Resting State fMRI

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fMRI Summer Course * 2018

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

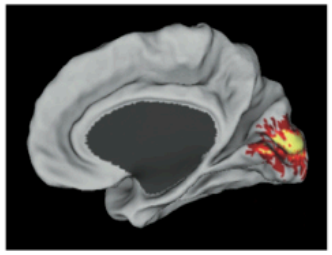
Resting-state fMRI

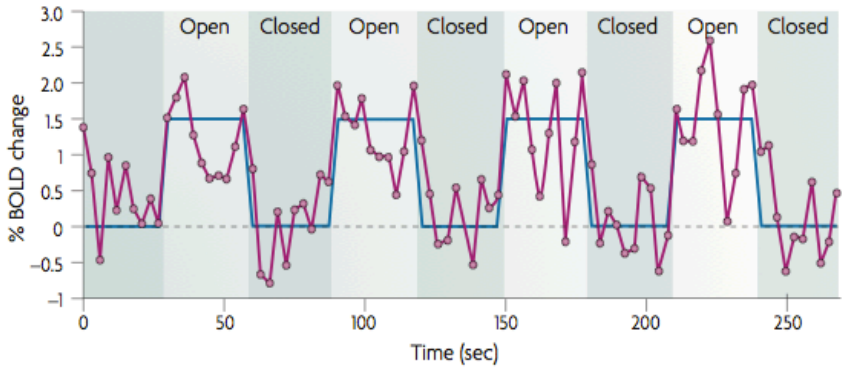
- Background & motivation
- Data analysis
- Interpretation
- Directions

Task vs. resting-state fMRI

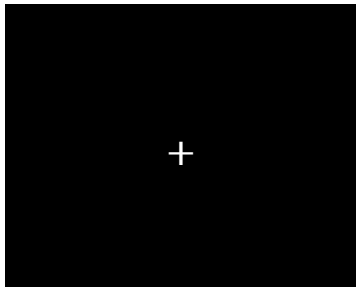
adapted from: Fox & Raichle, 2007

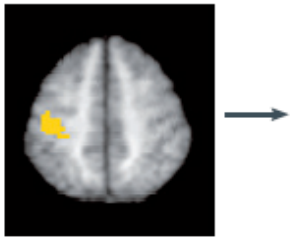
Task-based fMRI

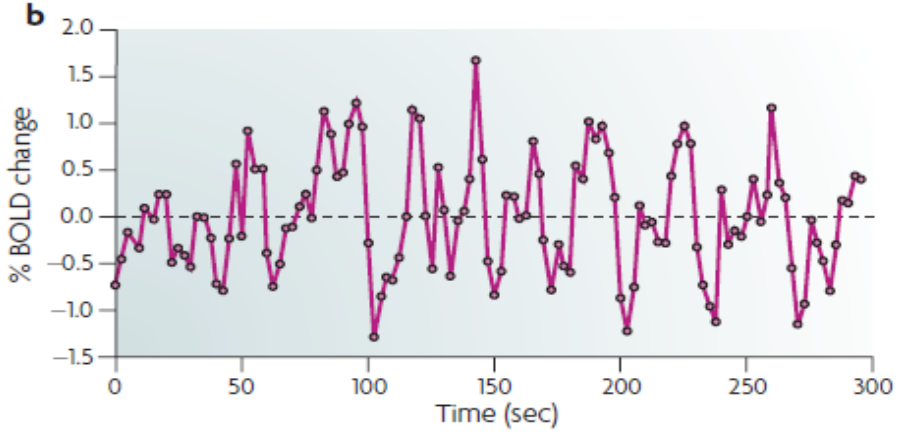




Resting-state fMRI

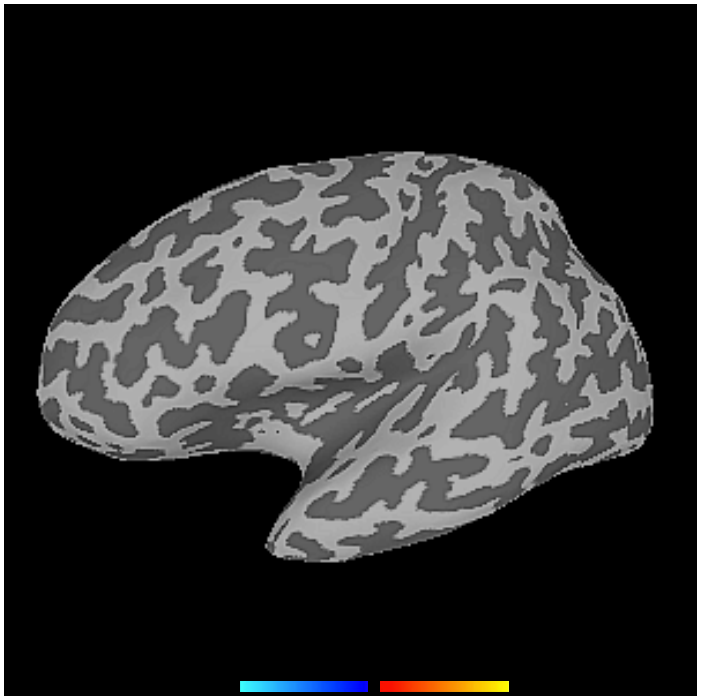






- no task/stimuli
- instructions like: “keep eyes closed” or “keep eyes open and fixate”
- usually 5-15 minutes long

Spontaneous brain activity

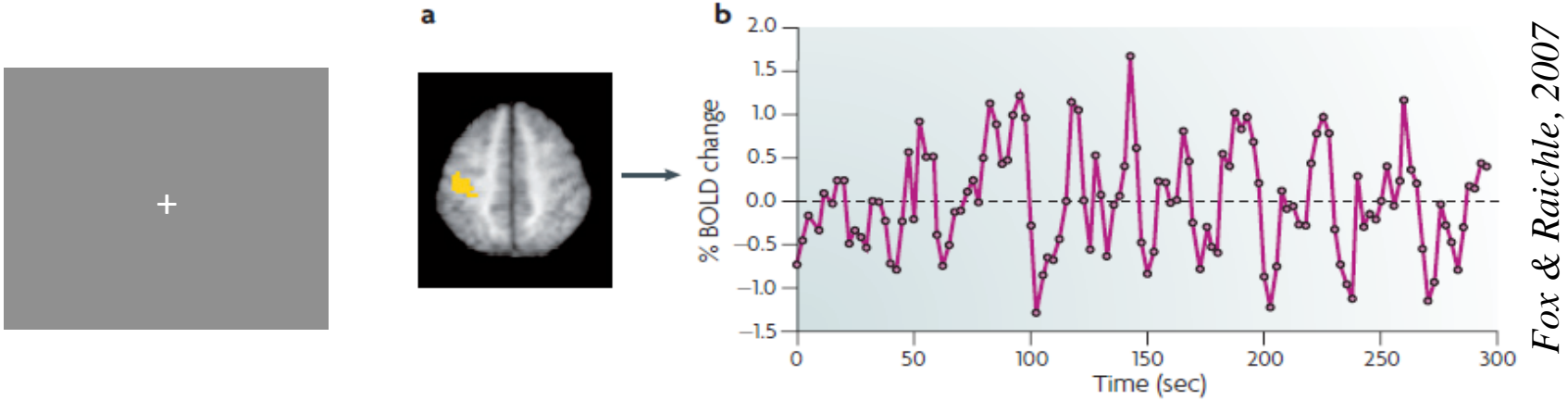


courtesy Zhongming Liu

- activity that cannot be attributed to experimental task/stimuli
- accounts for most of the brain's energy consumption[1]
- can we learn more about brain function by studying spontaneous activity?

[1] *Raichle & Mintun, 2006*

How to extract information from resting-state data?

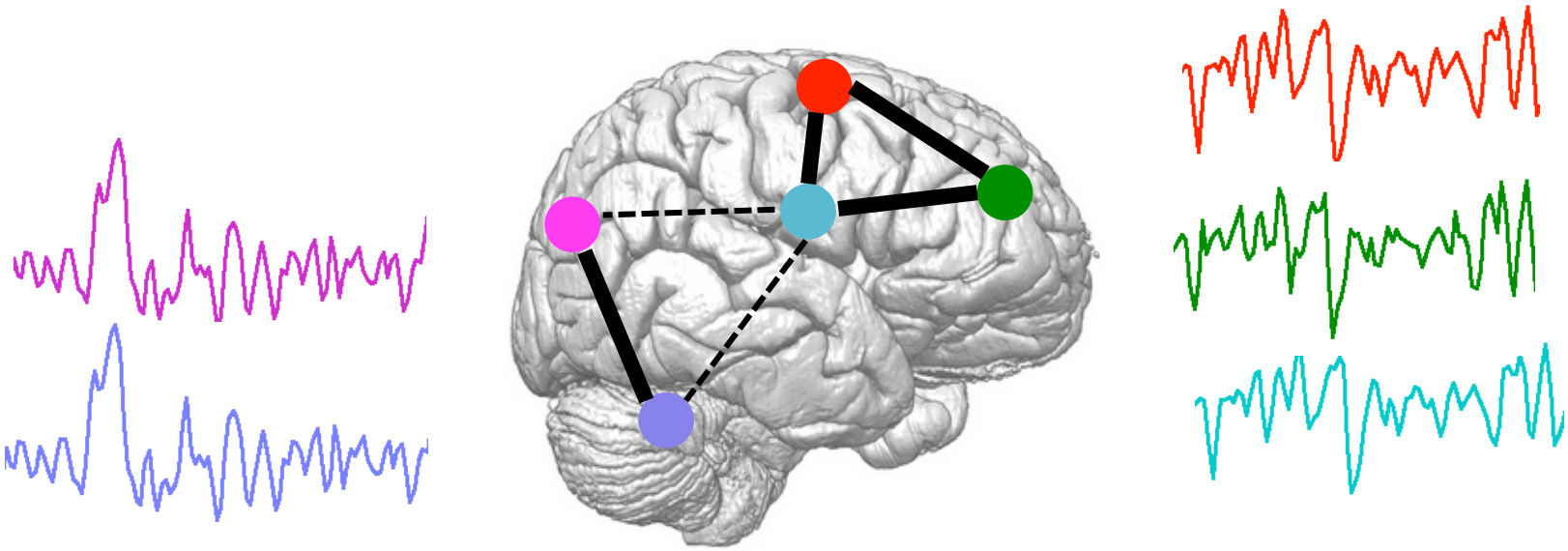


? no (known) conditions to compare

? how to separate "signal" (neurally driven component) from noise/artifacts

? how to interpret ongoing neural activity

Functional connectivity



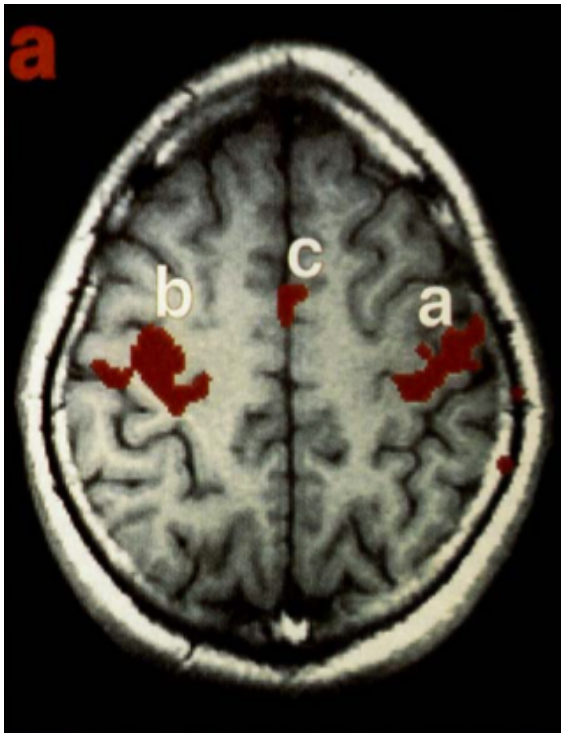
- FC: statistical dependence (e.g. correlation) between the time courses of different brain regions
- suggests “network” interactions, though interpretation is complicated!

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

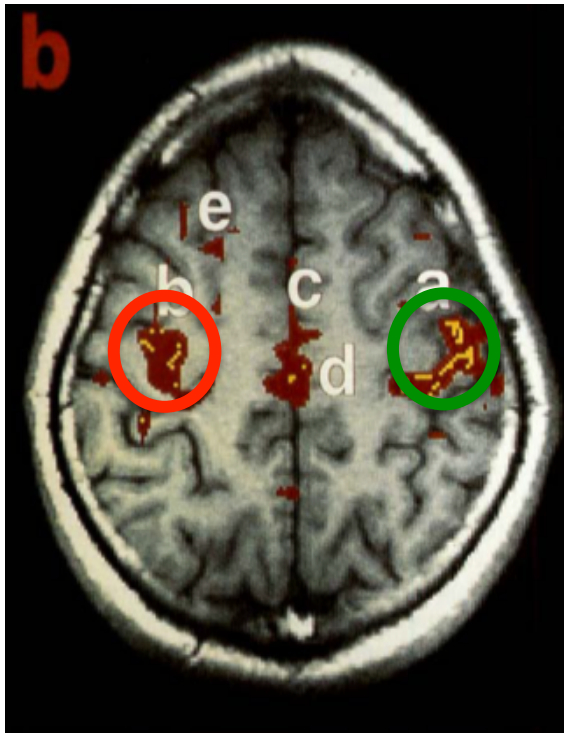
Bharat Biswal, F. Zerrin Yetkin, Victor M. Haughton, James S. Hyde

