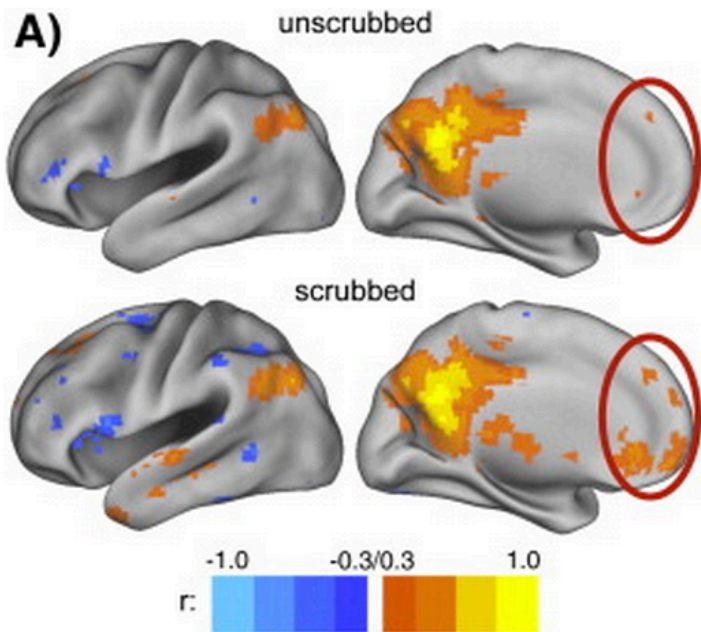


time (sec)

*data from Chang et al. 2009*

*Birn et al. 2006*

# Head motion



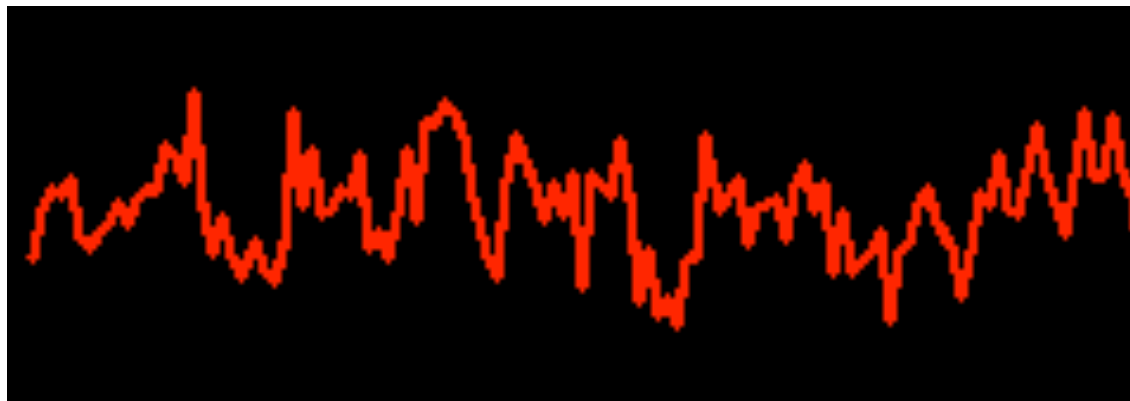
*Power et al. 2010*

- Systematic differences in head motion across age groups caused spurious functional connectivity effects



