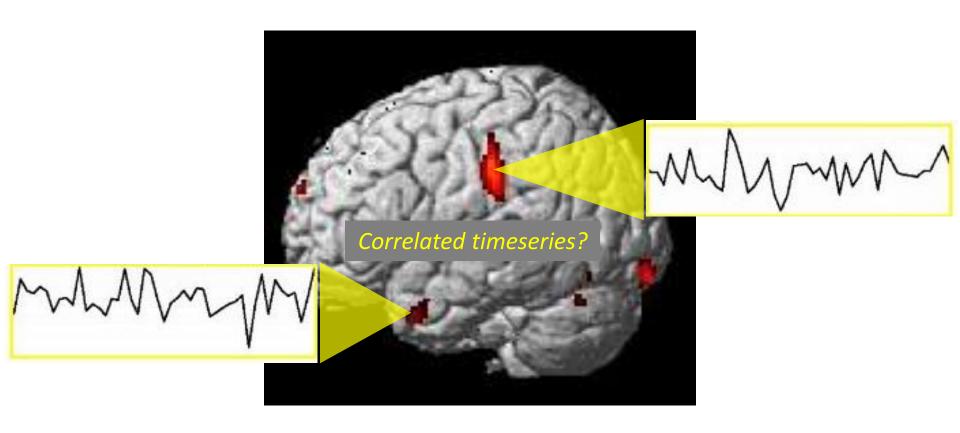
Lab session 11: Functional connectivity analysis (FCA)

(No assignment)

Andrew Bauer 04/06/16

Session no.	Date (all Wednesday)	Topic/activity	Topic of quiz that day	Topic of lab write-up (assignment) due that day
1	13-Jan	Lab overview		
2	20-Jan	Brain anatomy		
3	27-Jan	Data preprocessing	Brain anatomy (no. 1)	
4	3-Feb	Set up GLM model	Functional brain anatomy (no. 2)	
5	10-Feb	Single-subject SPM contrasts	Data preprocessing and GLM model (no. 3)	Brain anatomy (no. 1)
6	17-Feb	Within-subject MVPA		Single-subject SPM contrasts (no. 2)
7	24-Feb	SIBR tour and review for mid-term exam		Within-subject MVPA (no. 3)
No lab	2-Mar	No lab (mid-term exam)		
No lab	9-Mar	No lab (spring break)		
8	16-Mar	Group-level SPM contrasts		
9	23-Mar	Between-subjects MVPA		Group-level SPM contrasts (no. 4)
10	30-Mar	Voxel-wise modeling		Between-subjects MVPA (no. 5)
11	6-Apr	Functional connectivity analysis (no assignment)		
12	13-Apr	Review for final exam		Voxel-wise modeling (no. 6)
No lab	20-Apr	No lab		
No lab	27-Apr	No lab (final exam)		

So far, we've inferred an interaction or cooperation between brain regions if they're co-active...

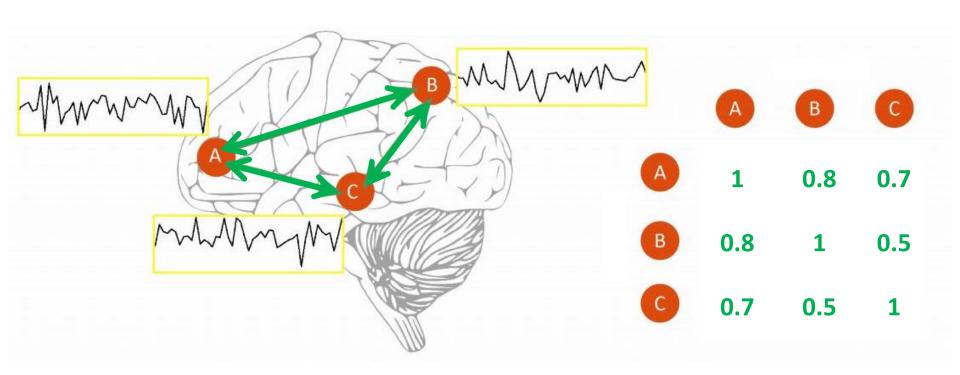


... but we can make our inference stronger by examining whether different brain regions' activity is correlated over time

Types of FCA

- Basic correlational approach
 - Does brain region A's activity correlate with brain region B's over time? If so: probably working together

