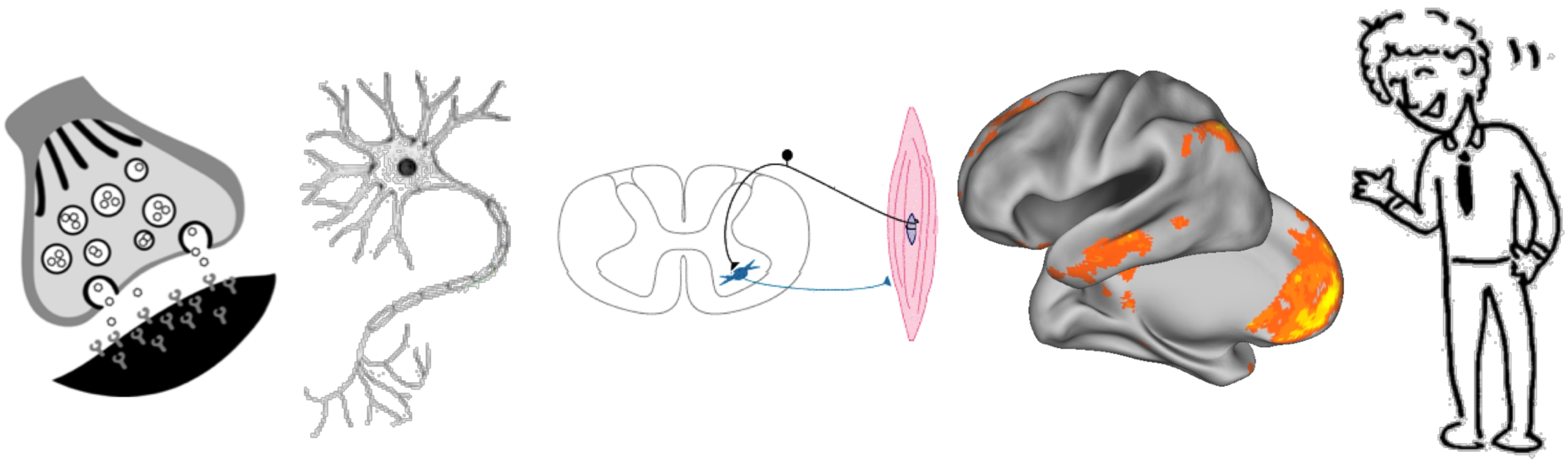
Martinos Center for Biomedical Imaging, Febr 21, 2013

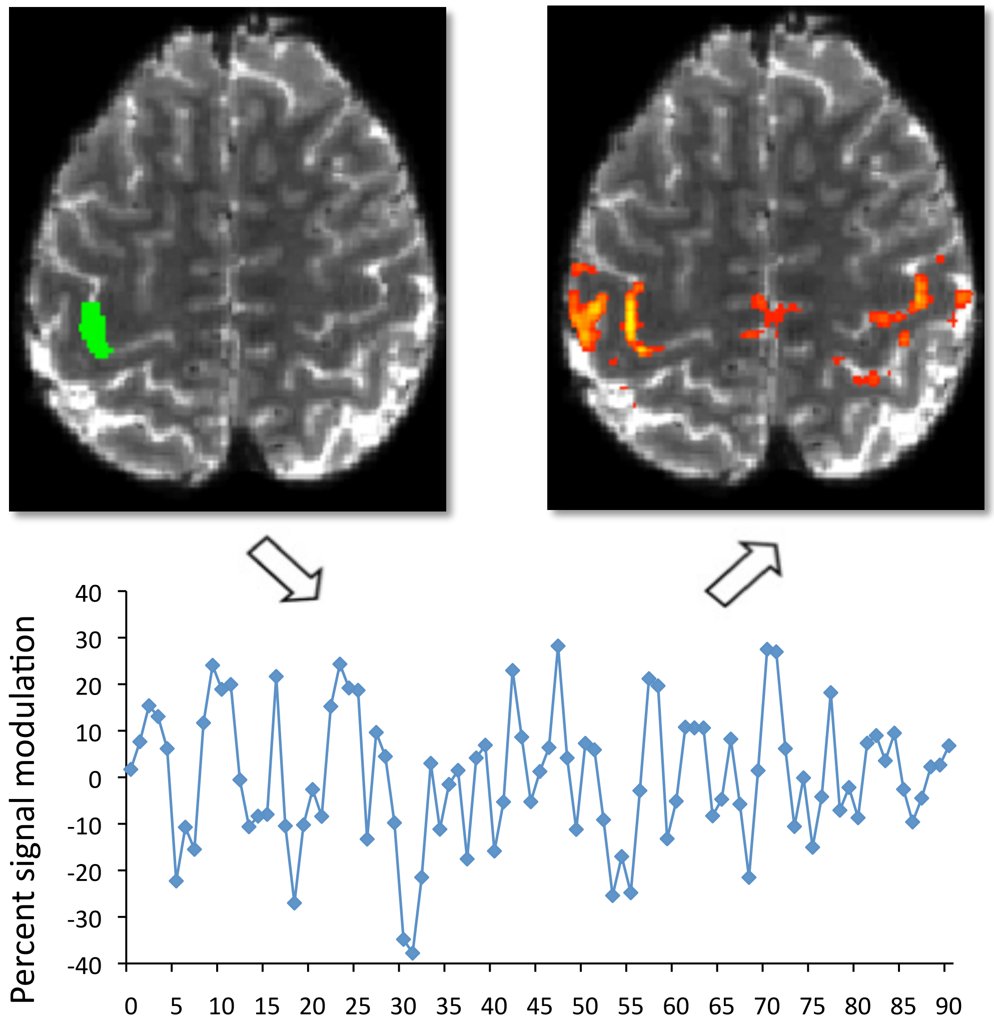
Why ‘n How: Functional connectivity MRI

Koene Van Dijk

Why

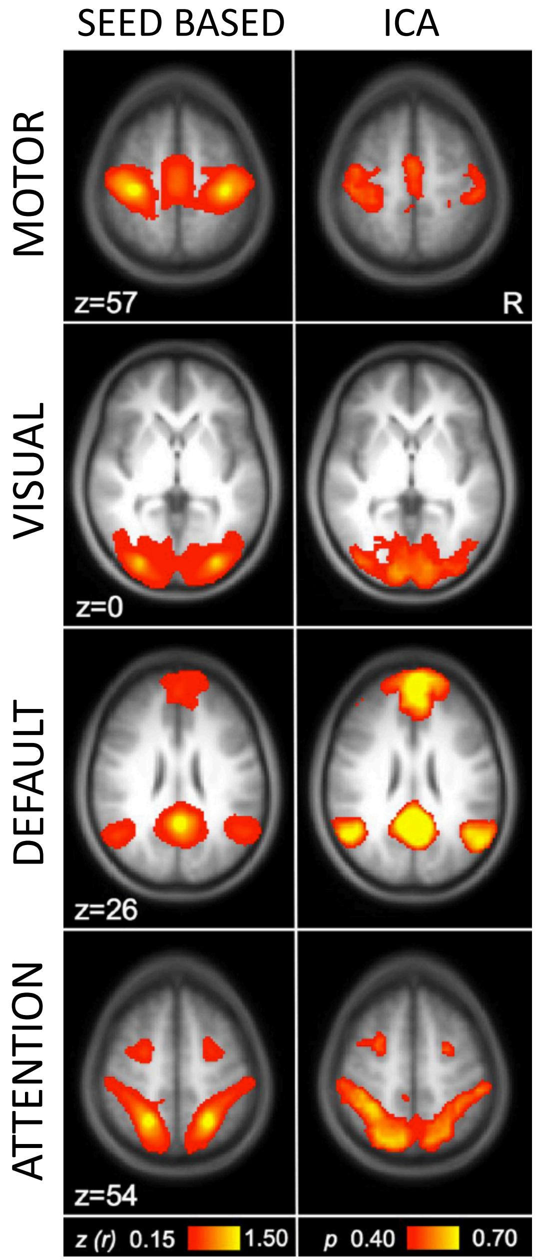


How

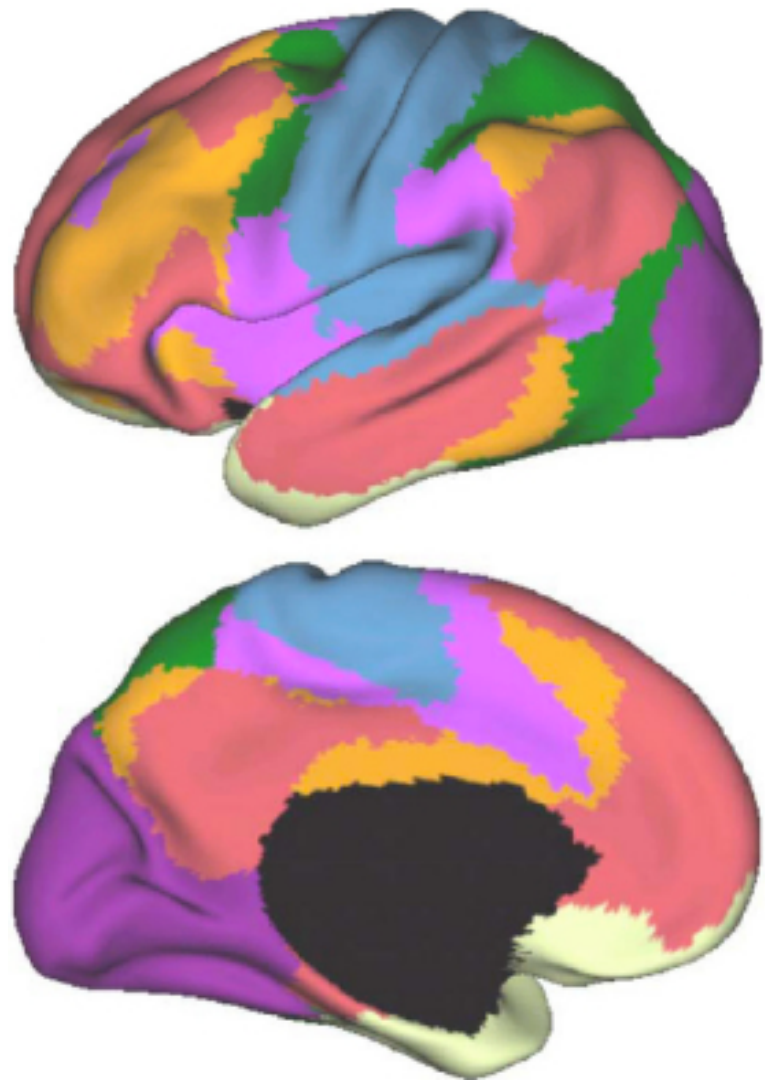


Spontaneous Activity Within Seed Region

Biswal et al., MRM, 1995



Van Dijk et al., 2010



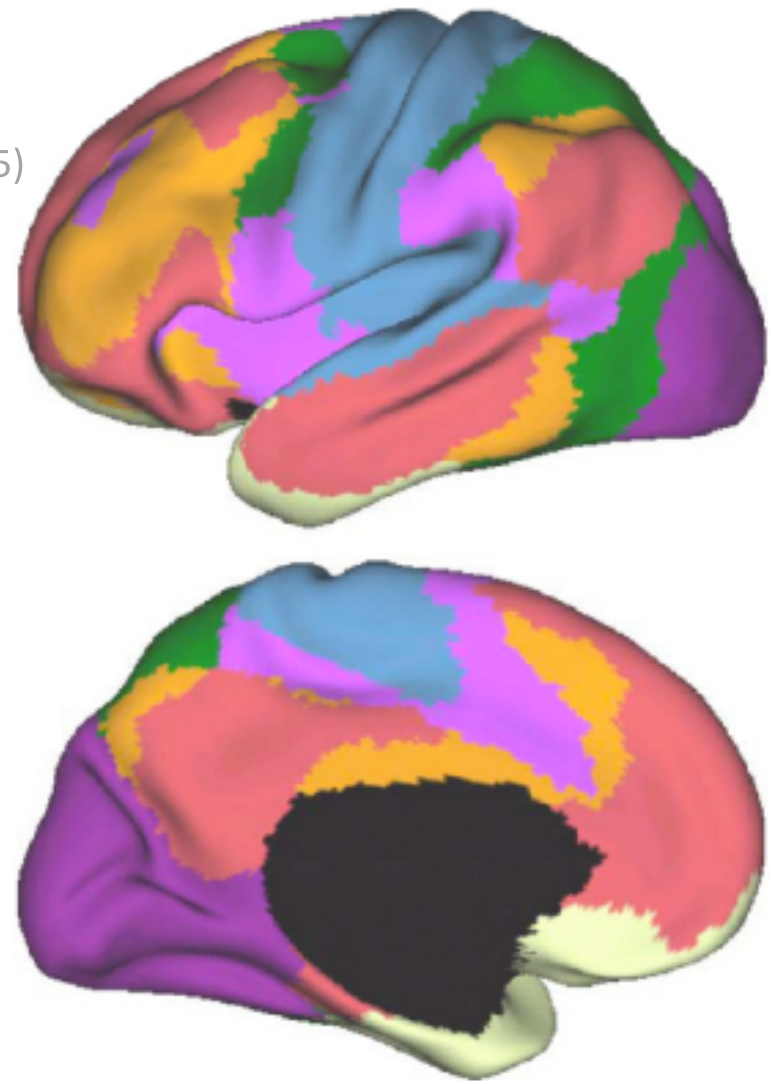
Yeo et al., 2011

Functional connectivity MRI (fcMRI)