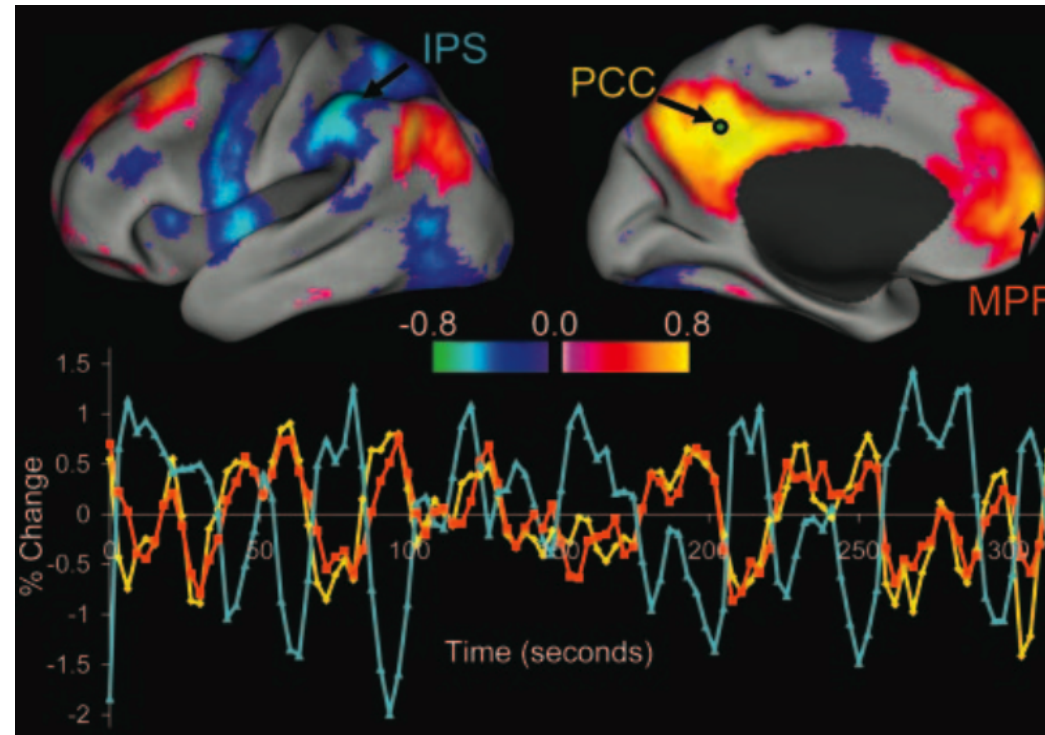
# What is noise, what is signal?

- no task/stimulus timing to help distinguish signal from noise
- trial averaging not possible
- resting-state FC quantifies relationships between fMRI time series across regions (each are signal + noise!)