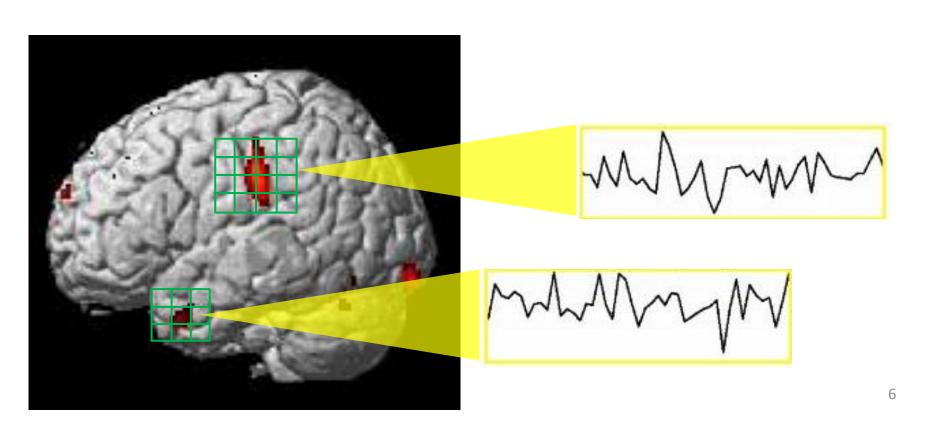
Basic correlational FCA: Pairwise correlations between nodes



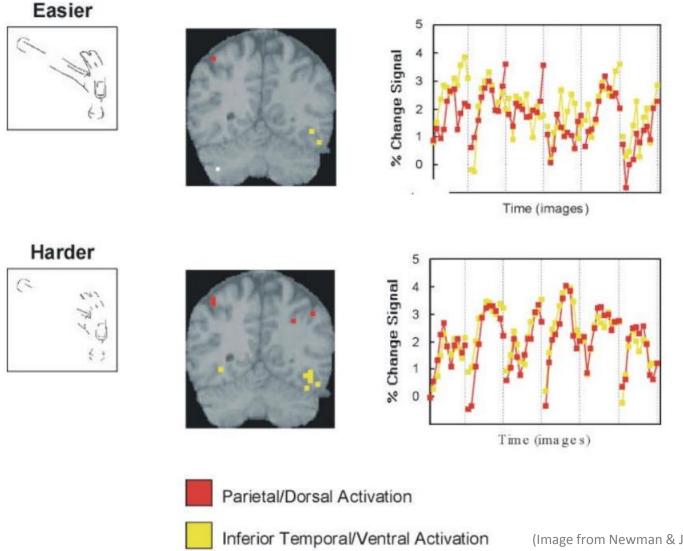
- Define network nodes (spatial coordinates or regions of interest)
- Identify a timeseries associated with each node
- Estimate the edge strengths, or connections between the nodes
 - For example, correlate each timeseries with every other timeseries

First must define regions of interest (ROI), a.k.a. nodes

- 1. Define a cube (your ROI, below) around a statistically significant cluster
- In this cube, average the timeseries only from the voxels that are statistically significant



Spatial (parietal) and visual (inf. temporal) brain activity synchronize *more* during the *harder* object recognition task

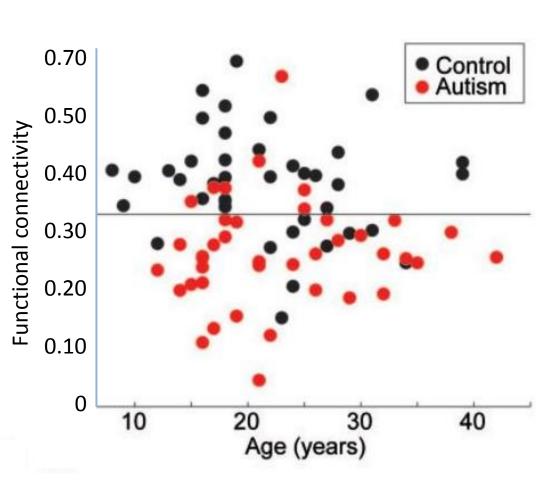


Can diagnose a subject based on functional connectivity as either: Autistic or Neurotypical (control)