Measures temporal coherence among brain regions (Biswal et al., 1995)

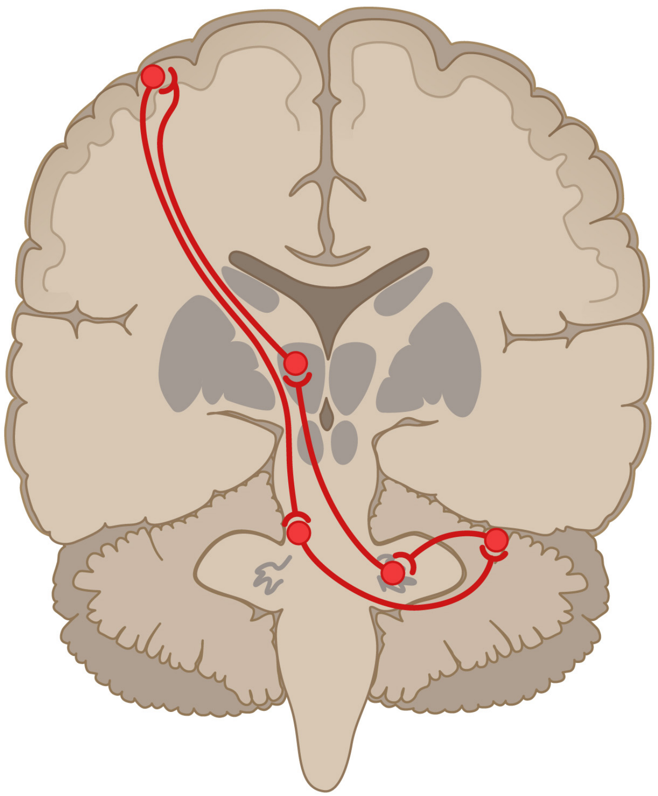
Shows existing functional-anatomical networks.

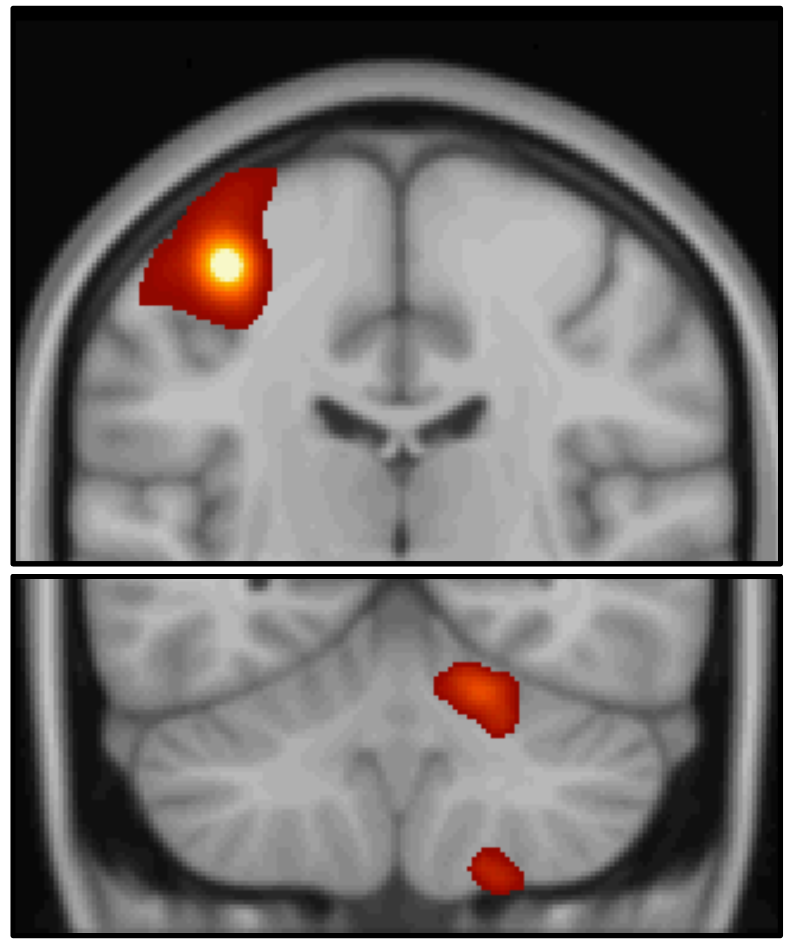
Most networks show coherent activity both during rest and during tasks (Fransson, 2006)



Yeo et al., 2011

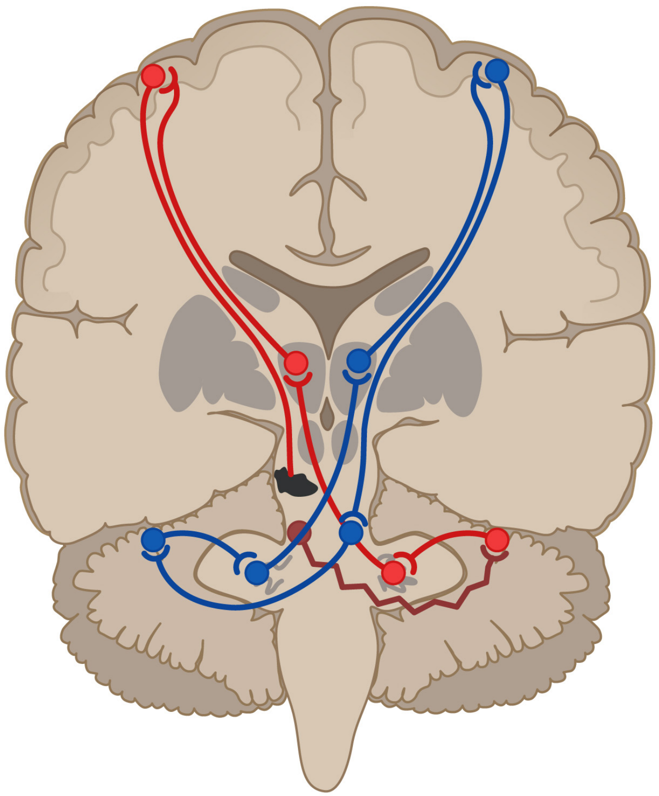
Cerebro-Cerebellar Circuits

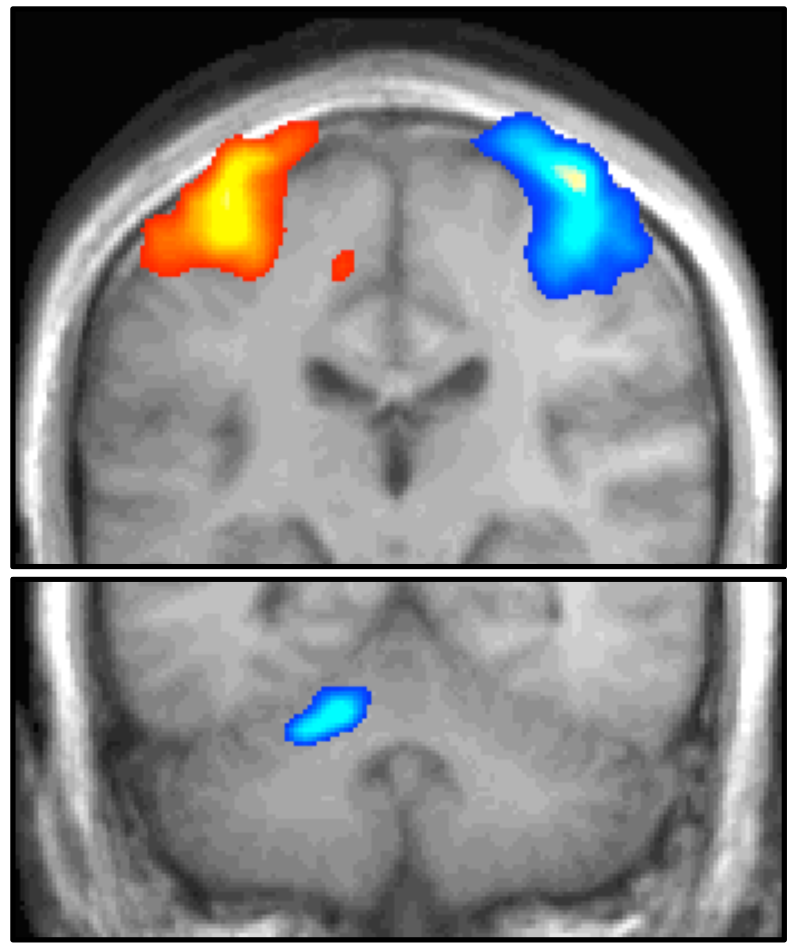




Krienen and Buckner, 2009, CerebCortex

Cerebro-Cerebellar Circuits





Lu et al., 2011, JNeurosci

fcMRI methods

1. Seed based analysis
2. Independent component analysis (ICA)
3. Graph analytic approaches
4. Clustering

Seed based analysis

- Standard fMRI pre-processing:
  - Slice time correlation
  - Motion correction
  - Spatial normalization to common atlas space (Talairach / MNI)
  - Spatial smoothing (Gaussian filter)

- Additional pre-processing:
  - Bandpass filter (retaining frequencies slower than 0.08 Hz or between 0.009 – 0.08 Hz)
  - Removal of any residual effects of motion by regressing out the motion correction parameters
  - **Removal of physiological noise**

    (i.e. mostly concerned with variability in heart rate and respiration)

Removal of physiological noise

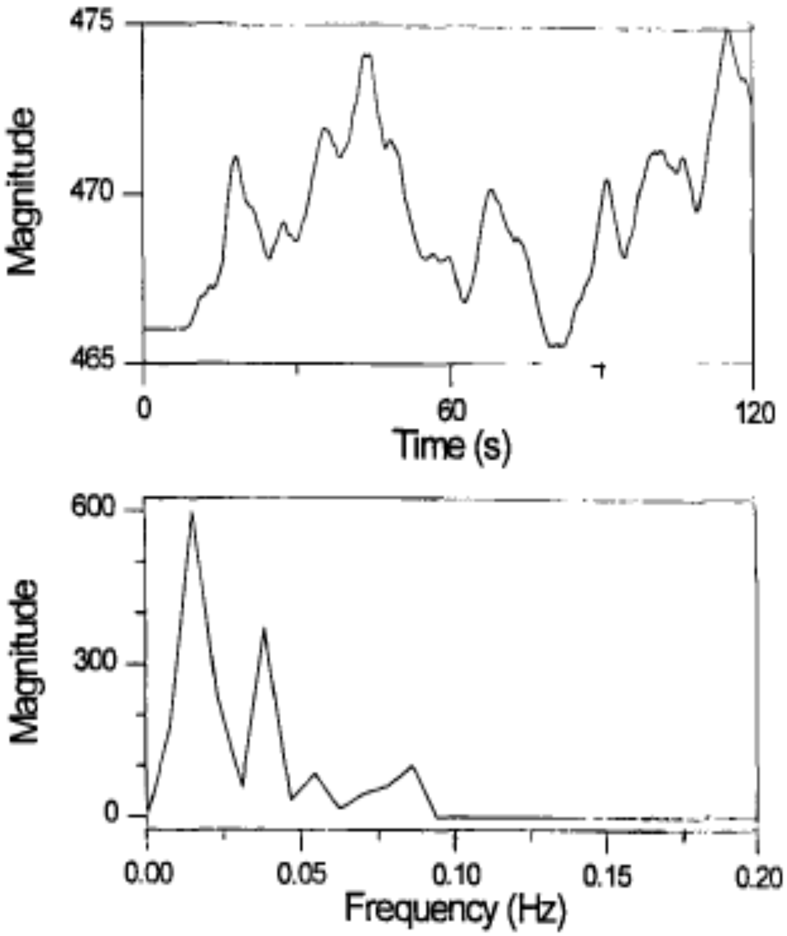
- By regressing out signals in the brain that are believed to contain noise:
  - Signal from ventricles
  - Signal from white matter
    (Dagli et al. 1999; Windischberger et al. 2002)
  - Signal averaged over the whole brain (Desjardins et al., 2001; Corfield et al., 2001; Macey et al. 2004)

