Course outline: NROD60 Cognitive Neuropharmacology
FALL: 2002

Course Details

Instructor: Norton W. Milgram
Classroom and Scheduled Times:
Friday, 11:00 - 1:00, Room R-3231

Course Description

1. General Purpose

The overall goal of this course is to provide a critical overview of the drug development process as applied to pharmaceuticals used to modify cognitive function. The target population for the application of these drugs consists of (1) individuals showing impairment linked to age (age associated memory impairment); and (2) cognitive disorders associated with neuropathology, including Alzheimer's disease, Frontal-Temporal Dementia, and Parkinson's disease.

2. Topics Covered

The first part of the course will focus on the theory underlying treatment of cognitive dysfunction with pharmaceuticals, and the actual developmental process. Topics that will be covered include:

a. Use of drugs to modify behavior: lessons learned from the study of psychotherapeutic drugs.
b. Components of cognition. Before we can even consider drug design, we have to have an identifiable target system. The course will take a neuropsychological perspective, which attempts to distinguish various cognitive processes on the basis of underlying neurobiological structure.
c. Animal models of cognitive decline. What species and what types of tasks can be used to model human cognition? How do we model cognitive impairment.
d. What is the neurobiological basis of cognition? Can we identify the neural structure underlying memory? What is the contribution of various neurotransmitter systems to cognitive performance? Are their common underlying cellular substrates?
e. Clinical evaluation of cognitive function. What kinds of tools are used to evaluate cognition in humans? How reliable are they? Do the different tests measure different functions?
f. Mechanisms of action of putative cognitive enhancing therapies. How do the drugs work.
g. The entire process – from identification of a need to drug approval for cognitive impairment.

These topics will be covered using a lecture-discussion format over the first 6-7 meetings. Test 1 will follow the conclusion of this part of the course.

The second half of the course will consist of presentations that will examine critically examine recent studies involving attempts to manipulate cognition pharmacologically.

You will be required to select a recent publication on the same topic that you are doing your term paper on. One week before your presentation, you should hand out copies of the paper to everyone in the class. The presentation should last a maximum of 15 minutes (including questions). The presentation should describe the study and discuss it critically.

In addition, you also hand out:
a. An outline/summary of the presentation.
b. Three potential test questions, and answers.

3. Grades:

Grades will be based on:

a.	Performance on examinations	- 30%
b.	Seminar	- 15%
c.	Class discussion	- 15%
d.	Term paper	- 40%

a. The term papers will also deal with specific interventions. The papers should summarize pertinent research on both human and animal models, discuss potential mechanisms of action. The papers should be broken down by headings in subsections, that include Summary, Introduction, Discussion, and References. The papers should follow the format of the Publication Manual of the American Psychological Association. The length excluding references must not exceed 15 double spaced pages.

Grading will be based on organization, clarity, scholarship (thoroughness of literature search).

The following are potential interventions for seminar and term paper.
a. anticholinesterases (including, but not limited to tacrine and aricept)
b. ampakines
c. adrenergic agonists
d. antioxidants
e. cerebral vasodilators (hydergine)
f. gonadal hormones (estrogen and testosterone)
g. selegiline hydrochloride (l-deprenyl)
h. adrafinil and modafinil
i. secretase inhibitors
j. serontonergic agonists and antagonists
k. statins
l. stimulants (methylphenidate, amphetamines, caffeine)
m. nootropics
n. growth factors (NGF, BDNF)
o. neuropeptides (ACTH and vasopressin analogs)
p. vaccines
q. memantine
r. NSAIDS

Readings

Bartus, R.T. (2000) The cholinergic hypothesis a generation later: Perspectives gained on the use and integration of animal models. In: Emerich, D.F., Dean, R.L, & Sanberg, P.R. (Eds). Central Nervous System Diseases: innovative animal models from lab to clinic. Human Press, pp3-45

Boller, F., & Duyckaerts, C. (1997). Alzheimer Disease: clinical and anatomic aspects. Chapter 41 in Behavioral Neurology and Neuropsychology. T.E. Feinberg and M.J. Farah (Eds). McGraw Hill, pp 521-544.

D'Mello, G.D., & Steckler, T. (1996). Animal models in cognitive behavioural pharmacology: an overview. Cognitive Brain Research, 3, 345-352.

Harvey, P.D., & Mohs, R.C. (2001). Memory changes with aging and dementia. In: Hof, PR and Mobbs, CV (Eds): Functional Neurobiology of Aging. Academic Press, San Diego, pp 53-63.

Head, E., Milgram, NW., & Cotman, CW. (2001). Neurobiological models of aging in the dog and other vertebrate species. In: Hof, PR and Mobbs, CV (Eds): Functional Neurobiology of Aging. Academic Press, San Diego, pp 457-467.

Morrison, J.H., & Hof, P.R. (1997). Life and death of neurons in the aging brain. Science, 278, 412-424.

Olshanski, J., Haflick, L., & Carnes, BA. (2002). No truth to the fountain of young. Scientific American, 286 (June), 92-95.

Valenstein, E., (1998). Blaming the brain. The Free Press.

Zivin, J.A. (2000). Understanding clinical trials. Scientific American, 282m 69-75

Tentative Schedule

Date	Topic	Assigned Reading
1 -Sept 13	Introduction - Course outline, a review of synaptic transmission processes	
2 -Sept 20	**NO CLASS**	Valenstein
3- Sept 27	Use of drugs to modify behavior I	Valenstein
4- Oct 4	Use of drugs to modify behavior I Cognitive Processes and Aging-	Valenstein Havey and Mohs
5- Oct 11	Cognitive Processes and Aging- Neurobiology of Aging	Boller & Duyckaerts Morrison & Hof
6- Oct 18	Animal Models	D'Mello & Steckler, Bartus, Head et al
7- Oct 25	Midterm Exam – Animal Models	
8 -Nov 1	Animal models - Clinical Trials	Olshanski, Zevin
9 - Nov 8	Seminars TBA	
10 -Nov 15	Seminars TBA	
11 -Nov 22	Seminars TBA	
12 -Dec 6	Final Exam -	