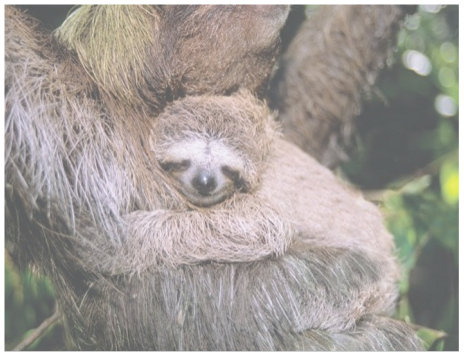
Resting State fMRI



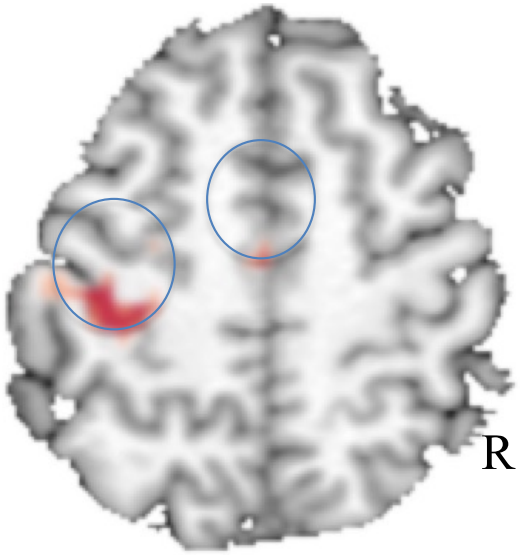
Catie Chang
Advanced MRI Section, NINDS, NIH
fMRI Summer Course * 2016

http://eandt.theiet.org/magazine/2012/01/images/640_baby-sloth.jpg

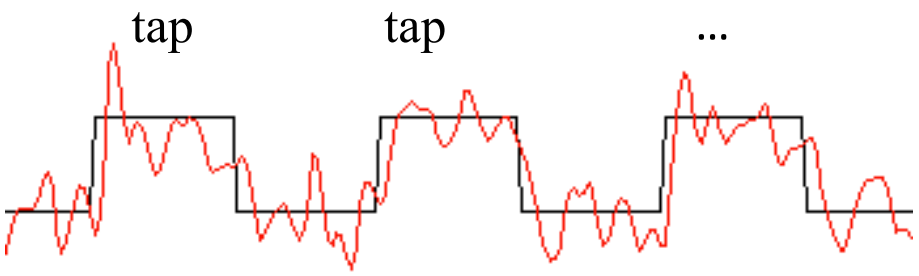
Outline

- **What is it?**
- Analyzing resting-state data
- Issues & interpretation
- Summary & discussion

Task v. resting-state fMRI



Right-hand fingertapping task

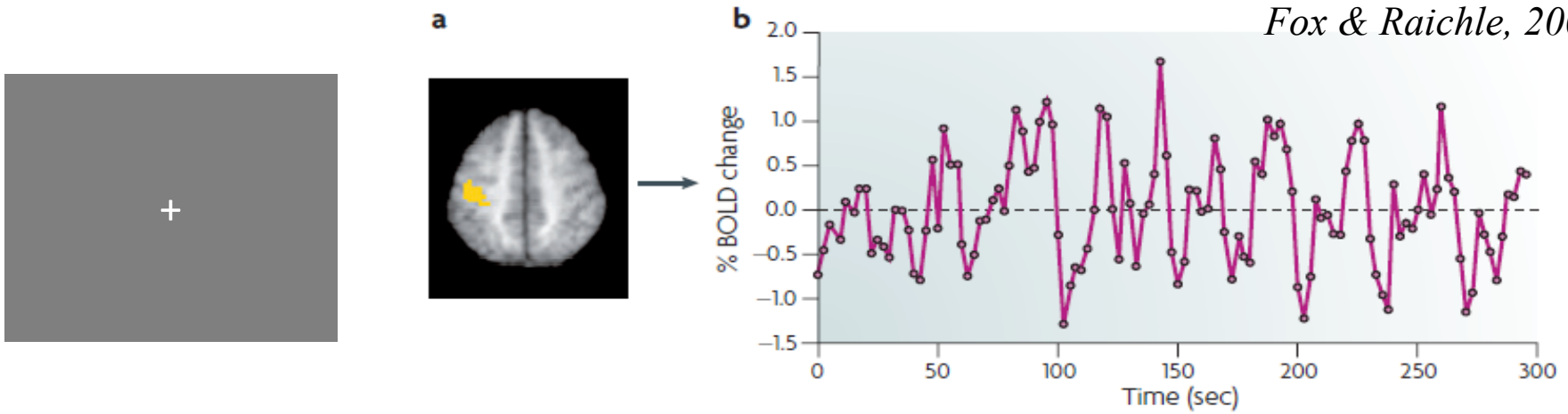


Spontaneous/intrinsic activity

- that which cannot be attributed to experimental task/stimuli (c.f. "evoked activity")
- accounts for most of the brain's energy consumption
- what can we learn by studying it?

courtesy Jen Evans (NIMH)

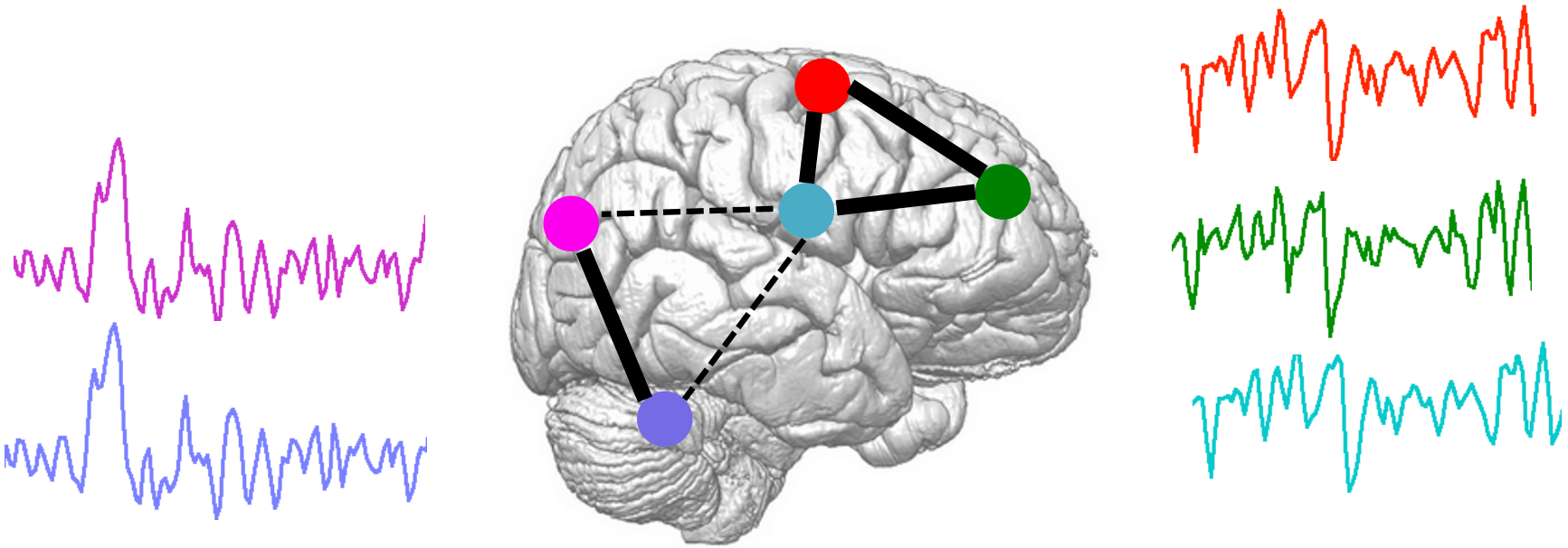
Resting-state fMRI



- No task or stimuli (minimal instructions, e.g. keep eyes closed)
- fMRI data reflect spontaneous activity (+ the usual fMRI noise)
- How to find useful information from this data?

? no (known) conditions to compare
? no idea what the subject is thinking
? how to separate "signal" from "noise"

Functional connectivity



- FC: statistical dependence (e.g. correlation) between the activity of different brain regions
- suggests "network" interactions, though interpretation is complicated

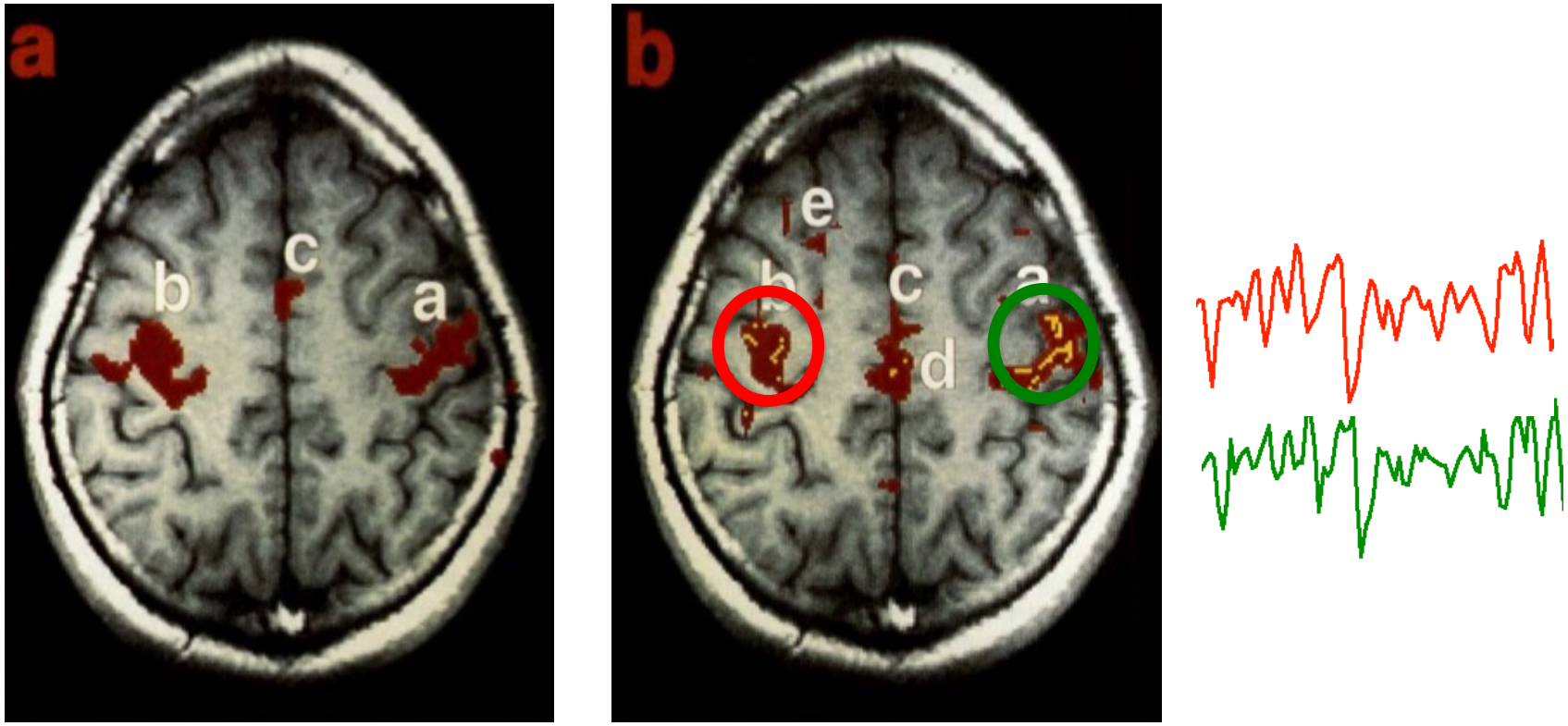
Brain image adapted from: http://www.cgl.ucsf.edu/home/goddard/temp/highlight14/highlight14.html

Functional Connectivity in the Motor Cortex of Resting Human Brain Using Echo-Planar MRI

Bharat Biswal, F. Zerrin Yetkin, Victor M. Haughton, James S. Hyde

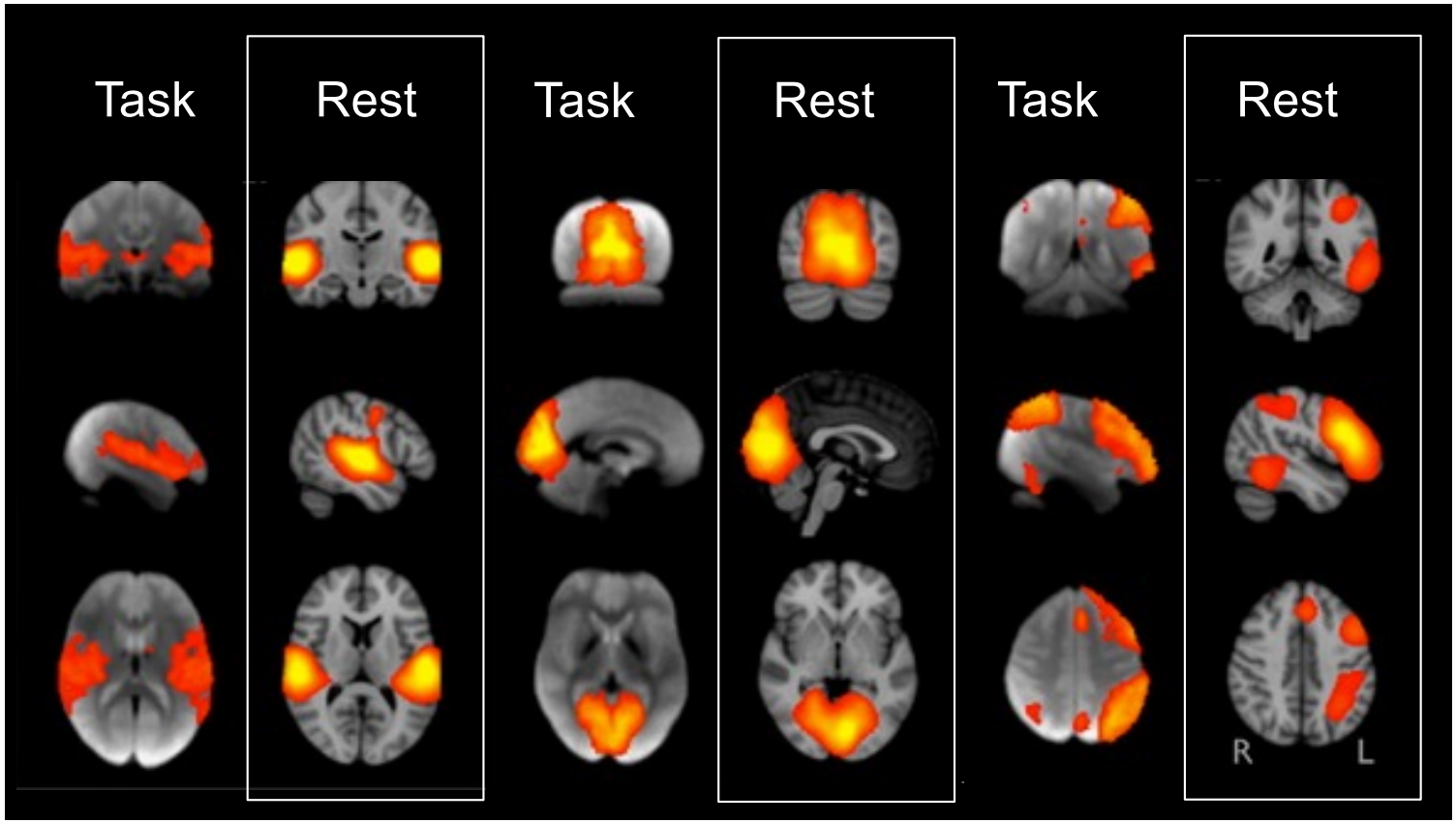
finger-tapping task
activation

resting state
functional connectivity



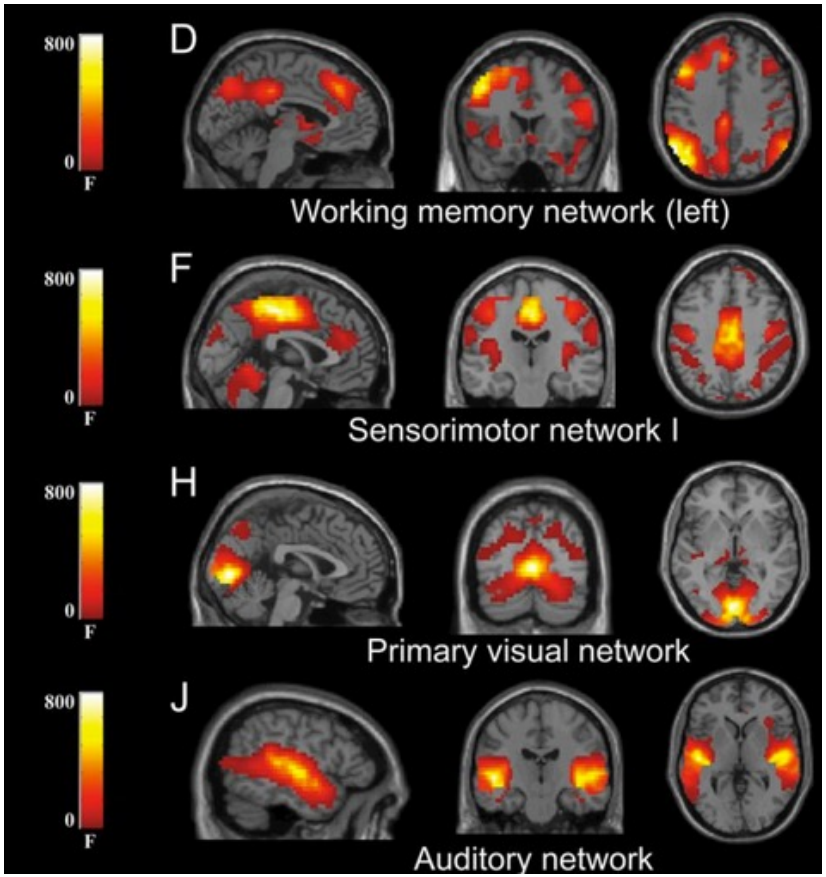
- areas that operate as functional networks tend to correlate with one another in resting-state scans