- By measuring variability in heart rate and respiration and regressing it out:
  - RETROICOR (Glover et al., 2002)
  - RVT (Birn et al., 2006)
  - RVHRCOR (Chang and Glover, 2009)

- By estimating variability in heart rate and respiration and regressing it out:
  - PESTICA (Beall and Lowe, 2007; 2010)
  - CompCor (Behzadi et al., 2007; also implemented in Sue Whitfield-Gabrieli's Conn toolbox)
  - CORSICA (Perlbarg et al., 2007)

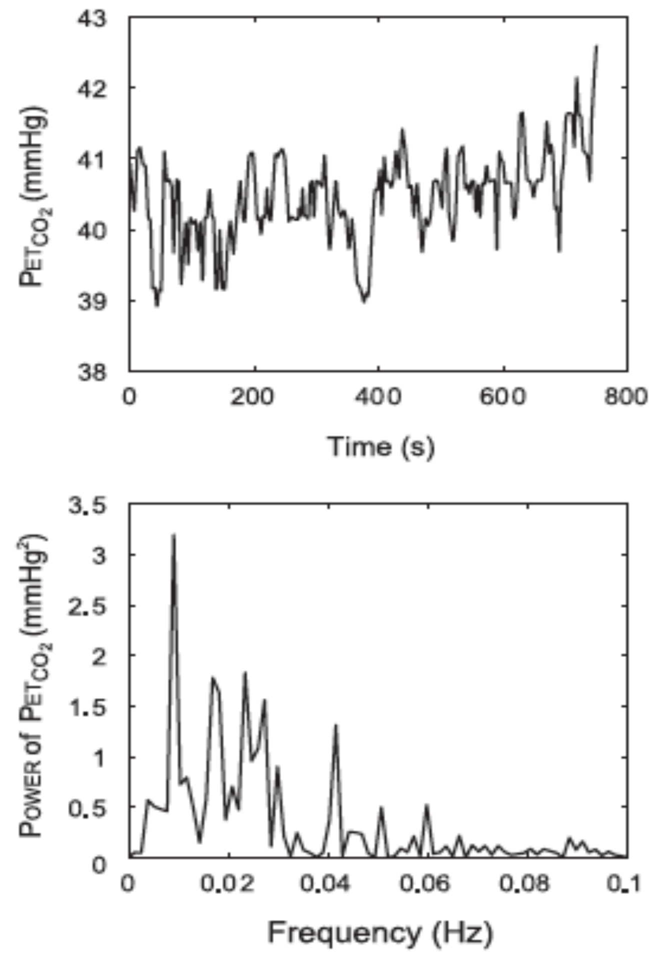
Removal of physiological noise

Low frequency BOLD fluctuations



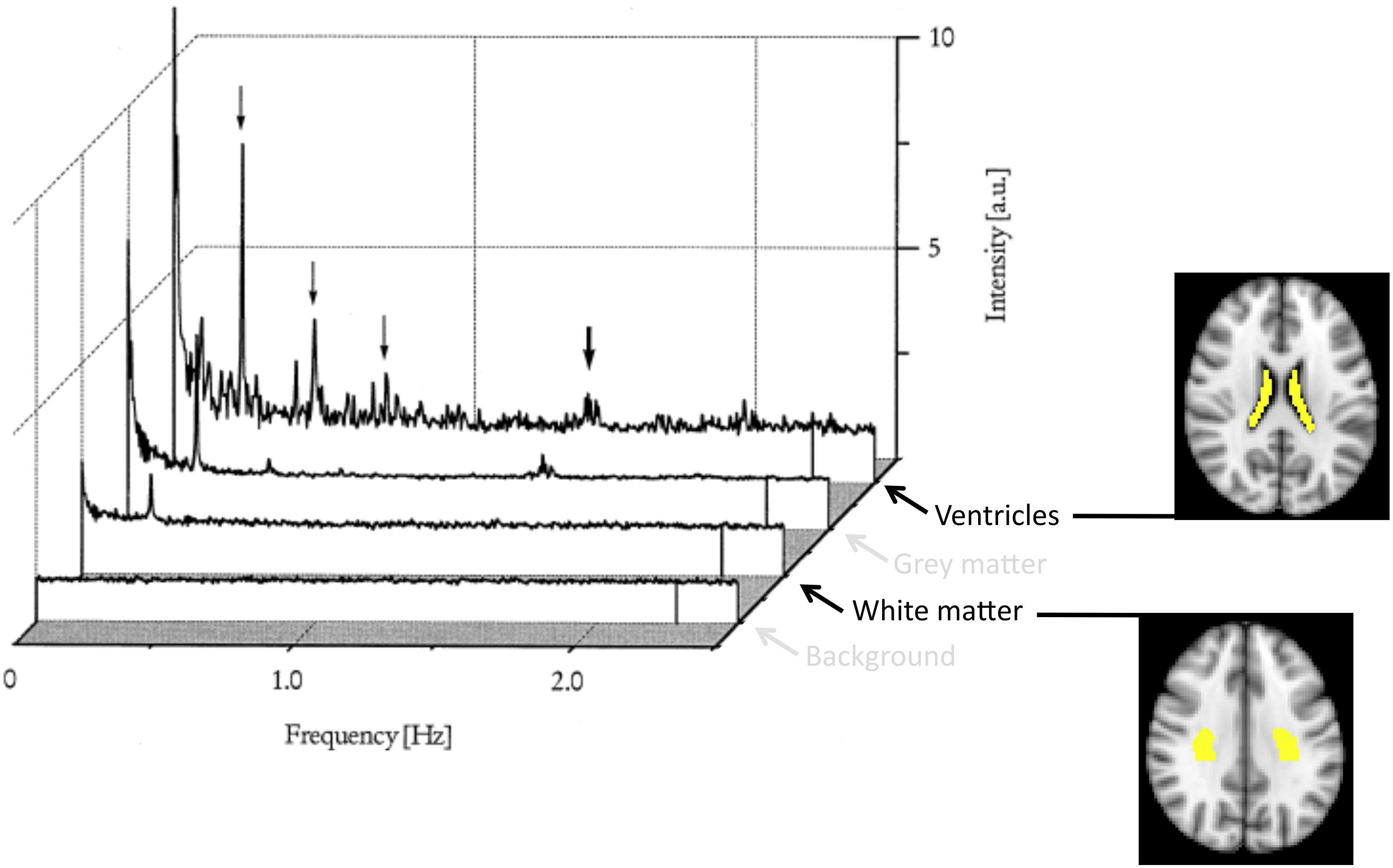
Biswal et al., 1995

Carbon dioxide fluctuations



Wise et al., 2004

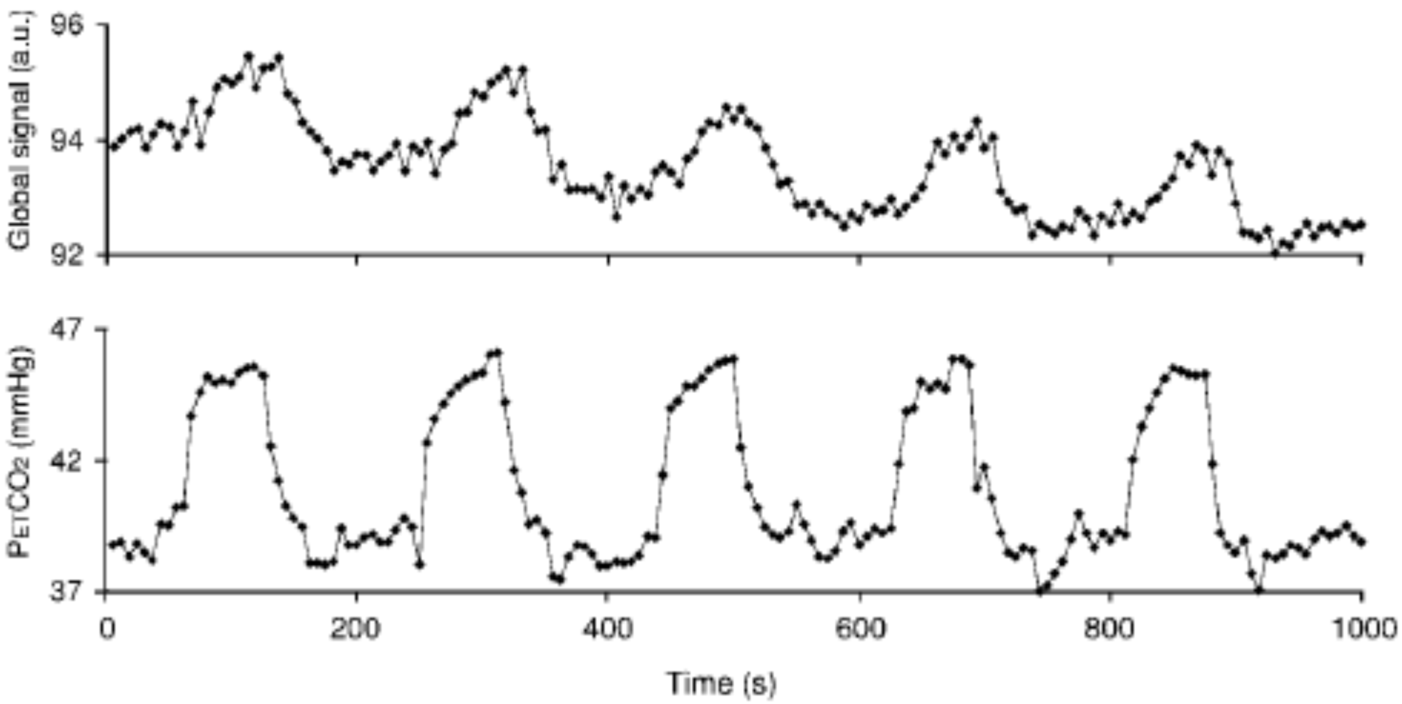
Ventricles and white matter signal

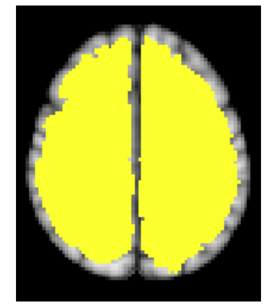


Windischberger et al. 2002

Whole brain signal

Whole brain signal is related to end-tidal carbondioxide during periods of hypercapnia

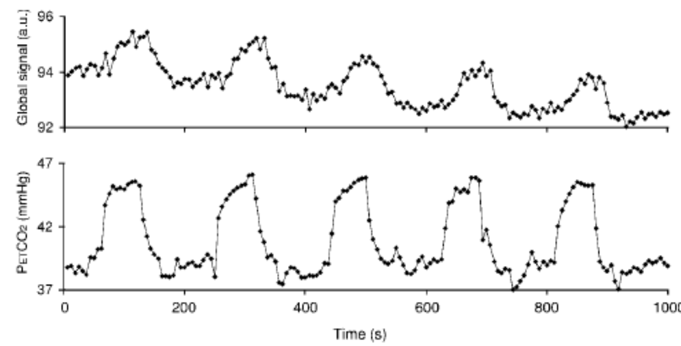




Corfield et al., 2001

Removal of whole brain signal

Pros:

