The Functional and Structural Human Brain Connectome

Syllabus MBB 980V Spring 2020

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General Information

Magnetic Resonance Imaging (MRI) has revolutionized our ability to study the living human brain. Studies of functional connectivity (FC) of the human brain using functional MRI data collected during wakeful rest have transformed our understanding of the brain's organization at the network level, revealing a canonical set of brain networks that are "active" in the absence of goal-directed activity and that are also the same networks engaged during task performance. More recently, structural MRI has revealed gray matter structural covariance networks, and advances in diffusion MRI have made it possible to study the white matter structural connectome via *in vivo* fiber tracking. MRI-based connectomics is a rapidly growing field, with new methods and applications evolving at an incredibly fast pace. The goal of this class is to understand how MRI methods are used to study the living human brain connectome. This course is designed for students in the MBB programs who are interested in learning about neuroimaging techniques for studying brain connectivity, including those who are interested in neuroscience applications and brain disorders and those interested in bioinformatics/computer science/statistics/physics applications in neuroimaging.

In this course, we will learn the basics of the workhorse MRI methods used for connectomics research, including structural, diffusion, and functional MRI. The basics of each method will be primarily conceptual, with some exposure to the physics and math underlying each technique. We will learn how each of these techniques is used to study the structural and functional connectome of the human brain. Key methodological and interpretational issues for each technique will be discussed, including comparative neuroanatomy research that aims to integrate MRI connectomic measures with findings from translational studies using tracer injections to gain an understanding of the mechanisms underpinning MRI measures of connectivity. We will discuss brain networks that have been reported in the literature using these methods, and the links between structural and functional connectomes, with a focus on networks implicated in addiction. We will do a survey of widely used open access tools for connectivity and connectome analyses. Last, throughout the course we will discuss open access resources for connectomics research, with a specific focus on the Human Connectome Projects, which will be the hypothetical data sources for your final research projects.

Grading is based on the following:

Class Participation:	15%
Quizzes:	10%
Pre-Proposal:	10%
Presentations on Aims & Significance	15%
Presentation on Final Project	15%
Final Project (Written):	35%

Class Participation: The success of this course depends upon your participation. You will be expected to read all assigned articles ***prior*** to each class and be prepared to discuss your thoughts, ideas, and questions on each topic. You will submit one question per article for the discussion on the day of the class via the Canvas website. Class attendance is required.

Extra readings are provided in case you are interested in exploring a topic in more depth or in seeing examples of data analysis pipelines, but are not required reading.

Assigned readings may be changed a bit if I find something that seems like a better compliment to the topic.

Quizzes: Three quizzes will be given throughout the course. These will be short and are primarily to ensure that everyone understands the topics we have discussed.

Pre-Proposal: Each student will submit a couple of candidate ideas for the Final Project. There should be about a paragraph for each candidate idea, with a few key references, so I can provide feedback to guide your choice of topic for the Final Project.

Final Project: Each student will prepare a four-page research paper modeled after the Research Plan for an HMS fellowship application. I will provide additional details of the structure of the application.

Presentations on Final Project Elements: Each student will do two short presentations on the elements of the Final Project. The first will be on the Specific Aims & Significance to get feedback from the class on your project topic, the second will be on the final project (all sections). You will be expected to prepare a powerpoint (or similar) presentations. The length of the presentations will depend on final class enrollment. Guidelines on the elements of the Final Project, including all presentations, will be given to you.

Academic Honesty

I expect that all students will uphold the standards of academic integrity according to the Harvard honor code. You are strongly encouraged to interact with your classmates on your Final Project to refine, focus, and develop your research study, and you will have ample opportunities in class to obtain feedback from me and your classmates on your proposed study. However, your written project must be the result of your own research and writing. You will be expected to produce your own academic work of integrity – that is, work that adheres to the scholarly and intellectual standards of *accurate attribution of sources and transparent acknowledgement of the contribution of others to their ideas, discoveries, interpretations, and conclusions*. Please see the Harvard Guide to Using Sources for further information (https://usingsources.fas.harvard.edu/). Cheating on quizzes also will not be tolerated and will result in a failure for that quiz.

Week 1 (1/28): A Case Study on Brain Connectivity: Ventral Medial Prefrontal Cortex

Assigned Readings:
Nieuwenhuis I and Takashima A. 2011. The role of ventromedial prefrontal cortex in memory consolidation. Behav Brain Res 218:325-334.

Ongur D and Price J. 2000. The organization of networks within the orbital and medial prefrontal cortex of rats, monkeys and humans. Cerebral Cortex 10:206-219.

Extra:
Schneider B & Koenigs M. 2017. Human lesion studies of ventromedial prefrontal cortex. Neuropsychologia 107:84-93.

Week 2 (2/4): Introduction and History of the Human Connectome.

Assigned Readings:
Sporns O. 2011. The human connectome: A complex network. Annals NY Acad Sci 1224: 109-125.
Catani M et al. 2013. Connectomic approaches before the connectome. Neuroimage 80:2-13.

Week 3 (2/11): Properties of Brain Networks, Parcellation and the Connectome.

