

R Psy 326 Seminar in Biopsychology: Parkinson's disease

Spring 2008
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In this seminar we will discuss the history of Parkinson's disease, the underlying cellular and molecular changes associated with this disease, and the range of symptoms. Both motor, cognitive, and emotional disturbances will be studied. Current treatments and potential future therapies will be covered. Prerequisites: a course in experimental methods, a course in statistics, a course in neuroscience, and permission of the instructor. Enrollment limited to 12.

We will begin by discussing our pre-reading ("The Case of the Frozen Addict") and the lecture by Dr. Fahn on the PDF.org website. During the month of February, students will work in teams to present an overview of select areas of research on PD. During the following month, we will study one article from each of these areas, and critique the article in detail. Students will develop two major works: a podcast targeted to the general public, and a research proposal targeted to a NIH panel of reviewers.

Schedule of topics:

Jan 31 - Introduction and overview (history, symptoms)

Feb 7 – Genetic and environmental causes

Discussion leaders: MyDzung Chu, Julia Vorhees, Emma Coleman

- Watch DVD on reserve Neilson Library "*Shake Rattle and Roll*"
- Listen to lecture by Caroline Tanner "Are there advances in environmental epidemiology?" www.pdf.org webcast
- Read: Farrer MJ (2006) Genetics of Parkinson disease: paradigm shifts and future prospects, *Nature Reviews Genetics* 7: 306-318.
- Read: Tan et al. (2003) Dose-dependent protective effect of coffee, tea, and smoking in Parkinson's disease: a study in ethnic Chinese. *J. Neurol. Sci*, 216: 163-7.
- Optional reading: Di Monte DA et al. (2002) Environmental factors in Parkinson's disease. *NeuroToxicology* 23:487-502 (focus on pages 493-497).

Feb 14 – Cellular and molecular studies

Elizabeth Deschene, Faythe-Anne MacKenzie, Jennifer Tyson

- Watch DVD - *Louie, Louie: A portrait in Parkinson's*
- Listen to lecture by Ana Marie Cuervo "Protein degradation, aggregation, misfolding" www.pdf.org webcast. Also suggested: "Mitochondria and Other Genes: DJ-1, PINK1" by Mark Cookson
- Read Wood-Kaczmar A et al (2006) Understanding the molecular causes of Parkinson's disease. *Trends in Molecular Medicine* 12:521-528.

- Read Abstract, Introduction, Mitochondrial Involvement in PD and Conclusion sections of Petrozzi et al.(2007) Mitochondria and Neurodegeneration, Biosci. Rep. 27:87-104.
- Optional reading: Mukaetova-Ladinskia and McKeith (2006) Pathophysiology of synuclein aggregation in Lewy body disease, Mechanisms of Aging and Development 127: 188-202.
- Optional reading: Engelender S (2008) Ubiquitination of α -synuclein and autophagy in Parkinson's disease, Autophagy 4:1-3.

Feb 21 – Cognitive and emotional symptoms, Aging and pathogenesis

Holly Boyle, Alexandra Ubell, Marlowe Dieckmann,

- Watch DVD – *The bridge at midnight trembles*
- Listen to lecture from pdf.org: Depression, Anxiety, Compulsiveness, Psychiatric Impairment - Christopher Goetz, M.D.
- Read: Levy G (2007) The Relationship of Parkinson Disease and Aging, Ach Neurol 64: 1242-1246.
- Read: Barker S et al (1998) Parkinson's Disease: A Holistic Approach, Am J Nursing 98:48A-48H
- Optional Reading: Matson N (2002) Made of Stone: A view of Parkinson 'off' periods, Psychology and Psychotherapy 75: 93-99

Feb 28 – Treatments

Yena Kang, Melecia Miller, Amanda Anderson

- Watch DVD – *Shaken: Journey into the mind of a Parkinson's patient*
- Listen to PDF webcast “Gene Therapy– Current and Future Approaches” Jeffrey Kordower, Ph.D.
- Read Singh N et al (2007) Advances in the treatment of Parkinson's disease, Prog Neurobiol 81:29-44
- Read Bjorklund et al (2003) Neural transplantation for the treatment of Parkinson's disease, Lancet 2:437-445
- Read Linazasoro et al (2008) Pharmacological treatment of Parkinson's disease: life beyond D2/D3 receptors? J Neural Transm
- Read Smith and Zigmond (2003) Can the brain be protected through exercise? Lessons from an animal model of parkinsonism Exptl Neurol 184: 31-39.