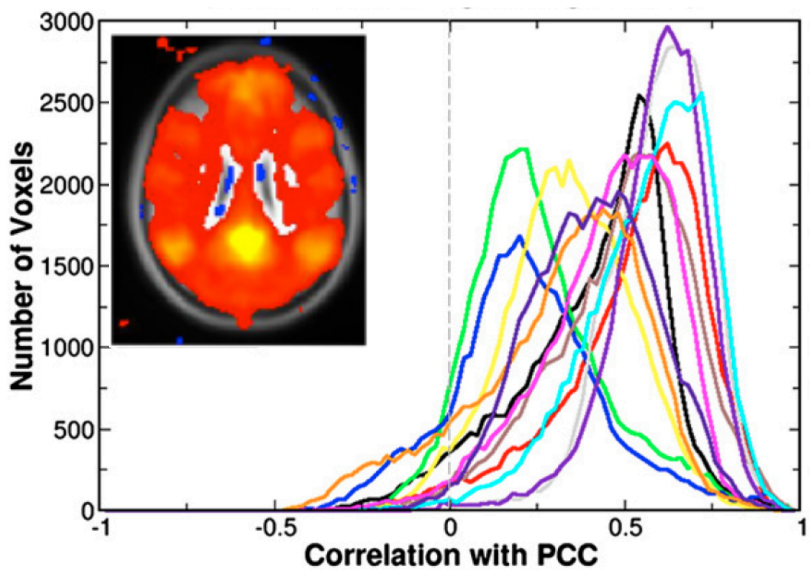


- Captures breathing variations (Corfield et al., 2001)
- Known to remove noise (Macy et al., 2004)
- Increased specificity of functional connectivity maps of the motor system (Weisenbacher et al., 2009)
- Shows fine neuroanatomical specificity not seen without global signal correction (Fox et al., 2009)

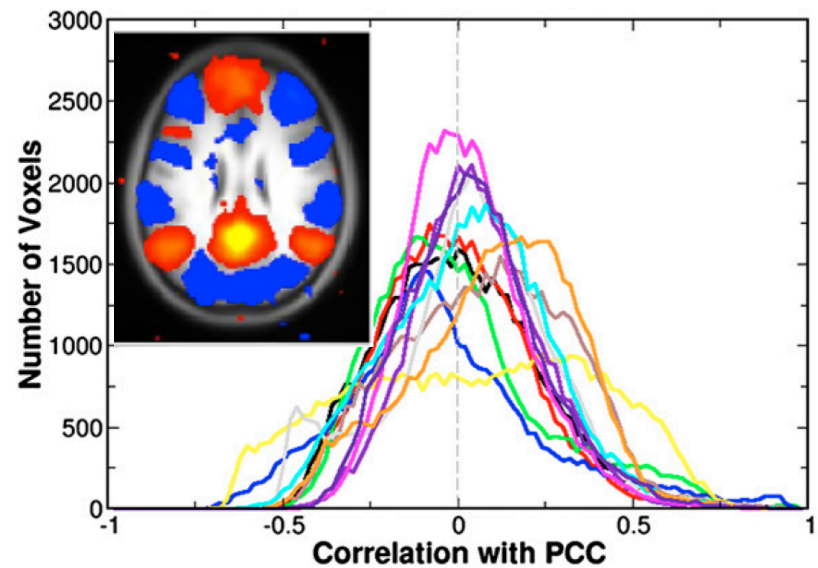
Removal of whole brain signal

Cons:

Before



After



Murphy et al. 2009; Van Dijk et al., 2010

See for discussion: Vincent et al., 2006; Fox et al. 2009; Murphy et al. 2009; Weissenbacher et al., 2009; Van Dijk et al., 2010; Saad et al., 2012

Removal of whole brain signal

What does this practically mean?

- Whenever possible collect heart rate (with e.g. pulse oximeter or ECG) and respiration signals (with e.g. pneumatic belt around the abdomen or with a mouth piece that measures airflow)

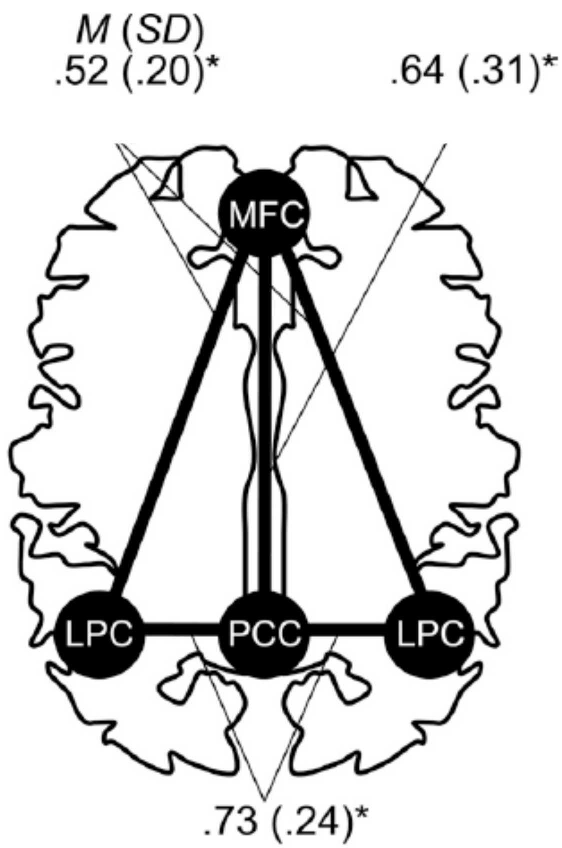
- Removal of the whole brain signal is a viable step especially if one has not measured the actual variability in heart rate and respiration.

- Negative correlations after whole-brain signal regression should be interpreted with utmost caution.

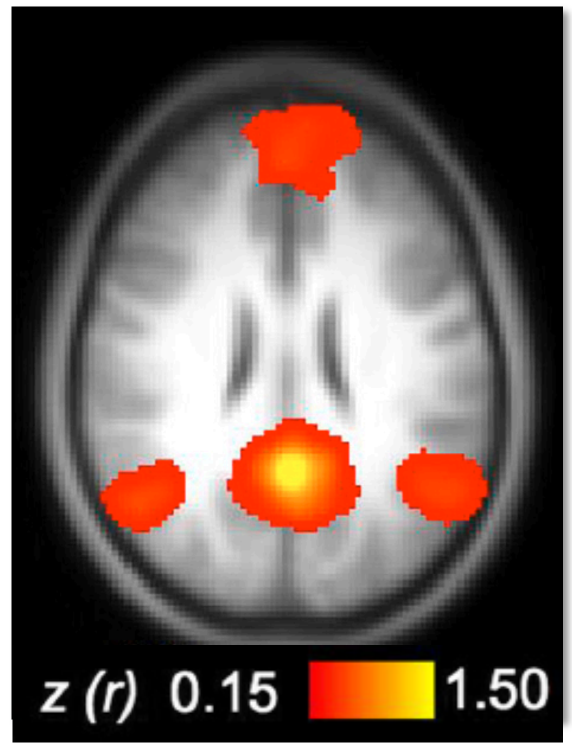
See for discussion: Vincent et al., 2006; Fox et al. 2009; Murphy et al. 2009; Weissenbacher et al., 2009; Van Dijk et al., 2010; Saad et al., 2012

Basic measures seed based analysis

A. Correlation values between regions of interest:



B. A map from a seed region of interest:

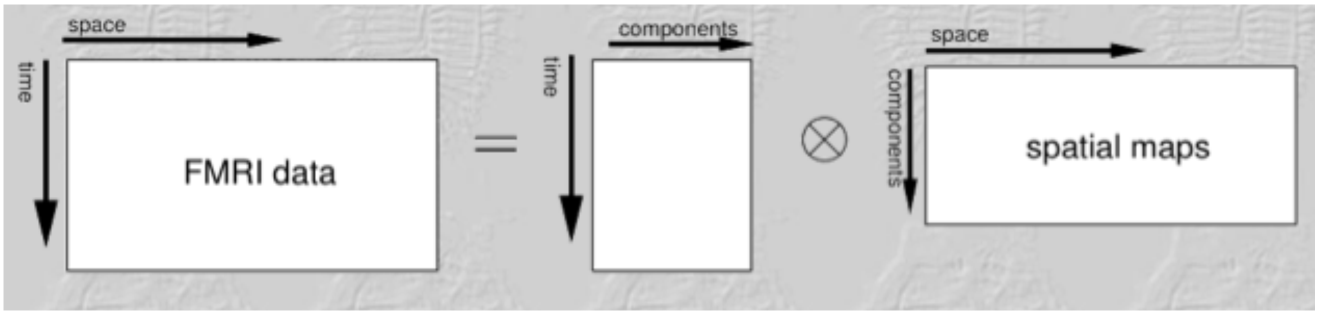


fcMRI methods

1. Seed based analysis
2. Independent component analysis (ICA)
3. Graph analytic approaches
4. Clustering

Independent component analysis (ICA)

SINGLE SUBJECT



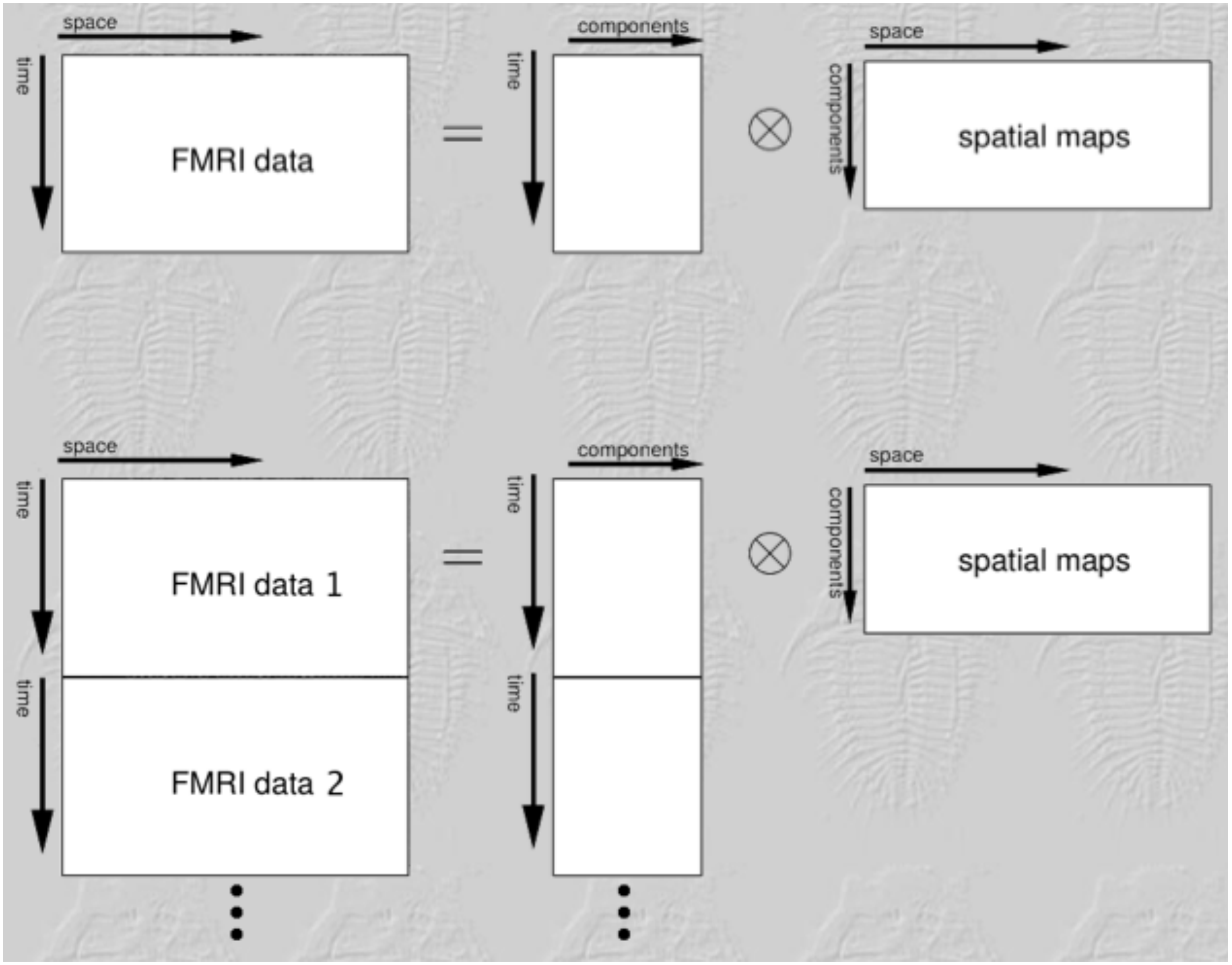
Data is decomposed into a set of <u>spatially independent</u> maps and corresponding time courses

[MELODIC: http://fsl.fmrib.ox.ac.uk/fsl/melodic/](http://fsl.fmrib.ox.ac.uk/fsl/melodic/) Beckmann et al., 2005
[GIFT: http://mialab.mrn.org/software/](http://mialab.mrn.org/software/) Calhoun et al., 2001

