

# Course outline: NROD60 Cognitive Neuropharmacology

## FALL: 2006

### **Course Details**

Instructor: Norton W. Milgram  
Classroom and Scheduled Times:  
Friday, 11:00 - 1:00, Room AA 208

### **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 process involved in developing interventions for treatment of behavioral disorders, with the main goal being to develop a pharmacological strategy for treatment of cognitive dysfunction. The second part will examine specific strategies currently under development and the underlying theoretical basis. Topics that will be covered include:

- a. Use of drugs to modify behavior: lessons learned from the study of psychotherapeutic drugs.
- b. The drug approval process
- c. 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.
- d. 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.
- e. Neurobiological basis of cognition and dementia? 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?
- f. 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?
- g. Strategies for development of intervention – Currently approved.
- h. Strategies for development of intervention – Future.

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

### 3. Grades:

Grades will be based on:

- a. Performance on examinations - 45%
- b. Class participation - 15%
- c. Term paper - 40%

The term paper must deal with a specific type of intervention. The paper should summarize pertinent research on both human and animals and discuss potential mechanisms of action. If possible the research and developmental process should be linked to the material discussed in the course. 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) and originality.

The following are potential interventions that can be used in your term paper. The topic you select must be approved.

The following are potential interventions that can be used in your term paper.

- a. anticholinesterases (including, but not limited to tacrine and aricept)
- b. ampakines
- c. adrenergic agonists
- d. antioxidants
- e. gonadal hormones (estrogen and testosterone)
- f. selegiline hydrochloride (l-deprenyl)
- g. adrafinil and modafinil
- h. secretase inhibitors
- i. serotonergic receptor-specific agonists and antagonists
- j. statins
- k. stimulants (methylphenidate, amphetamines, caffeine)
- l. nootropics
- m. growth factors (NGF, BDNF)
- n. neuropeptides (ACTH and vasopressin analogs)
- o. vaccines and other beta amyloid modifying therapeutics
- p. memantine
- q. NSAIDS (Non-steroidal anti-inflammatories )
- r. Exercise and/or cognitive stimulation
- s. Phosphatidylserine
- t. Omega 3 Fatty Acids (DHA and EPA)
- u. Lipoic acid and acetyl l carnitine
- v. Medium chain triglycerides (MCTs)

## 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.
- Brown, K. (2004). A radical proposal. *Scientific American*, 14, 30-35.
- Collie, A & Maruff, P. (2000). The neuropsychology of preclinical Alzheimer's disease and mild cognitive impairment. *Neuroscience and Biobehavioral Reviews*, 24, 365-75.
- 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, P.R. and Mobbs, C.V. (Eds): *Functional Neurobiology of Aging*. Academic Press, San Diego, pp 53-63.
- Morrison, J.H., & Hof, P.R. (1997). Life and death of neurons in the aging brain. *Science*, 278, 412-424.
- Sinclair, D & Guarente, L. (2006). Unlocking the secrets of longevity genes. *Scientific American*, 294, 48-57.
- Tapp, P.D., & Siwak, C.T. (2006). The canine model of human brain aging: cognition, behavior and neuropathology. In: *Handbook of models for human aging*. Academic Press, pp 415- 434.
- Valenstein, E., (1998). *Blaming the brain*. The Free Press.
- Van Reekum, R, Black, S.E, Conn, D & Clark, D. (1997). Cognition-enhancing drugs in dementia: a guide to the near future. *Canadian Journal of Psychiatry*, 42, 35-49.
- Wolf, M.S. (2006). Shutting down Alzheimer's. *Scientific American*, 294, 72-79.
- Zivin, J.A. (2000). Understanding clinical trials. *Scientific American*, 282, 69-75

## Tentative Schedule

Date	Topic	Assigned Reading
1 -Sept 15	Introduction - Course outline	
2 -Sept 22	Use of drugs to modify behavior I	Valenstein (1998)
3- Sept 29		Valenstein
4- Oct 6	Use of drugs to modify behavior I The drug approval process	Valenstein Zevin (2000)
5- Oct 13	Targets for Cognitive modifying drugs Cognitive Processes and Aging-	Harvey and Mohs Collie and Maruff (2000)
6- Oct 20	Neuropathology Clinical Assessment	Morrison & Hof (1997) Van Reekum et al (1997)
7- Oct 27	Midterm Exam	
8 -Nov 3	Animal models -	D'Mello & Steckler (1996) Tapp and Siwak (2006)
9 - Nov 10	Cholinesterase Inhibitors	Bartus (2000)
10 -Nov 17	Beta amyloid modifying drugs	Wolfe (2006)
11 -Nov 24	Nutritional and genetic strategies	Brown (2004) Sinclair and Guarente (2006)
12 -Dec 1	Final Exam (Comprehensive)	Term Paper Due Date