Resting-state "networks" closely resemble task-activated networks



Smith et al, 2009

"Resting-state networks"

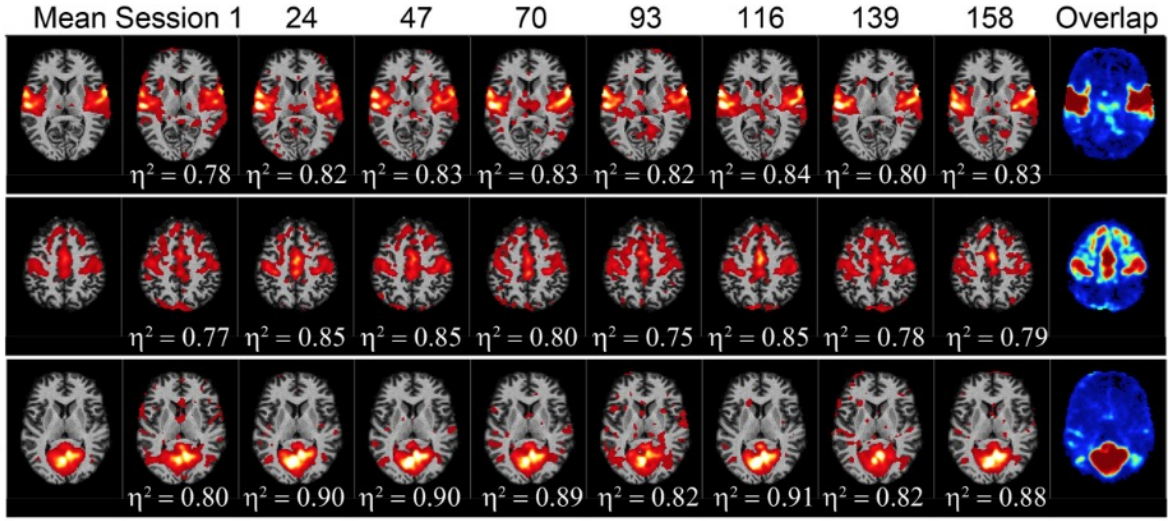


Rocca et a. 2012

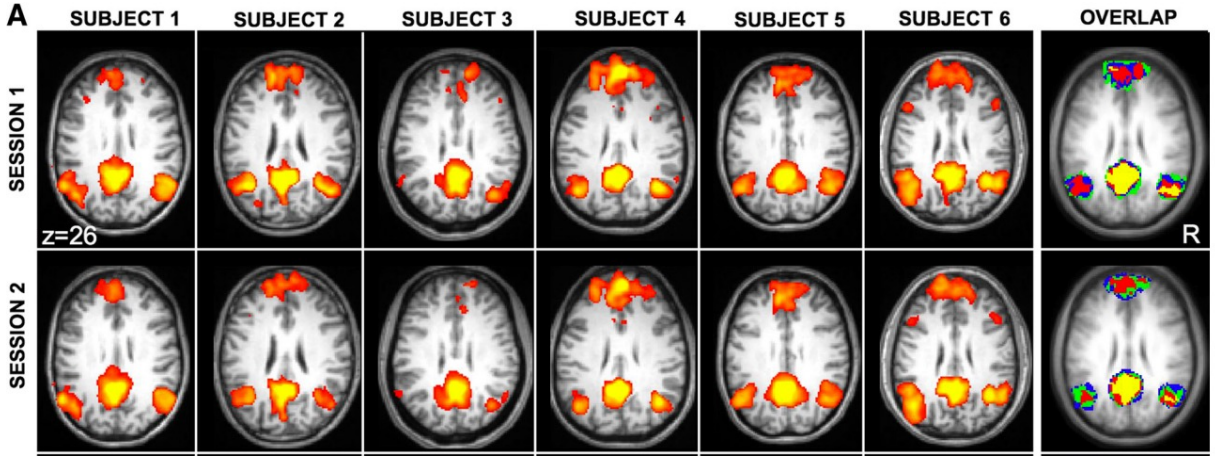
- **Resting-state network** : set of regions ("nodes") with mutually high functional connectivity in resting state
  - approx 10-15 reliable patterns at this spatial granularity
  - often named after the functional areas with which they overlap

- Fixed # of networks??
  - FC can be studied at multiple scales (spatial and temporal)

Stability of resting-state networks

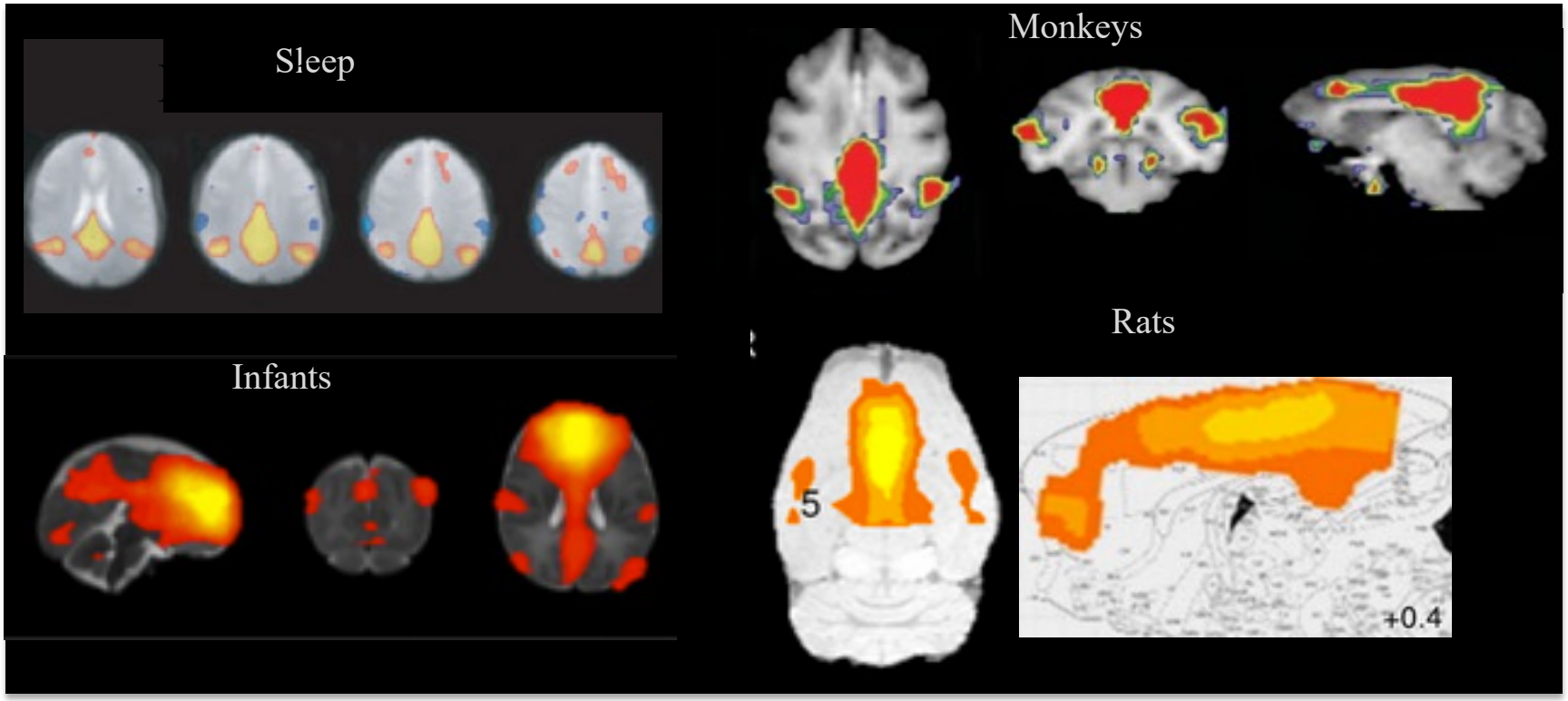


Choe et al, 2015



Van Dijk et al. 2010

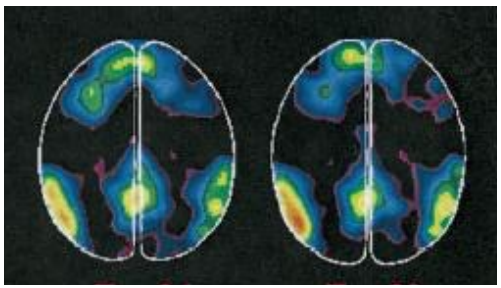
Stability across time, states, species

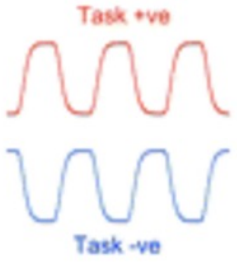


Horovitz et al. 2008; Doria et al. 2010; Vincent et al. 2007; Lu et al. 2007

Default-mode network

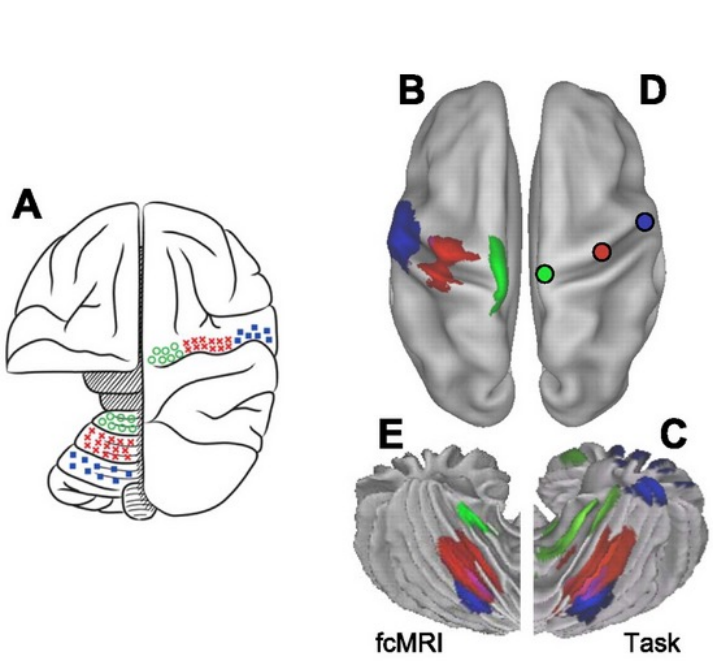
Raichle at el., 2001->
Greicius at el., 2003