Functional connectivity between frontal and parietal areas 0.19 subj1 subj2 0.74 subj3 0.32 0.63 subj4 subj5 0.17 subj6 0.64 subj7 0.39

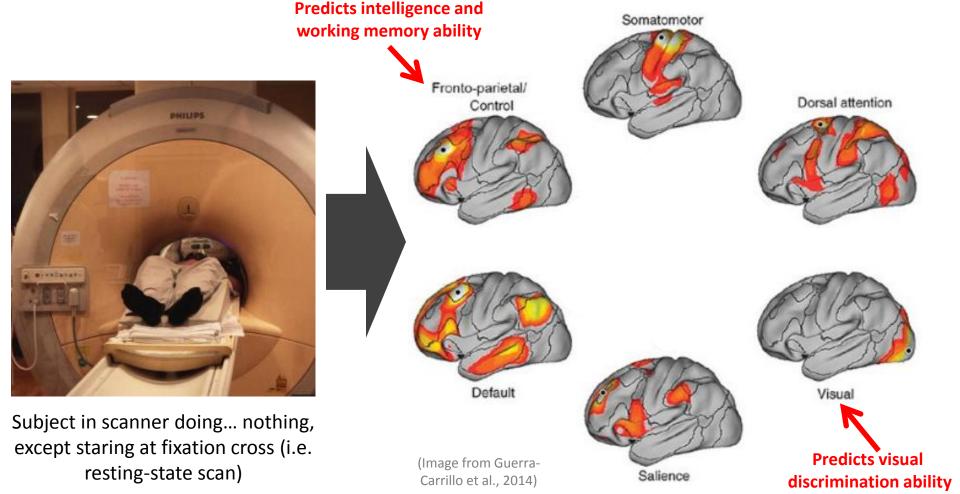
Neurotypical
(control)?

Classifier's
decision for each
subject
Autistic?



Resting-state functional connectivity networks Taking functional neuroanatomy to the spatio<u>temporal</u> level

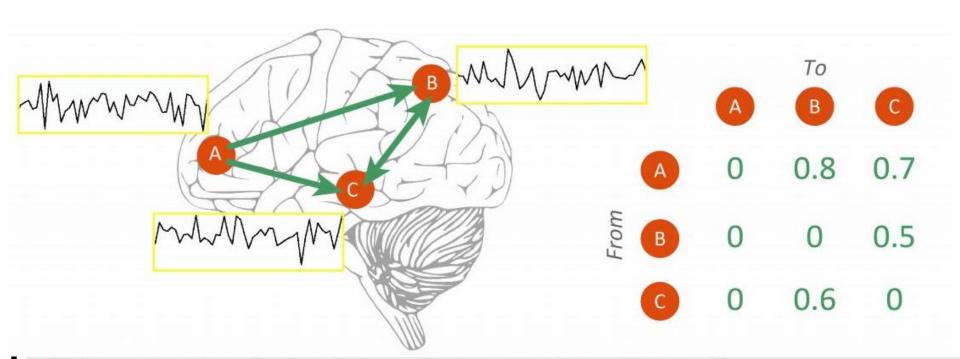
 Brain networks at rest reflect the history of interactions between regions during day-to-day activities



Types of FCA

- Basic correlational approach
 - Does brain region A's activity correlate with brain region B's over time? If so: probably working together
- Causal(-esque) approach (vs. correlational)
 - Does brain region A's activity cause brain region B's?
 - More specific interaction than "they might work together"

Going from *correlational* to *causal* FCA (a.k.a. from *functional* to *effective* connectivity) (note differences here from Slide 5)



- Define network nodes (spatial coordinates or regions of interest)
- Identify a timeseries associated with each node
- Estimate the edge strengths, or connections between the nodes
 - For example, correlate each timeseries with every other timeseries
 - If the data (and method for estimating edges) permits the estimation of causality,
 the edges may be uni-directional, resulting in an asymmetric network matrix