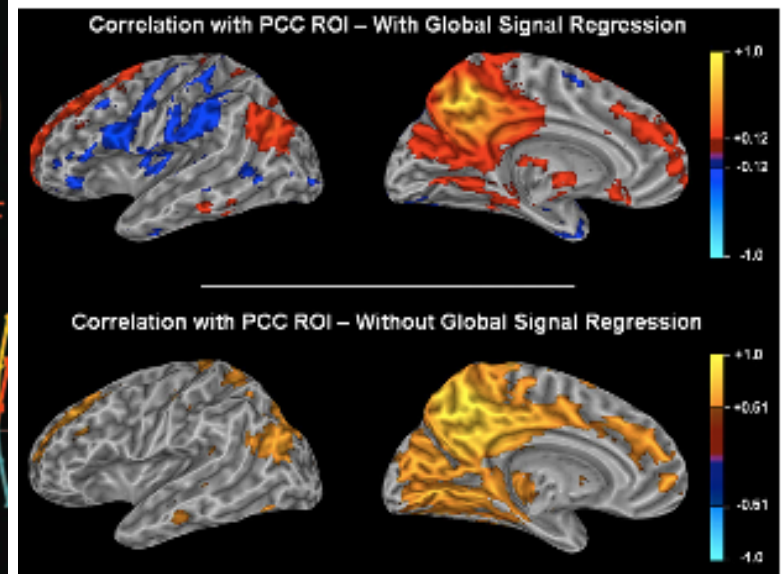


# Noise reduction strategies can affect results



*Fox et al, 2005*

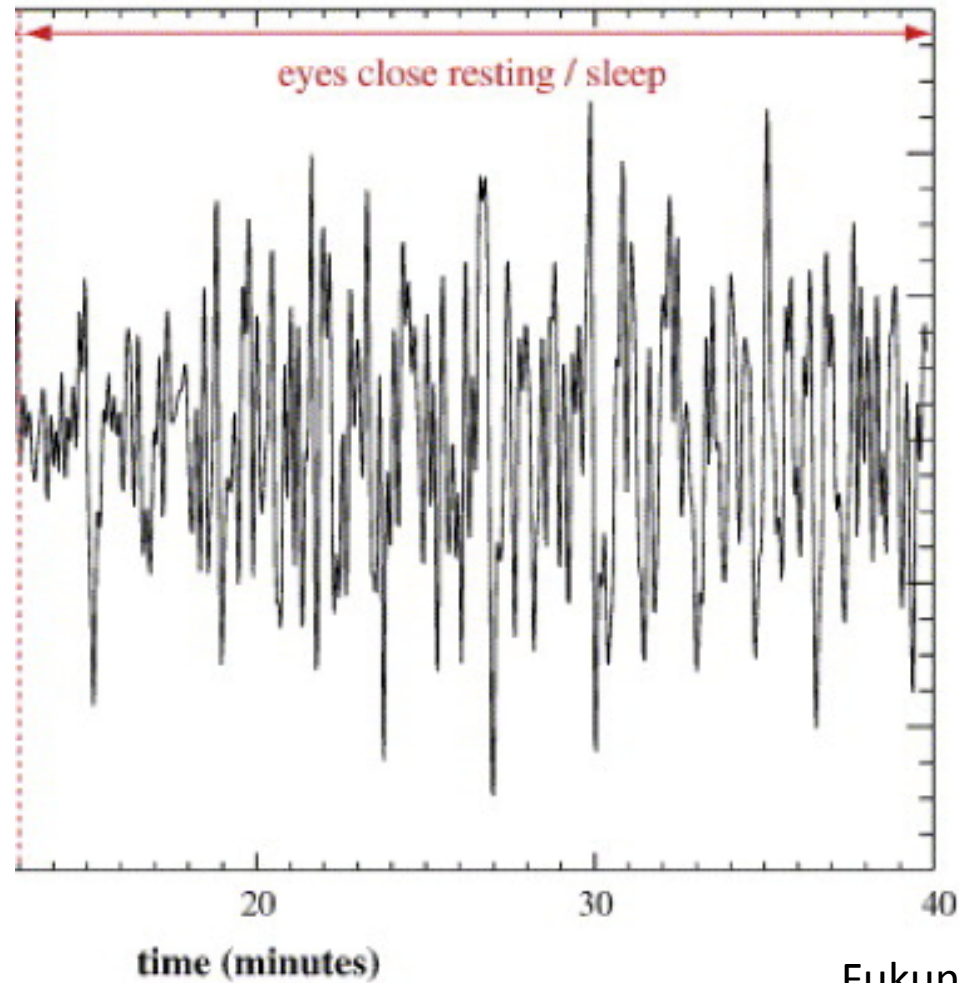
*Fransson 2005*



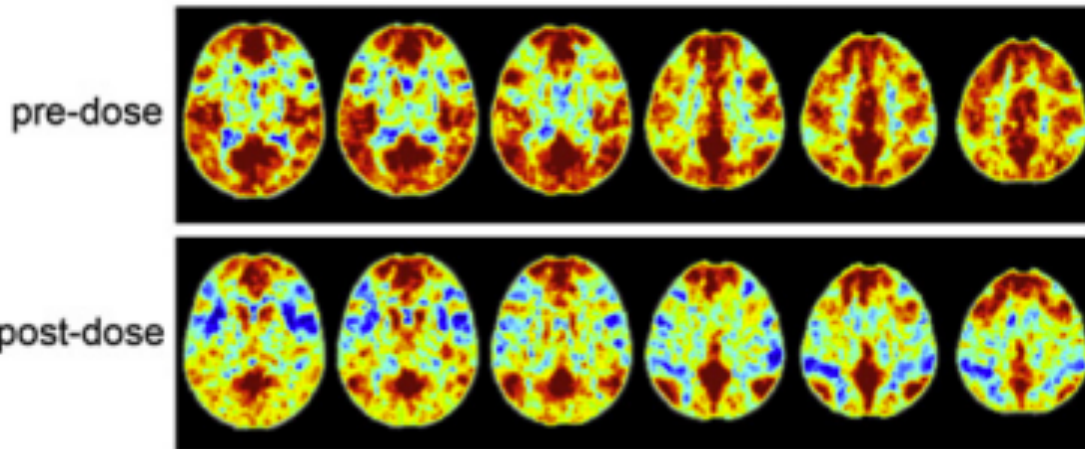
*Murphy et al, 2009*

- and how can we tell which is correct?