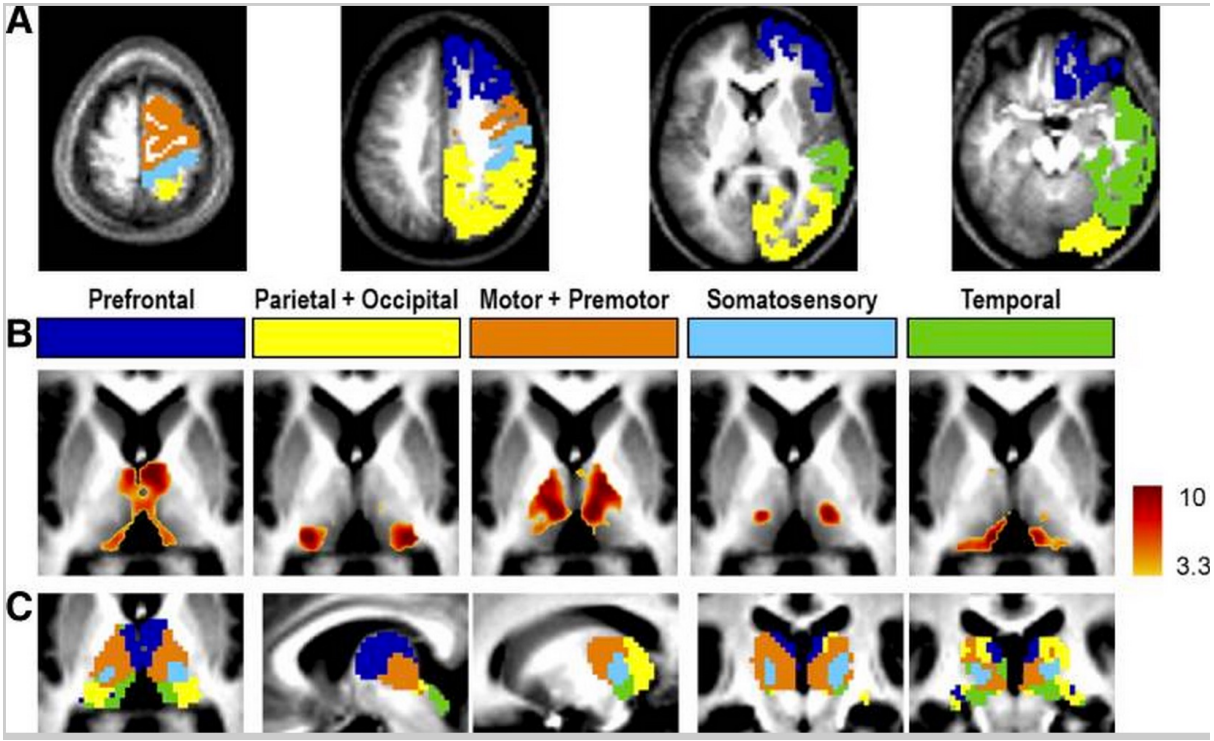


Leech et al., 2015

Correspondence with known fine-grained anatomic/functional organization



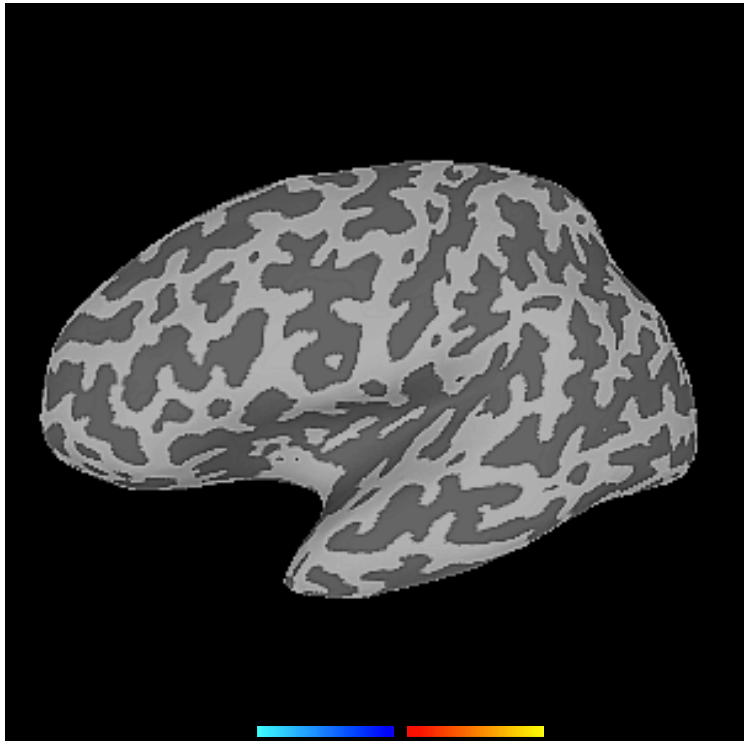
Buckner et al. 2011



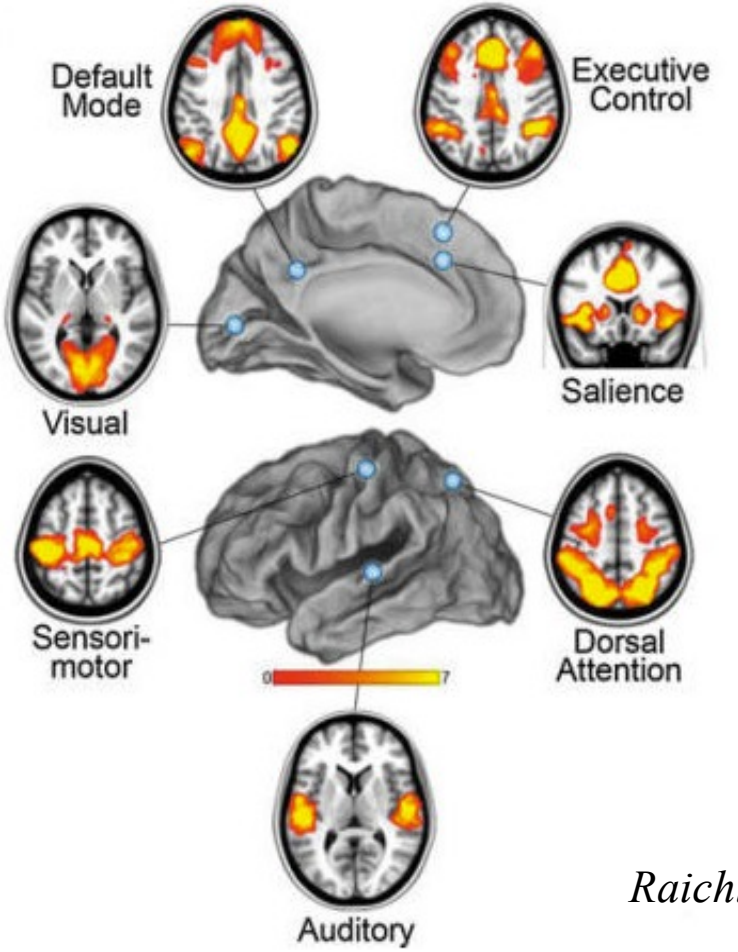
Zhang et al. 2008

(however, there is not a one-to-one correspondence between FC and structural connectivity)

Resting-state data appears to provide info about functional organization

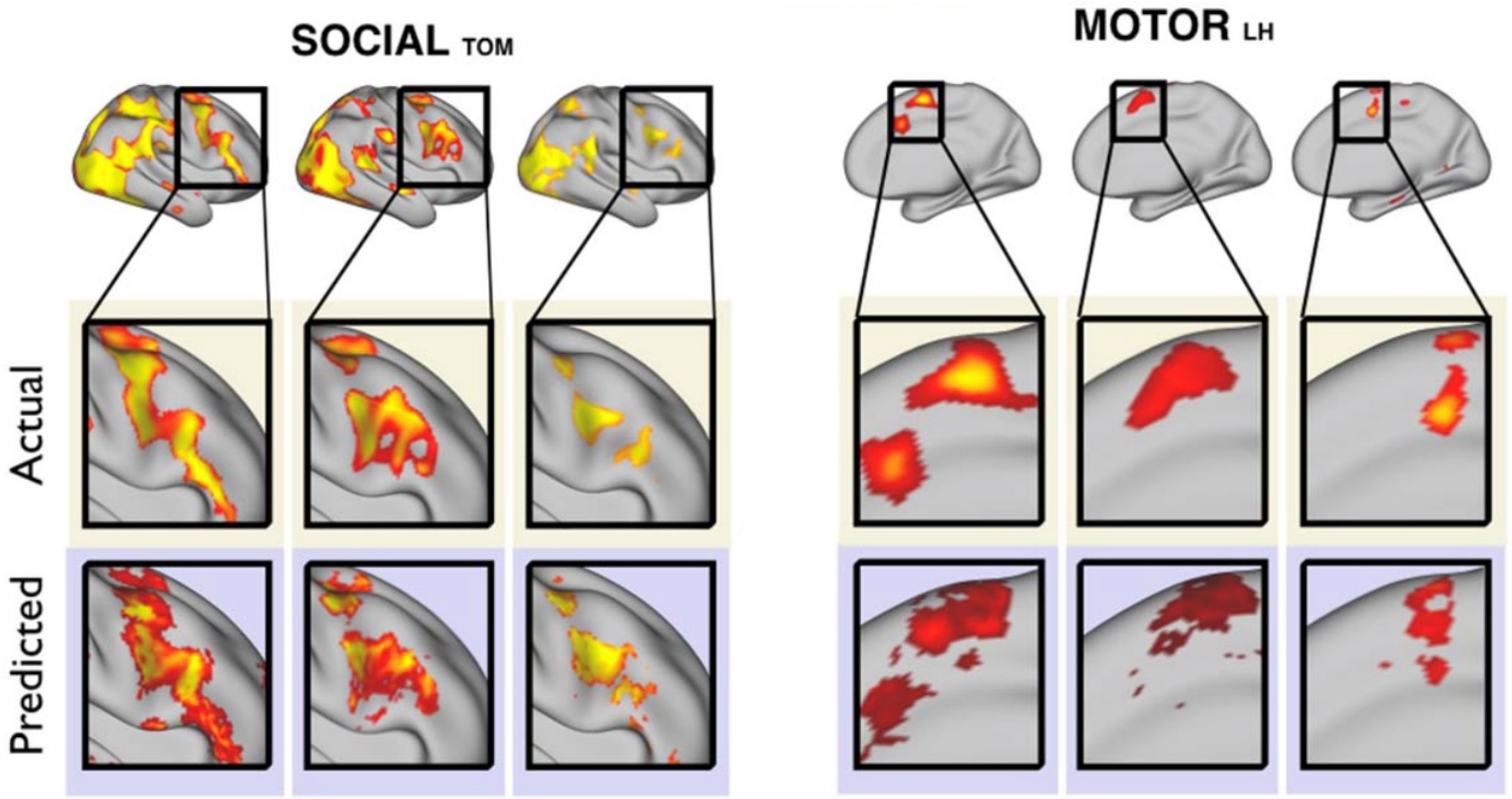


courtesy Zhongming Liu



Raichle, 2011

Resting-state data can predict task activation



Tavor et al. 2016

If we can map functional networks from resting-state data….

Implications:

+ can derive many networks from one set of task-free data
+ no task or task compliance needed
+ tool for studying disease-related differences in functional organization

Resting-state fMRI is a topic of much current interest

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)

Disorder/Condition	# studies
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

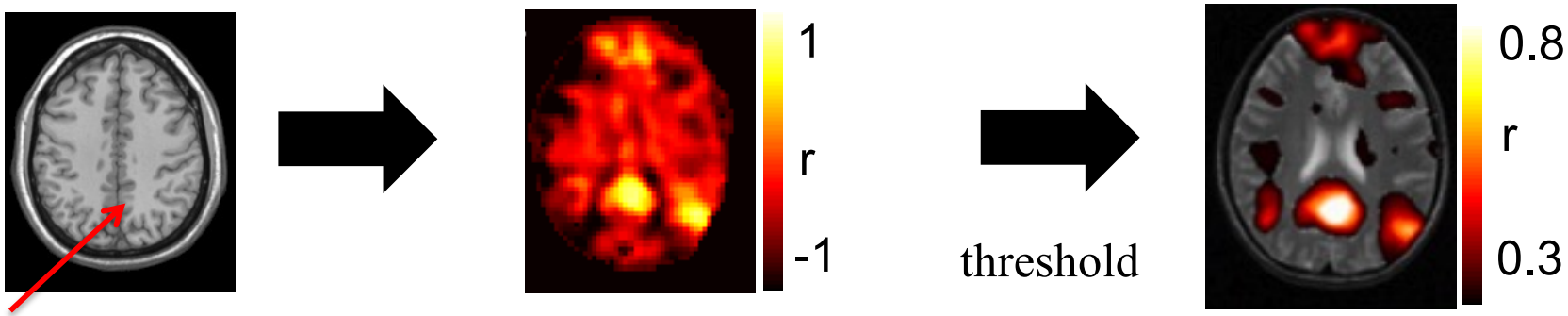
Kelly et al. 2012

Outline

- What is it?
- **Analyzing resting-state data**
  - **seed-based correlation**
  - **ICA**
  - **complex network analysis**
- Issues & interpretation
- Summary & discussion

Seed-based correlation

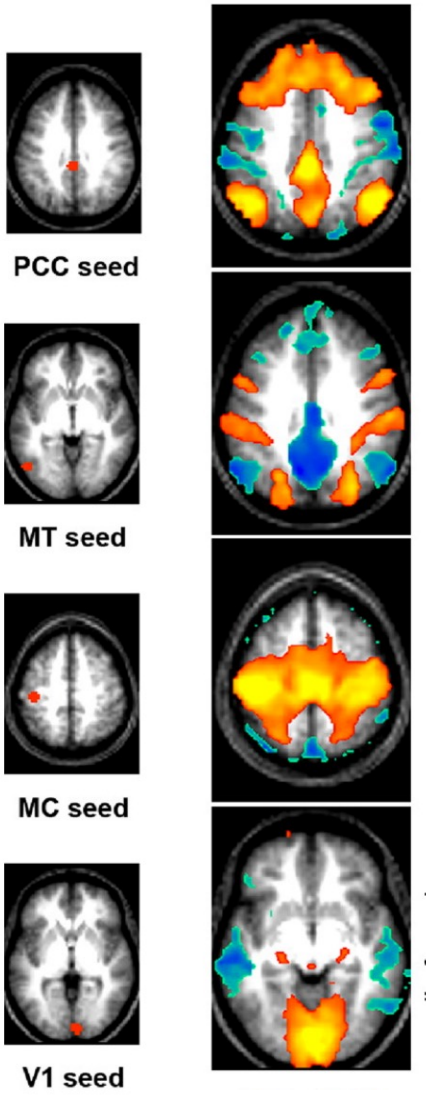
- Which areas are most highly correlated with a region of interest ("seed") ?
- Implemented with GLM (linear regression)



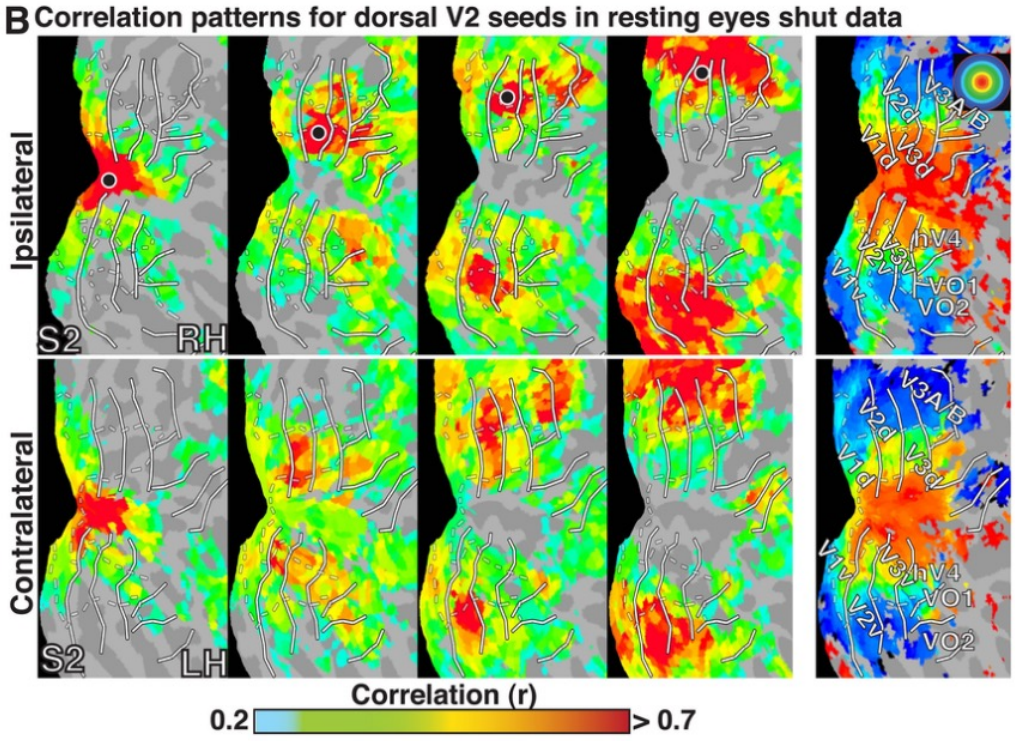
seed

correlate seed's time series with every other voxel's time series

Seed-based correlation



Fox et al. 2009



Arcaro et al. 2015

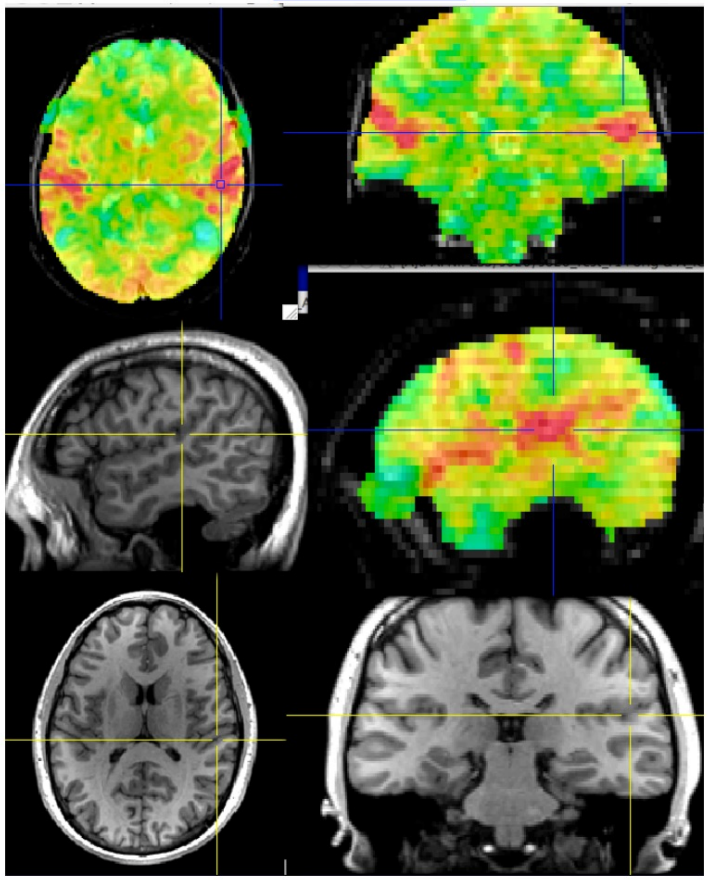
Seed-based correlation

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

–1–

AFNI InstaCorr

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



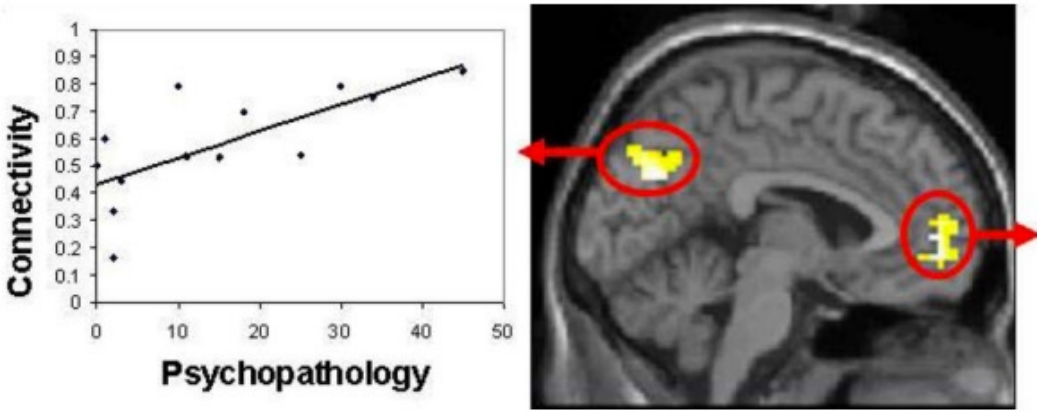
- On-the-fly **insta**ntaneous **corr**elation map of resting state data with interactively selected seed voxel
- **Setup phase**: prepares data for correlations (several-to-10+ seconds)
- **Correlation phase**: you select seed voxel, correlation map appears by ***magic***

Seed-based correlation: examples

Sample questions:

- Are there any areas whose FC with my seed ROI is significantly different in [condition A] v. [condition B]?
- Any areas whose FC with my seed ROI changes with disease severity?