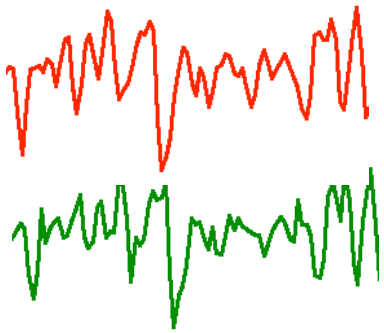
Mag. Res. Med. 1995, ~5300 citations

task *activation*

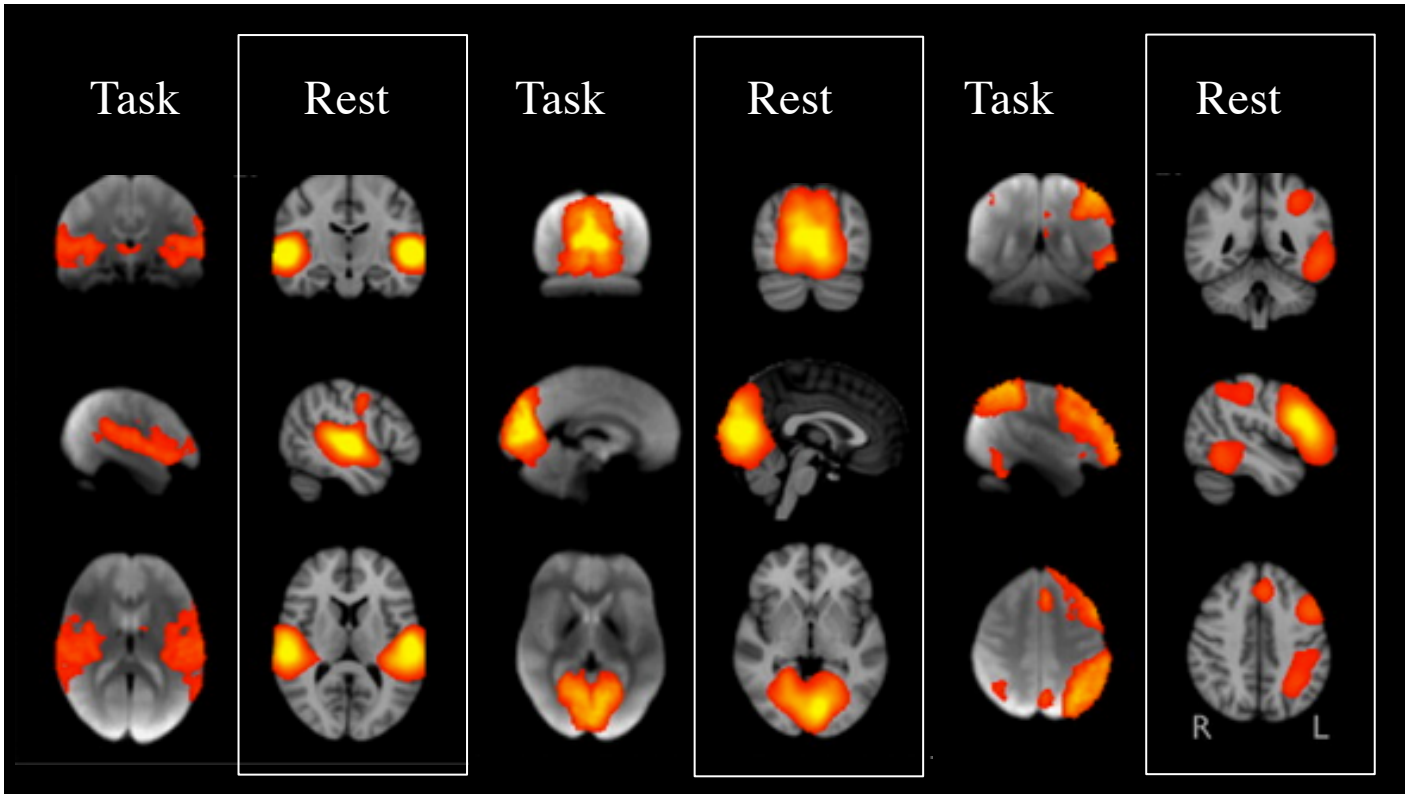


resting state *correlation*





Resting-state "networks" resemble task-activated networks

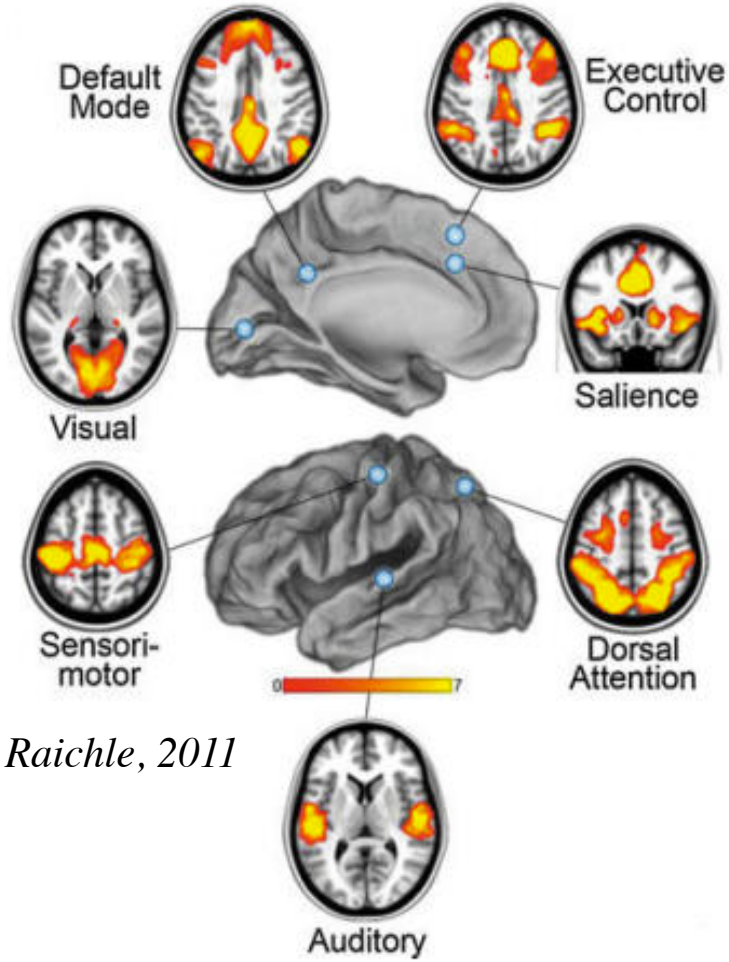


adapted from Smith et al, 2009

- Suggests we may be able to map multiple functional networks without needing tasks
- Would allow for studying functional networks in populations and brain states where tasks are not feasible

"Resting State Networks"

a.k.a. "intrinsic networks"

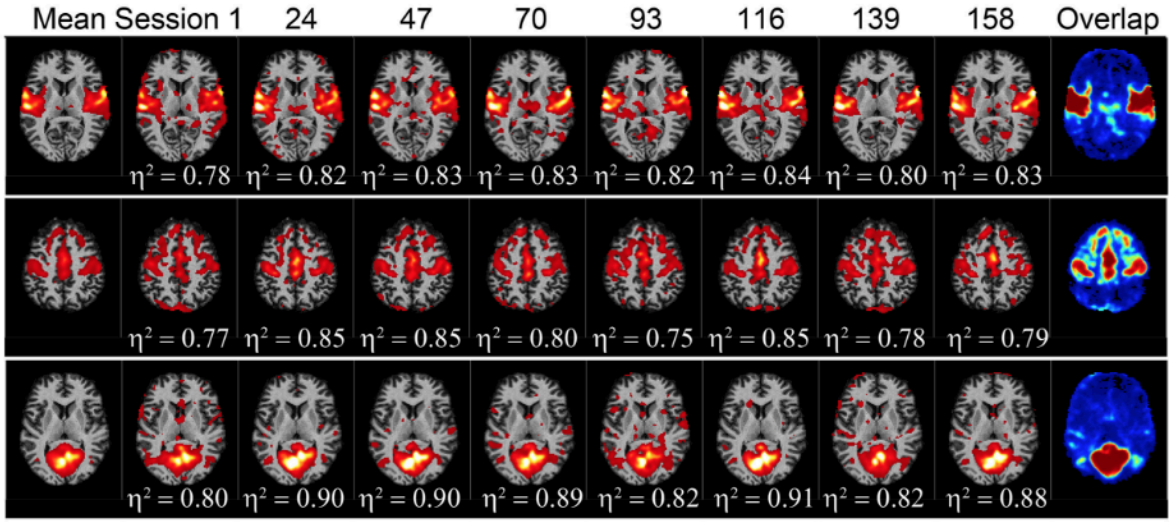


Raichle, 2011

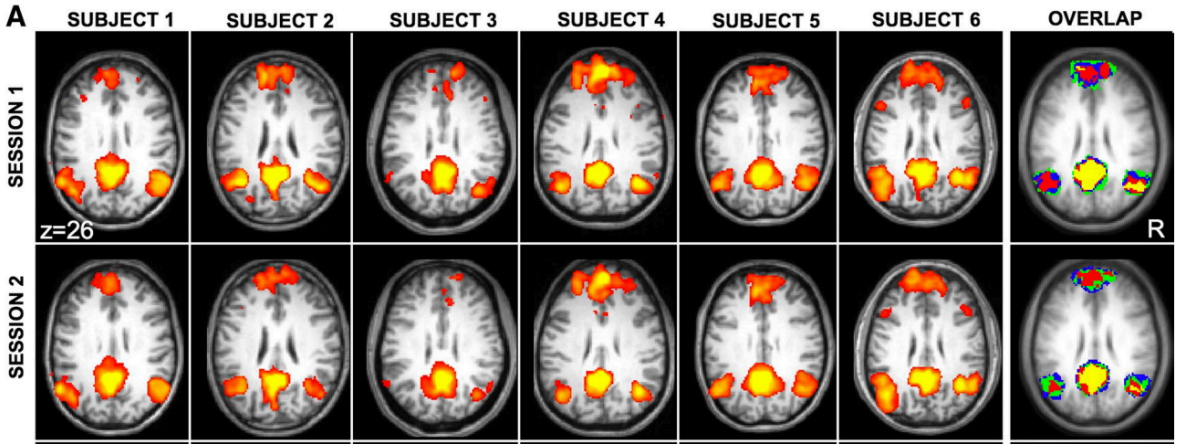
Sets of regions ("nodes") with mutually high functional connectivity in resting state

- often named after the functional areas with which they overlap
  (careful: terminology not standardized)
- approx. 10-15 reliable patterns at the spatial granularity shown here
- FC/networks can be studied at multiple spatial and temporal scales

Reliability of resting-state networks

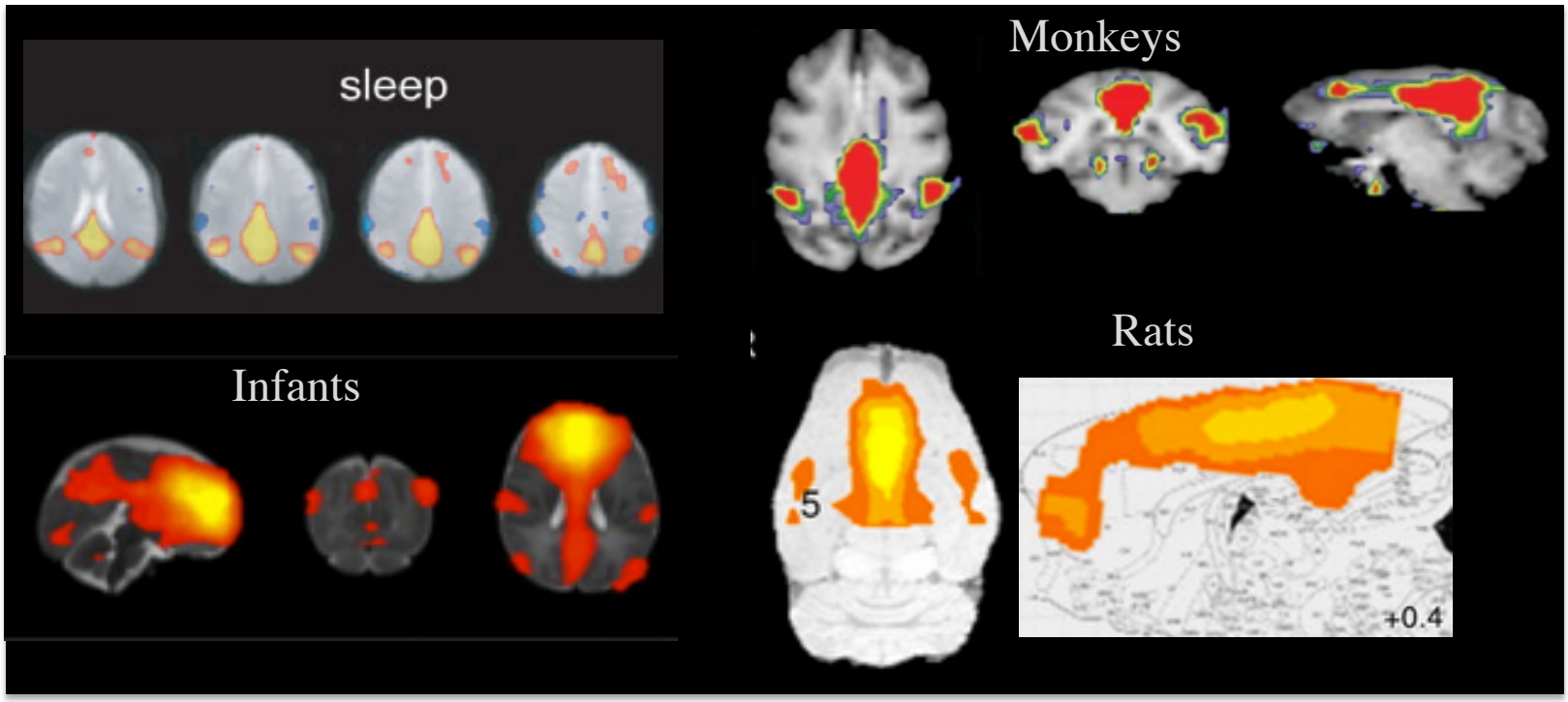


Choe et al, 2015



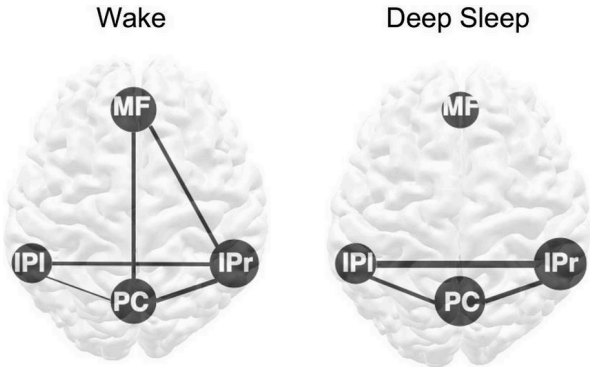
Van Dijk et al. 2010

Reliability of resting-state networks

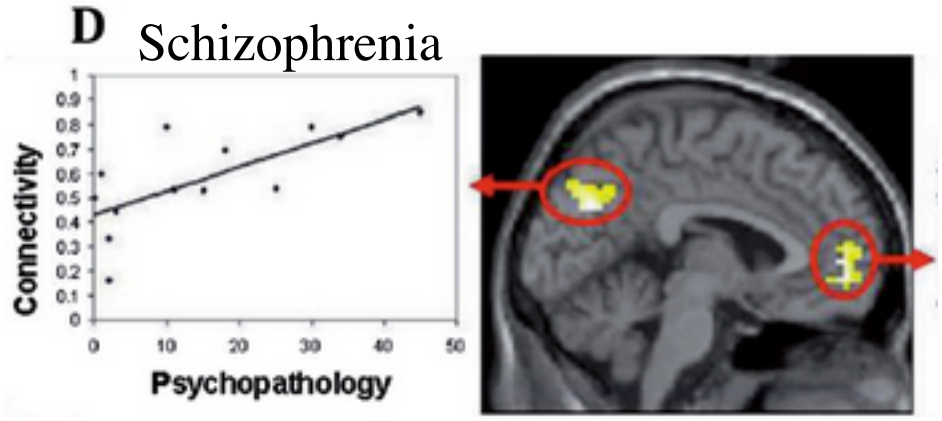


Horovitz et al. 2008; Doria et al. 2010; Vincent et al. 2007; Lu et al. 2007

Variability of resting-state networks



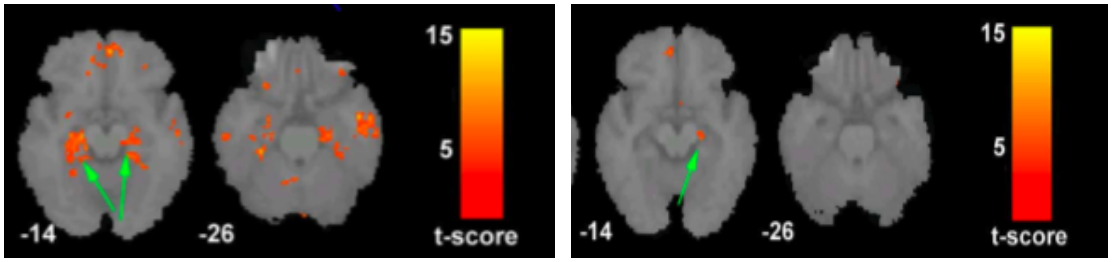
Horovitz et al., 2009



Whitfield-Gabrieli et al. 2009

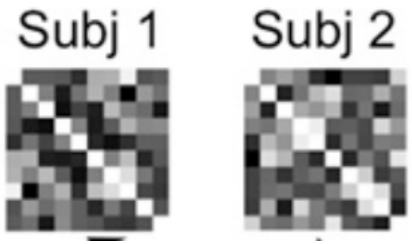
Healthy controls

Alzheimer's Disease



Greicius et al. 2004

Individual differences



Finn et al. 2015

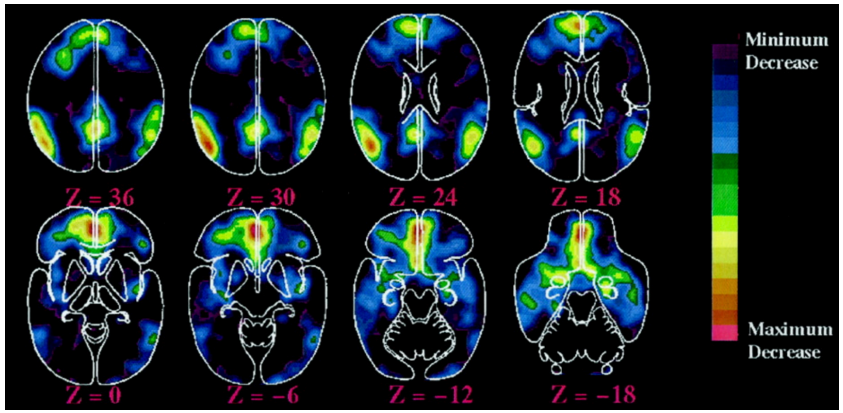
- Potential for resting-state fMRI to yield biomarkers