Mar 6 – Target article critique - Genetic and environmental causes

- Tanner CM et al (2002) Smoking and Parkinson's disease in twins. Neurology 58:581-8
- Singleton AB et al. (2003) α -Synuclein locus triplication causes Parkinson's disease. Science 302:841.

Mar 13 – Target article critique - Cellular and molecular studies

- Clark IE et al (2006) *Drosophila pink1* is required for mitochondrial function and interacts genetically with *parkin*, Nature 441:1162-6.

Mar 15-23 Spring Break

Mar 27 – Target article critique - Cognitive and emotional symptoms, Aging and pathogenesis

- Williams-Gray CH et al. (2007) Evolution of cognitive dysfunction in an incident Parkinson's disease cohort, *Brain* 130:1787-1798.
- Alternative article: Braak H et al. (2003) Staging of brain pathology related to sporadic Parkinson's disease, *Neurobiology of Aging* 24 (2003) 197-211.

Apr 3 – Target article critique – Treatments

- Kaplitt MG et al. (2007) Safety and tolerability of gene therapy with an adeno-associated virus (AAV) borne GAD gene for Parkinson's disease: an open label, phase I trial, *The Lancet*, 369 : 2097-2105.
- (optional background) Lewis TB and Standaert DG (2008) Design of clinical trials of gene therapy in Parkinson disease, *Experimental Neurology* 209:41-47.

Training on editing podcasts (1h)

Apr 10 – Open

Apr 17 – Video conference – Mark Cookson, National Institutes of Health

- Listen to webcast lecture by Dr. Cookson “Mitochondria and other genes: DJ-1, PINK1”
- Reading TBA

Apr 24 and May 1 – Presentation of research proposals

Requirements:

1. A proposal for graduate research, final version submitted by May 9.

Directed to NIH, a “Research Design and Methods” essay for an F30 (MD/PhD students) or F31 (PhD students) application. Research plan limited to 10 pages, single-spaced. See instructions on page I-23 (paragraph on lower left) of this document:

<http://grants.nih.gov/grants/funding/416/phs416-1.pdf>

Note this advice: “The typical successful grant application has as its basis a testable hypothesis in a biological area of high current interest. It includes a short, concise series of specific aims that address the central hypothesis. A well written background section is used to indicate the significance of the proposed work and review important information gleaned from the literature and the investigator's previous work that would allow reviewers to easily understand the hypothesis. Proposed experiments are clearly described in detail, with suggestions for proceeding with the work should they fail to produce the expected outcome. There is a body of solid preliminary data that demonstrates the likelihood for success of these experiments.”

From: http://www.niddk.nih.gov/fund/grants_process/grantwriting.htm

2. A podcast for the general public, final version submitted by May 1.

Students will work in pairs. Aim for 5-7 min in length. The topic chosen should not overlap significantly with that from other students in the class. Deadlines: Feb 28 –

submit paragraph describing goals and outline, as well as a test interview. Mar 13 – submit questions for interview. Mar 31 – submit interview on CD. May 1 – edited and posted.

3. Critiques of other students' research proposals and podcasts.
4. Article critiques, due 24 h prior to the class period, submitted electronically.

Grade:

10% Feb class presentation

10% Article critiques

10% Class participation (attendance, prompt arrival, active participation in all class sessions, lack of major sleep deprivation)

10% draft of NIH proposal one month prior to final submission deadline (April 10)

10% peer-editing of podcasts

25% NIH research proposal final product

25% podcast final product