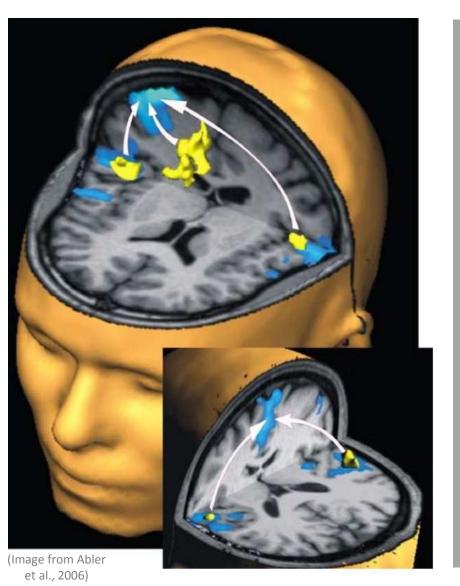


One method of causal(-esque) FCA: Granger causality (Pure causality is hard to measure due to poor fMRI temporal resolution)

If brain region A's timeseries "Granger-causes" brain region B's, then:

Past activation values of A should help predict B's activation *above and beyond* the information contained in past activation of B alone

Granger-causal flow of brain activity following the auditory command: "press left button"



Main picture:

Significant Granger causality: FROM auditory cortex and SMA

TO right motor cortex

Small picture:

Significant Granger causality: FROM auditory cortex

TO SMA

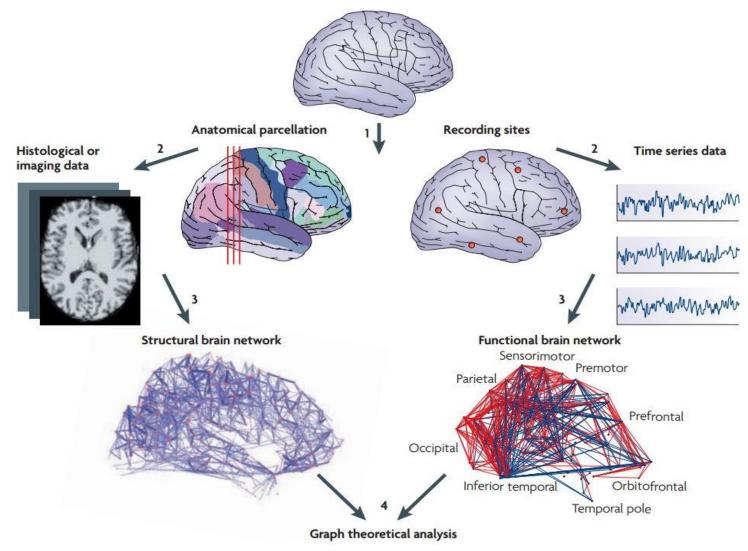
Types of FCA

- Basic correlational approach
 - Does brain region A's activity correlate with brain region B's over time? If so: probably working together

- Causal(-esque) approach (vs. correlational)
 - Does brain region A's activity cause brain region B's?
 - More specific interaction than "they may work together"

- Comparing functional and <u>structural</u> connectivity
 - E.g. diffusion tensor or spectrum imaging (DTI/DSI)

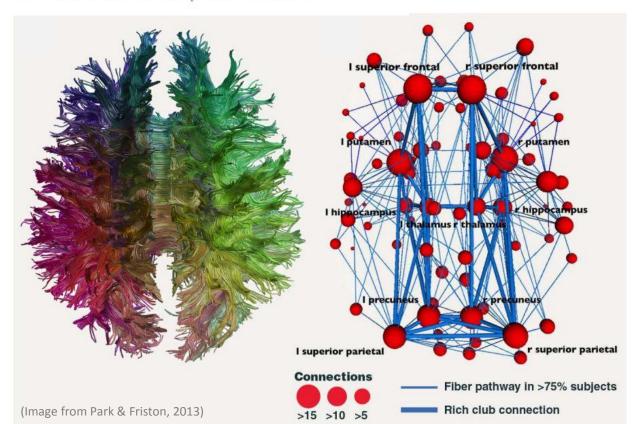
Can compare *structural* (left) and *functional* (right) connectivity measures

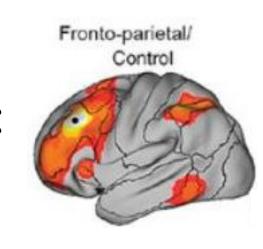


The "rich club" (left; discovered structurally) partially overlaps with the intelligence/control network (right; discovered functionally)

The brain's wiring allows for the rapid transmission of information, with a set of particularly well-connected hubs, known as the **rich club**, directing much of the traffic between different parts of the brain