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

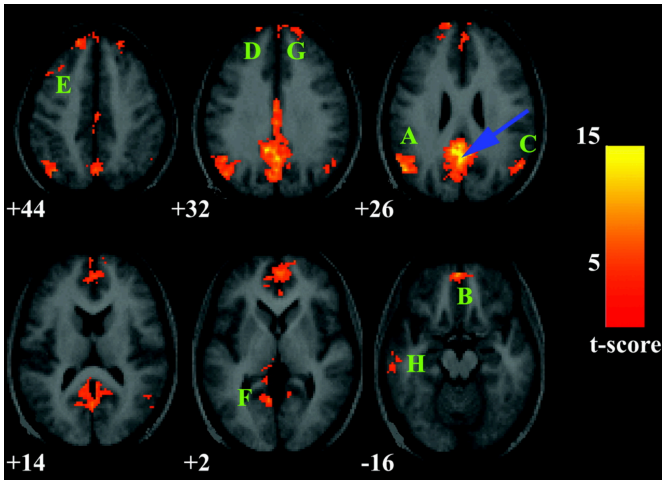
Kelly et al. 2012

Default Mode Network



Raichle at el., 2001

"A default mode of brain function"



Greicius et al., 2003,

" Functional connectivity in the resting brain: a network analysis of the default mode hypothesis"

- Preferentially active when not focused on the external environment
- Possible functions include**:** autobiographical memory retrieval, envisioning the future, and conceiving the perspectives of others
  - review: Buckner et al., 2008 Ann N Y Acad Sci

Recap

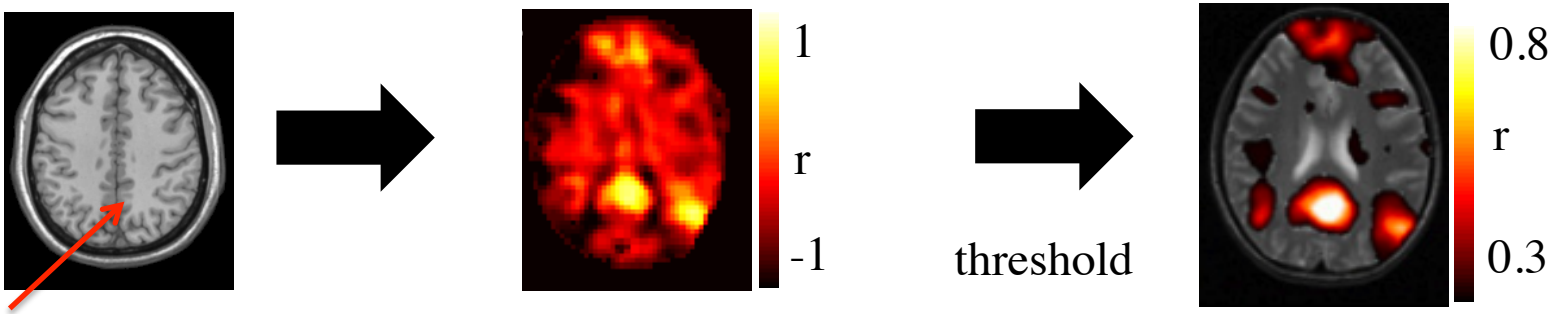
- Resting-state fMRI scan:
  - no task or stimuli, minimal instructions
  - study spontaneous brain activity
- Can reliably identify spatial patterns of temporally correlated activity that correspond with known functional networks
  - “resting-state networks”
  - no task or task compliance needed
- Promising tool for studying natural or disease-related differences in functional organization

Resting-state fMRI

- Background & motivation
- **Data analysis**
  - **seed-based correlation**
  - **independent component analysis (ICA)**
  - **complex network analysis**
- Interpretation
- Challenges / directions

Seed-based correlation

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



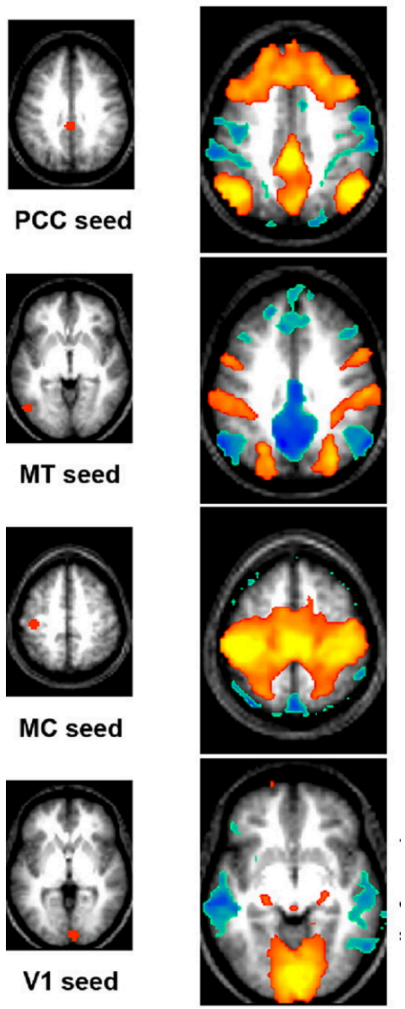
seed

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

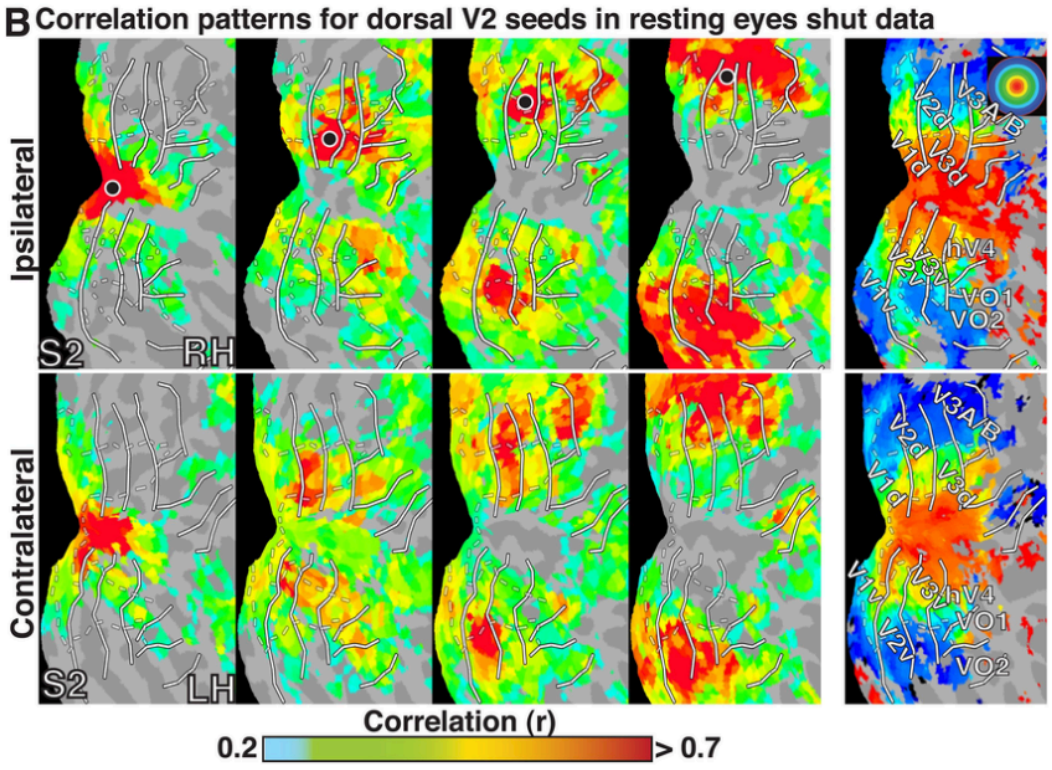
example questions:

- Are there any areas whose correlation with my seed ROI is significantly different in *condition A* v. *condition B* / *patients v. controls* ?
- Any areas whose FC with my seed ROI is proportional to [behavioral measure / outcome measure, etc.]

Seed-based correlation: examples



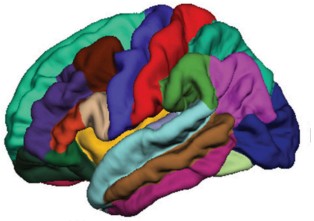
Fox et al. 2009



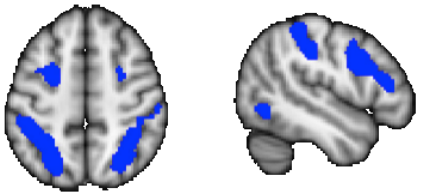
Arcaro et al., 2015

Choosing the seed region

E.g., from atlas, published coordinate, structrual image, activation map (single-sub, group-level)