Independent component analysis (ICA)

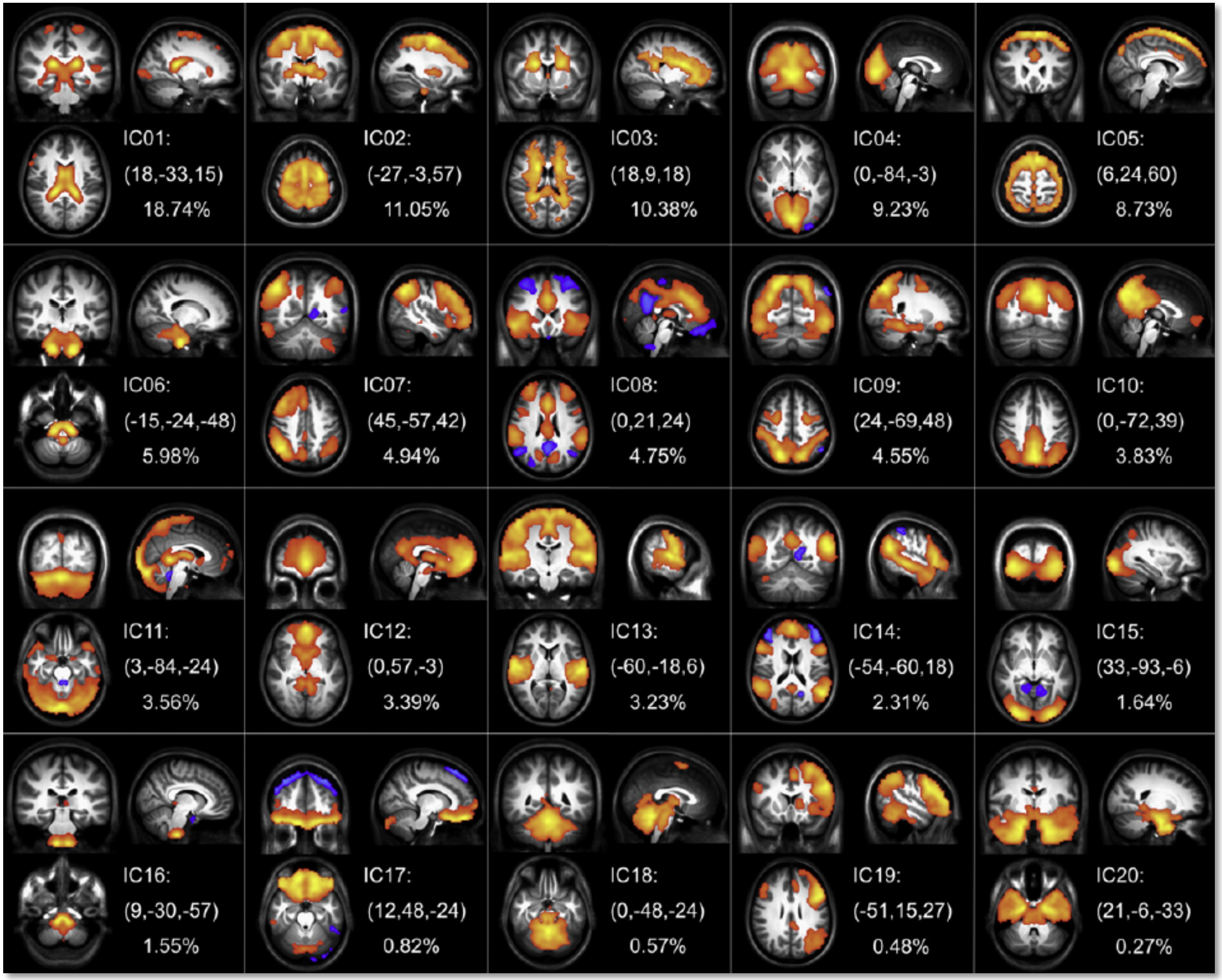
SINGLE SUBJECT

MULTI SUBJECT



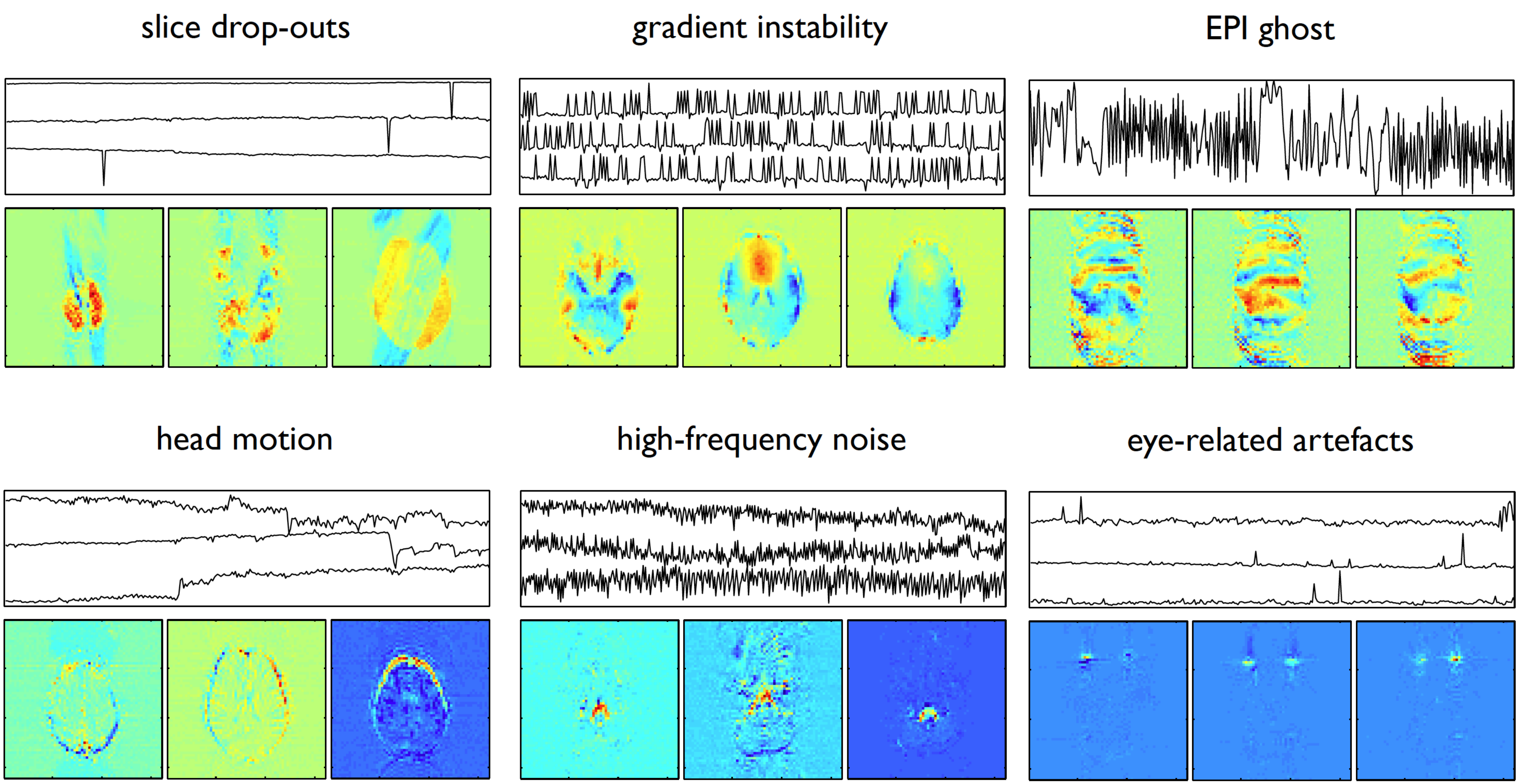
MELODIC: http://fsl.fmrib.ox.ac.uk/fsl/melodic/ Beckmann et al., 2005

GIFT: http://mialab.mrn.org/software/ Calhoun et al., 2001



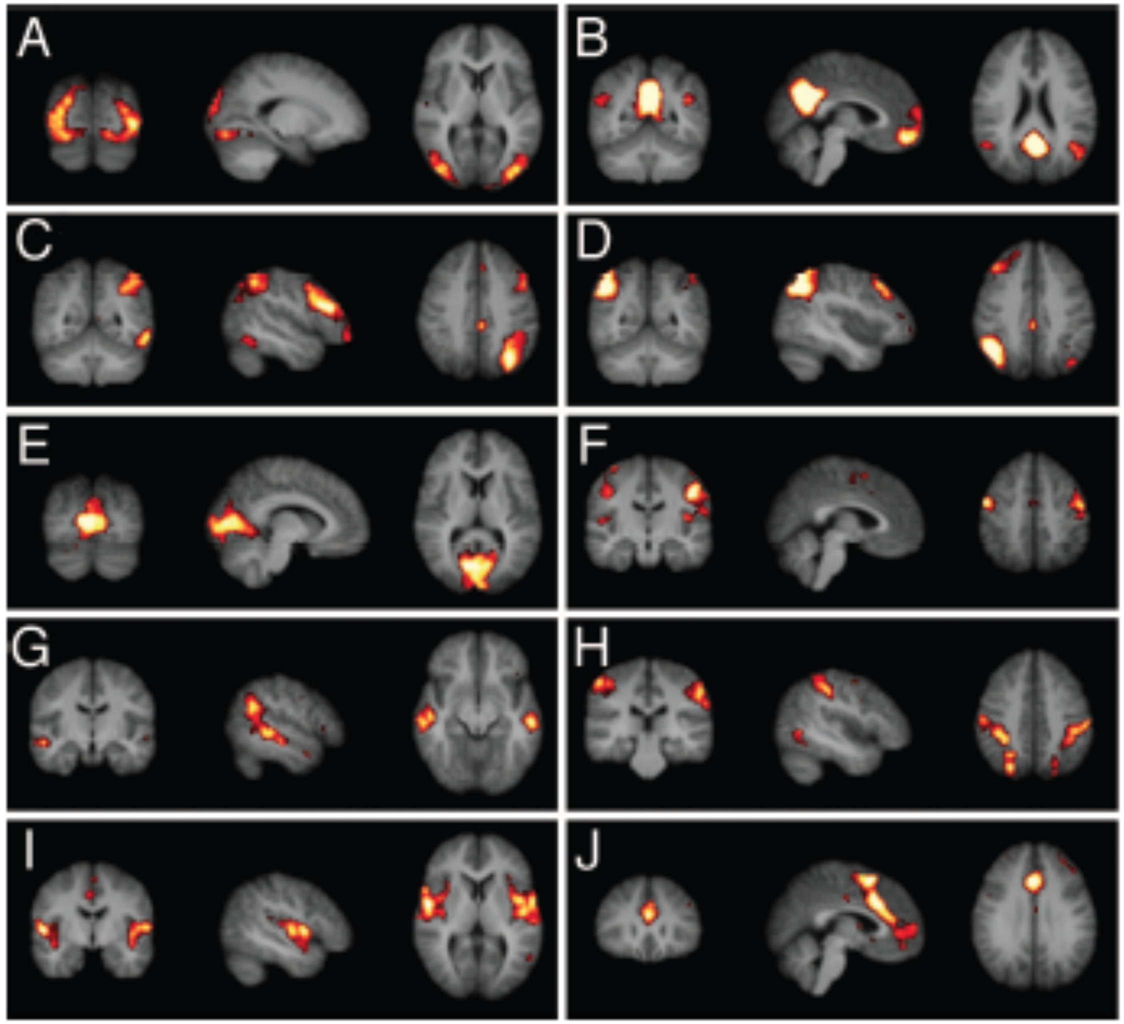
Zou et al., 2010

Noise components



Beckmann et al., 2000 & http://www.fmrib.ox.ac.uk/fslcourse/lectures/melodic.pdf

Neuronal network components



Damoiseaux et al., 2006

Imperial College London

FMRIB
Oxford Centre for Functional MRI of the Brain

Group comparison of resting-state FMRI data using multi-subject ICA and dual regression

1) Concat ICA:

Multiple fMRI data sets are concatenated temporally and ICA is applied in order to identify *large-scale patterns of functional connectivity in the sample*

2) Dual regression:

This is used to identify, within each of the *individual* subjects' fMRI data, spatial maps and associated timecourses corresponding to the multi-subject ICA components.