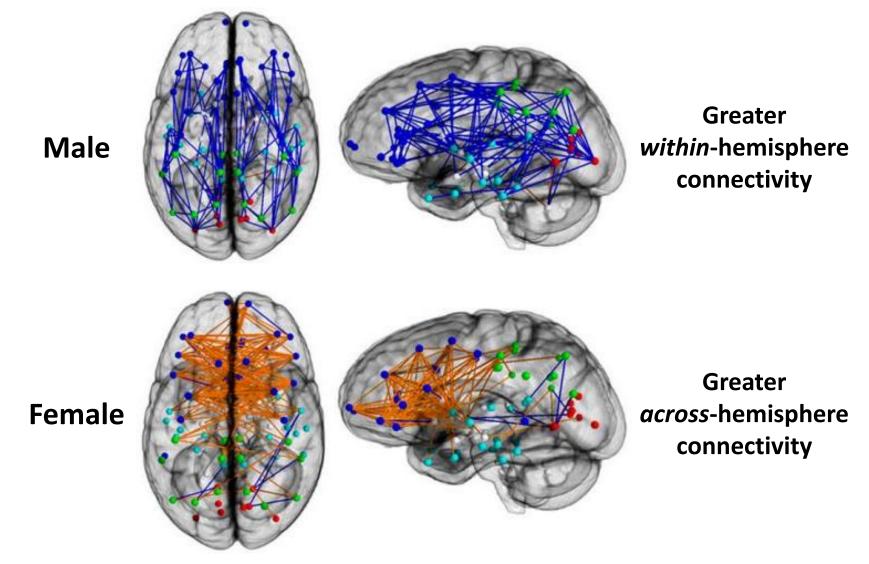
This group may be crucial for integrating all the thoughts and feelings that make up our conscious experience





Sex differences in major structural connectivity

(Image from Ingalhalikar et al., 2013)



... but what do these results mean in terms of brain function and behavior?

References

Abler, B., Roebroeck, A., Goebel, R., Höse, A., Schönfeldt-Lecuona, C., Hole, G., & Walter, H. (2006). Investigating directed influences between activated brain areas in a motor-response task using fMRI. *Magnetic Resonance Imaging*, 24(2), 181–5. doi:10.1016/j.mri.2005.10.022

Anderson, J. S., Nielsen, J. A., Froehlich, A. L., Dubray, M. B., Druzgal, T. J., Cariello, A. N., Lainhart, J. E. (2011). Functional connectivity magnetic resonance imaging classification of autism. *Brain: A Journal of Neurology*. doi:10.1093/brain/awr263

Bullmore, E., & Sporns, O. (2009). Complex brain networks: graph theoretical analysis of structural and functional systems. *Nature Reviews. Neuroscience*, *10*(3), 186–98. doi:10.1038/nrn2575

Guerra-Carrillo, B., Mackey, A. P., & Bunge, S. A. (2014). Resting-State fMRI: A Window into Human Brain Plasticity. *The Neuroscientist: A Review Journal Bringing Neurobiology, Neurology and Psychiatry*, (February). doi:10.1177/1073858414524442

Ingalhalikar, M., Smith, A., Parker, D., Satterthwaite, T. D., Elliott, M. A., Ruparel, K., Verma, R. (2013). Sex differences in the structural connectome of the human brain. *Proceedings of the National Academy of Sciences*, 1–6. doi:10.1073/pnas.1316909110

Newman, S. D., & Just, M. A. (2005). The neural bases of intelligence: A perspective based on functional neuroimaging. *Psychology*. In Robert J. Sternberg & Jean Pretz (Eds.) (2005). Cognition and intelligence: Identifying the mechanisms of the mind (pp. 88-103). New York: Cambridge University Press

Park, H. J., & Friston, K. (2013). Structural and functional brain networks: from connections to cognition. *Science (New York, N.Y.)*, 342(6158), 1238411. doi:10.1126/science.1238411

Smith, S. M., Vidaurre, D., Beckmann, C. F., Glasser, M. F., Jenkinson, M., Miller, K. L., Van Essen, D. C. (2013). Functional connectomics from resting-state fMRI. *Trends in Cognitive Sciences*, *17*(12), 666–82. doi:10.1016/j.tics.2013.09.016