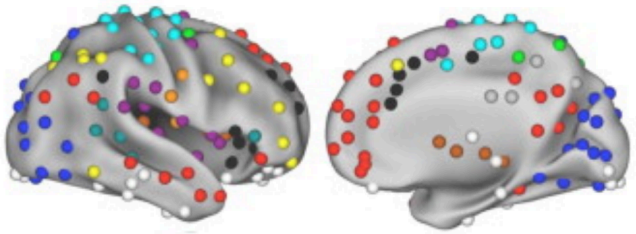


Klein et al. 2012

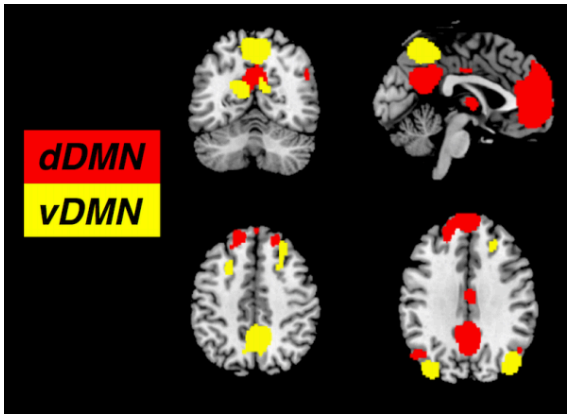


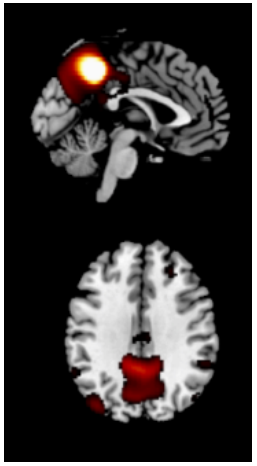
Stanford "FIND" atlas

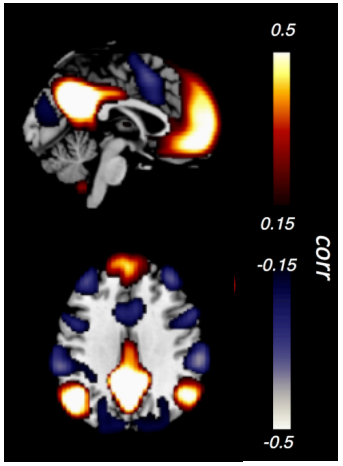
Shirer et al. 2011



Power et al. 2011



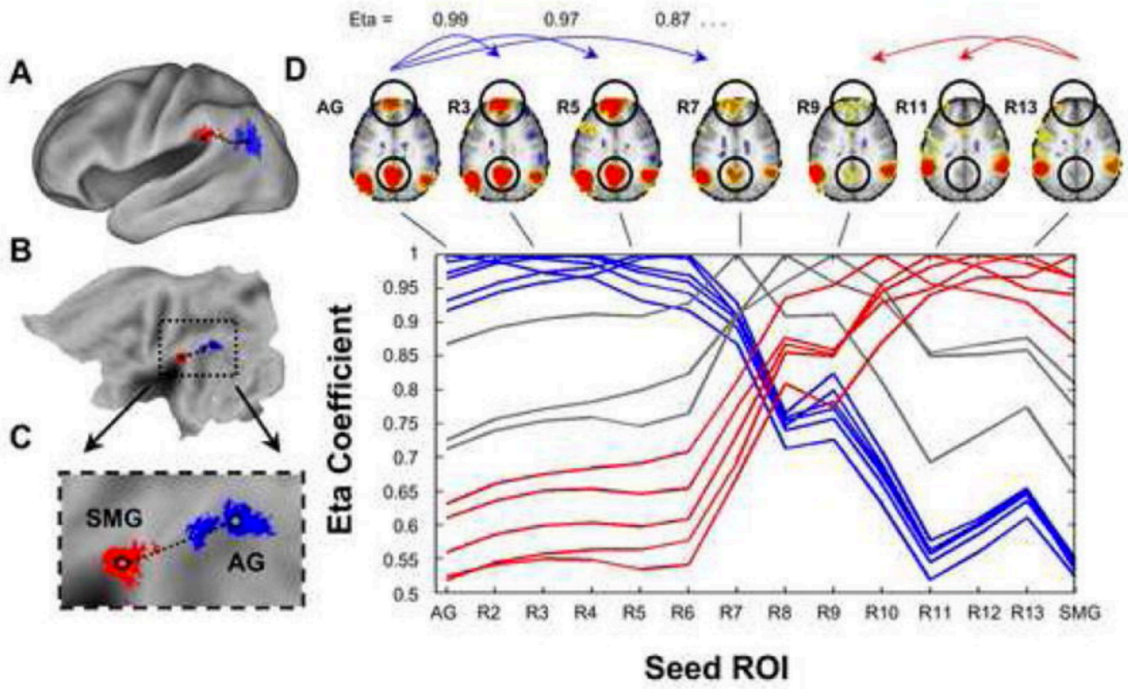


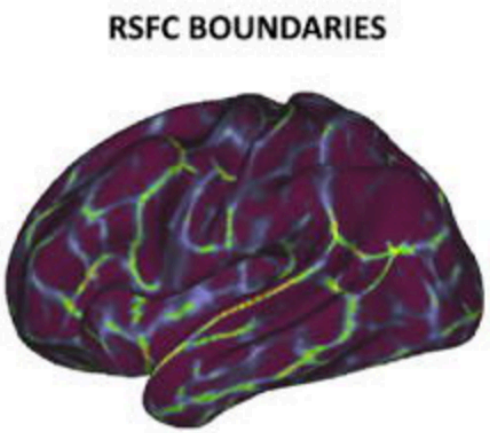


Differences in seed location can explain discrepancies across papers

Chen et al. 2017

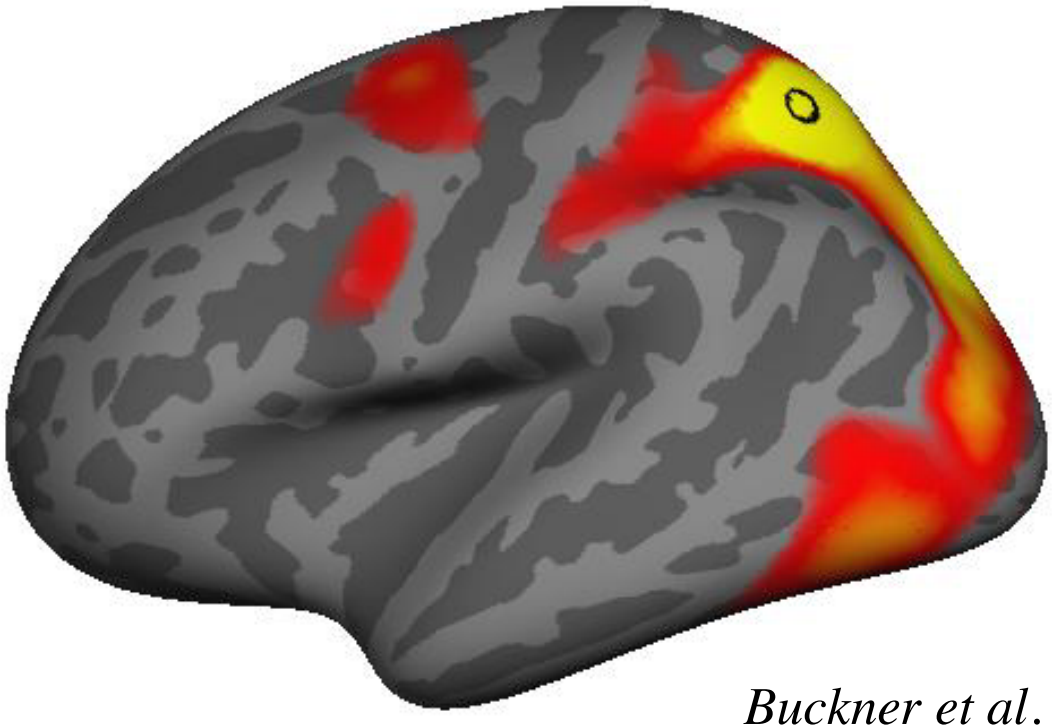
Choosing the seed region





Cohen et al. 2008

Choosing the seed region



Buckner et al. 2013

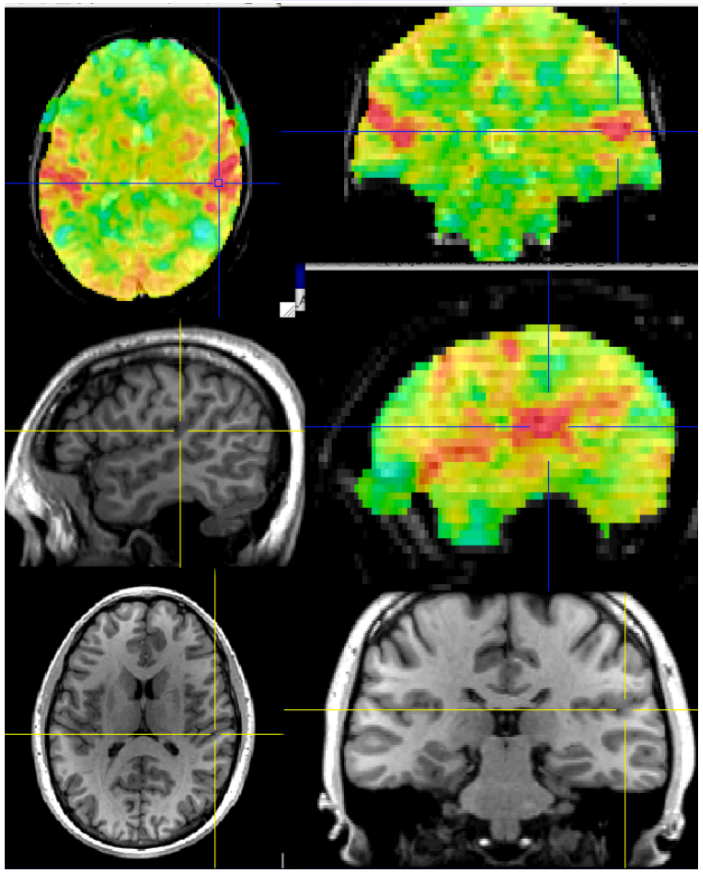
Exploratory seed-based correlation in AFNI

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

–1–

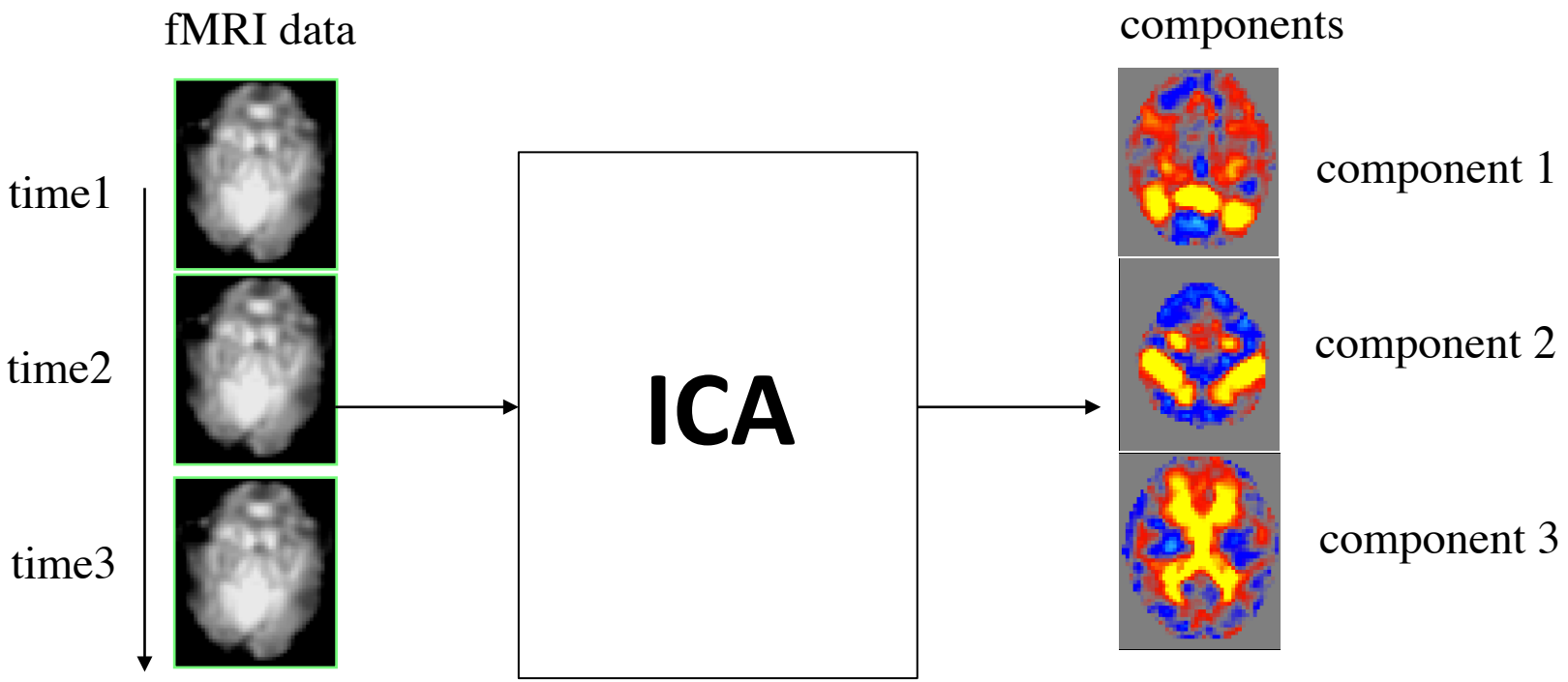
AFNI InstaCorr

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

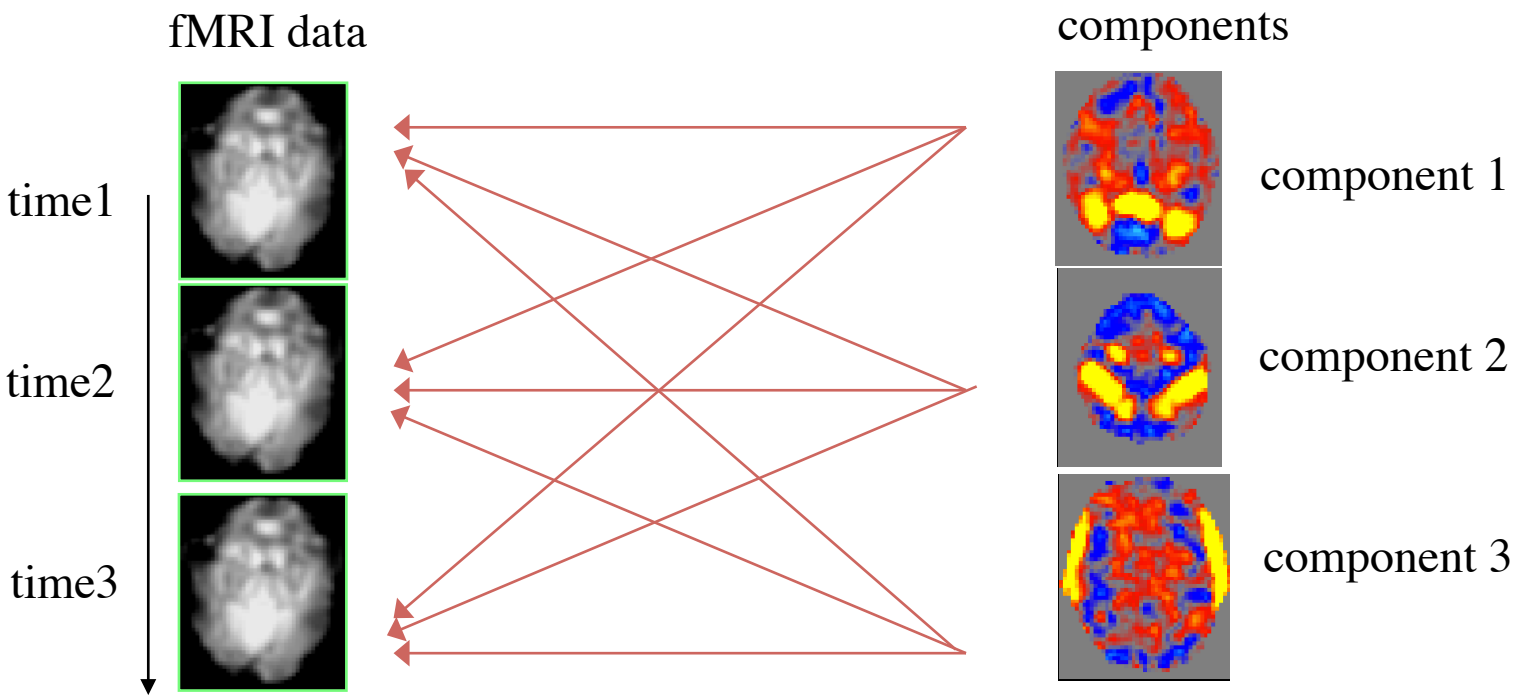


- On-the-fly **insta**ntaneous **corr**elation map of resting state data with interactively selected seed voxel
- **Setup phase**: prepares data for correlations (several-to-10+ seconds)
- **Correlation phase**: you select seed voxel, correlation map appears by ***magic***

2. Independent Component Analysis (ICA)



Independent Component Analysis (ICA)



