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
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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

images courtesy Jen Evans (NIH)
Resting State fMRI
Functional connectivity

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

Brain image adapted from: http://www.cgl.ucsf.edu/home/goddard/temp/highlight14/highlight14.html
Resting-state functional connectivity

Biswal et al., 1995
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)

Torrisi et al. 2015
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

Kenet et al, 2003
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

Fox et al. 2014

Greicius et al. 2004
Table 1. Number of publications in which fC or resting state approaches have been used to study a variety of disorders and conditions (PubMed search on 25 January 2012)

<table>
<thead>
<tr>
<th>Disorder/Condition</th>
<th># studies</th>
</tr>
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<tbody>
<tr>
<td>Schizophrenia</td>
<td>45</td>
</tr>
<tr>
<td>Alzheimer’s Disease</td>
<td>44</td>
</tr>
<tr>
<td>Depression</td>
<td>42</td>
</tr>
<tr>
<td>Mild Cognitive Impairment (MCI)</td>
<td>33</td>
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<tr>
<td>Aging</td>
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<td>Epilepsy</td>
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<td>Substance Dependence</td>
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<td>ADHD</td>
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<tr>
<td>Multiple Sclerosis</td>
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<tr>
<td>Autism</td>
<td>12</td>
</tr>
<tr>
<td>Parkinson’s Disease</td>
<td>11</td>
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<tr>
<td>Pain</td>
<td>10</td>
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<tr>
<td>Anxiety Disorders</td>
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<td>Sleep</td>
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</tr>
<tr>
<td>Miscellaneous Neurological Disorders</td>
<td>10</td>
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<tr>
<td>Stroke</td>
<td>7</td>
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<tr>
<td>Obsessive Compulsive Disorder (OCD)</td>
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<tr>
<td>Posttraumatic Stress Disorder (PTSD)</td>
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<td>Amnesia</td>
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<tr>
<td>Brain Lesions</td>
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<tr>
<td>Dementia</td>
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<td>Seizure</td>
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<tr>
<td>Trauma</td>
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<tr>
<td>Bipolar Disorder</td>
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<td>Personality Disorders</td>
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<td>Cerebral Palsy</td>
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<td>Psychopathy</td>
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<td>Learning Disabilities</td>
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<tr>
<td>Tourette Syndrome</td>
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</tr>
</tbody>
</table>

Kelly et al. 2012
Clinical applications

Healthy control

Alzheimer’s

Schizophrenia

Whitfield-Gabrieli et al. 2009

Greicius et al. 2004
Outline

- What is it?
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Seed-based correlation

- Select a seed voxel.
- Correlate the seed’s time series with every other voxel’s time series.
- Apply a threshold (e.g., $r > 0.3$).
- The resulting “network” shows regions with significant correlations.
Seed-based correlation

AFNI InstaCorr

- 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

All data herein from Alex Martin, et al. [NIMH IRP]
Seed-based correlation

Buckner et al. 2013
Independent Component Analysis (ICA)

fMRI data

time1

time2

time3

ICA

components “networks”

component 1

component 2

component 3
Independent Component Analysis (ICA)

fMRI data

time1

time2

time3

components “networks”

component 1

component 2

component 3
Independent Component Analysis (ICA)

fMRI data

components “networks”

component 1

component 2

component 3
Independent Components

\[ \text{raw_data}(t) = a_1(t) + a_2(t) + \cdots + a_{N-1}(t) + a_N(t) \]
RSNs from ICA

Damoiseaux et al. 2006

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

David M. Cole¹, Stephen M. Smith² and Christian F. Beckmann¹,²*
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

Sadaghiani et al. 2015
Outline

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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”

Birn et al. 2006

data from Chang et al. 2009
Systematic differences in head motion across age groups caused spurious functional connectivity effects

*Power et al. 2010*
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

- and how can we tell which is correct?
Drowsiness

Fukunaga et al. 2006
Drowsiness

Wong et al. 2010

Chang et al. 2013
Drifting to sleep...

- Functional connectivity patterns change with sleep stage

Horovitz et al., 2009

Tagliazzucchi 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