Topics in Neurobiology and Behavior: Focus on Autism-related Research G4440
Fall 2017, Mondays 4.10-6PM
Schmerhorn 405
Instructor: Helen Brew, PhD
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Office hours: Wednesday 3-5pm, Schermerhorn 356

Course overview: Research on autism spectrum disorder, or ASD, is highly multi-disciplinary, because it is a behaviorally defined disorder known to depend strongly on genetics, with some single candidate genes and their protein products having strong effects. We will explore the nature of ASD by examining studies in genetics, epidemiology, neurobiology and behavior. We will examine the results from neurobiological experiments on animal models of ASD at the behavioral, systems, cellular, molecular and genetic levels. Questions to be considered will include: Is ASD really a single disorder? Which theories of ASD causation are the most compelling? Has there really been a rise in ASD prevalence? What makes a good animal model of ASD? Can neurobiological experiments on animals lead to treatments for ASD? Can any oddities of animal behaviors be considered directly analogous to those comprising a human behavioral disorder? Will the future bring “personalized medicine” with dedicated animal or human stem cell models for every person with ASD? What types of environmental insult contribute to ASD? What are the links between the immune and nervous systems in ASD? How do current behavioral findings from people with ASD direct neurobiological research?

Prerequisites: Mind, Brain and Behavior (Psych 1010) or an equivalent biological-based psychology class is required. Courses in statistics, research methods or genetics would be helpful, but are not required. The permission of the instructor is required in order to register.

Course objectives: This course fulfills the Seminar Requirement for the Psychology Major and the Advanced Seminar Requirement for the Neurobiology and Behavior Major.

The goals of this course are:

- to gain an advanced understanding of neurobiological research related to ASD by reading primary scientific literature
- to gain an advanced understanding of current knowledge on the neurobiology of ASD
- to read, understand and orally present primary scientific literature from psychology and neuroscience journals
- to be able to critically evaluate published research and discuss its merits, caveats and alternative interpretations
- to develop a review commentary or research proposal on a research topic by reading and evaluating published research

Course requirements:
Weekly readings/assignment and participation (20%): You will be expected to carefully and thoroughly read and understand three or four scientific research papers each week. The chosen papers will usually be primary research reports from seminal findings on the topic of the week. Some basic background knowledge of the topic is expected. In some cases, this may need to be supplemented through textbooks or other references cited in the assigned reading. Everyone will post a substantial comment, thought or question on the paper before class on the Discussion Board of Courseworks, which will serve as a basis for discussion during class. Each week, Dr Brew will also present relevant background material.

Presentation of two papers (40%): Each week, 2 student leaders will each present one of the assigned readings in an approximately 30 minute slide presentation and initiate a short discussion of the paper. Each student will present 2 papers during the semester. Written feedback will be provided one week following the presentation. Ideally, obtain help with your presentation from Dr. Brew well before class, e.g. during Wednesday office hours.

Short mid-term (5%): The students take a half-hour long written midterm quiz covering the material presented by Dr Brew, in the papers and the class discussions. 15 minutes will be multiple choice questions,
and 15 minutes will be a short essay chosen from three topic options. This will take place on Monday 16\textsuperscript{th} October, and will be with open notes. The main reason for having it is to give me an idea of your writing skills and how well you are keeping up factually, so that I can help you choose an appropriate term project topic.

**Research proposal or review paper (30\%):** A term project will be required, on a topic of your choosing from material covered during the seminar (~10-15pg). It may consist of either a research proposal or a research review paper. Detailed information will be given at the start of the course. The project will require that you meet individually with the instructor to get approval on the topic and outline. Outline due November 13\textsuperscript{th}.

**Short presentation based on term paper (5\%):** Each student will give a ten minute presentation of an interesting aspect of their term project paper on December 11\textsuperscript{th}, the final day of class.

**Class policies:**

Attendance: You are expected to come to class each week prepared to discuss the assigned papers. Your unexcused absence will be noted and reflected in your participation grade. Make-up ‘participation’ for preapproved excused absences will be arranged on an individual basis.

Assignments: Paper presentations are assigned based on solicited preferences during the first week of the semester and once assigned may not be changed. In the case of a documented medical or family emergency, alternate arrangements will be made to present the paper individually during office hours. The due date for the term paper is firm, and as such, one letter grade will be deducted for each day it is late.

Academic Integrity: "The intellectual venture in which we are all engaged requires of faculty and students alike the highest level of personal and academic integrity. As members of an academic community, each one of us bears the responsibility to participate in scholarly discourse and research in a manner characterized by intellectual honesty and scholarly integrity. . . . In practical terms, this means that, as students, you must be responsible for the full citations of others’ ideas in all of your research papers and projects; you must be scrupulously honest when taking your examinations; you must always submit your own work and not that of another student, scholar, or internet agent." From the Faculty Statement on Academic Integrity - [www.college.columbia.edu/academics/integrity-statement](http://www.college.columbia.edu/academics/integrity-statement). Cheating on assignments or exams and plagiarism are very serious violations within the academic community. Students are expected to do their own work on all tests and assignments for this class. You are expected to always act in accordance with the Columbia honor code. Any student found cheating or plagiarizing in this class will be reported to Columbia’s Office of Judicial Affairs and Community Standards for evaluation and academic discipline. If you have questions about any aspect of academic integrity at Columbia, please refer to the following link: [www.college.columbia.edu/academics/integrity](http://www.college.columbia.edu/academics/integrity) and if you have specific questions about the judicial process, please see [www.college.columbia.edu/academics/disciplinaryprocess](http://www.college.columbia.edu/academics/disciplinaryprocess).