Schizophrenia

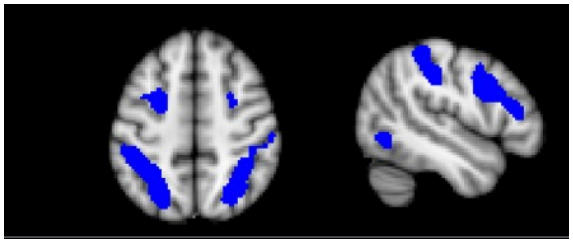


Whitfield-Gabrieli et al. 2009

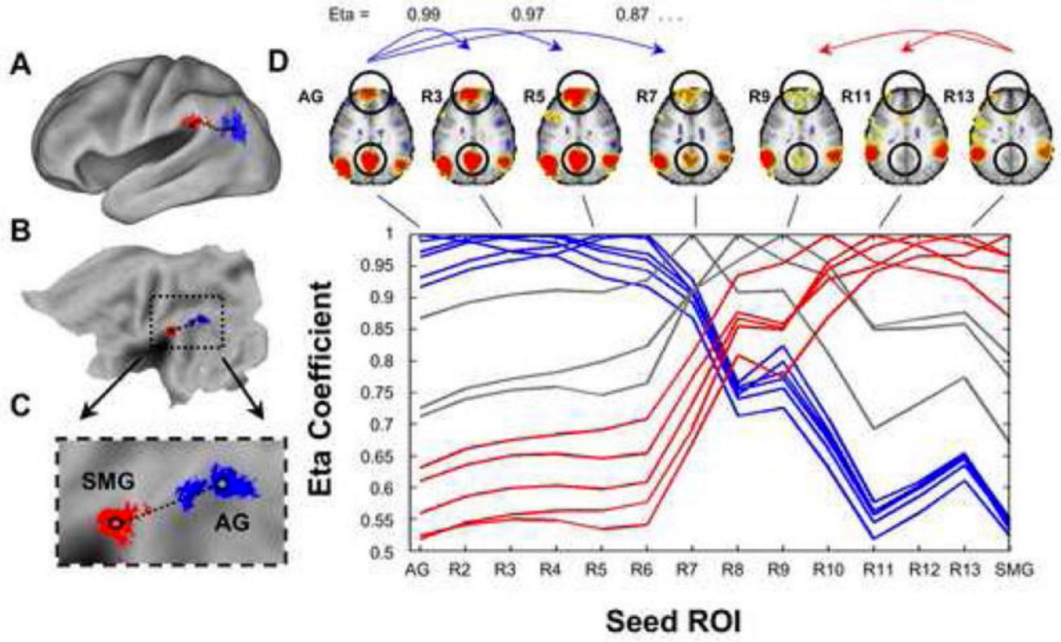
Seed-based correlation: considerations

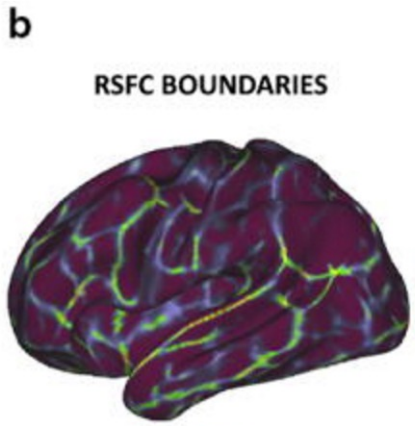
- Placement/size of seed ROI?
  - atlas, structrual image, activation map (single-sub, group-level)

Klein et al. 2012



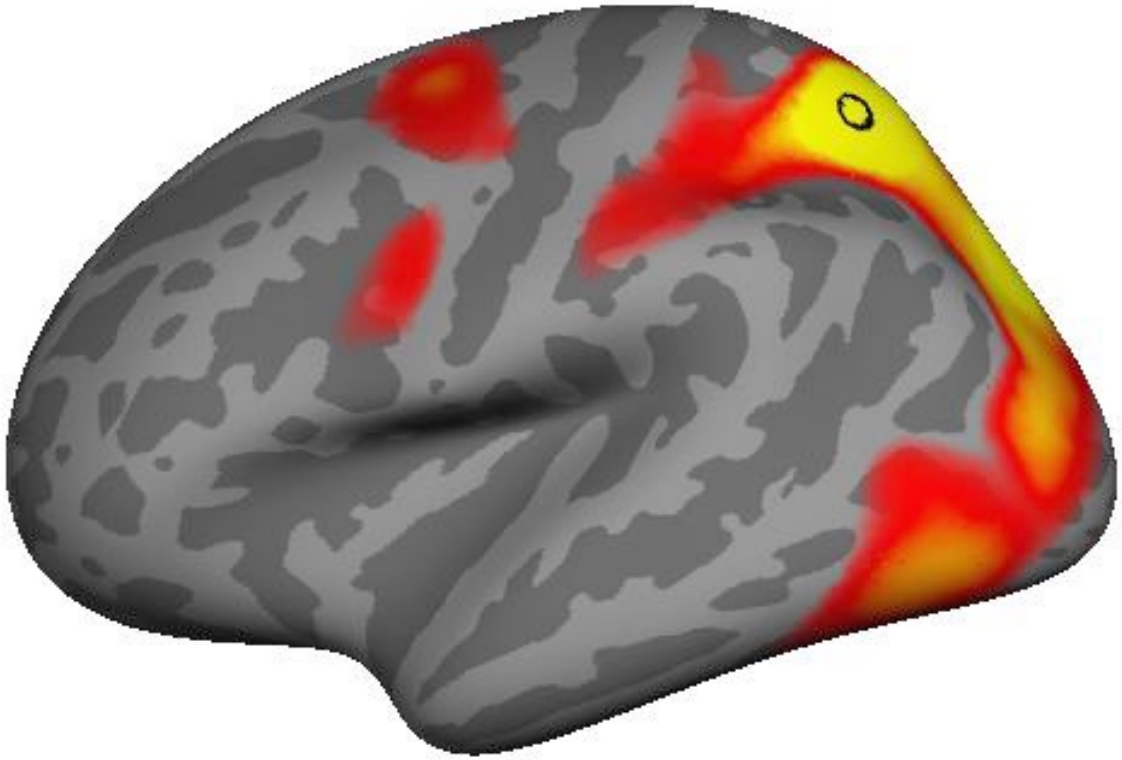
Stanford "FIND" atlas; Shirer et al. 2011





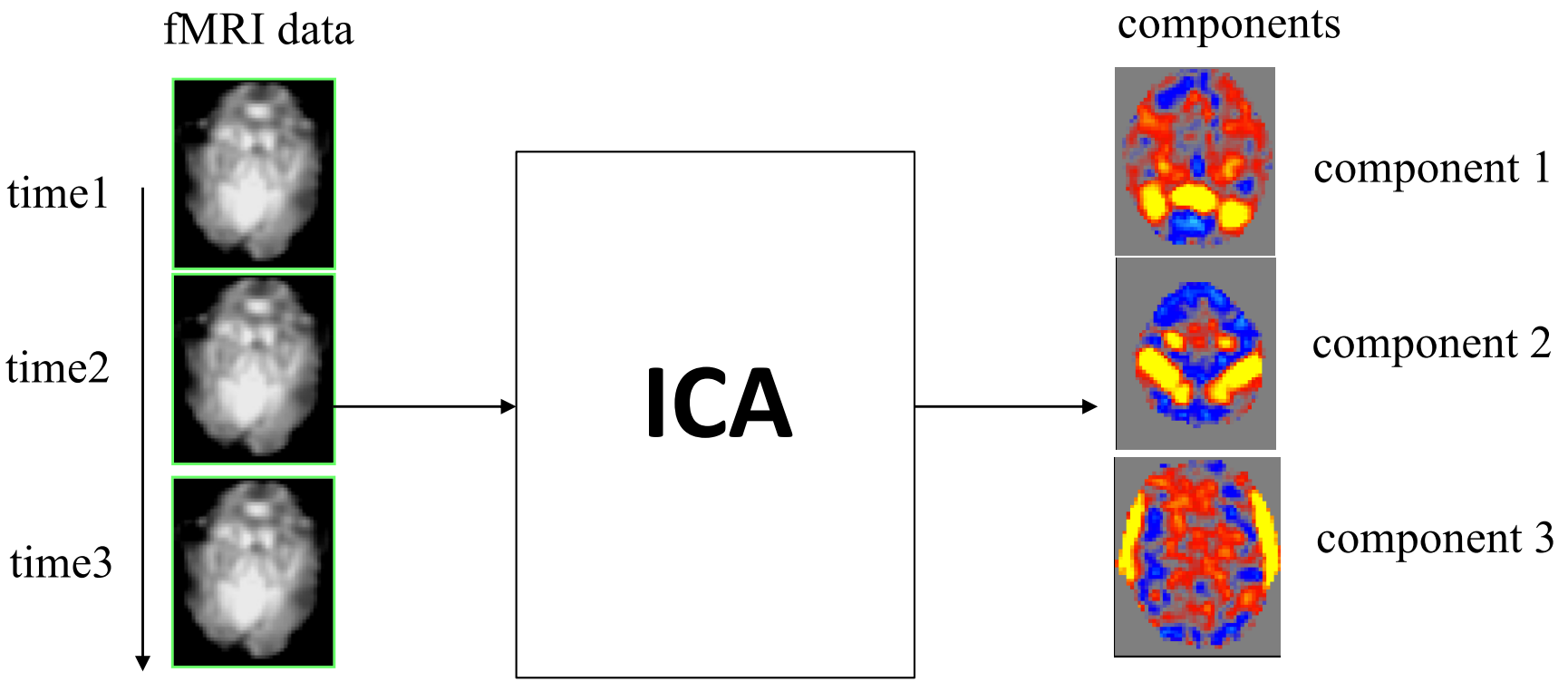
Cohen et al. 2008

Seed-based correlation



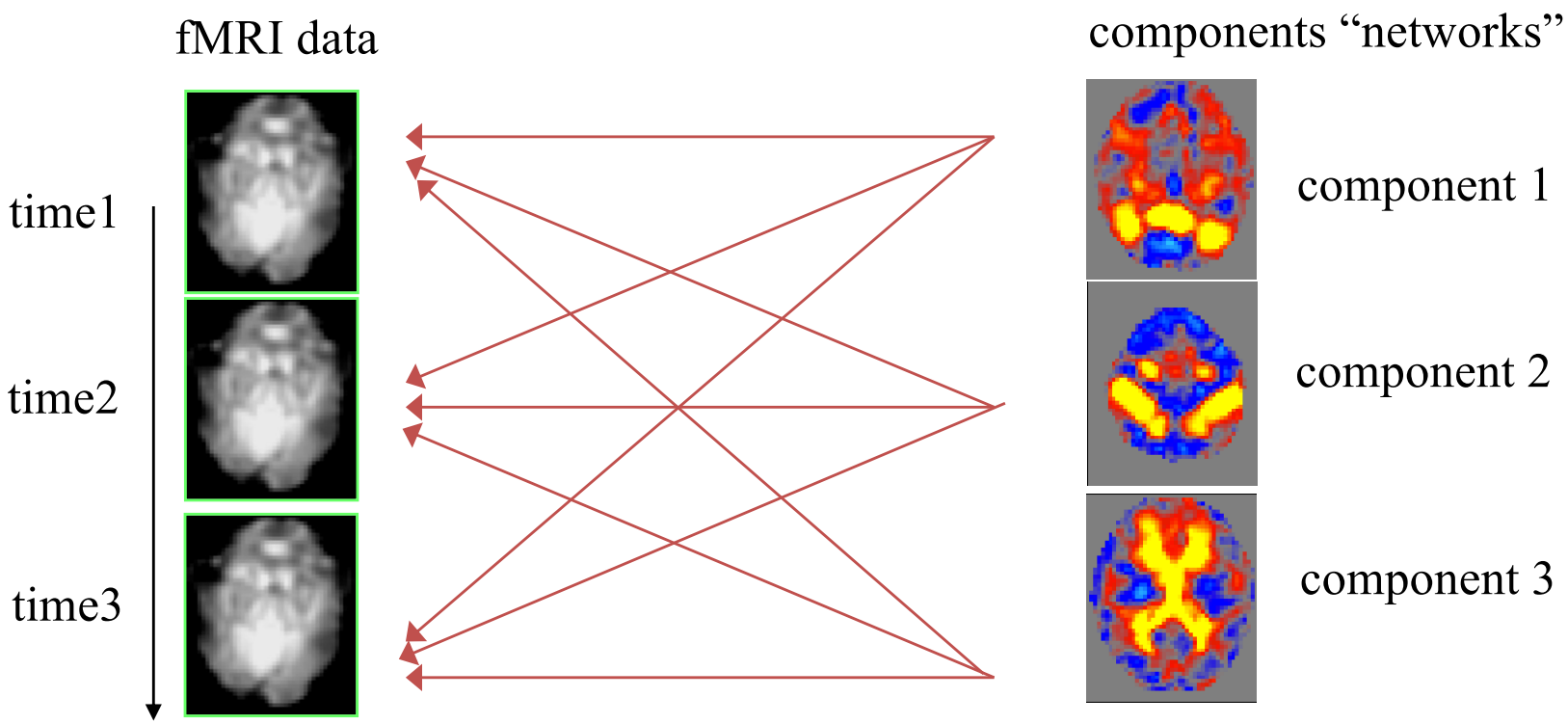
Buckner et al. 2013

Independent Component Analysis (ICA)