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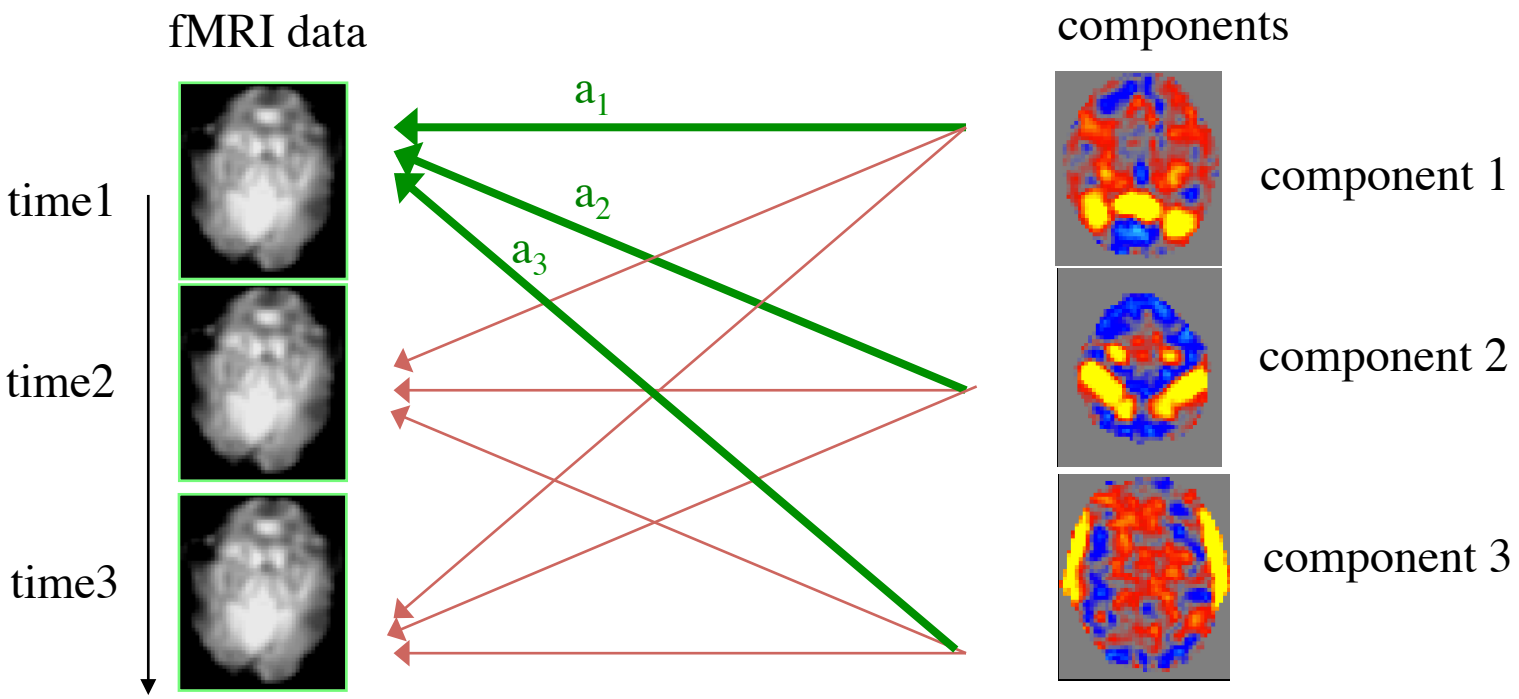
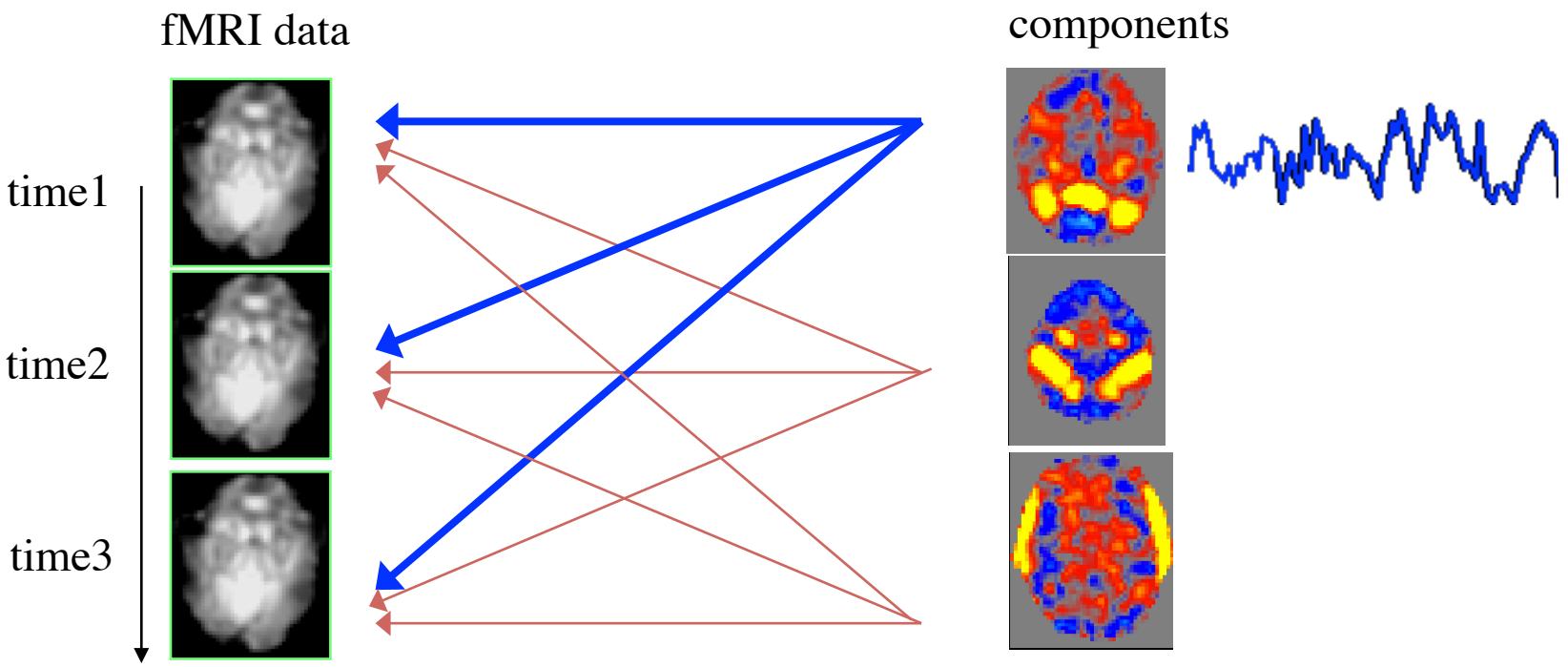
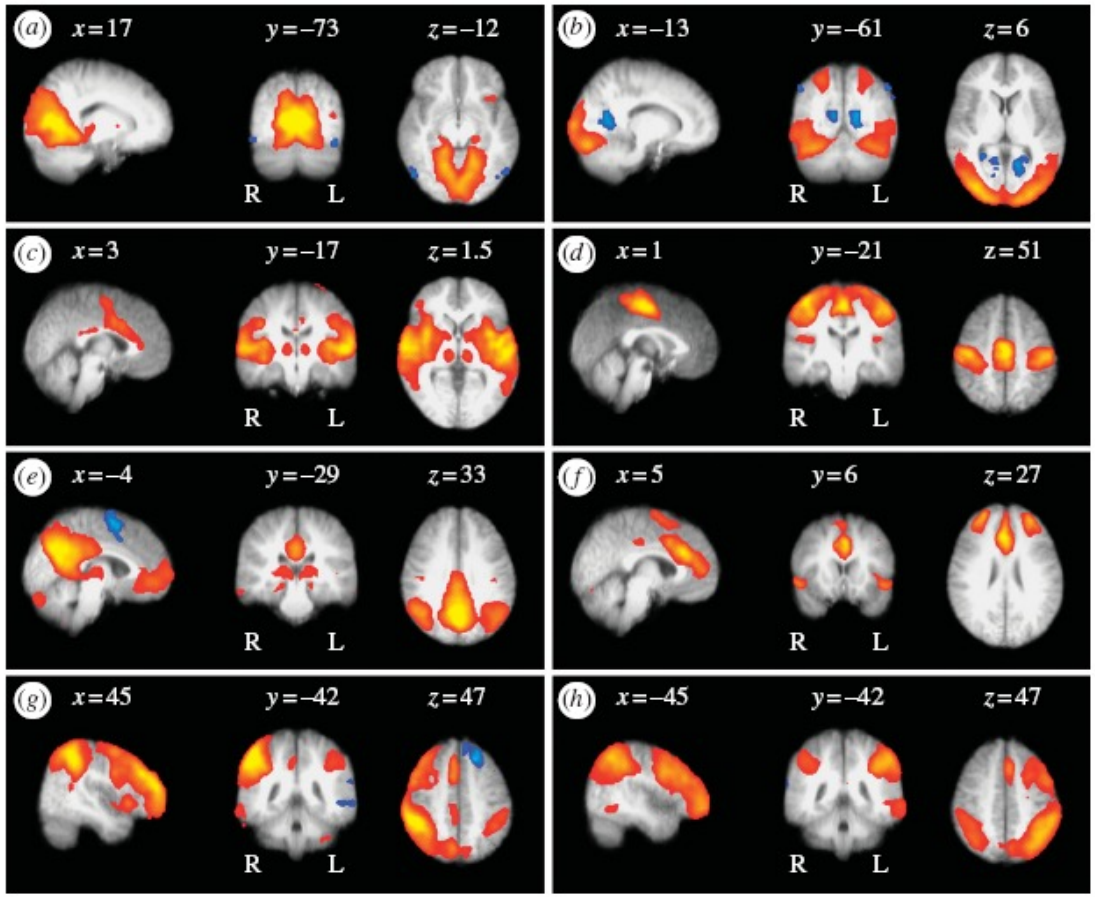


Independent Component Analysis (ICA)



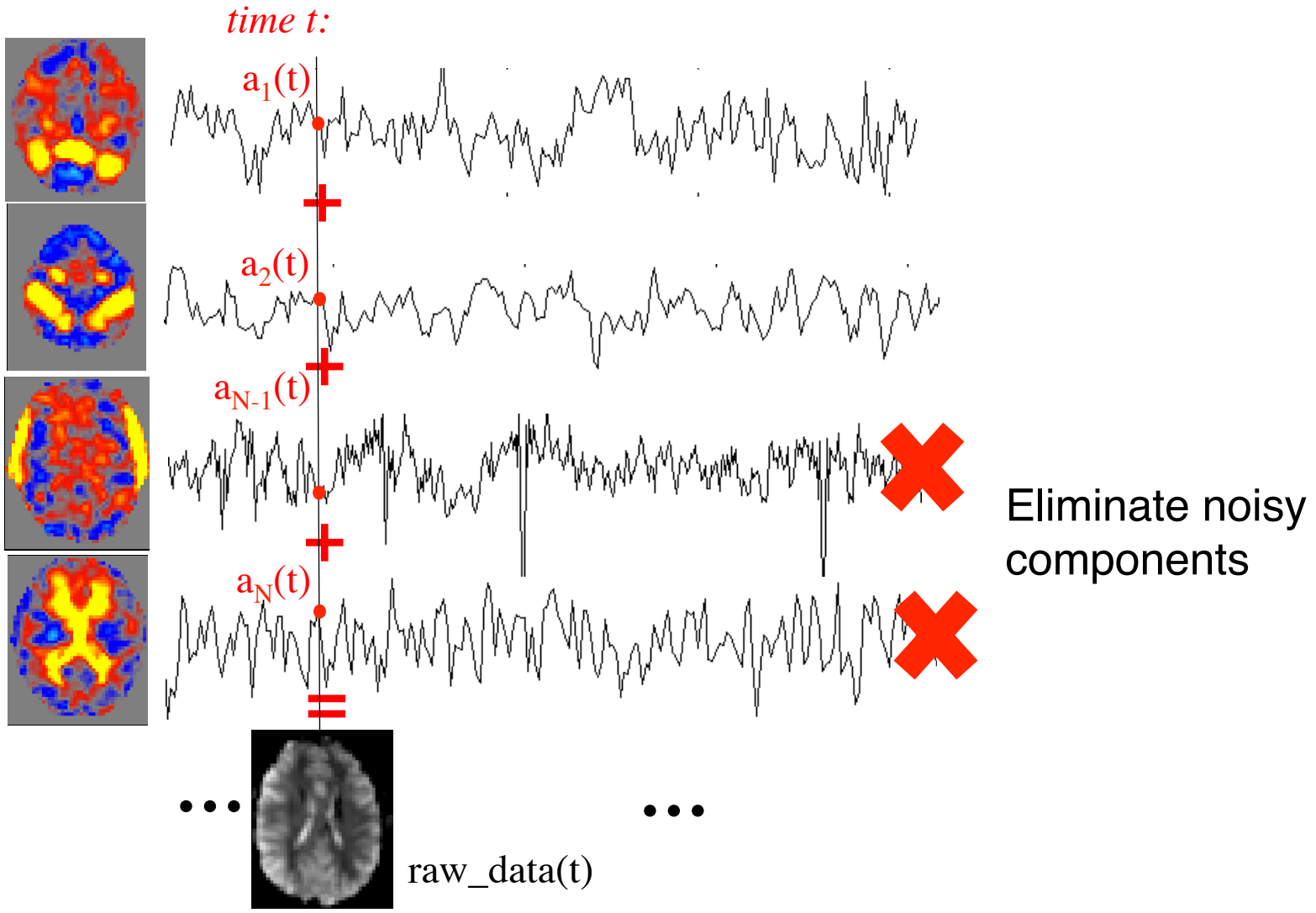
- Analogy: “cocktail-party problem”
- Uses assumption of spatial independence

“Networks” from ICA



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

ICA reveals structured neural & artifact patterns

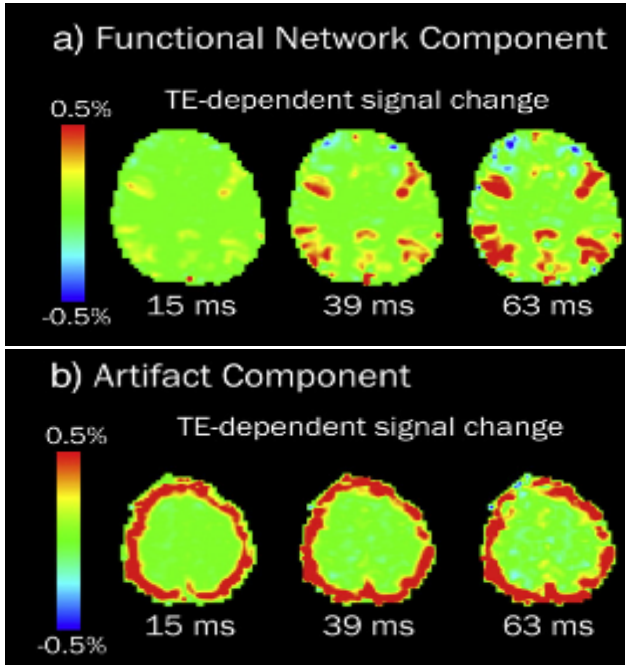


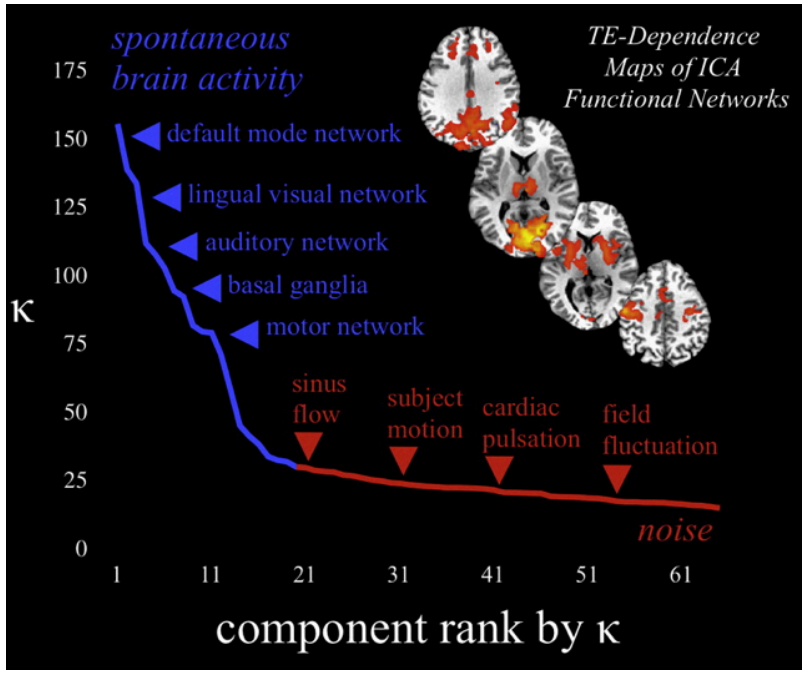
Identifying noise components?

- 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

- ICA is multivariate; extract many "networks" (components) at once
- Doesn't require seed, but need to specify some parameters
  - e.g., number of components - this can greatly impact your results (networks "split" when increasing the number of components)
- Can be used for network analysis and noise reduction
  - must objectively select components
  - not all types of artifact are easily separable with ICA
- see also: **dual regression** (Filippini et al. 2009)
- Interpretation more complicated than seed-based analysis

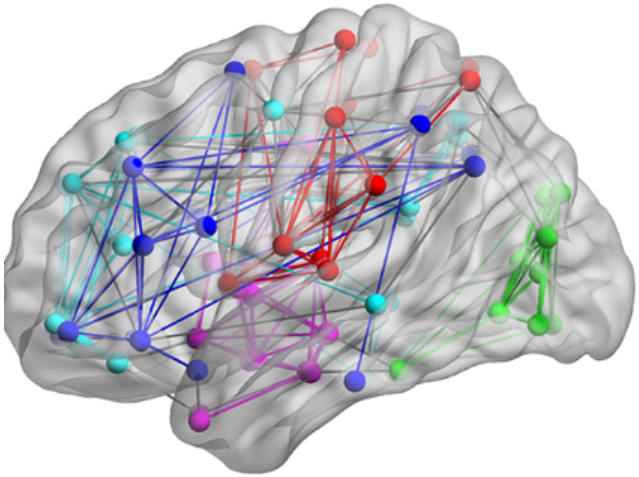
frontiers in
SYSTEMS NEUROSCIENCE

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

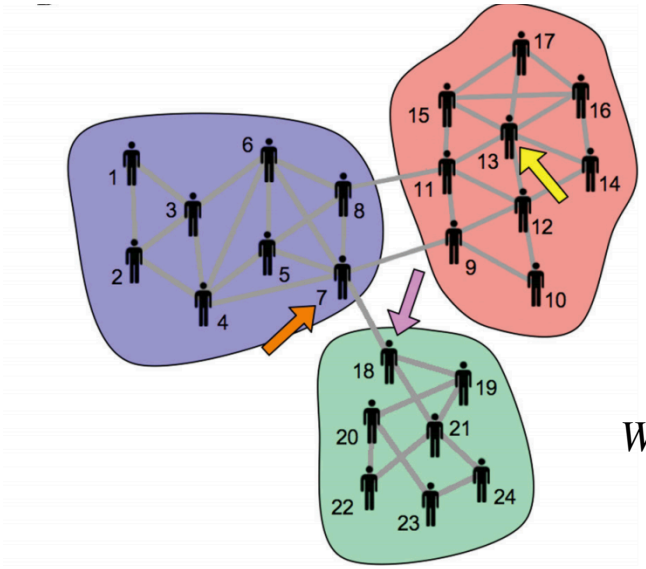
Advances and pitfalls in the analysis and interpretation of resting-state FMRI data