**Class Schedule**

Please note that readings and topics may be subject to change based on enrollment number and student preferences. **Papers in bold are particularly important.** (Papers in parentheses are optional background reading which you can skim-read to get overview and perspective).

**Week 1. September 11\textsuperscript{th}. What is ASD? And Introduction to seminar**

Information on: course format, evaluation, discussion board posts, presentation of papers, class discussion, term paper. **Students will select at least one of their presentation topics today.** Please choose one paper from weeks 2-7, the other from weeks 8-12. Everyone will thoroughly read the two papers selected for presentation. (Dr Brew will briefly include the remaining one or two papers in her weekly presentations of background material).

**Introduction to ASD and theories of autism** The clinical definition and diagnosis of ASD, including broadening definition and changes in diagnostic criteria over time. The strong genetic basis of autism, concordance. **Theories:** Excitatory-inhibitory imbalance, theory of mind, neural disconnection, overgrowth,
male brain, noisy brain, synaptic dysfunction, faulty synaptic pruning, striatum/cerebellum/frontal cortex, environmental effects, (vaccines).

(Rubenstein, J. L. R., & Merzenich, M. M. (2003). Model of autism: increased ratio of excitation/inhibition in key neural systems. *Genes, brain, and behavior, 2*(5), 255–67). This paper introduced one of the well-known theories of autism: excitatory/inhibitory imbalance. The fact that epilepsy is a common co-morbidity with ASD means this was not all that controversial.


**Week 2. September 18th. Examples of behavioral and neurobiological abnormalities in ASD.**

Biological motion perception, face recognition, noisy brain, empathy versus social cognition.


**Week 3. September 25th. The genetics of ASD.** Chromosomal deletions and duplications conferring risk. Syndromic autism versus “idiopathic” autism. Specific genes conferring risk, especially CHD8 and SCN1A. Abnormal expression of networks of synaptic genes and microglia genes.


**Week 4. October 2nd. What makes a good animal model? Is it possible to model ASD?**

Face validity, construct validity and predictive validity. Which is most important for which type of testing? Which (if any) animal behaviors are analogous to human ASD behavioral symptoms? Repetitive behaviors and social abnormalities. Consideration of developmental age, and species and strain differences. Advances due to CRISPR techniques.
Mouse models of synaptic-associated genes implicated in ASD: Fragile X syndrome, Dravet syndrome, Timothy syndrome, SCN2A and Shank genes.


**Week 5. October 9th. More genetic mouse models** These models are of ASD-related genes that seem less directly related to synapses: Rett syndrome, CHD8, PTEN, Ube3a


**Week 6. October 16th** Short mid-term quiz for first half hour of class (see Course Requirements section above for more details).

Do particular parts of the brain show structural or functional abnormalities in ASD? Where in the brain should we look, based on behavioral evidence from people with ASD? Social brain areas? Movement areas? Which parts of the brain are abnormal in mouse models of ASD? (E.g. striatum, forebrain, cerebellum).


Week 7. October 23rd. Characteristics of autism in females


Week 8. October 30th. The vaccine story.

There is a huge amount of literature on this whole story, which is more sociology (scare journalism, mass hysteria, conspiracy theories) than psychology, let alone neuroscience. Most importantly please read one or both of the epidemiology studies (papers 1 and 2). If someone feels like volunteering to present topic 3….an overview of the whole vaccine scare….great! If not I will lead a structured discussion on topic 3.


3. The retracted Wakefield et al paper and commentaries since:


And here is a link to a series of papers by the main journalist uncovering what went wrong……..


Monday November 6th is an academic holiday.

Week 9. November 13th. Biomarkers and early diagnosis, baby sib studies. Studies of the baby siblings of older kids with ASD can allow longitudinal studies from birth or even before birth.


**Week 10. November 20th. Maternal infection…..immune system and gut…probiotics**
(also relevant to microglia, synaptic pruning, mTOR)

Lee et al (2015) Maternal hospitalization with infection during pregnancy and risk of autism spectrum disorders. Brain Behav Immun. Feb;44:100-5…..this is a study of 2.4 million people showing risk of autism increases by 37% if Mom hospitalized with infection.


**Week 11. November 27th. Treatment approaches supported by models of ASD**


**Week 12. December 4th. Can cells in dishes help find ASD treatments?**


**Week 13. December 11th. Which theories of ASD are the most compelling? Which research should be most urgently funded?**

Presentations of Term Papers: Persuade the class of your opinion or convince the class that we should fund your research proposal (10 minutes each). No assigned reading this week.