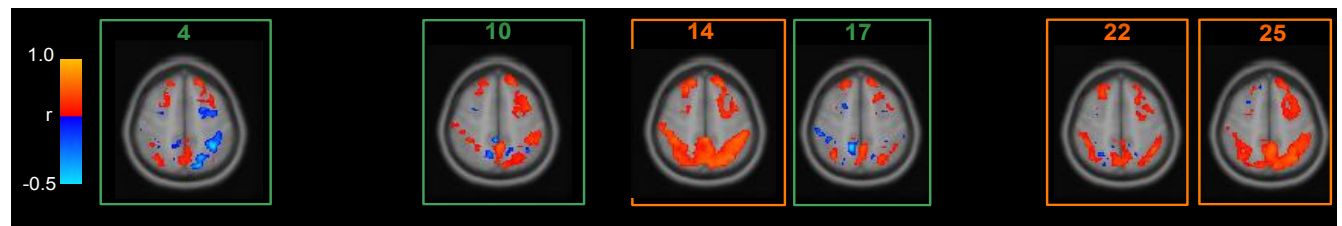
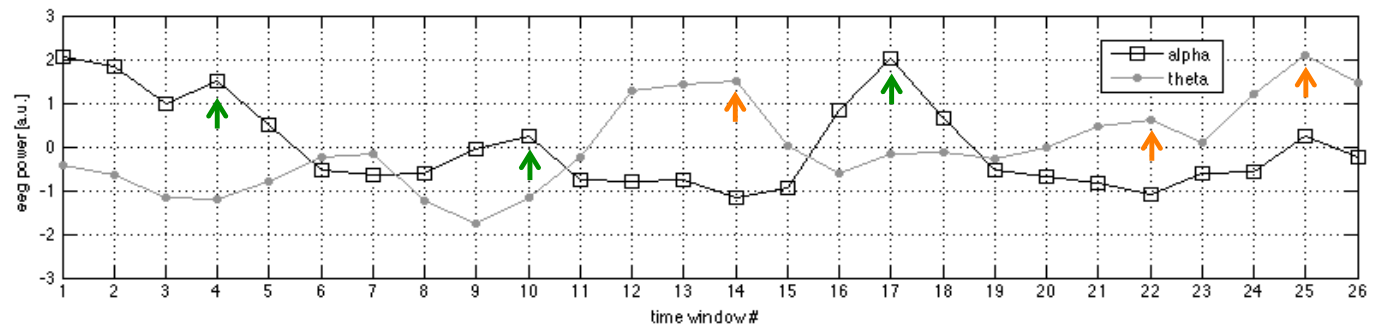
# Drowsiness