Beckmann et al., poster HBM, 2009

First papers using dual regression approach:
- Filippini, et al., Distinct patterns of brain activity in young carriers of the APOE-epsilon4 allele. *Proc Natl Acad Sci U S A*. 2009;106(17):7209-14.
- Glahn et al., Genetic control over the resting brain. *Proc Natl Acad Sci U S A*. 2010;107(3):1223-8.

Seed based

Pros:

- Quantification of network strength: one number per subject (easy to relate to other measures such as behavior, white matter (Andrews-Hanna et al., 2007), amyloid pathology (Hedden et al., 2009))
- Input for other other metrics: graph analytic approaches, clustering, multivariate approaches

Cons:

- One needs to choose networks based on prior knowledge of brain systems (e.g. from anatomy, seed regions from the literature)
- Methods for removal of physiological noise not without controversy (Fox et al. 2009; Murphy et al. 2009)

ICA

Pros:

- No prior knowledge of brain systems necessary
- Automatic removal of physiological noise (to a certain extent)

Cons:

- Obtaining one number per subject is not straightforward (goodness-of-fit metric is not without controversy (Franco et al., 2009))

More regarding methods

J Neurophysiol 103: 297–321, 2010.
First published November 4, 2009; doi:10.1152/jn.00783.2009.

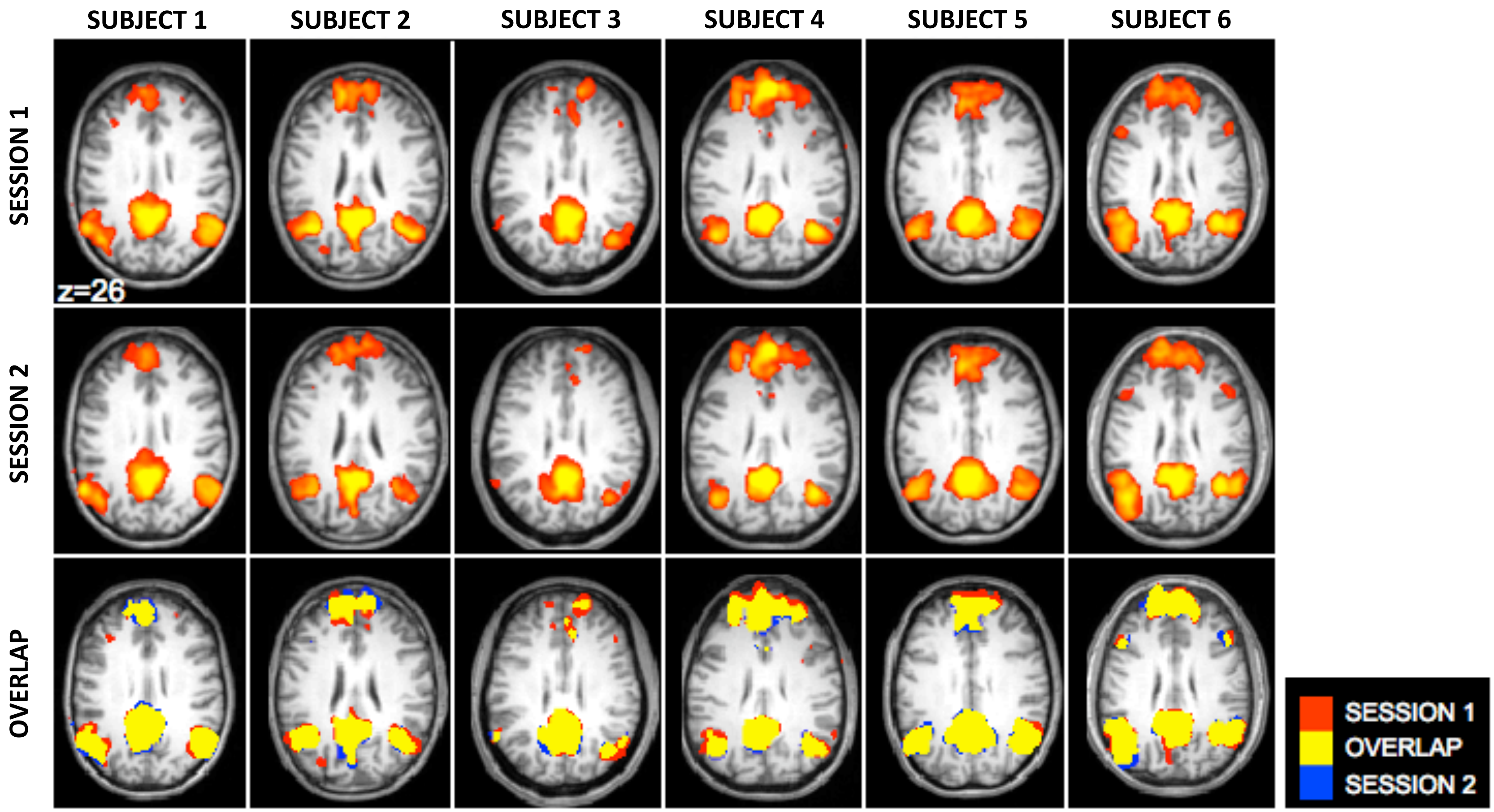
Intrinsic Functional Connectivity As a Tool For Human Connectomics: Theory, Properties, and Optimization

Koene R. A. Van Dijk,[1,2,3] Trey Hedden,[1,2] Archana Venkataraman,[4] Karleyton C. Evans,[5] Sara W. Lazar,[5] and Randy L. Buckner[1,2,5,6]

- Test-retest reliability
- Effects of scan length
- Seed-based analysis versus ICA
- "Time on task" effects within a resting resting-state run
- Differences between:
  - Two scans of 6 min versus one scan of 2 min
  - Temporal resolution: TR=2.5 versus TR=5.0
  - Spatial resolution: 2x2x2 versus 3x3x3
- Effects of task/instruction (eyes open, eyes closed, word classification task)

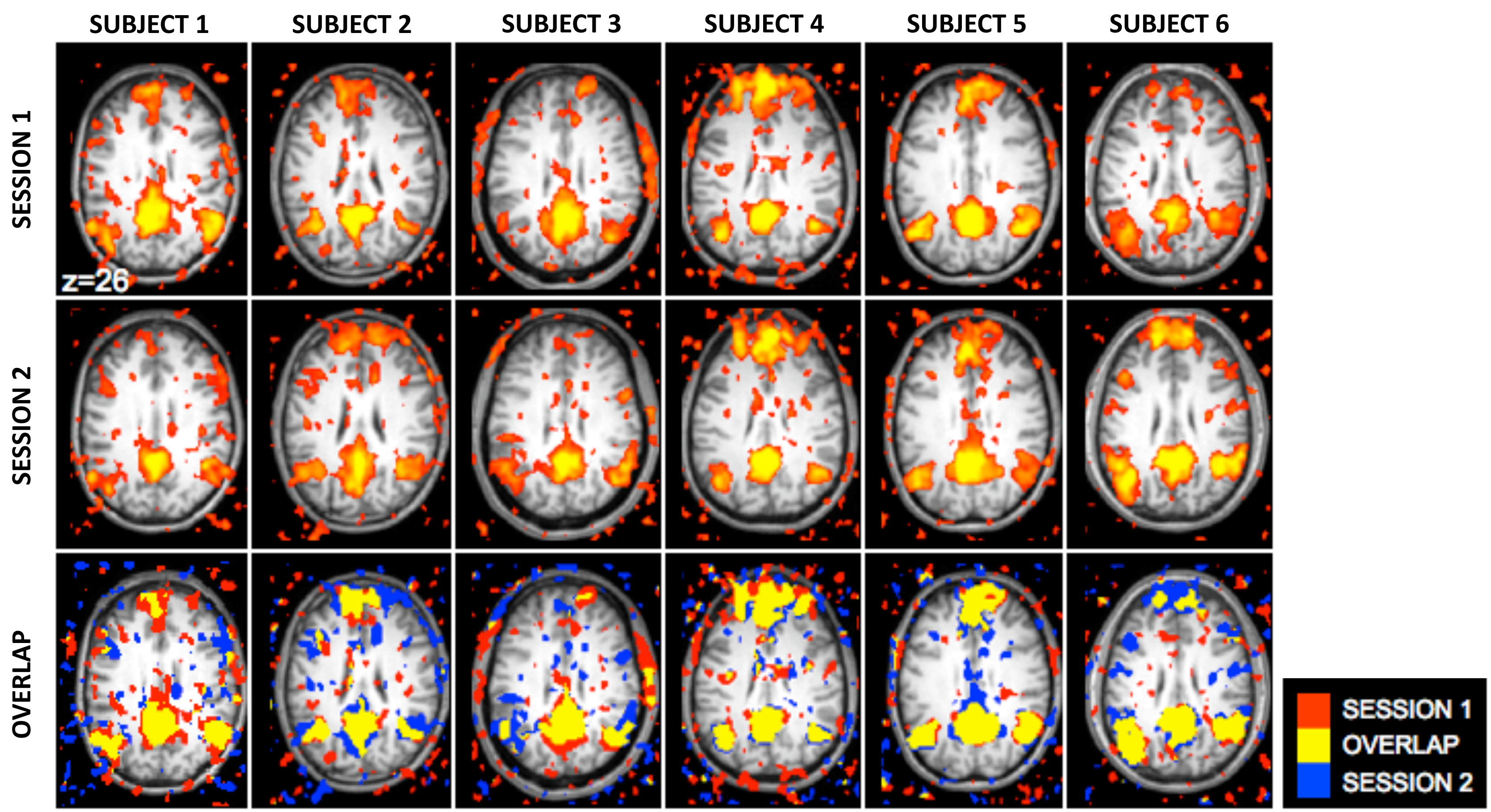
Free online access: http://jn.physiology.org/content/103/1/297.full