Assigned Readings:
Mesulam M. 2012. The evolving landscape of human cortical connectivity: Facts and inferences. Neuroimage 62:2182-2189**. Only the section on "Characteristics of large-scale neurocognitive networks".**
Sporns O. 2013. The human connectome: Origins and challenges. Neuroimage 80:53-61. **Only the section on "Challenges".**
Ardesch D., et al. 2019. The human connectome from an evolutionary perspective. Progress in Brain Research 250:129-151.

Week 4 (2/18): The Young Adult, Aging, Development, and Disease Connectome Projects and Other Open Access Data

Assigned Readings:
Van Essen D., et al. 2013. The WU-Minn Human Connectome Project: An overview. Neuroimage 80:62-79. **Pp. 62-64.**
Barch D. 2017. Resting state functional connectivity in the Human Connectome Project: Current status and relevance to understanding psychopathology. Harvard Rev Psychiatry 25:209-217. **All pp**.
Barch D., et al. 2013. Function in the human connectome: Task-fMRI and individual differences in behavior. Neuroimage 80:169-189. **Pp. 169-179 (stop at fMRI data acquisition)**

Quiz 1. Connectome Introduction Block (Take-Home, due 2/25)

Week 5 (2/25): Fundamentals of MRI

Assigned Readings:
Huettel S., et al. 2009. Functional Magnetic Resonance Imaging, 2nd Edition. Sinauer Associates, Inc., Sunderland, MA. pp. 31-43, 57-67, 90-97, 121-131.

Week 6 (3/3): Gray Matter Structural Morphometry and Gray Matter Structural Covariance Networks

Assigned Readings:
Alexander-Bloch A., et al. 2013. Imaging structural covariance between human brain regions. Nat Rev Neurosci 14:322-336.

Extra:
Seeley W., et al. 2009. Neurodegenerative diseases target large-scale human brain networks. Neuron 62:42-52.

Project Pre-Proposal Due

Week 7 (3/10): Introduction to Functional MRI and Functional Connectivity

Guest Discussion Leader: Poornima Kumar, Ph.D. Assistant Professor HMS
https://www.mcleanhospital.org/profile/poornima-kumar

Assigned Readings:
Bandettini P. 2012. Functional MRI: A confluence of fortunate circumstances. Neuroimage 61:A3-A11.
Fox M. and Raichle M. 2007. Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. Nature Neuroscience Reviews 8:700-711.

Week 8 (3/16-3/20) Spring Break

Week 9 (3/24): Intrinsic Connectivity Networks and Challenges of FMRI Connectivity

Assigned Readings:
Uddin et al. 2019. Towards a universal taxonomy of macro-scale functional human brain networks. Brain Topography 32:926-942.
Buckner R. et al. 2013. Opportunities and limitations of intrinsic functional connectivity MRI. Nature Neuroscience 16:832-837.

Due by 3/27 Recorded presentations: Aims and Significance

Week 10 (3/31): Introduction to Diffusion MRI and Structural Connectivity with Tractography

Guest speaker: Anastasia Yendiki, PhD. Associate Professor HMS
https://scholar.harvard.edu/a-y/research

Assigned Readings:
Mueller et al. 2015. Diffusion MRI and its role in neuropsychology. Neuropsychol Rev 25:250-271.

Extra:
Assaf Y., et al. 2019. The role of diffusion MRI in neuroscience. NMR in Biomed 32e3762, pp. 1-16.

Due by 4/3 Review of Significance and Aims Presentations
4/2 Quiz 2. Anatomical and Functional MRI block (Take home due by 4/9)

Week 11 (4/7): Interpretation and Validation of dMRI Measures of White Matter Structure

Beaulieu C. 2014. The Biological Basis of Diffusion MRI in *Diffusion MRI 2nd Edition*. Edited by Heidi Johansen-Berg and Timothy Behrens. Elsevier. Pp. 155-183.

Due by 4/9 Quiz 2. Anatomical and Functional MRI block

Week 12 (4/14): Data Analysis Tools and Methods for MRI Connectomics

I will give a one hour presentation in the first hour, then we will discuss the assigned reading in the second hour.

Assigned Readings:
Sotiropolous S. and Zalesky A. 2016. Building connectomes using diffusion MRI: why, how and but. NMR in Biomed 32e3752, pp. 1-23.

Extra Readings:
Soares J., et al. 2013. A hitchhiker's guide to diffusion tensor imaging. Front Neurosci 7:31, pp. 1-14. Very nice listing of popular tools for DTI processing, discusses artifacts, subject level data processing.
Whitfield-Gabrieli S. and Nieto-Castanon A. 2012. Conn: A functional connectivity toolbox for correlated and anticorrelated brain networks. Brain Conn 2:125-141. Popular tool for seed-based functional connectivity, describes subject-level data processing.
Smith S., et al. 2004. Advances in functional and structural MRI image analysis and implementation as FSL. Neuroimage 23:S208-S219. Popular suite of tools for processing structural, diffusion, and functional MRI. Has a toolbox for network analysis.

Quiz 3. Functional Connectivity and Diffusion MRI block (Take home, due 4/21)

Week 13 (4/21): Cross-Modal and Cross-Species Comparisons of Structural and Functional Connectivity

Assigned Readings:
Reid et al. 2016. A cross-modal, cross-species comparison of connectivity measures in the primate brain. Neuroimage 125:311-331.

Week 14 (4/28): In class presentation: Final Project

Wednesday 5/6: Final Project papers due.