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

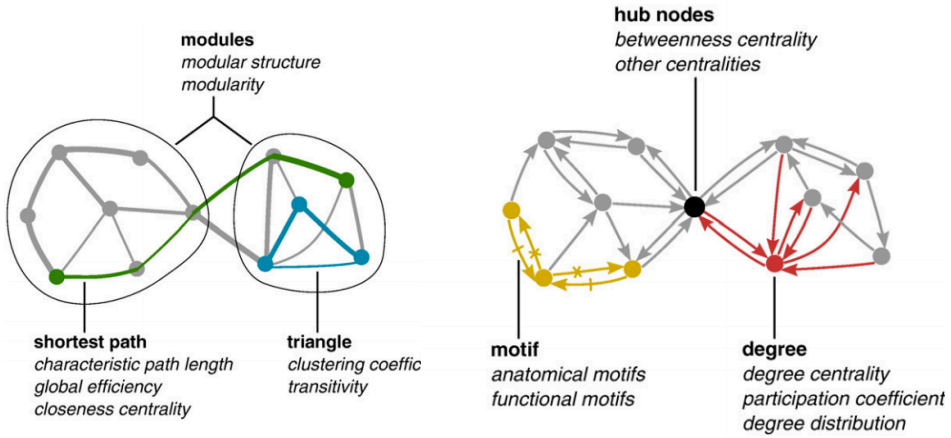
3. Complex network analysis



Xia et al., 2013

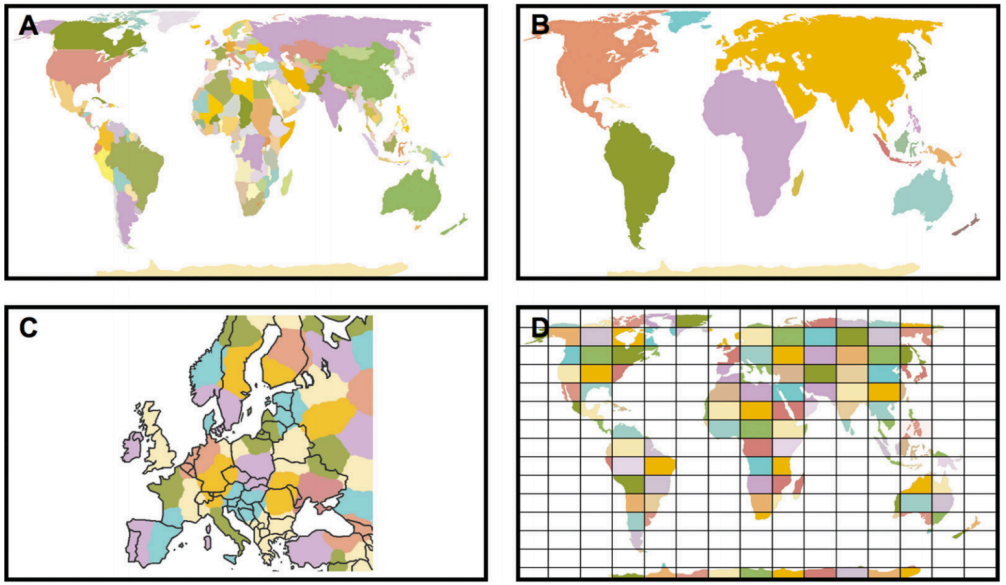


Wig et al. 2011

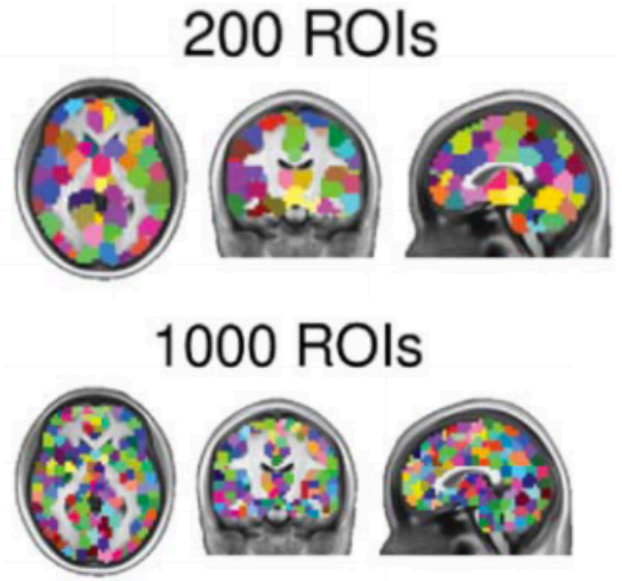


Reviews:
Rubinov & Sporns, 2010
Bassett & Sporns, 2017

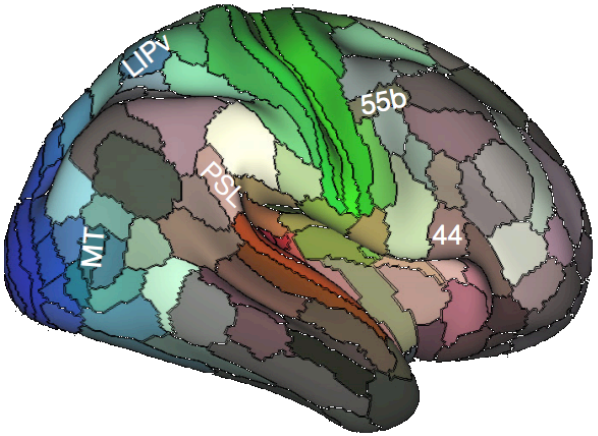
Choice of nodes ("parcellation")



Wig et al. 2011



Craddock et al. 2012



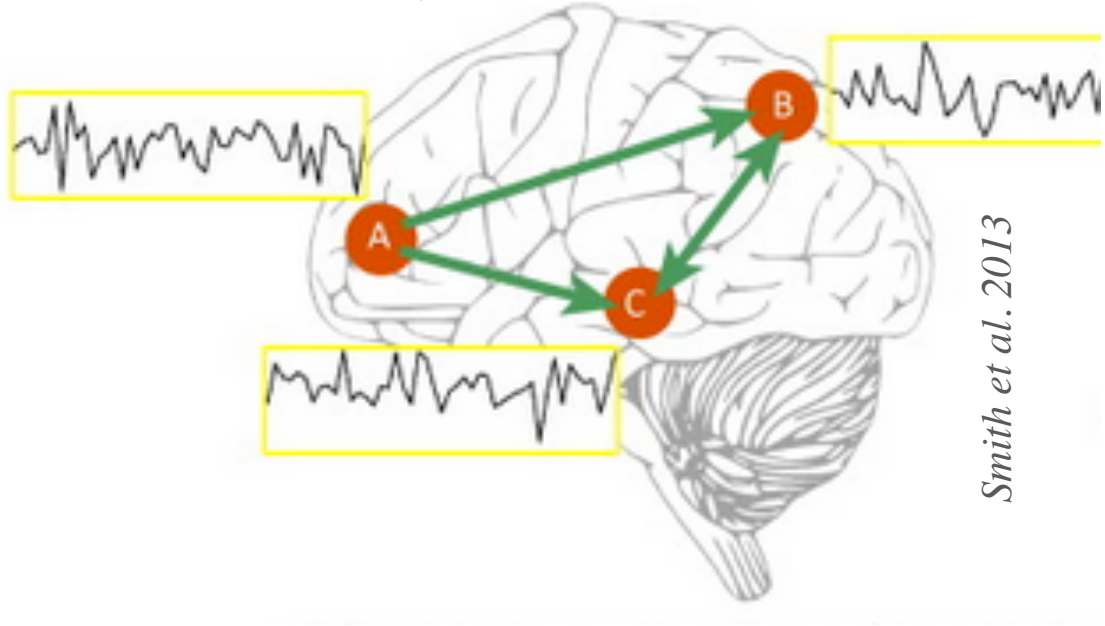
Glasser et al. 2016

Resting-state fMRI

- Background & motivation
- Data analysis
- **Interpretation**
- Directions

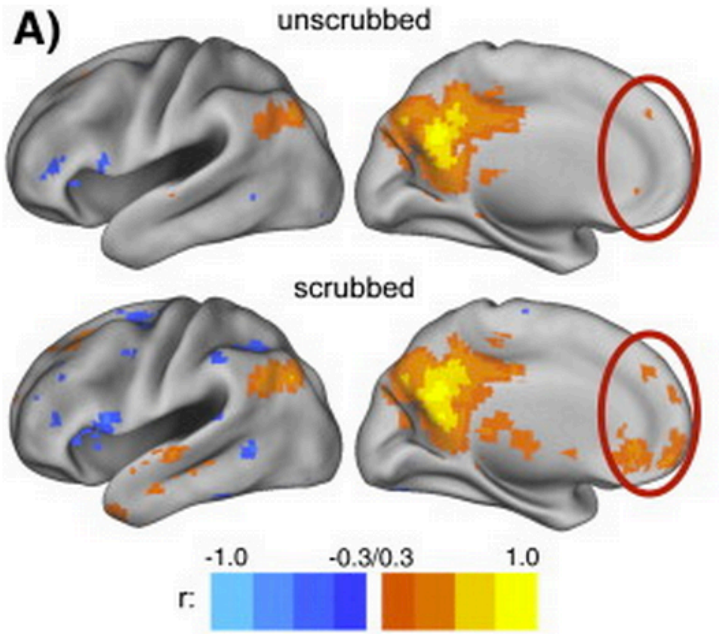
Resting-state fMRI: powerful but ambiguous

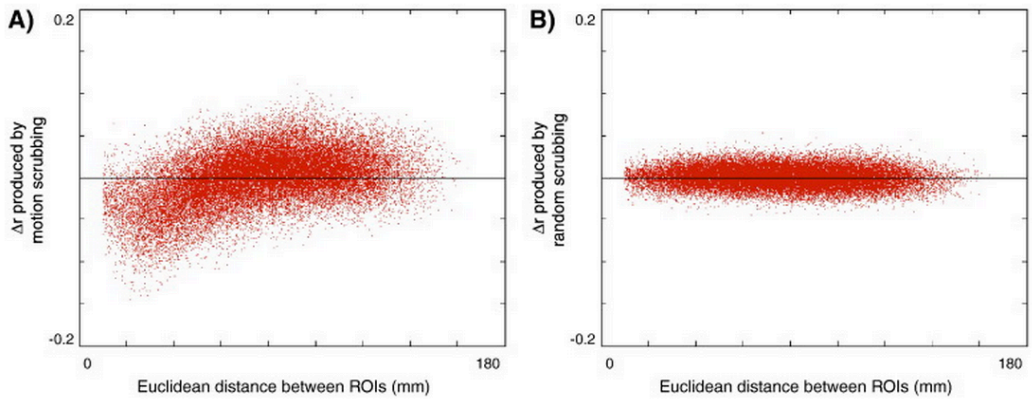
Functional connectivity is a powerful but ambiguous mapping tool
(Buckner et al. 2013 Nat. Rev. Neuro)



- Resting state data: mixture of many, largely unknown processes.
- Relationship with structural connectivity & electrophysiology not straightforward
- Data are noisy & sensitive to modeling and pre-processing decisions

Head motion



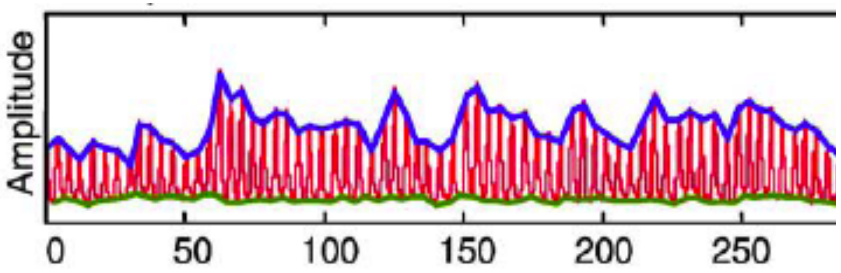


Power et al. 2010

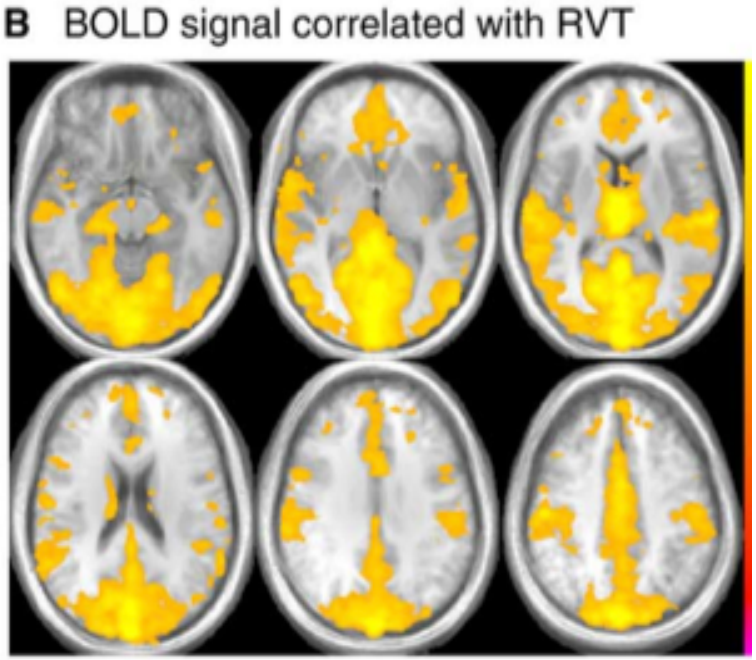
Systematic differences in head motion across age groups caused spurious functional connectivity effects

Physiological effects in fMRI data

- e.g., fluctuations in breathing & heart rate correlate with fMRI



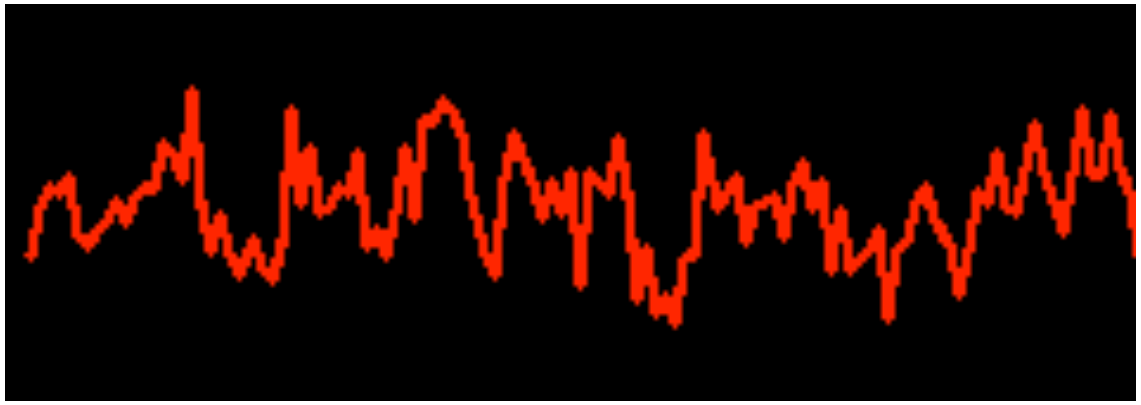
Birn et al. 2006



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

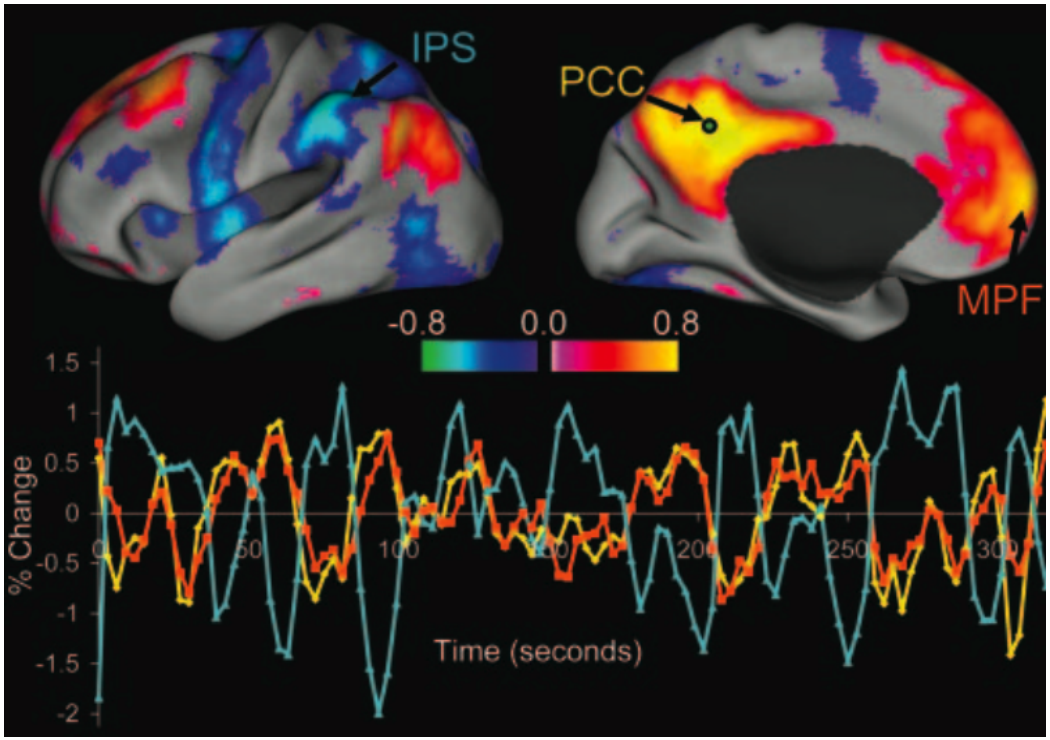
What is noise, what is signal?