Reliability of network measures



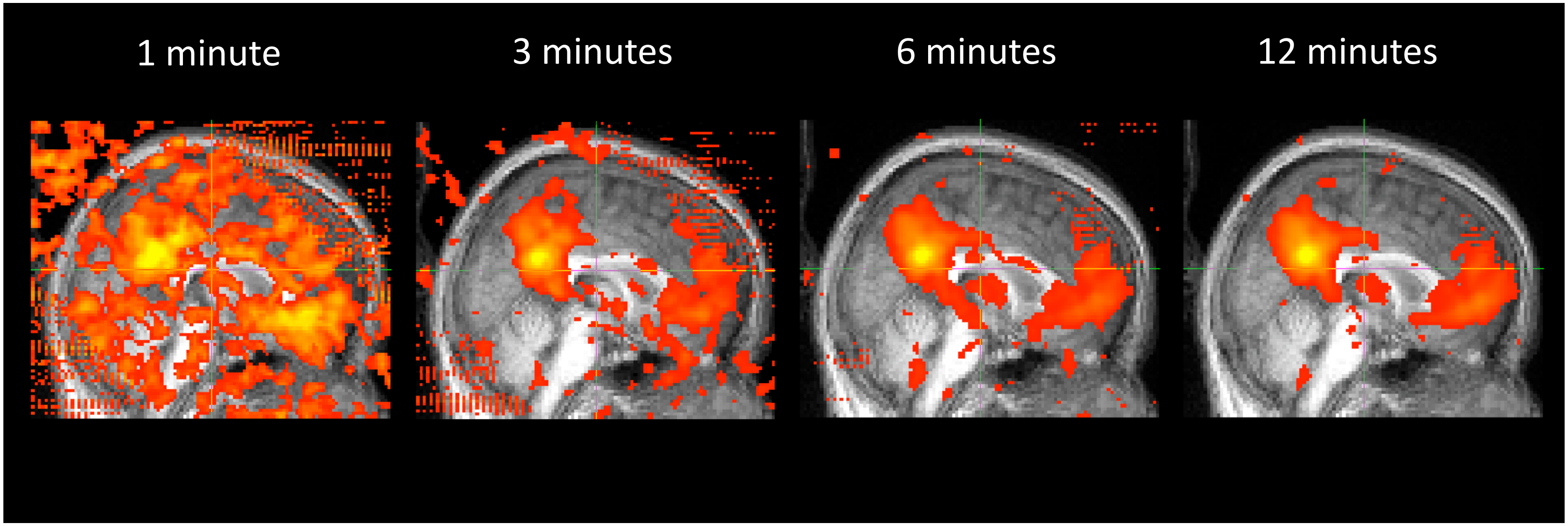
Van Dijk et al., 2010, JNeurophys

Reliability of network measures



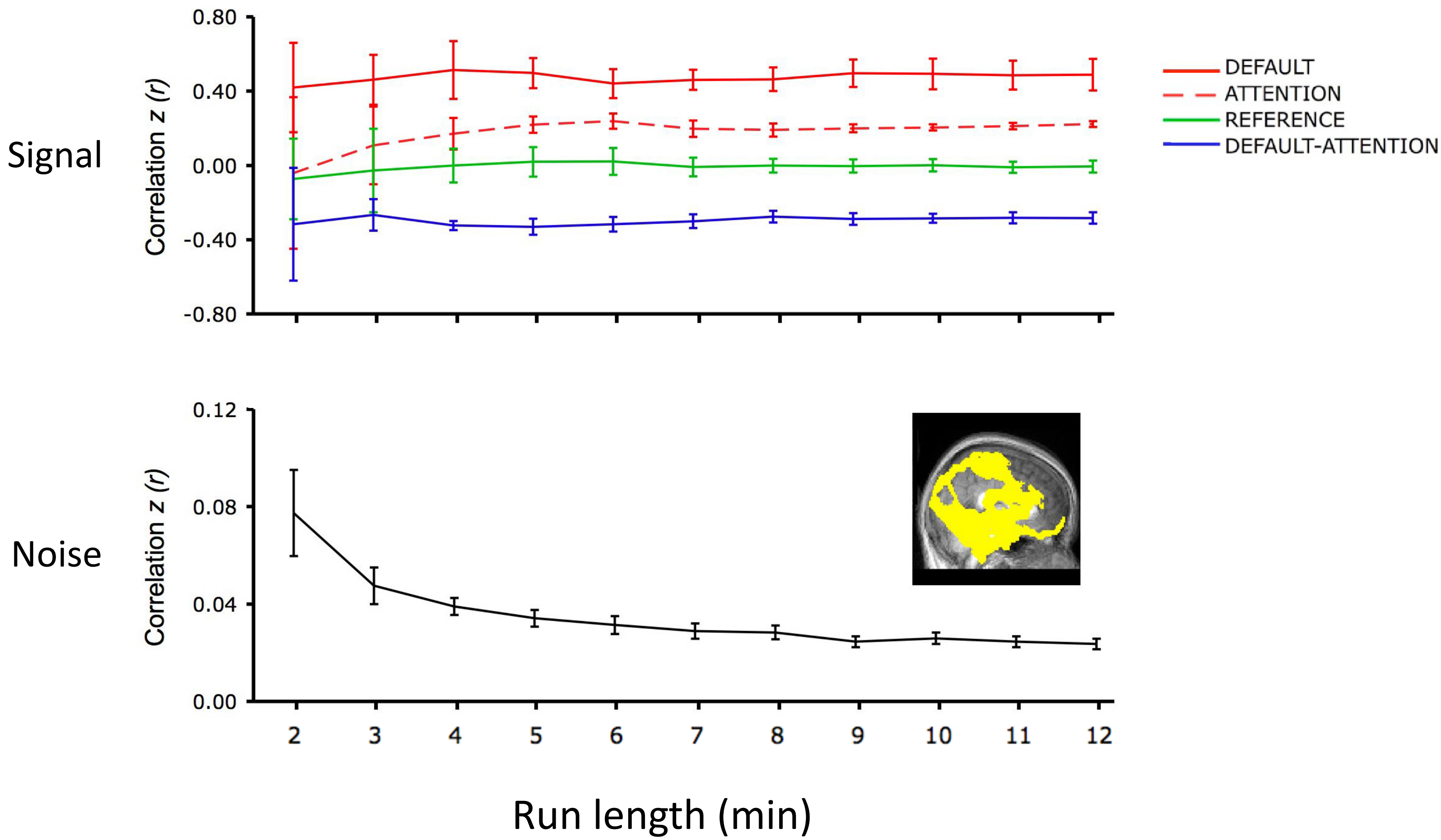
Van Dijk et al., 2010, JNeurophys

Short acquisition times are sufficient



Van Dijk et al., 2010, JNeurophys

Short acquisition times are sufficient



Van Dijk et al., 2010, JNeurophys

Confounding effects of head motion

NeuroImage 59 (2012) 431–438

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

The influence of head motion on intrinsic functional connectivity MRI

Koene R.A. Van Dijk [a,b], Mert R. Sabuncu [b,c], Randy L. Buckner [a,b,d,e,*]

NeuroImage 59 (2012) 2142–2154

Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion

Jonathan D. Power [a,*], Kelly A. Barnes [a], Abraham Z. Snyder [a,b], Bradley L. Schlaggar [a,b,c,d], Steven E. Petersen [a,b,d,e]

NeuroImage 60 (2012) 623–632

Contents lists available at SciVerse ScienceDirect

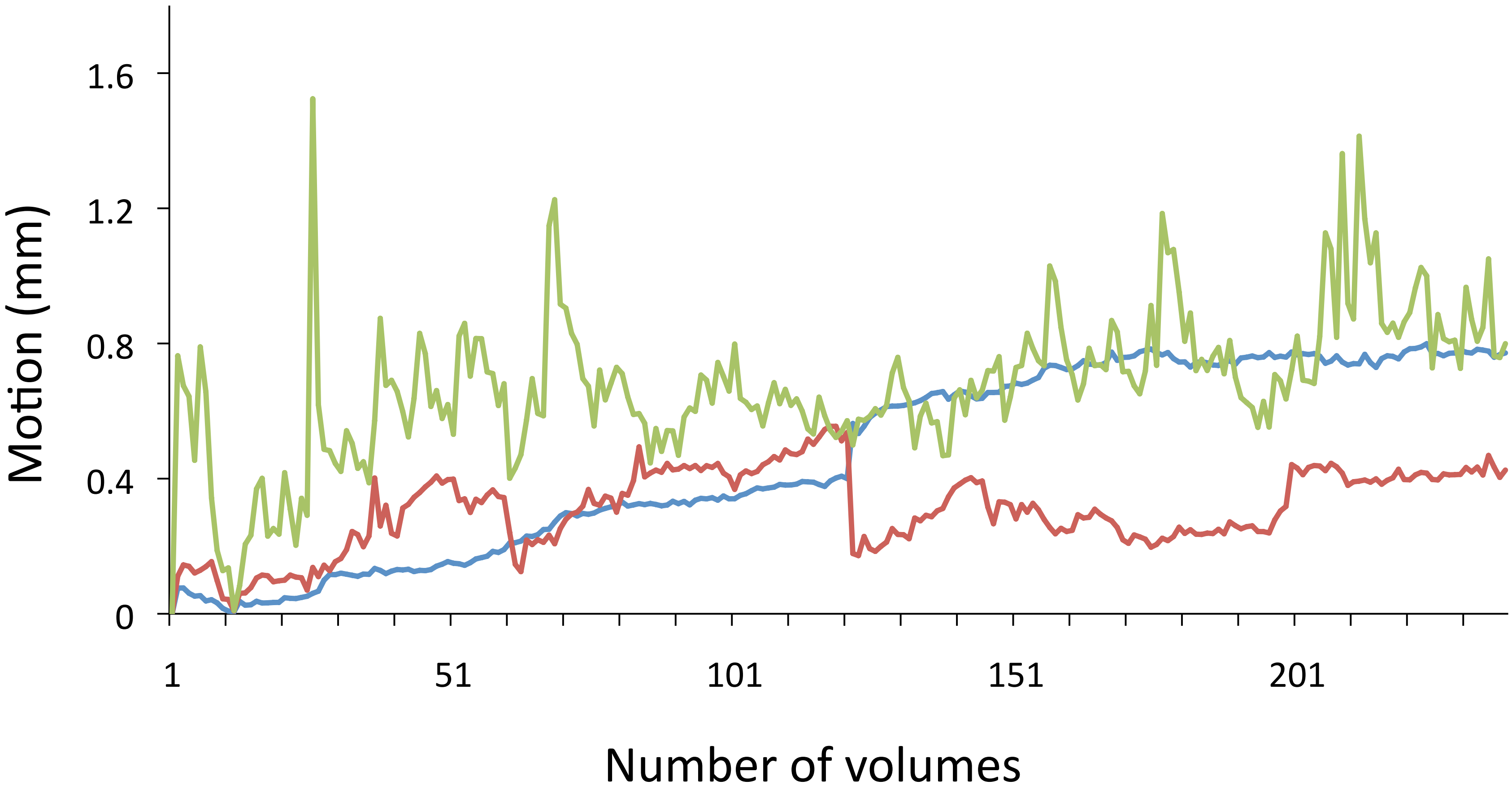
NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Impact of in-scanner head motion on multiple measures of functional connectivity: Relevance for studies of neurodevelopment in youth[☆]

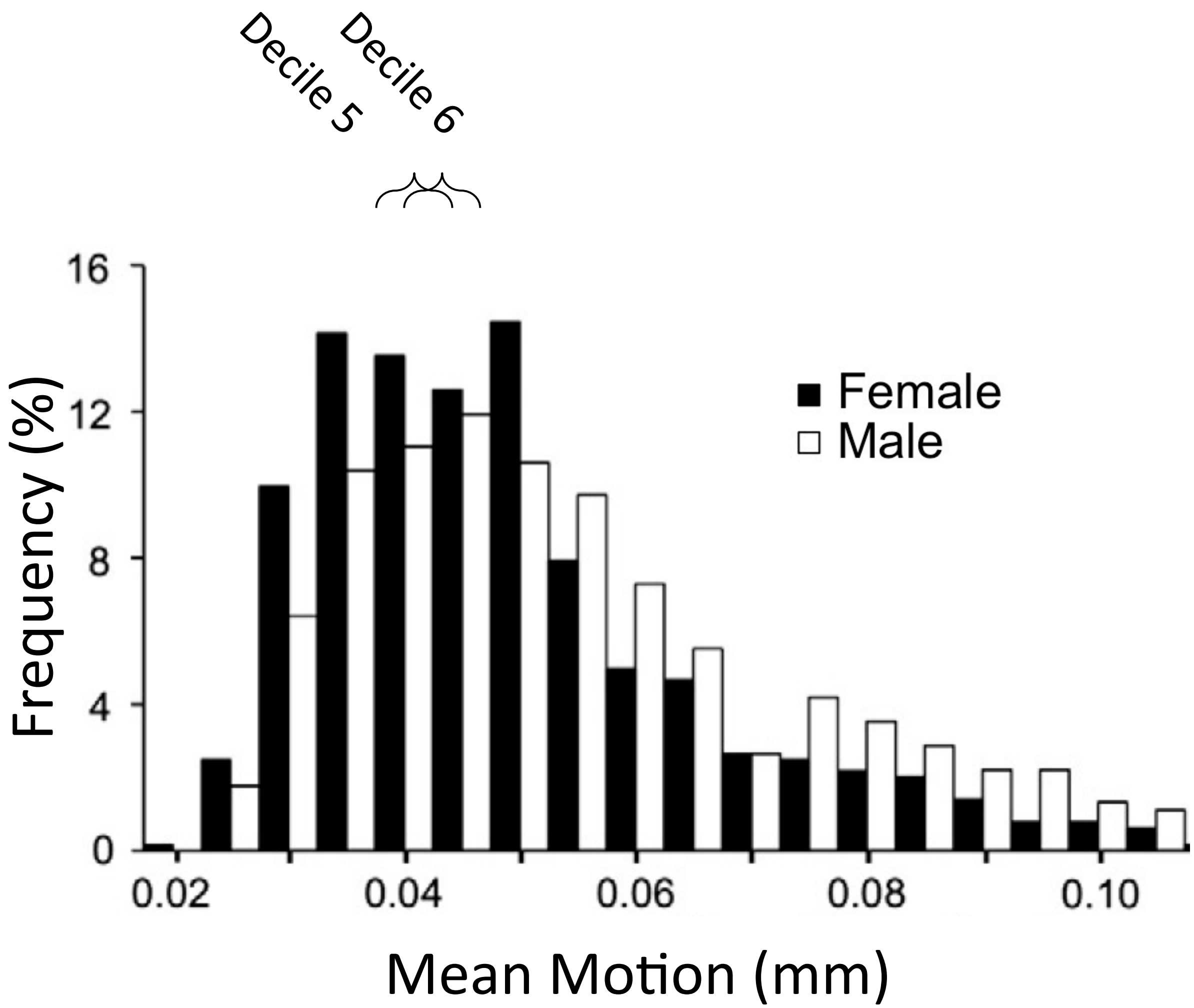
Theodore D. Satterthwaite [a,*], Daniel H. Wolf [a], James Loughead [a], Kosha Ruparel [a], Mark A. Elliott [b], Hakon Hakonarson [c], Ruben C. Gur [a,b,d], Raquel E. Gur [a,d]