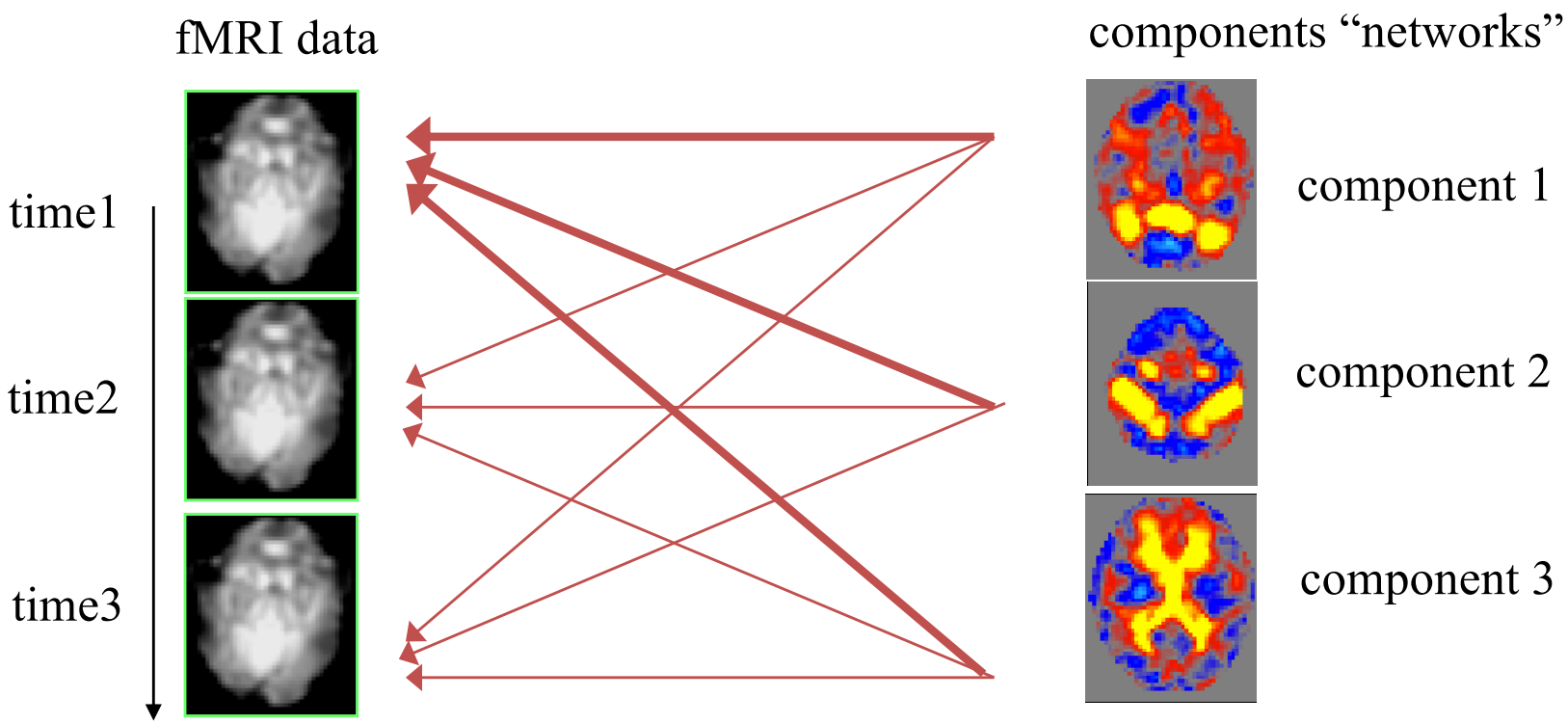


- Multivariate; many "networks" (components) at once
- Data-driven; no need to choose a seed
- Can be used for functional connectivity analysis and noise reduction

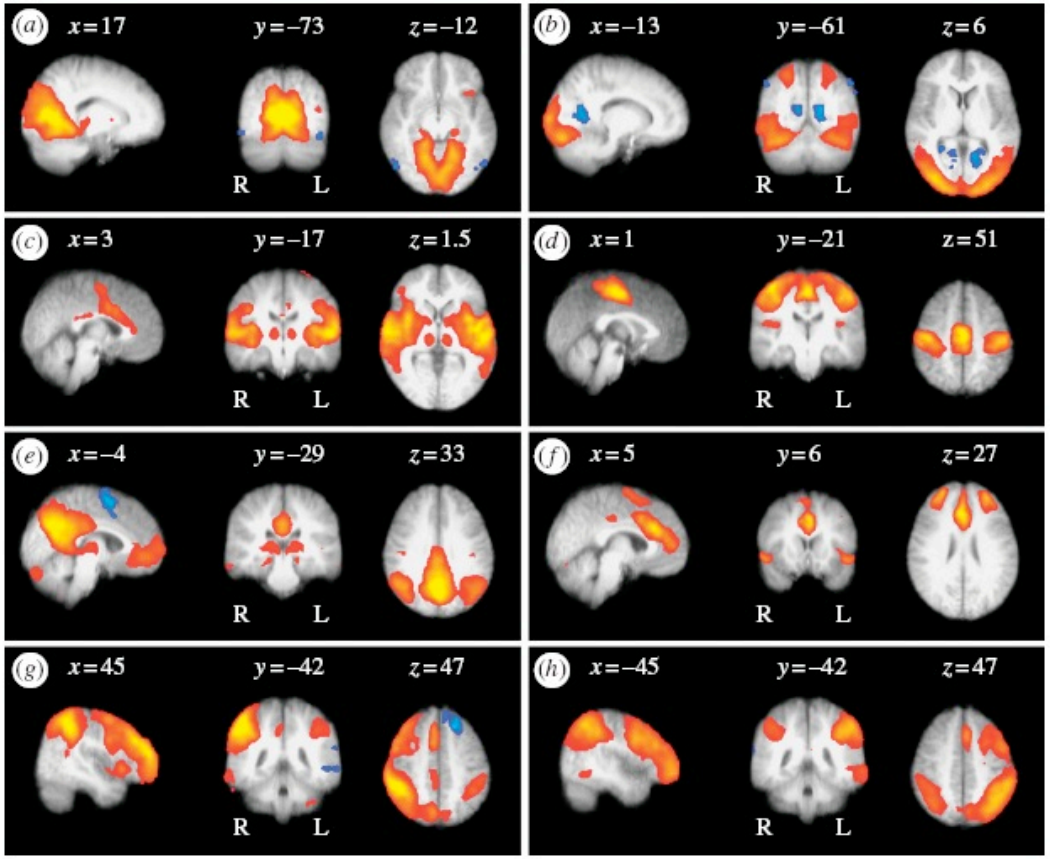
Independent Component Analysis (ICA)



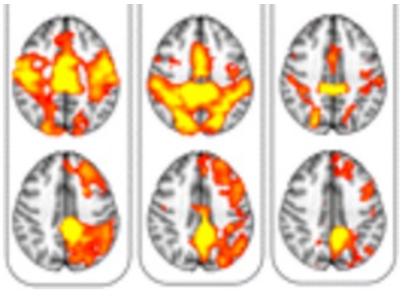
Independent Component Analysis (ICA)



“Networks” from ICA



7 10 15 components

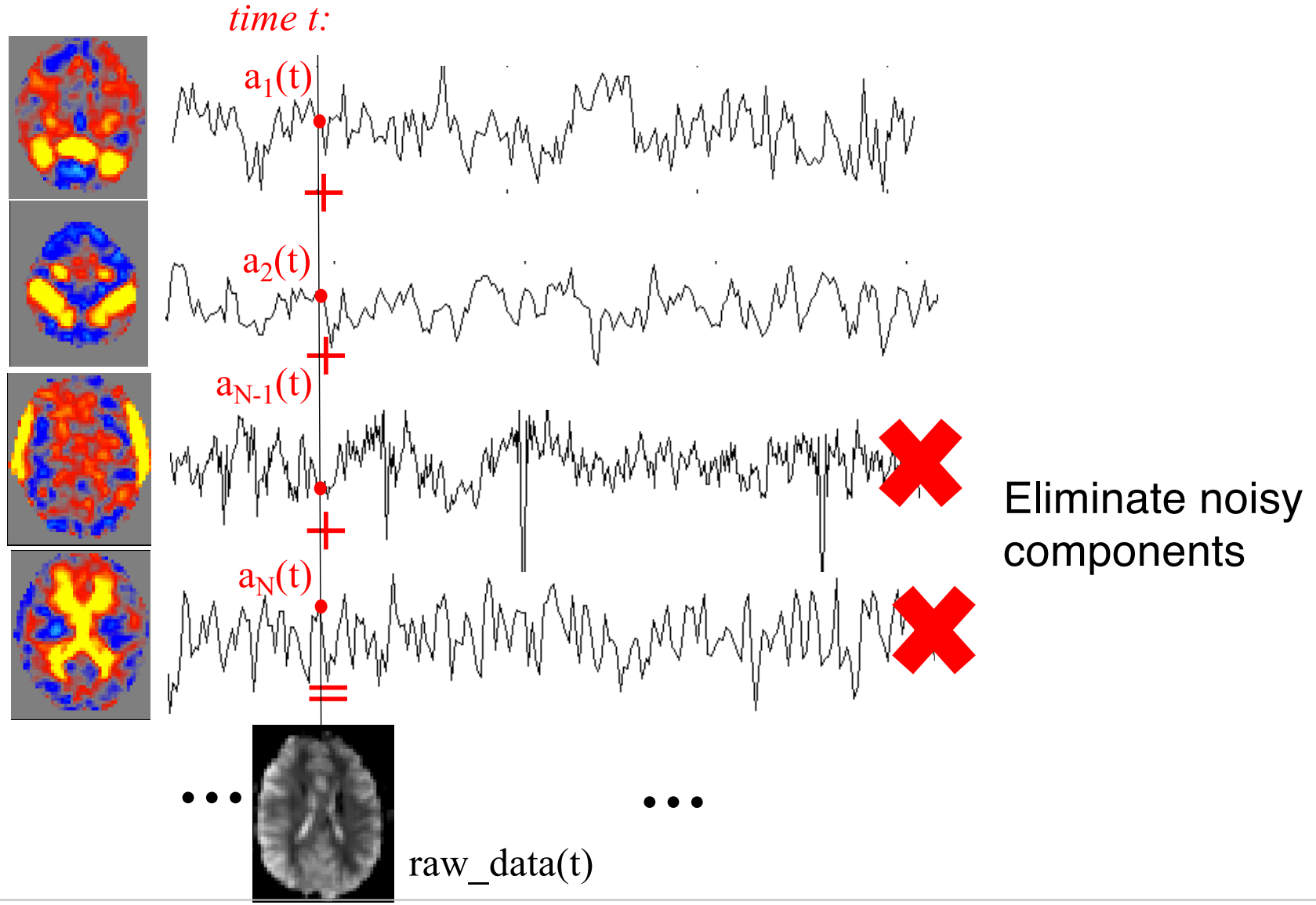


Leech et al., 2012

McKeown et al. 1998
<- Damoiseaux et al. 2006

- Component selection?
- Component “splitting”?
- Between-group comparisons?

Independent Components

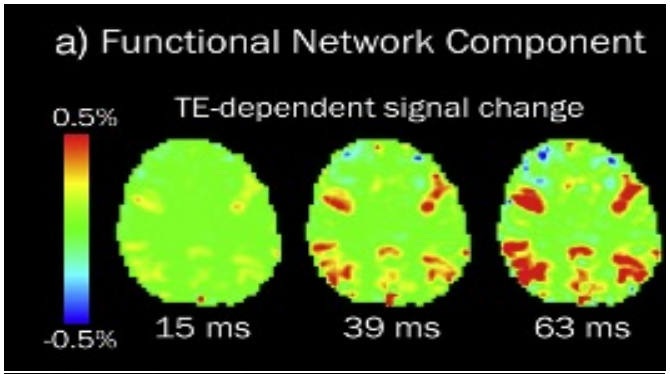


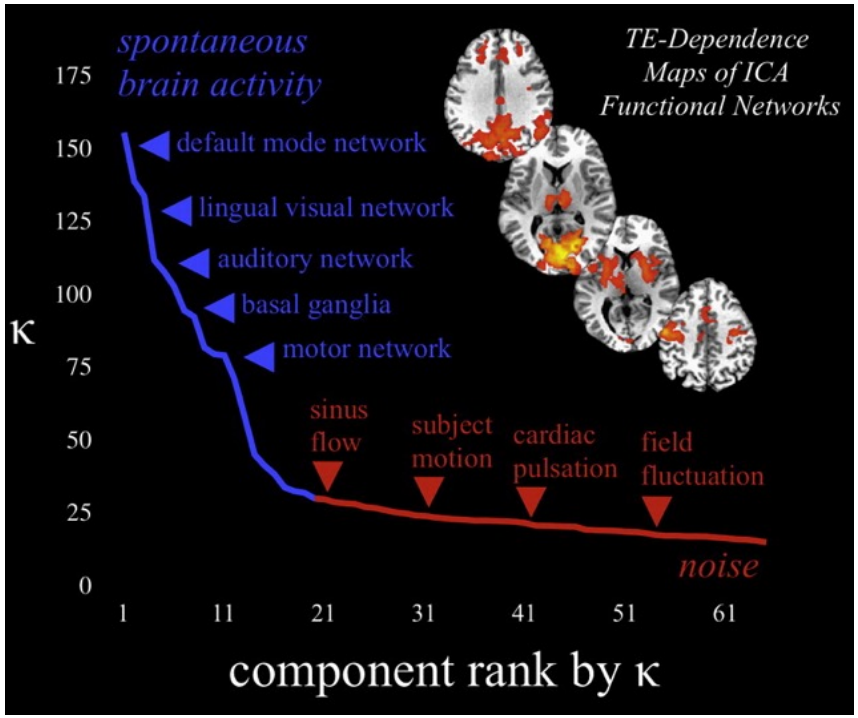
Identifying noise components?

- FIX: "FMRIB's ICA-based Xnoiseifier"

http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FIX

- Multi-echo ICA





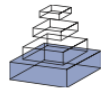
Kundu et al, 2012, 2013

ICA: considerations

- How many components to ask for?
  - Heuristics, but no "best" way
  - Similar networks may split when increasing the no. of components
- Interpretation more complicated than seed-based
  - Algorithm, non-biological criterion: spatial independence
- Must select noise and neural components
  - There are methods for automated selection
  - Not a clean separation

frontiers in
SYSTEMS NEUROSCIENCE

REVIEW ARTICLE
published: 06 April 2010
doi: 10.3389/fnsys.2010.00008

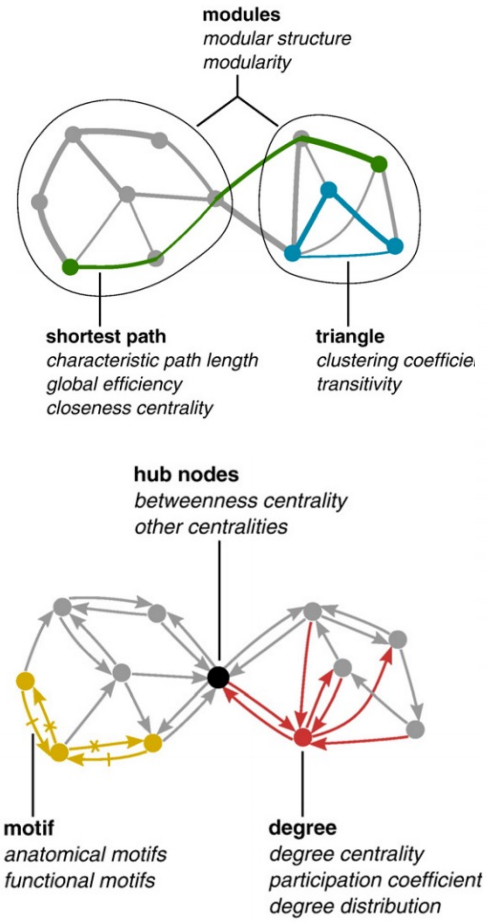


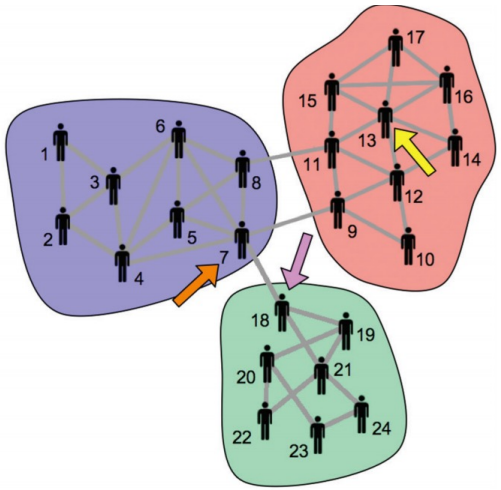
Advances and pitfalls in the analysis and interpretation of resting-state FMRI data