- no task/stimulus timing to help distinguish signal from noise
- trial averaging not possible
- “functional connectivity” quantifies relationships between regions (each are signal + noise!)

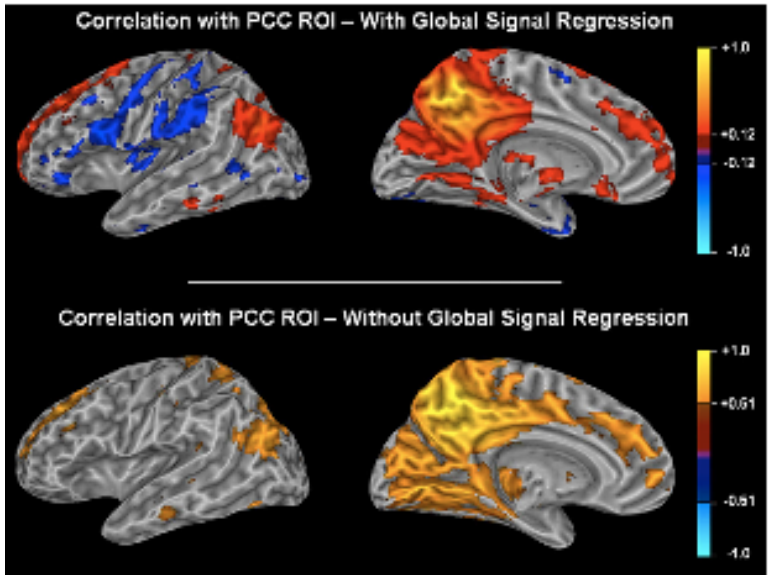


Pre-processing strategies can affect results

- and it's hard to evaluate pre-processing strategies – no ground truth
- saga of the global signal…



Fox et al, 2005



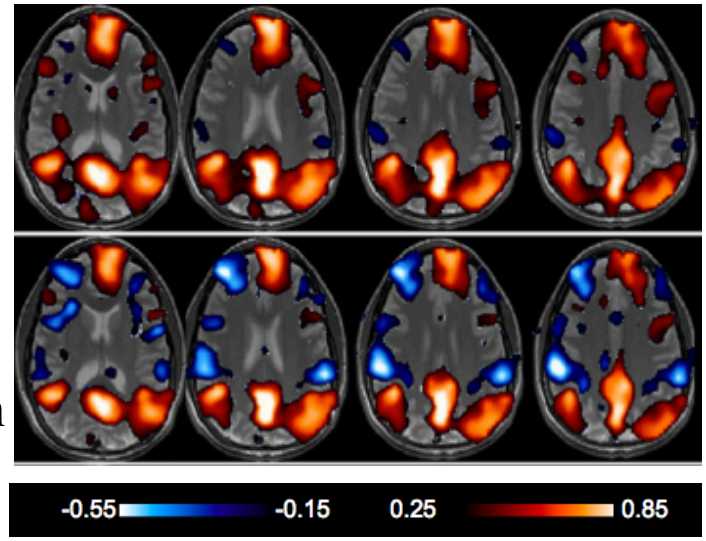
Murphy et al, 2009

Pre-processing strategies can affect results

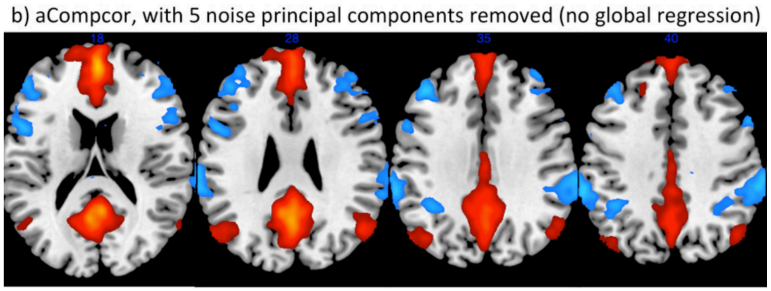
- physiological noise reduction
  can reveal anti-correlations

no correction

physiological
noise reduction

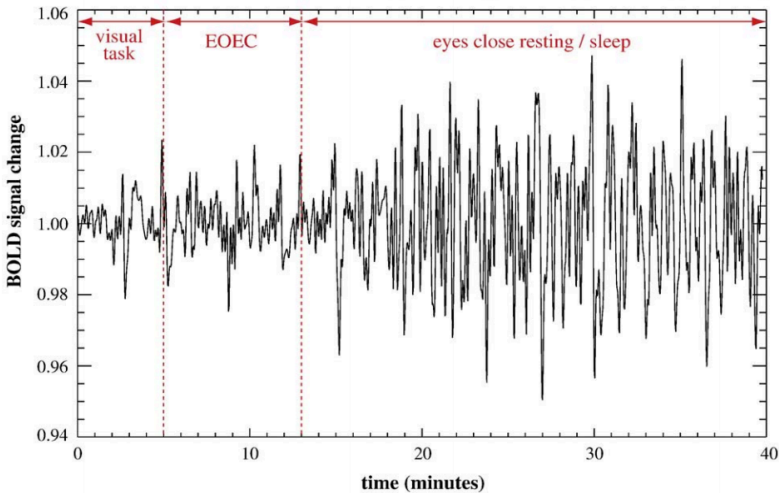


Chang et al, 2009



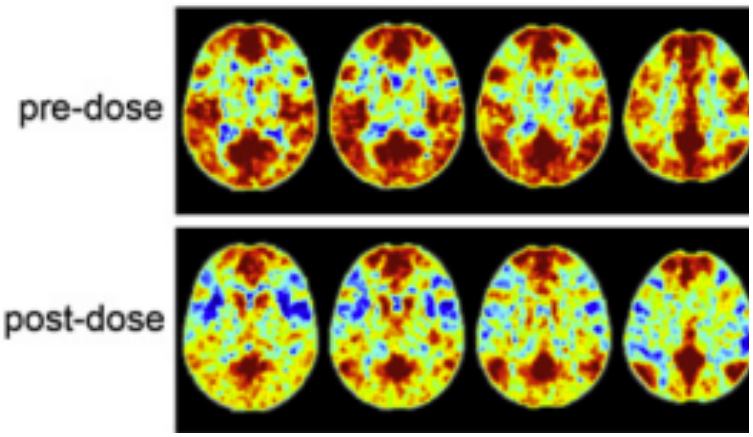
Chai et al, 2012

Fluctuations in alertness / vigilance

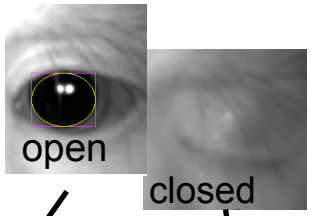


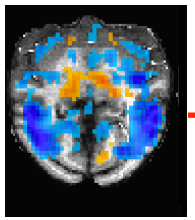
Fukunaga et al. 2006

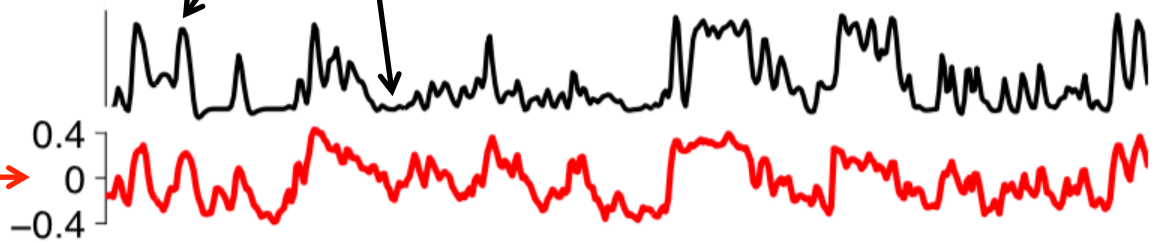
before v. after caffeine



Wong et al. 2010



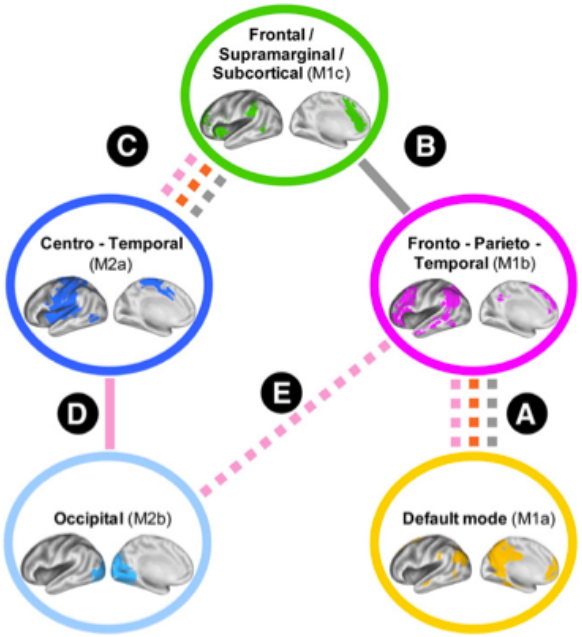




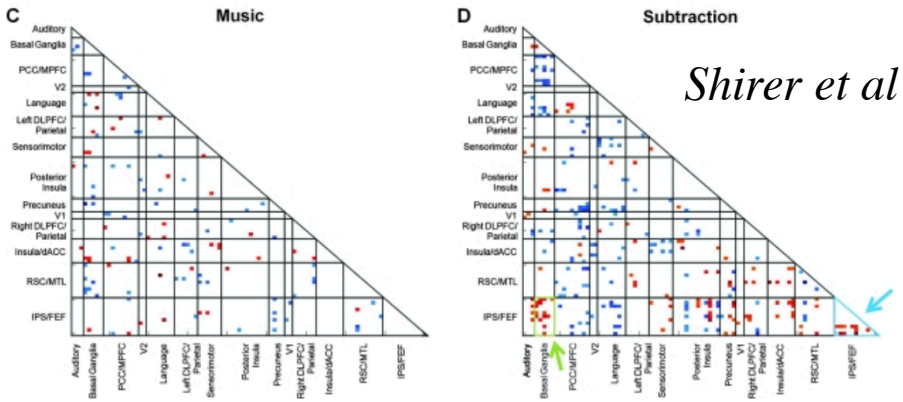
data-driven fMRI vigilnance estimate
(test dataset)