# Drowsiness



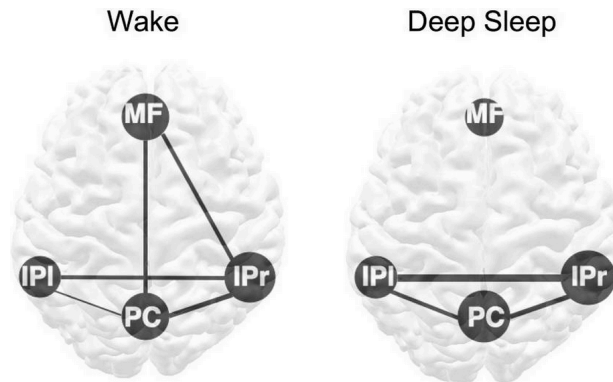
*Wong et al. 2010*



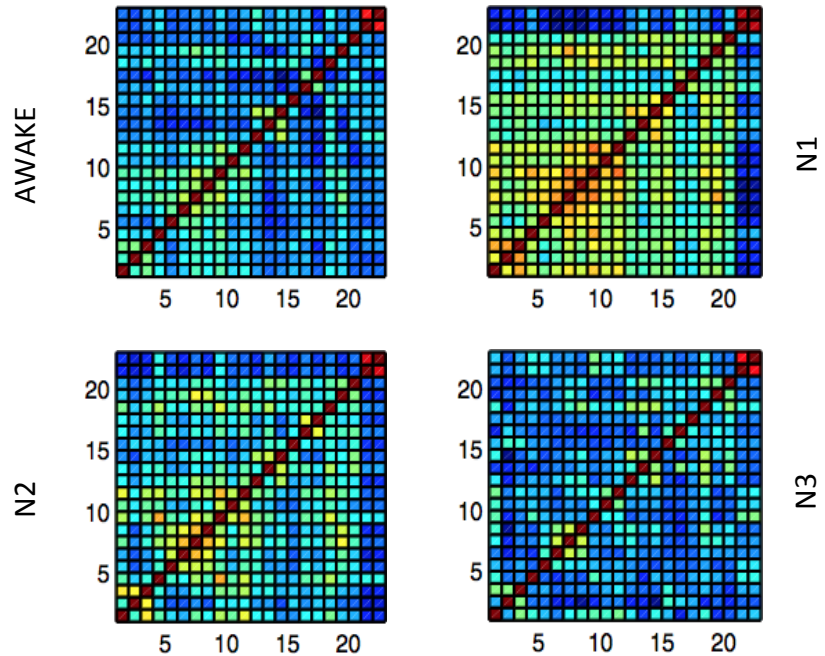
*Chang et al. 2013*

# Drifting to sleep...

- Functional connectivity patterns change with sleep stage

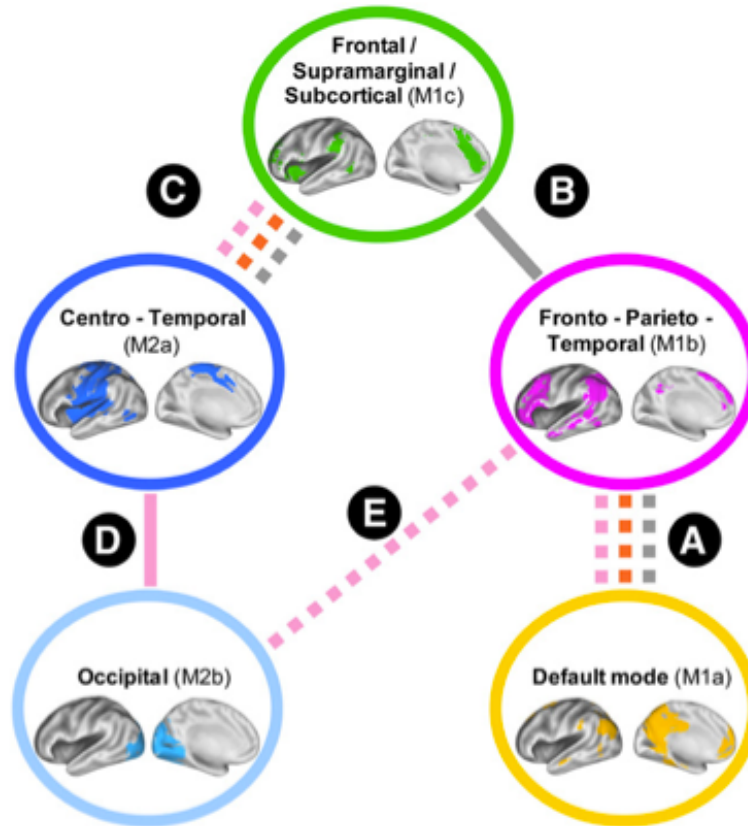


*Horovitz et al., 2009*



*Tagliazucchi et al. 2012*

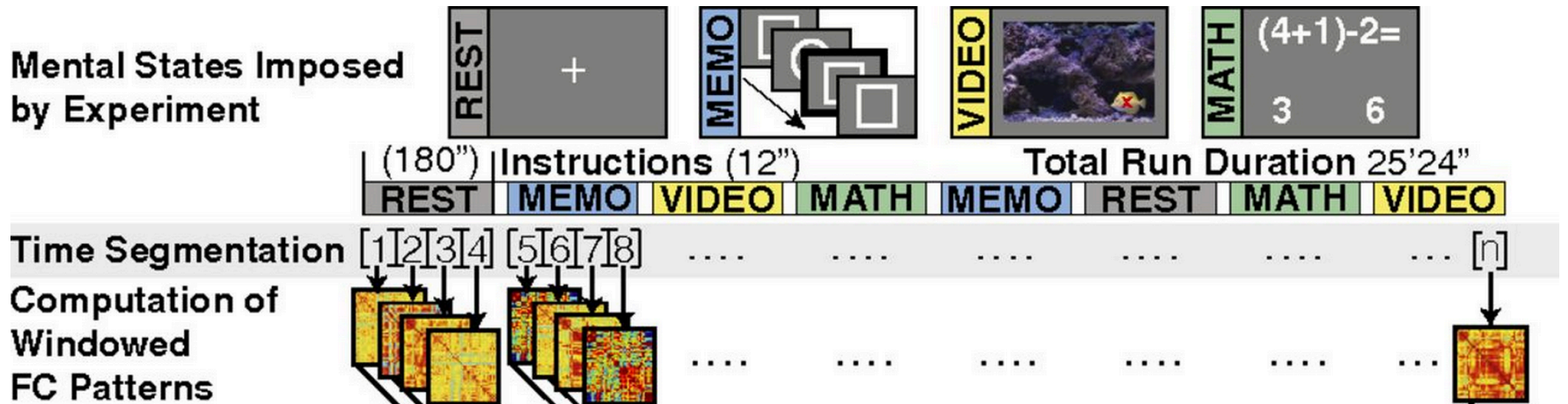
# Mind wandering



*Doucet et al. 2011*



# Mind wandering



*Gonzalez-Castillo et al. 2015*

# Summary

- Resting-state fMRI is proving valuable for clinical applications and basic neuroscience
  - RSNs relate to anatomic connectivity and electrophysiology, but precise relationship still not clear
- Understand analysis methods/tradeoffs
- Noise and neural variability can affect signal and connectivity measurements

# Thanks!



[http://eandt.theiet.org/magazine/2012/01/images/640\\_baby-sloth.jpg](http://eandt.theiet.org/magazine/2012/01/images/640_baby-sloth.jpg)