*David M. Cole[1], Stephen M. Smith[2] and Christian F. Beckmann[1,2]**

Complex network analysis

Meunier et al. 2011





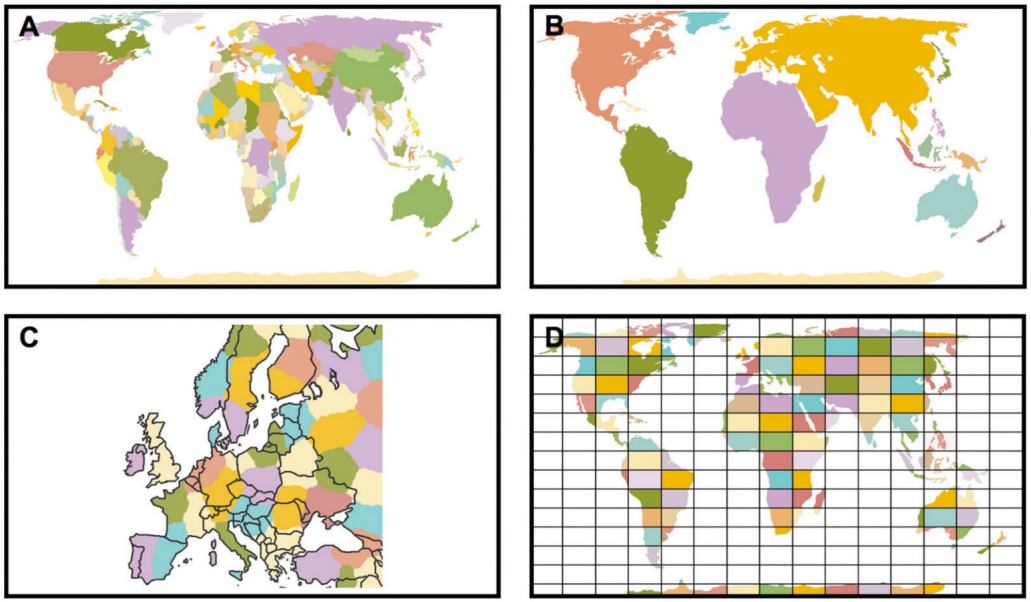
Wig et al. 2011

Reviews:

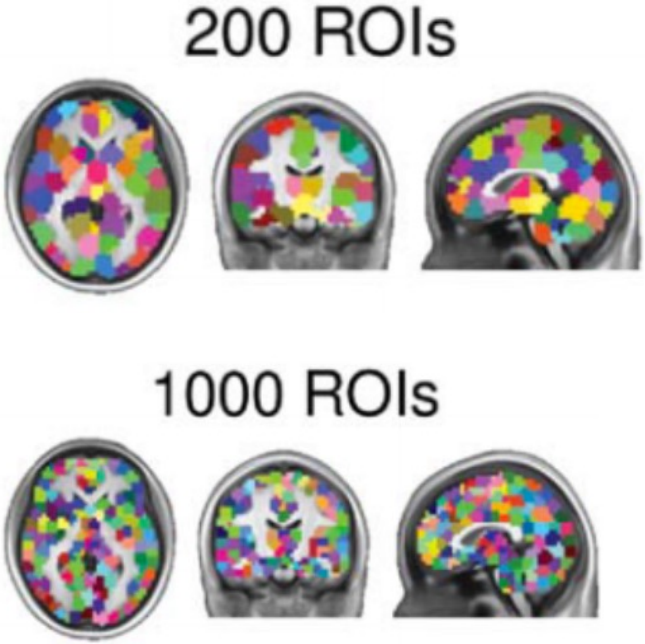
Rubinov & Sporns, 2010

Bullmore & Sporns, 2009

Complex network analysis

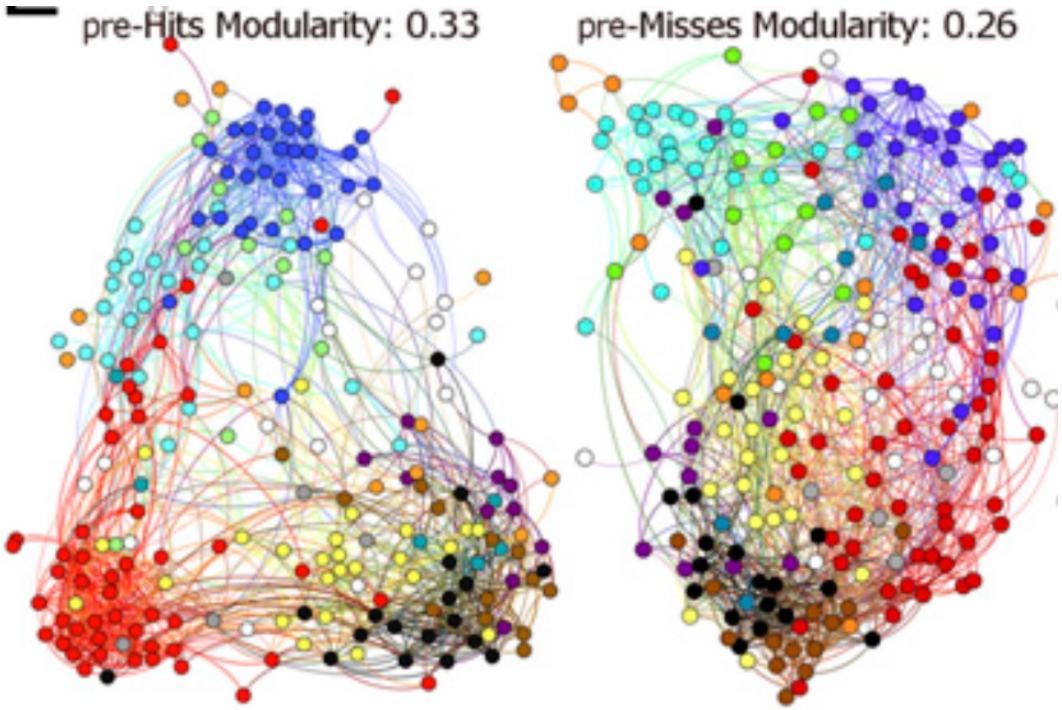


Wig et al. 2011



Craddock et al. 2012

Complex network analysis



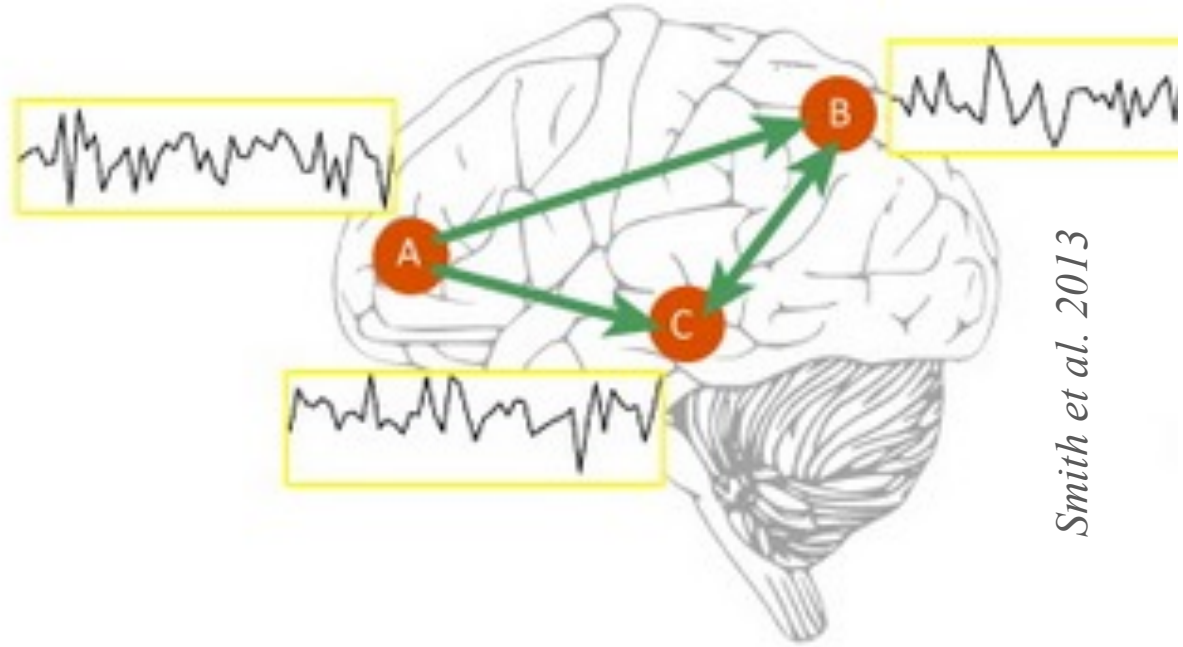
Modular structure predicted perception of near-threshold auditory stimulus

Sadaghiani et al. 2015

Outline

- What is it?
- Analyzing resting-state data
- **Issues & interpretation**
- Summary & discussion

Functional connectivity?



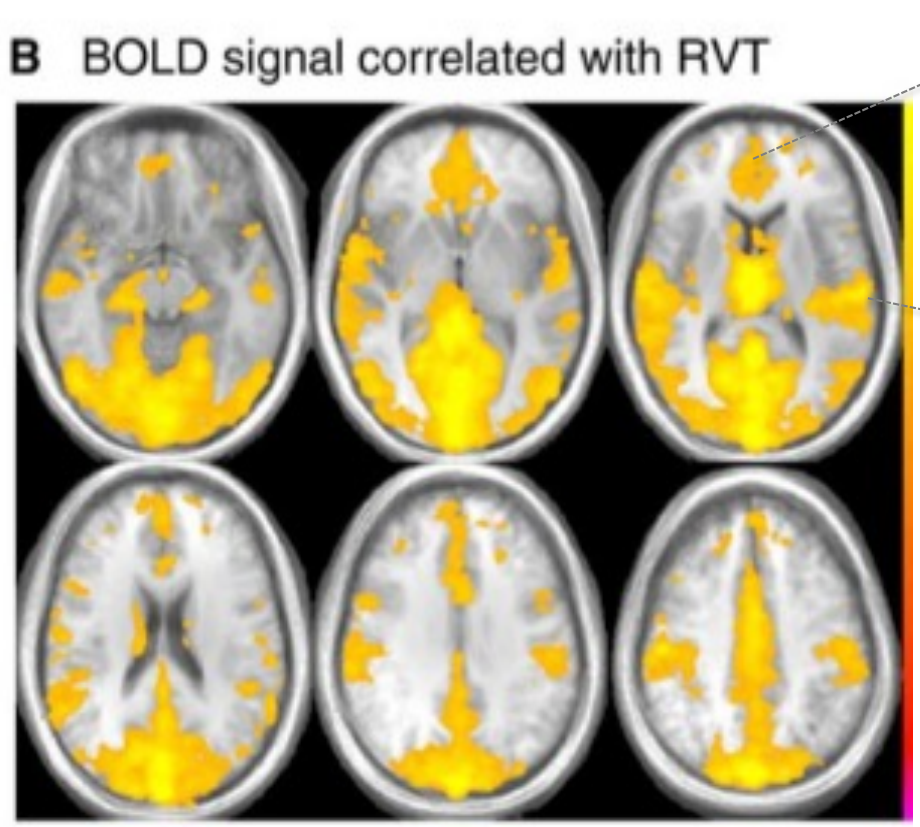
Functional connectivity is a powerful but ambiguous mapping tool

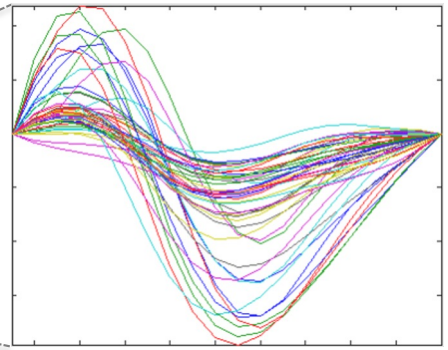
(Buckner et al. 2013 Nat. Rev. Neuro)

- Difficult to isolate process of interest from non-neural effects & other neural effects
- Sensitivity to modeling and pre-processing decisions
- Relationship with structural connectivity & electrophysiology not straightforward

Physiological noise

- Any non-neural fluctuations shared in common across regions will creates the appearance of "functional connectivity"