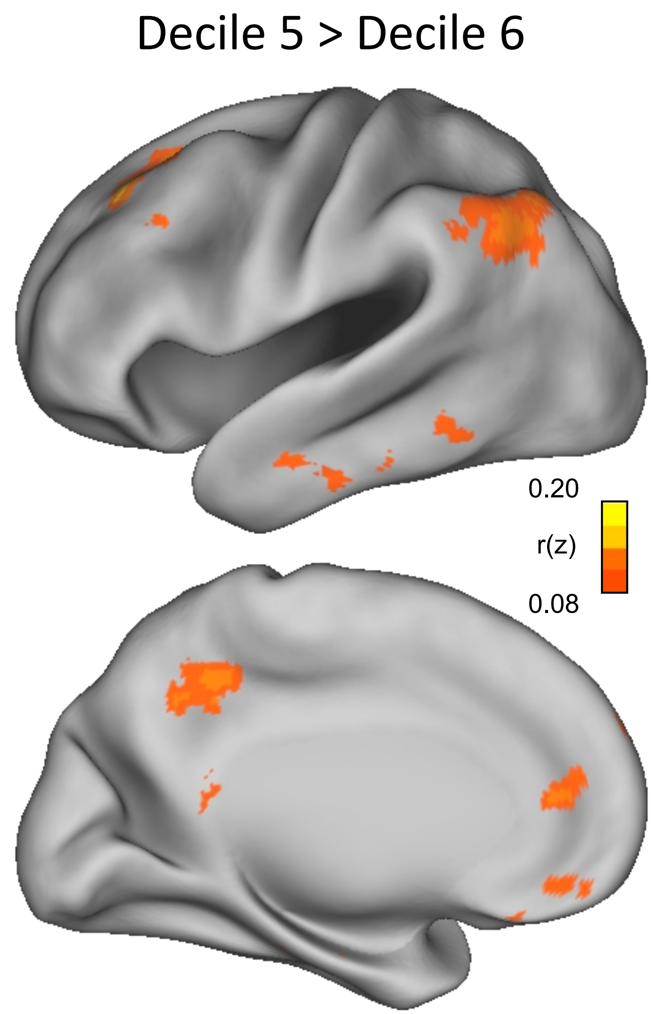
Translational motion of 3 subjects



Van Dijk et al., 2012, Neuroimage

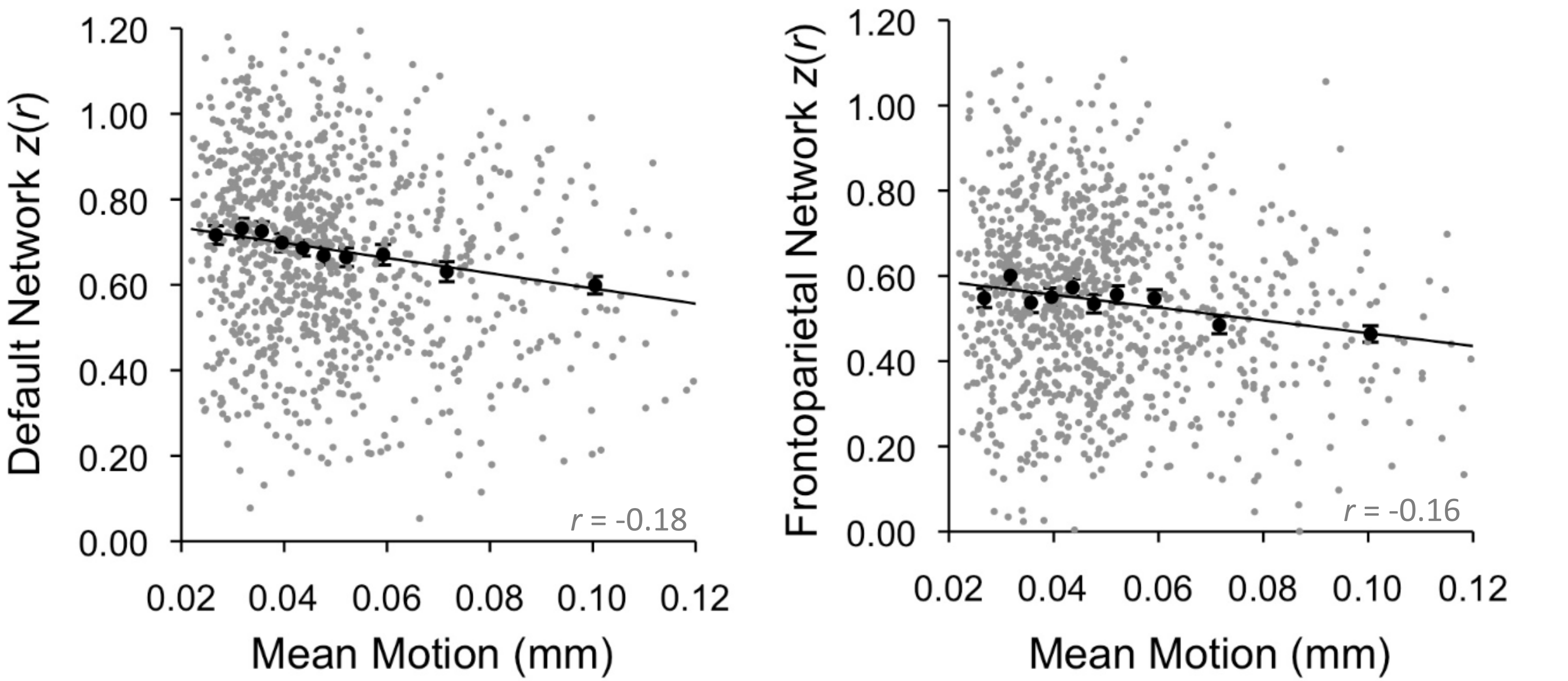
Head motion is a problem





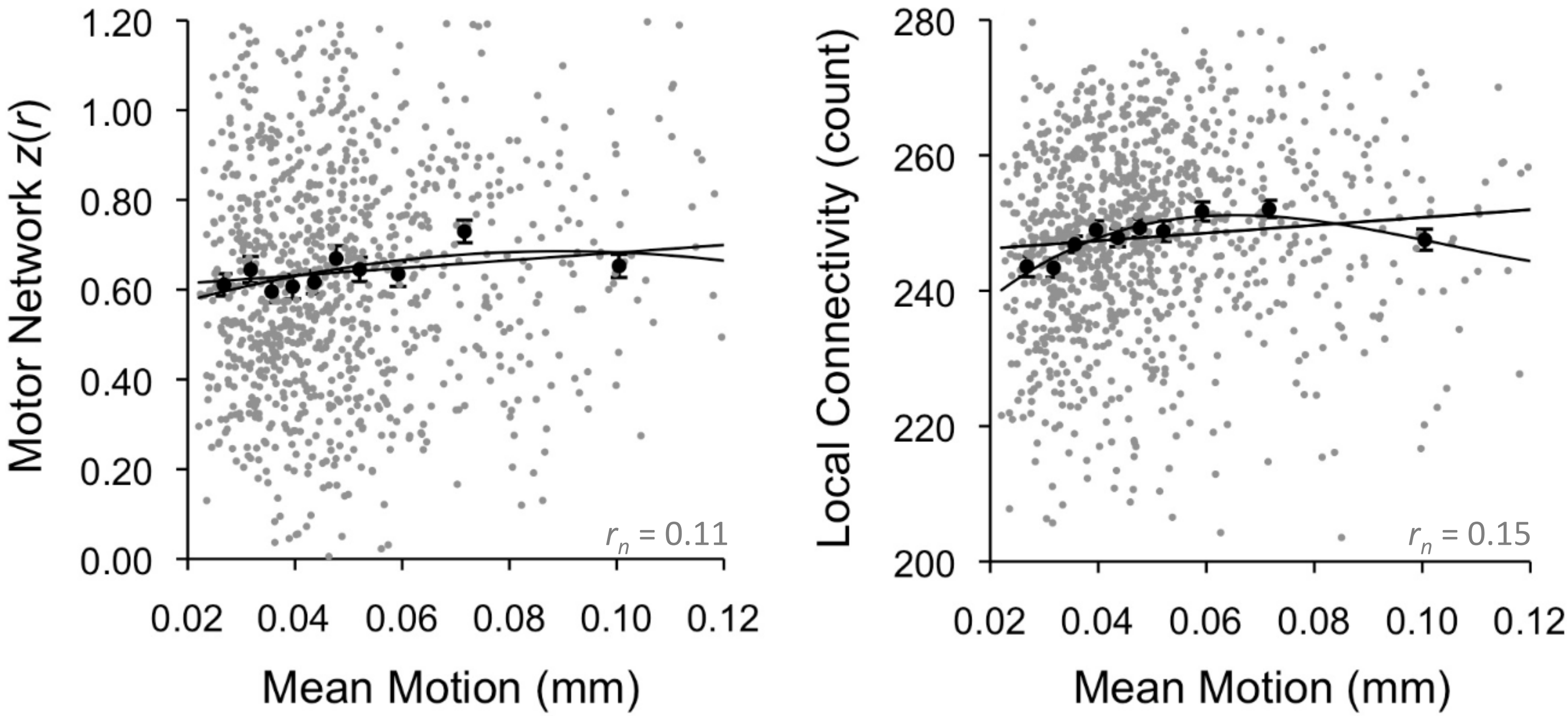
Van Dijk et al., 2012, Neuroimage

Motion decreases correlation strength in large-scale networks



Van Dijk et al., 2012, Neuroimage

Motion increases local functional coupling

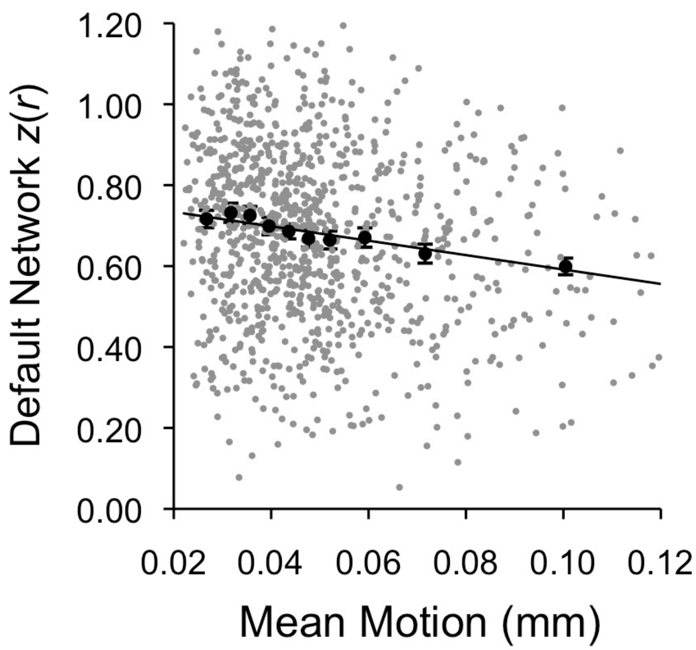


Van Dijk et al., 2012, Neuroimage

Conclusions regarding head motion

1. Head motion has a significant effect on measures of network strength

2. Most variance in fcMRI metrics is not related to motion



3. Carefully consider effects of head motion in studies that contrast groups:
   - Children vs adults
   - Old vs young
   - Patients vs controls

4. Improve effectiveness of current regression techniques

5. Consider "scrubbing" epochs were motion occurred *(e.g. Power et al., 2012)*

Van Dijk et al., 2012, Neuroimage

Thank you for your attention!

References:

Van Dijk KRA, Hedden T, Venkataraman A, Evans KC, Lazar SW, and Buckner RL (2010) Intrinsic Functional Connectivity As a Tool For Human Connectomics: Theory, Properties, and Optimization. *Journal of Neurophysiology.* 103: 297-321.
Full text at: http://jn.physiology.org/content/103/1/297.full

Van Dijk KRA, Sabuncu MR, and Buckner RL. (2012) The Influence of Head Motion on Intrinsic Functional Connectivity MRI. *NeuroImage*. 59(1):431-8.
Abstract at: http://www.sciencedirect.com/science/article/pii/S1053811911008214
(send me an e-mail if you would like a PDF)

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Web: http://www.nmr.mgh.harvard.edu/~kdijk/