Chang et al. 2016, Tagliazucchi et al. 2012

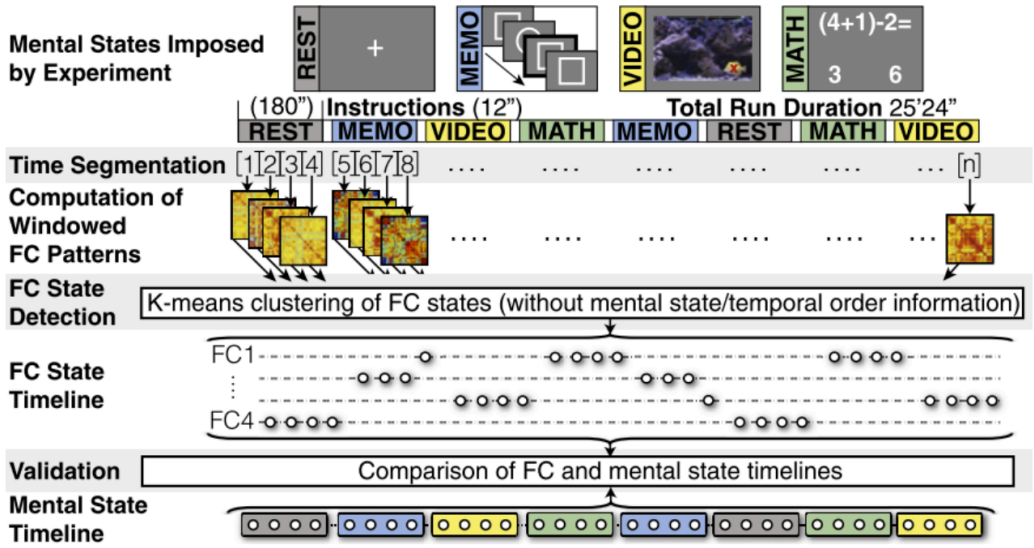
Thoughts, mind-wandering



Doucet et al. 2011

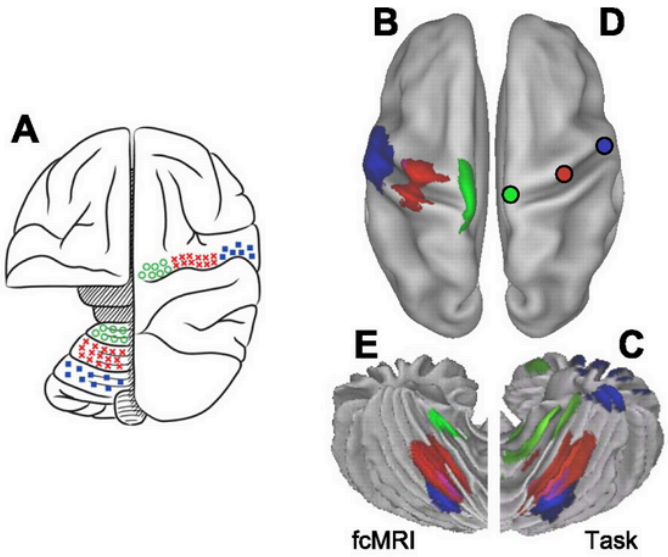


Shirer et al. 2012

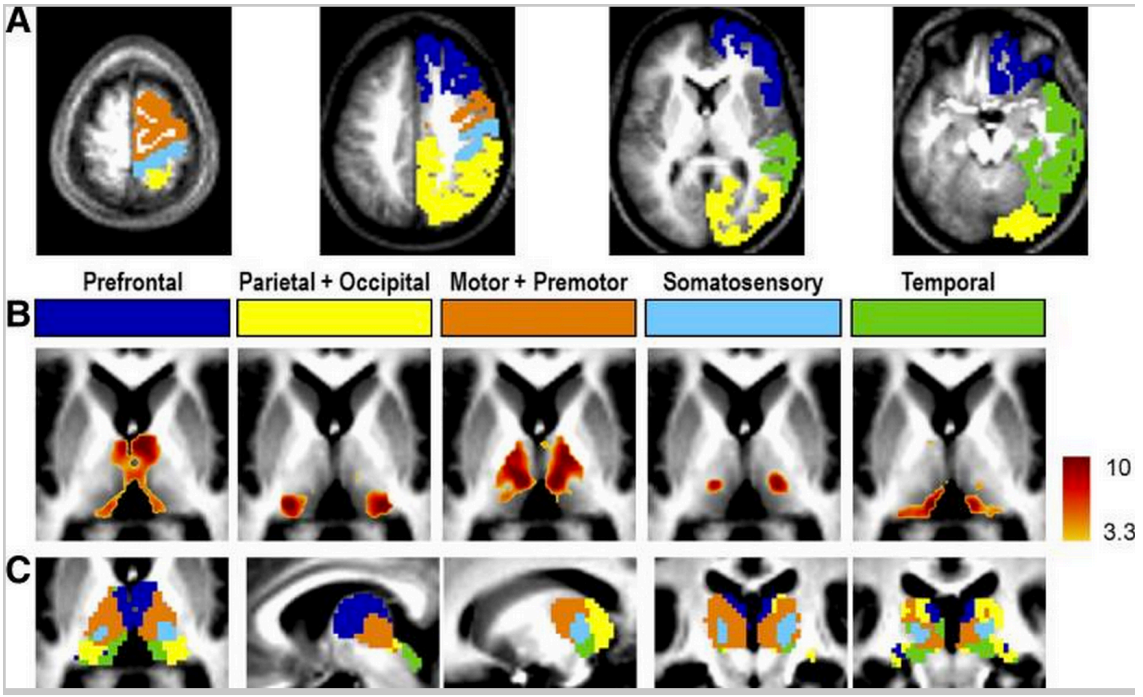


Gonzalez-Castillo et al. 2015

Correspondence with anatomic connectivity



Buckner et al. 2011



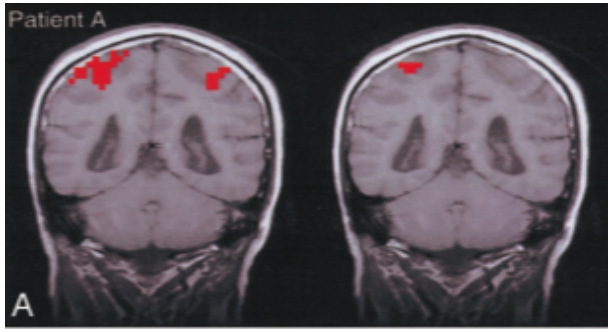
Zhang et al. 2008

Correspondence with anatomic connectivity

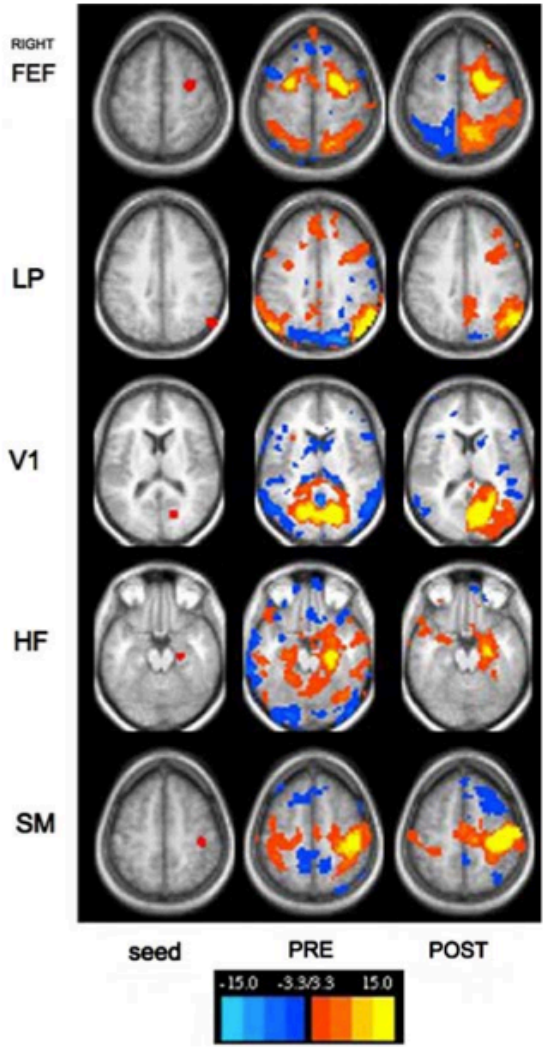
Agenesis of the Corpus Callosum

task

correlations (resting state)



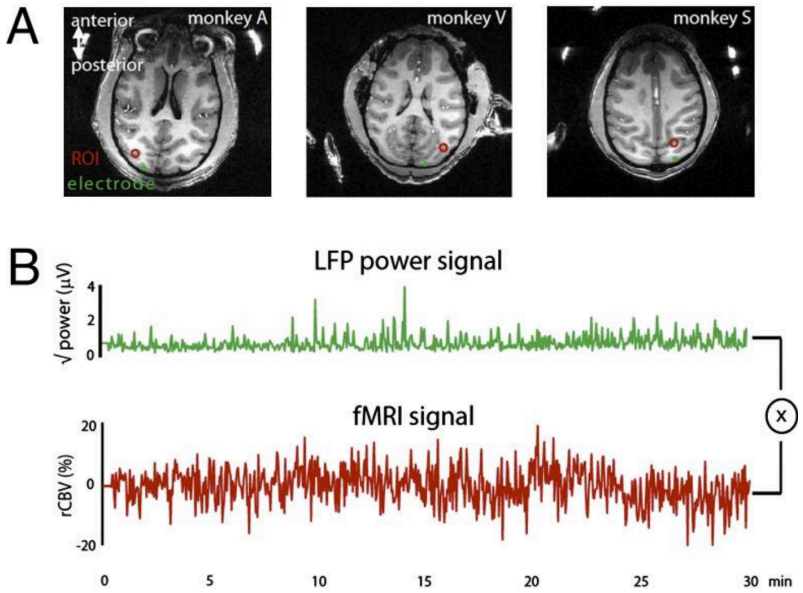
Quigley et al., 2003



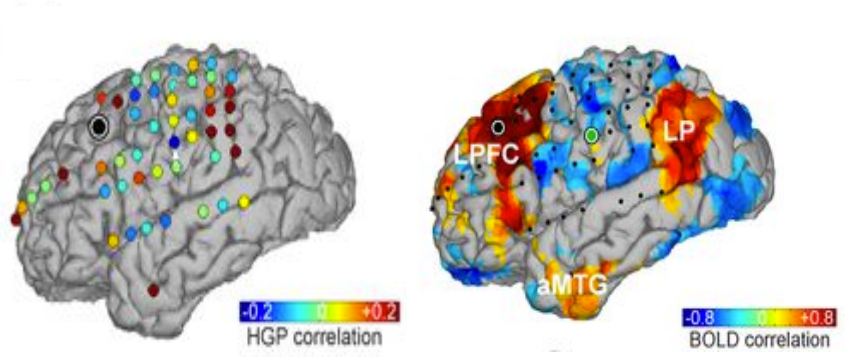
Johnston et al., 2008

via indirect connections?

Correspondence with electrophysiology



Schölvinck et al. 2010
Shmuel & Leopold, 2008



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)

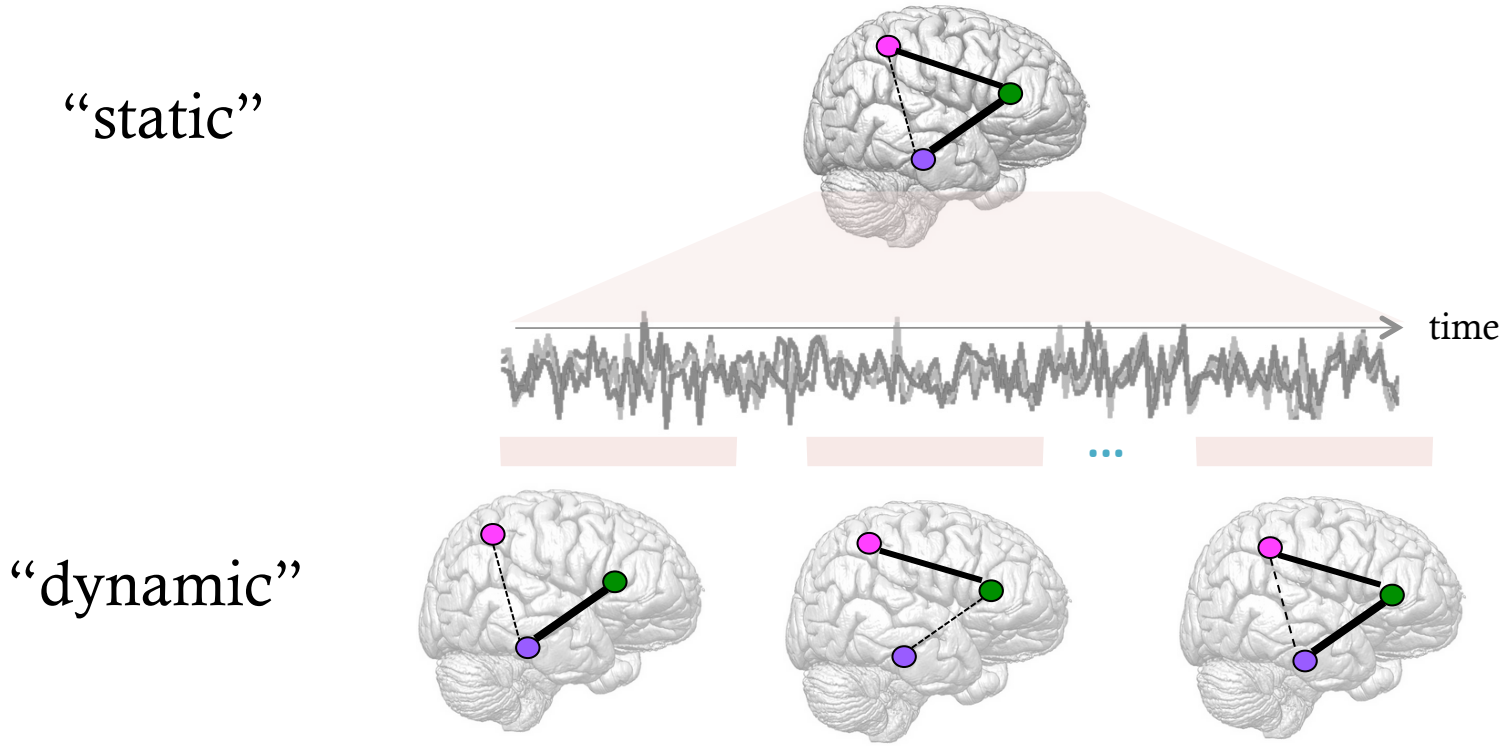
- **review**: Schölvinck, Leopold et al. 2013

Overall Summary

- Resting-state fMRI data exhibit spatio-temporal organization and is widely studied for clinical applications and basic neuroscience
- Understand analysis methods/tradeoffs
  - and stay close to the data
- Artifacts and neural variability can affect signal and connectivity measurements
- Interpretation is still not clear
  - understand neural, physiological basis

Directions

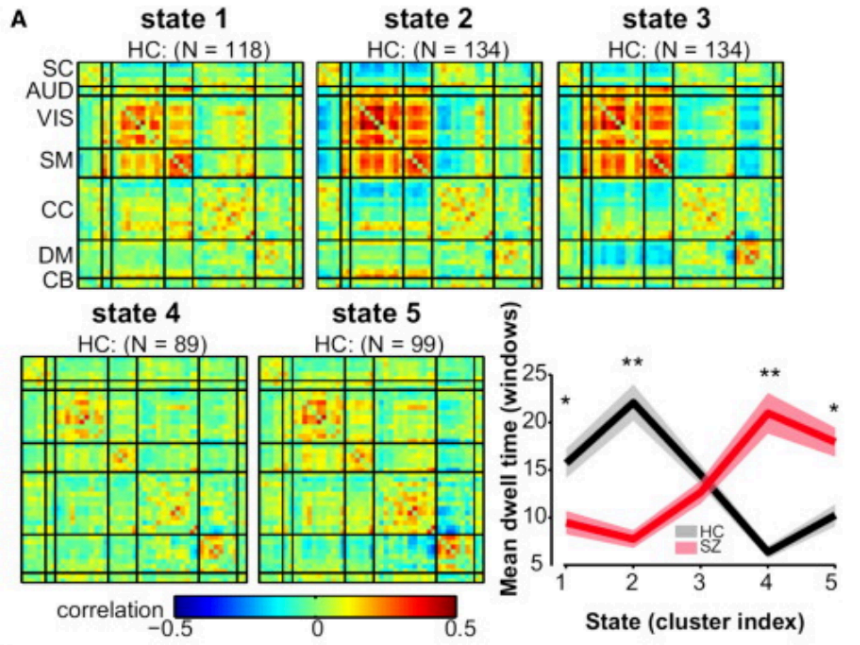
- Methods for analyzing spatio-temporal dynamics of brain activity (in rest & task)



Directions

- Methods for analyzing spatio-temporal dynamics of brain activity (in rest & task)

  e.g., time-varying analysis, brain "states"



Reviews:

Hutchison et al. Neuroimage 2013

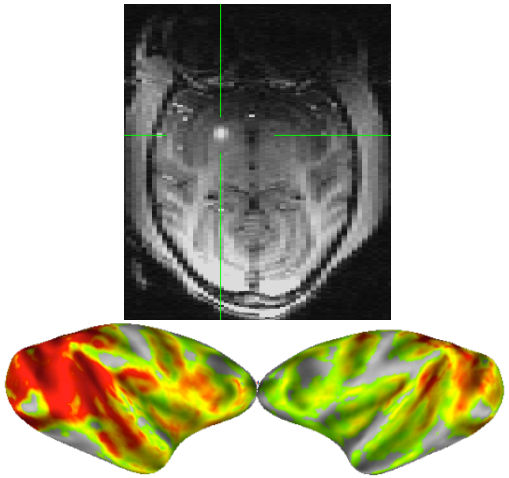
<--Calhoun et al. Neuron 2014

Keilholz et al. Brain Conn. 2017

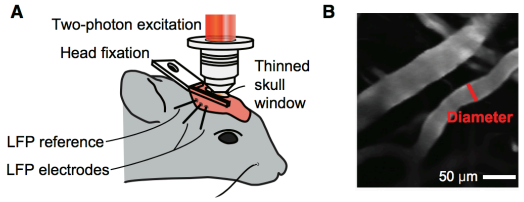
Directions

- Methods for analyzing spatio-temporal dynamics of brain activity (in rest & task)
  - e.g., time-varying analysis, brain "states"
- Improved understanding of neural & physiological basis
  - multi-modal recordings, causal manipulation

http://fmri.uib.no



Turchi et al. 2018

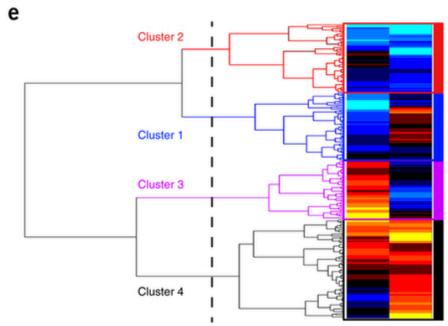


Mateo et al., 2017
He et al. 2018

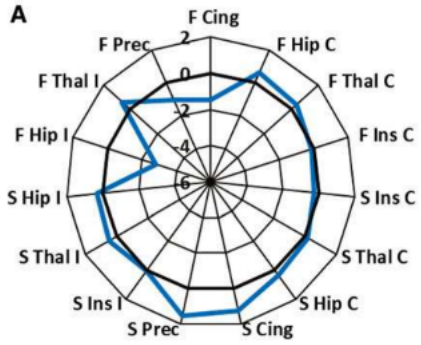
Directions

- Methods for analyzing spatio-temporal dynamics of brain activity (in rest & task)
  - e.g., time-varying analysis, brain "states"
- Improved understanding of neural & physiological basis
  - multi-modal recordings, causal manipulation
- Individual Differences, Clinical Applications

Drysdale et al. 2017
Subtypes of depression



Morgan et al. 2017
Epilepsy: prediction of seizure outcome



Data sharing & fMRI big data

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

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[d] *Center for Magnetic Resonance Imaging, University of Minnesota, Minneapolis, MN 55455, USA*

Thanks!