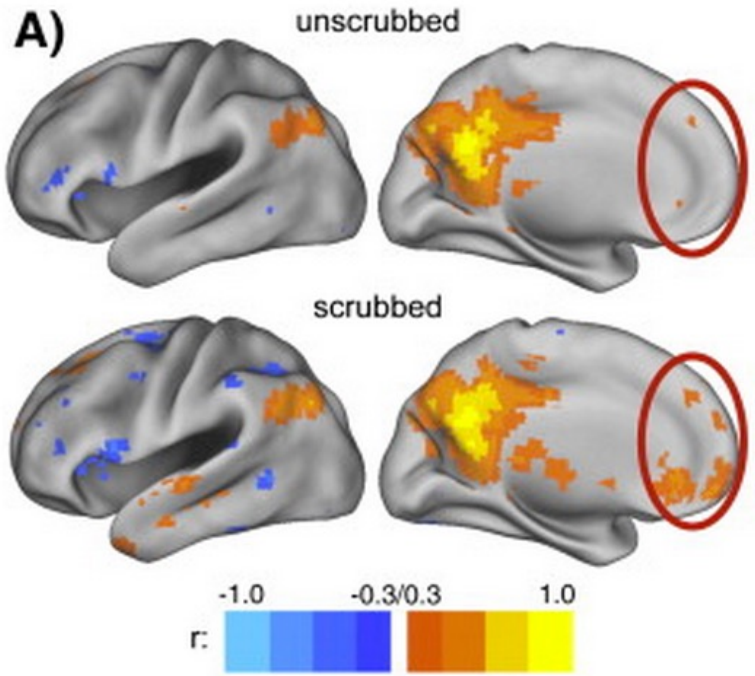


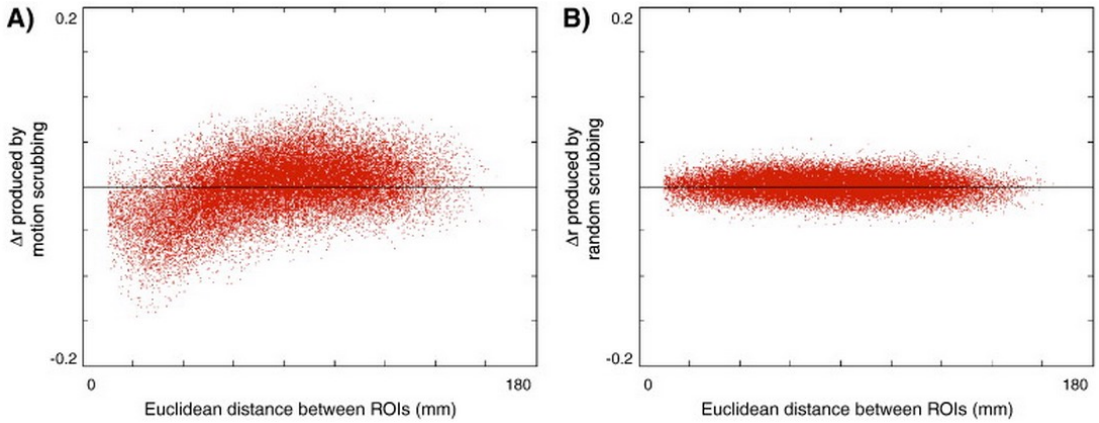


data from Chang et al. 2009

Birn et al. 2006

Head motion



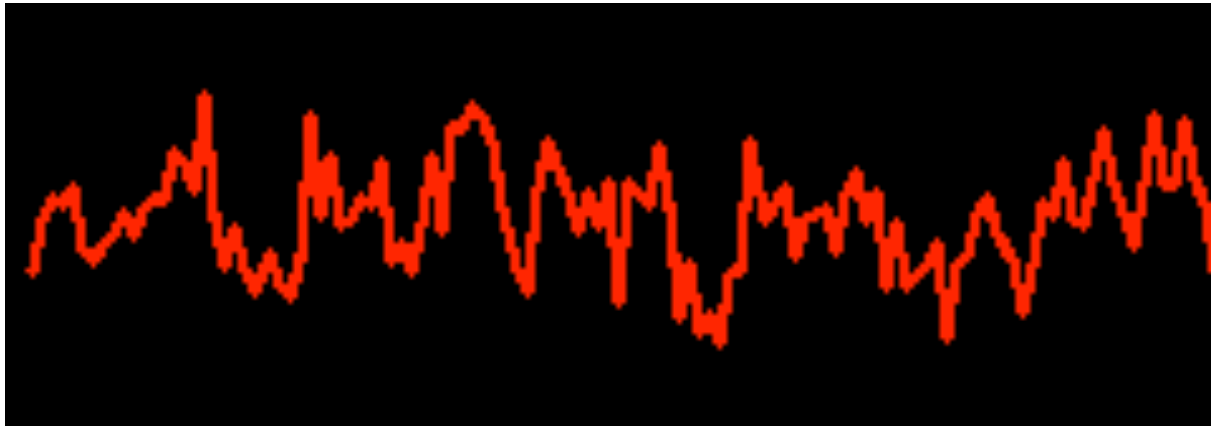


Power et al. 2010

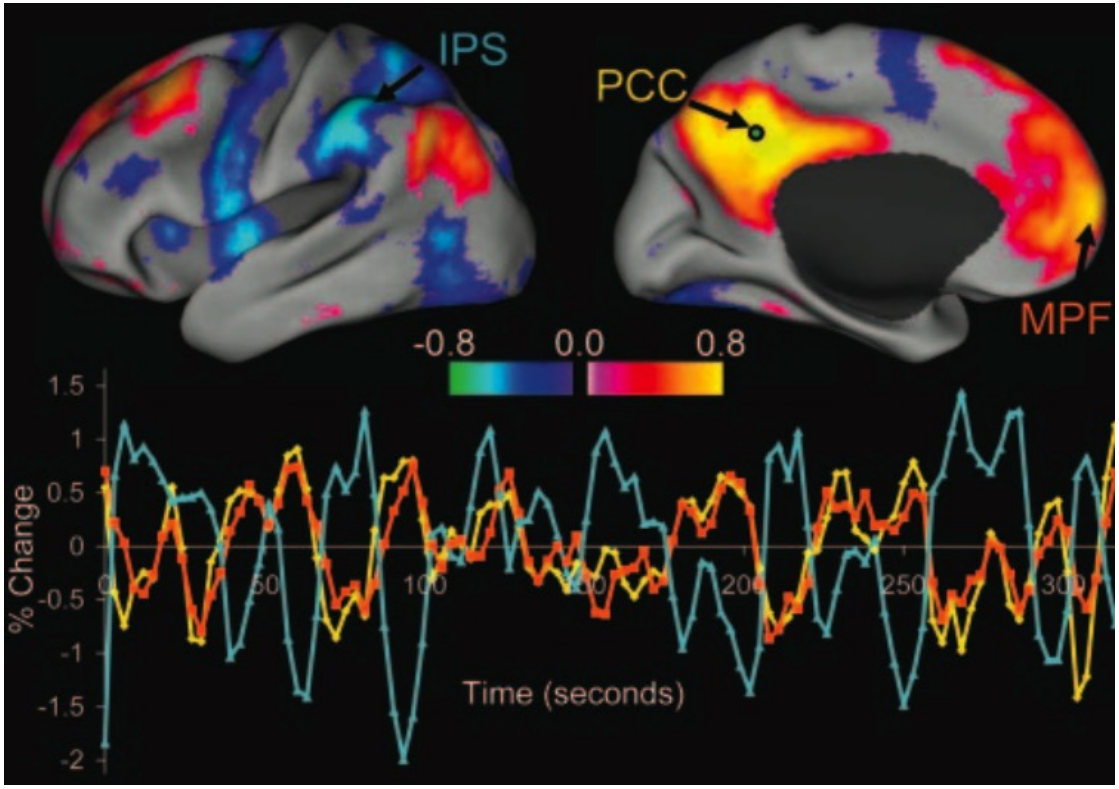
- Systematic differences in head motion across age groups caused spurious functional connectivity effects

What is noise, what is signal?

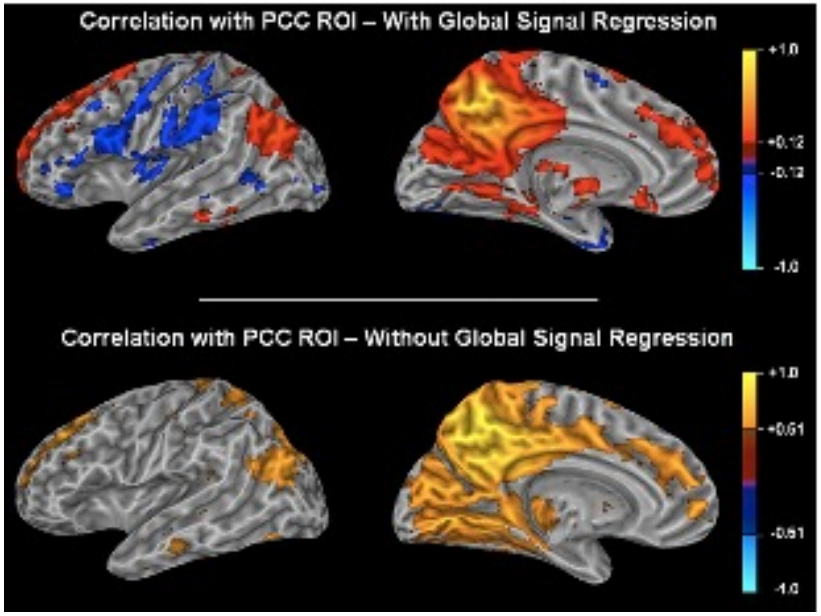
- no task/stimulus timing to help distinguish signal from noise
- trial averaging not possible
- resting-state FC quantifies relationships between fMRI time series across regions (each are signal + noise!)



Noise reduction strategies can affect results



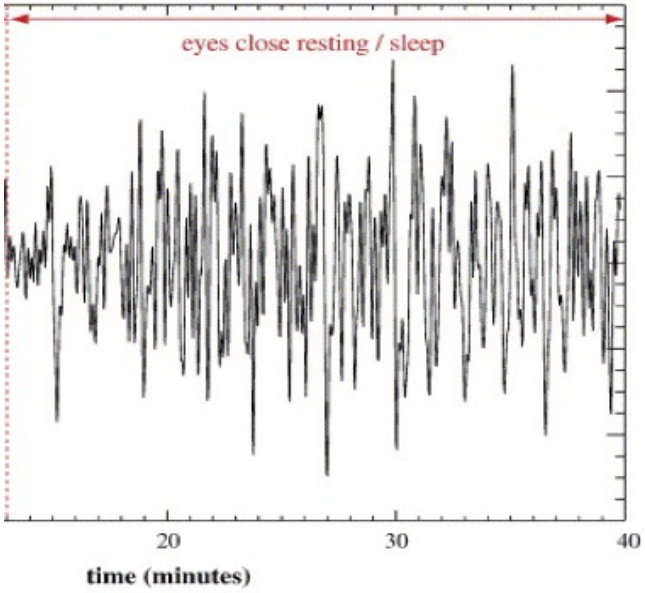
Fox et al, 2005
Fransson 2005



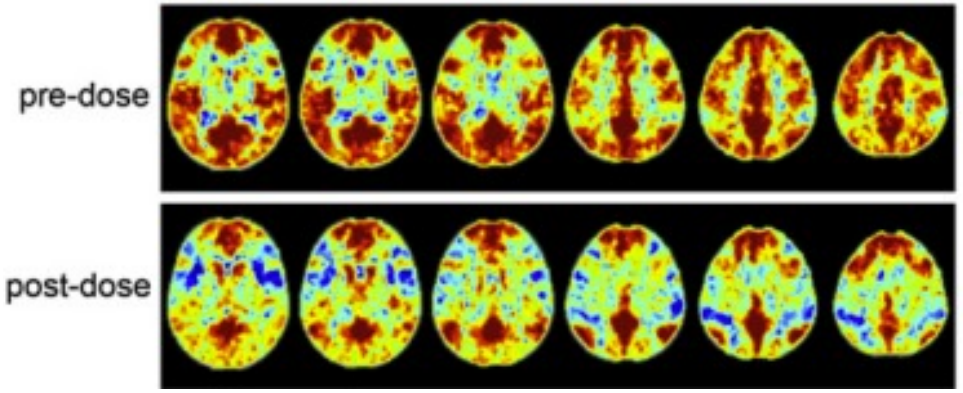
Murphy et al, 2009

- how can we tell which is correct?

Drowsiness



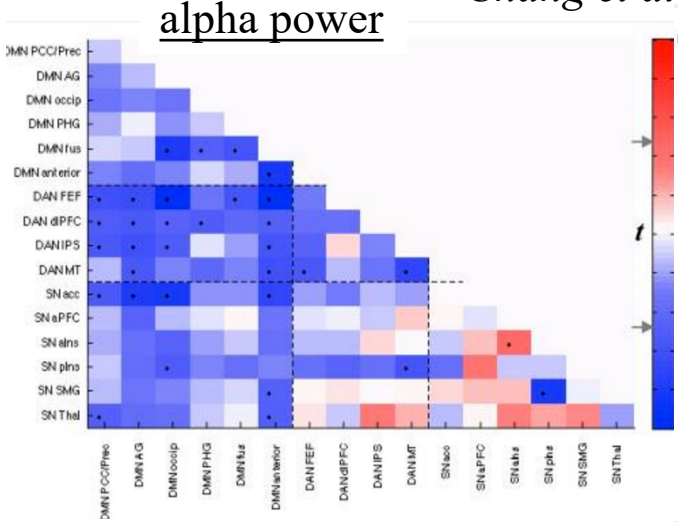
Fukunaga et al. 2006



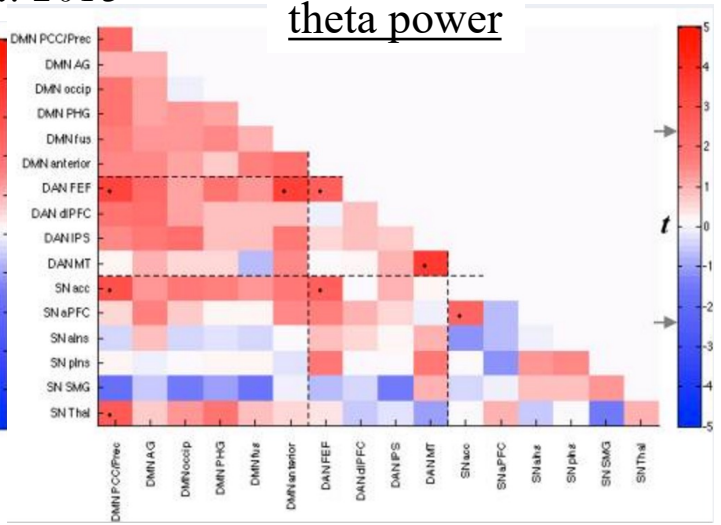
Wong et al. 2010

Chang et al. 2013

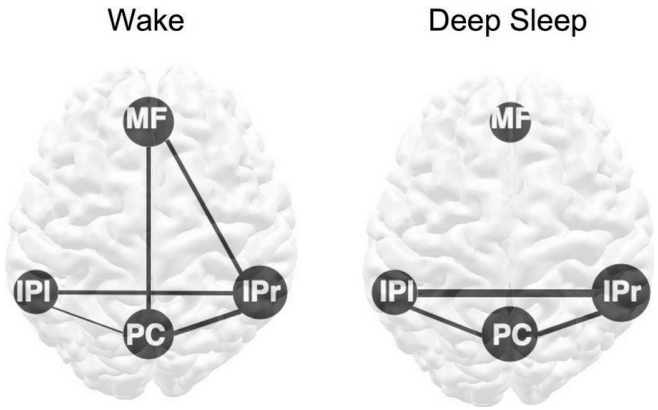
alpha power



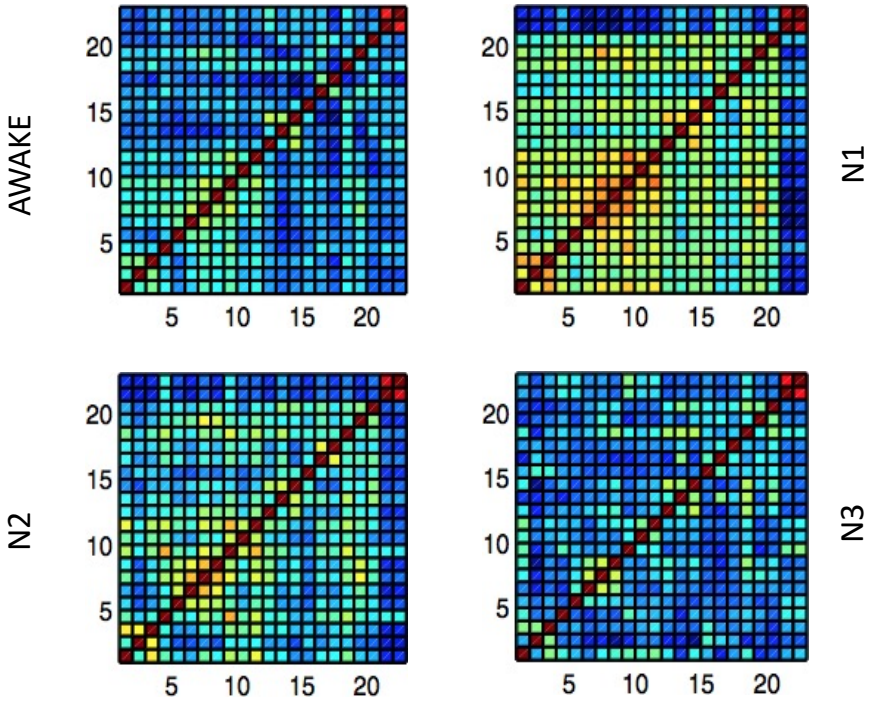
theta power



Drifting to sleep…

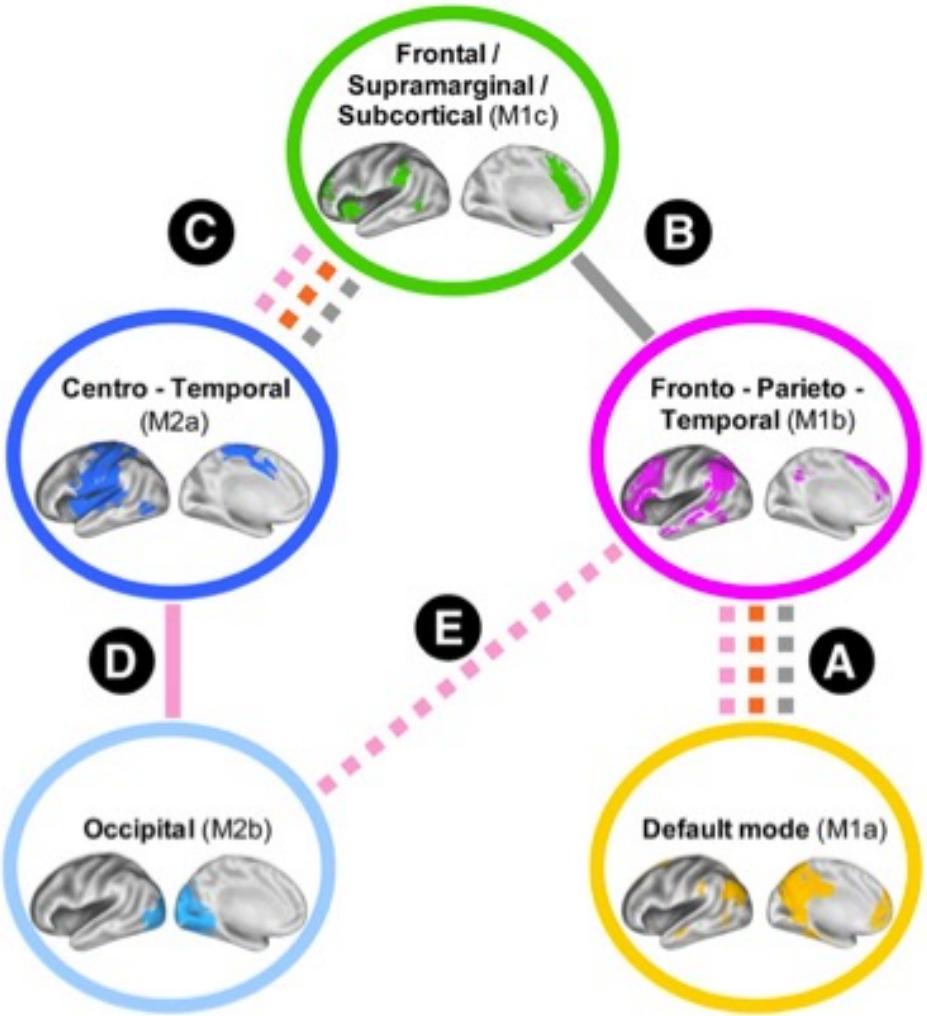


Horovitz et al., 2009



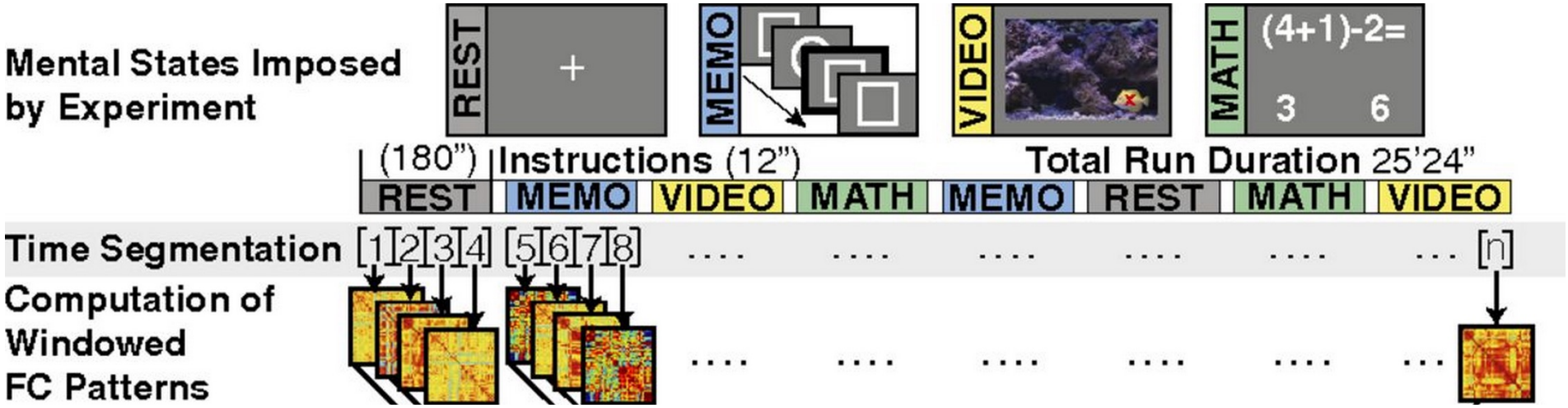
Tagliazucchi et al. 2012

Mind wandering



Doucet et al. 2011

Mind wandering



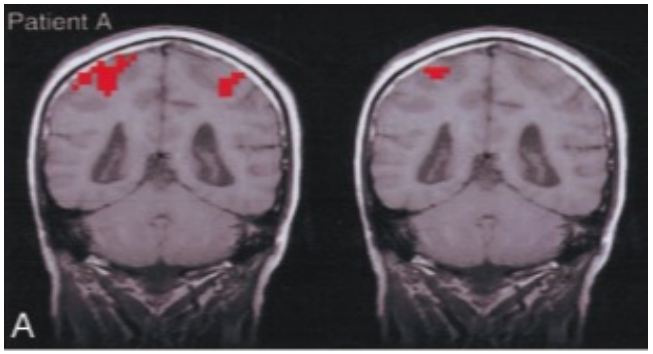
Gonzalez-Castillo et al. 2015

Structural connectivity shapes functional connectivity

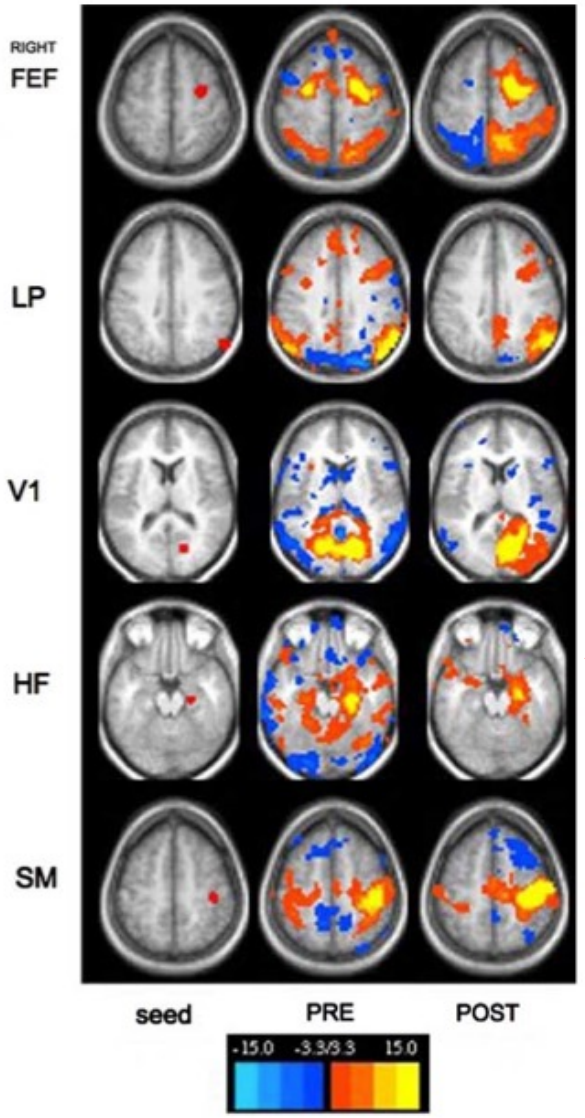
Agenesis of the Corpus Callosum

task

functional connectivity (resting state)



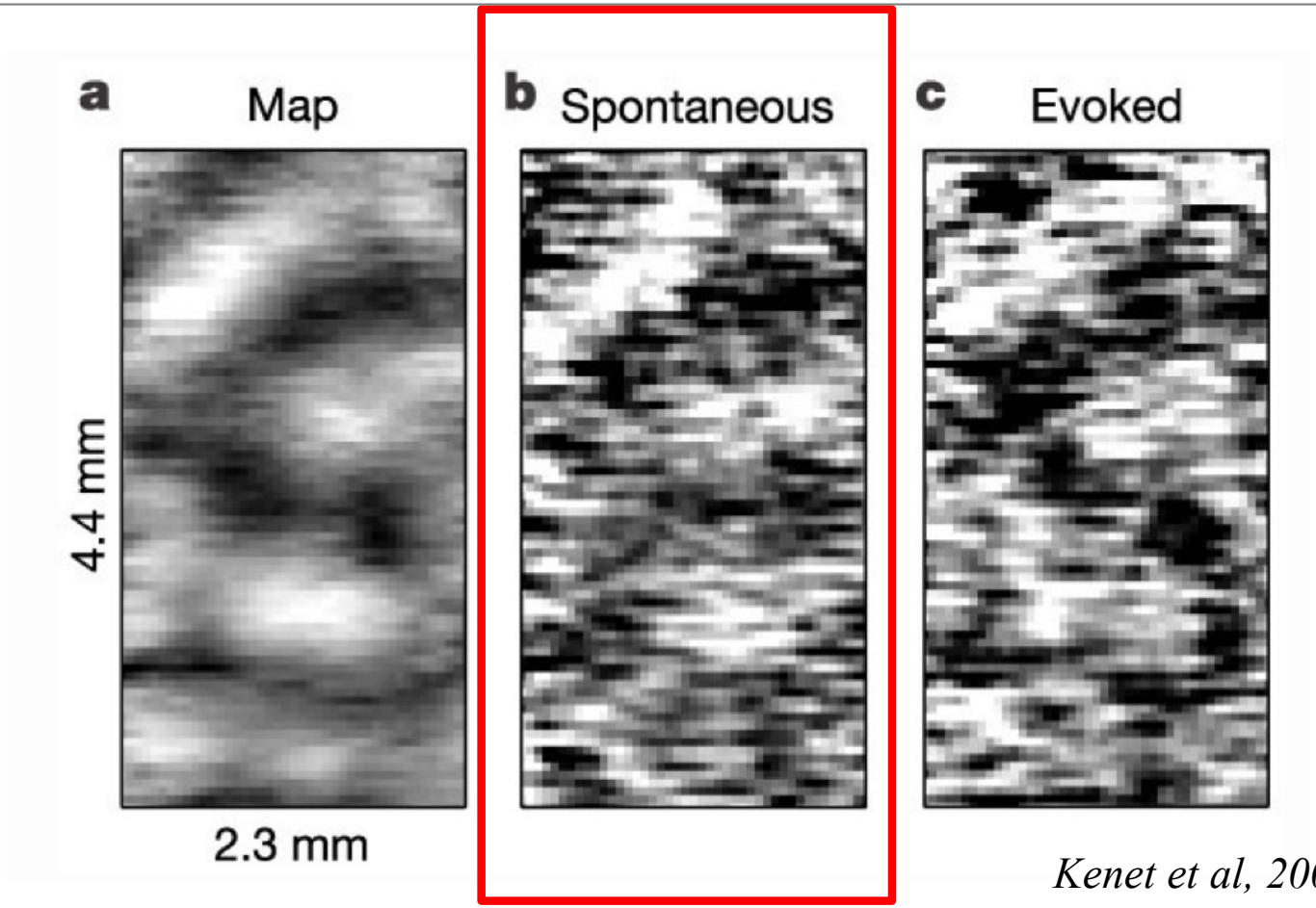
Quigley et al., 2003



Johnston et al., 2008

via indirect connections?

Coherence in spontaneous electrophysiological signals

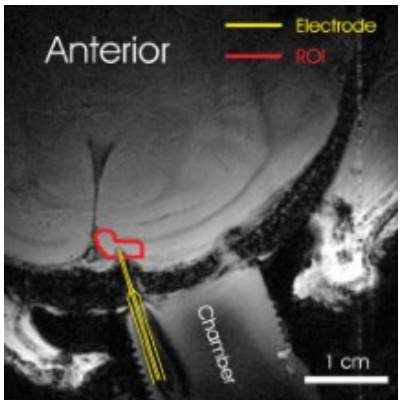


Kenet et al, 2003

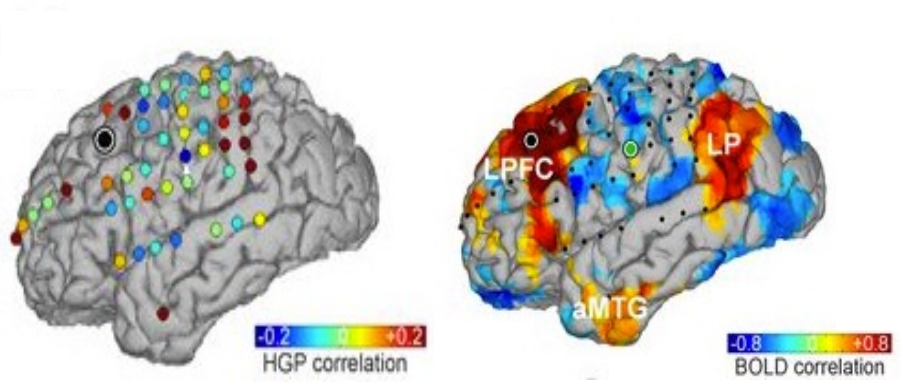
spontaneous fluctuations in membrane voltage resemble orientation columns & evoked activity

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

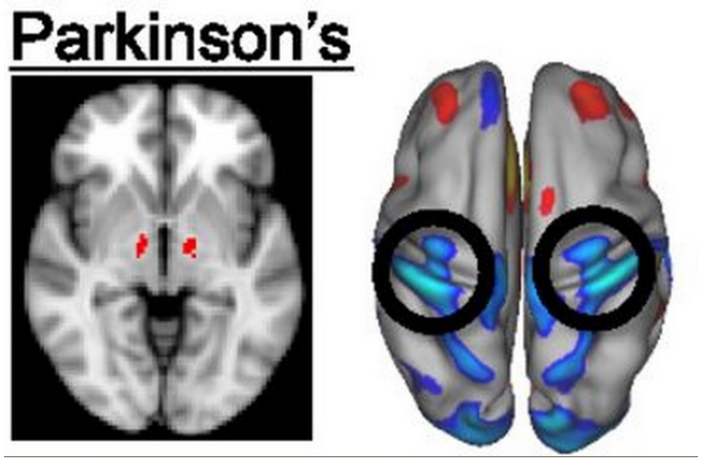
- slow cortical potential (e.g. He et al, 2010)
- distributed across frequency bands (e.g. Mantini et al. 2007)
- broadband (e.g. Liu et al. 2014)

- *review*: Scholvinck et al. 2013

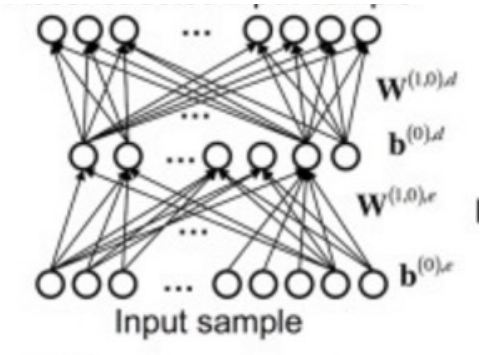
Outline

- What is it?
- Analyzing resting-state data
- Issues & interpretation
- **Summary & discussion**

Clinical applications

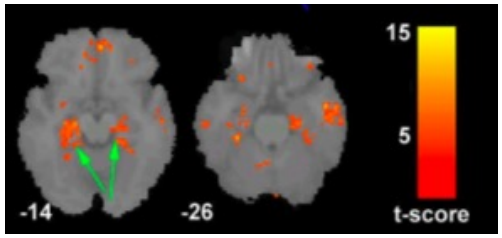


Fox et al. 2014

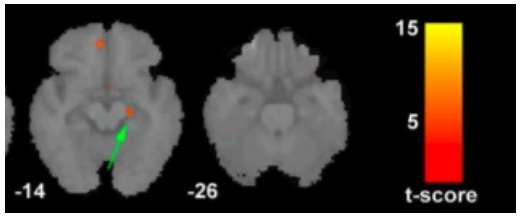


Kim et al. 2016

Healthy control



Alzheimer's



Greicius et al. 2004

- Many studies of network-level differences across disorders
- Applications to surgical planning, early diagnosis, treatment response…
- Differences in FC may not relate to network interactions or inter-areal communication
  - could reflect differences in anatomy, neuro-vascular coupling, SNR, physiological noise…

Data sharing & data mining

The WU-Minn Human Connectome Project: An overview

David C. Van Essen [a,*], Stephen M. Smith [b], Deanna M. Barch [c], Timothy E.J. Behrens [b], Essa Yacoub [d], Kamil Ugurbil [d], for the WU-Minn HCP Consortium

[a] *Department of Anatomy & Neurobiology, Washington University School of Medicine, 660 S. Euclid Avenue, St. Louis, MO 63110, USA*
[b] *FMRIB (Oxford Centre for Functional MRI of the Brain), Oxford University, Oxford, UK*
[c] *Psychology Department, Washington University, St. Louis, MO 63105, USA*
[d] *Center for Magnetic Resonance Imaging, University of Minnesota, Minneapolis, MN 55455, USA*

Summary

- Resting-state fMRI is proving valuable for clinical applications and basic neuroscience
- Understand analysis methods/tradeoffs
  - and stay close to the data
- Noise and neural variability can affect signal and connectivity measurements

Acknowledgments

Jen Evans

Mikail Rubinov

Summary

- Resting-state fMRI is proving valuable for clinical applications and basic neuroscience
- Understand analysis methods/tradeoffs
  - and stay close to the data
- Noise and neural variability can affect signal and connectivity measurements