Neurophysiology of Aging - Syllabus

Robin Looft-Wilson, Ph.D.
rlooft@wm.edu, 221-2784, 113 Adair Hall
Office Hours: Mon, Wed 3:30-4:30

Attribute: COLL 400. Satisfies the major writing requirement in Kinesiology, and Neuroscience

Prerequisites: Human Physiology (KINE 304) or Neurobiology (BIOL 345)

Textbook: None, we will use current scientific journal articles

Goals: To provide in-depth knowledge of the physiological changes in the nervous system with aging, including common pathologies, and to refine skills needed to evaluate and synthesize the scientific literature. This includes lectures on each topic, systematic analysis of the basic scientific literature, construction of an original research proposal, and oral presentation of the proposal.

Grading:

Research Paper Discussions	90 pts.	Weekly (9 total, 10 pts. each)
Abstract and References	10 pts.	(Due Feb. 24, 5:00 PM)
Written Research Proposal	80 pts.	(Drafts due Mar. 22 and May 5, 5:00 PM)
Oral Presentation	40 pts.	
Ask Questions During Presentations	10 pts.	(5 questions, 2 pts. each)
Quiz #1	40 pts.	(Mar. 3)
Quiz #2	40 pts.	(Apr. 5)
TOTAL	**310 pts.**	

Quizzes: Quizzes are multiple-choice, but you have the opportunity to explain any answer and potentially earn partial credit. It is possible to take a quiz early (if pre-arranged ~1 week in advance with instructor). Late quizzes are allowed in case of illness or personal hardship (as approved by Dean of Students). It is also allowed by choice, but will result in a point deduction (5% if taken within 1 week, 10% after 1 week).

Final Exam: Because this is a seminar course, there is no final exam.

Paper Discussions:

Paper discussions will consist of reading an assigned original research paper, and presenting an assigned figure/table with your small group **(10 pts. each paper, 90 pts. total)**.

Your figure/table presentation should include:

1) the overall purpose of the experiments
2) an explanation of each panel of data, including the methods/approach used (if not obvious)
3) the significance of the data and its importance to the paper overall
4) any limitations of the data

In class format:

1) instructor will present the background, hypothesis, and general methods of the paper
2) your small group will have some time to organize your figure/table presentation
3) small groups will then present figures to class
4) instructor will present conclusions, significance, limitations

Missed Discussions: If you are going to miss a paper discussion, you may turn in (by e-mail) a detailed written analysis (3-5 pages; essay style) which includes the purpose/hypothesis of the paper, an explanation of the data and significance of each figure/table, and overall conclusions, significance, and limitations of the paper. The analysis is **due by 5:00 on the day of the discussion**, or points will be deducted (5% if turned in within 1 week, 10% after 1 week). **You will only be able to take this option for 2 paper discussions**. If you miss more than 2 paper discussions, there is no opportunity to make-up the work, except in extraordinary circumstances.

Final grading:

Final grading is based on the standard scale cut-points (e.g., A=93%, A-=90%, B+=87%, B=93%, B-=80%, etc.), however, if the mean is <80%, then grading is on the curve, with the mean representing the lowest B. Grades are generally not rounded up unless the score is within 0.5 points of the next grade bracket. **This course does not offer extra credit assignments.**

Course Project:

Students will write an *original* research proposal ~8-10 pages in length (**80 pts**) related to one of the course topics, and present it to the class (**40 pts**) in a way that a non-scientist could understand. The topic idea is due Wed., Feb. 9, and a first draft of the Abstract and References is due on Wed., Feb. 23 (**10 pts**). The first draft of the written proposal is due Wed., Mar. 9 [with the opportunity to revise (final draft due on Wed., May 4)] and should include:

a) Abstract (1 paragraph): A summary of your proposal written in lay-person terms. It should describe the rationale for the study (1-2 sentences), the hypothesis (1 sentence), the basic experimental strategy that you propose (1-2 sentences), and the significance of the study (1 sentence).
b) Background/Rationale on the topic (2-3 pages): Explain the specific evidence that provides the rationale for your study. Include an explanation of the pathways/processes being studied, and rationale for the proposed experiment. This section should be heavily referenced in order to adequately explain the current knowledge on the topic and justify your approach.
c) Hypothesis (1 sentence): A prediction statement that is sufficiently focused so that it can be tested with one or more experiments.
d) Study Design (1 paragraph): Explain the overall experimental design including the test subjects/model, treatment scheme, and key measurements.
e) Methods (2-3 pages): Explain the methods in enough detail that the reader knows how you will perform the experiments, when you will make measurements, and the rationale for each. Include references for key methodology, and to justify specific approaches.
f) Potential Results/Interpretation (1 page): Explain what the experimental outcomes would mean. Consider outcomes that support or refute your hypothesis.

g) Significance (1 paragraph): Explain how your project would specifically contribute to our knowledge.
h) References: Include **at least 12 recent, original research articles** related to the proposal topic, **and one or more review articles**. Proper citation within the text (numbered or author, date) is required and each reference should be listed in the bibliography (listed by number or alphabetical by first author's last name). Only include cited references in the bibliography.

The oral presentation should be:

a) ~8 minutes in length (~8-10 Powerpoint Slides)
b) composed to communicate with a lay audience (mostly pictures, minimal text)
c) **Assertion-Evidence Format** (each slide has a conclusive title and visual image to provide evidence for the title, and minimal text)
d) in this slide format:
    1) Title (1 slide)
    2) Rationale (1-3 slides): Explain the reason for the study using evidence from previous studies. Include key data/figures/or models from previous studies (cite references in the notes section of the Powerpoint slides). Explain why the question is important. Each slide in this section should convey only one idea.
    3) Model (1 slide): Include a simple visual model of the pathway, process, or problem to be examined.
    4) Hypothesis (1 slide): State a clear, specific prediction on its own slide.
    5) Experimental Design/Approach (1 slide): A slide showing the treatment strategy and overall design. Include a timeline if appropriate.
    6) Methods (1-2 slides): Describe the measurements and techniques using picture and/or diagrams. Be prepared to discuss their limitations.
    7) Predicted Results/Interpretation (1 slide): Explain what the predicted results are and what they would mean.
    8) Significance (1 slide): Explain what key information your study will provide.

Ask Questions: You will be expected to ask a total of 5 questions during the student proposal presentations **(2 pts. each, 10 pts. total).**

Lecture Topics:

1) Introduction to Aging and Human Longevity
    a) What is Aging & How is it Studied
    b) History of Human Life Span
    c) Biological Hallmarks of Aging
2) General Changes in the Nervous System with Aging
    a) Structural changes in the brain – neuron number/function, glial cells, connectivity, synaptic plasticity, neurotransmitters
    b) Discrete areas of neuron loss
    c) Abnormal inclusions in the brain
    d) Overview of functional changes in the brain
3) Learning, Memory, Dementias, Alzheimer's Disease

a) Overview of brain areas and processes involved in learning and memory
b) Specific changes in memory and learning processes with aging
c) Types of dementias
d) Alzheimer's disease – risk factors, genetics, cellular/molecular mechanisms, treatments
e) Multi-infarct dementia and stroke

4) Motor Control, Parkinson's Disease
    a) Overview of brain areas and processes involved in motor control
    b) Specific changes in motor control and gait with aging
    c) Parkinson's disease – risk factors, genetics, cellular/molecular mechanisms, treatments
5) Sleep and Circadian Rhythms
    a) Overview of neural control of circadian rhythms and sleep
    b) Specific changes in circadian and sleep patterns with aging
    c) Link between sleep disturbances and dementia
    d) Discovery and importance of the glymphatic system and the role of sleep in its function
6) Vision and Hearing
    a) Overview of the visual system
    b) Changes in the structure and function of the visual system with aging
    c) Diseases of the eye with aging – pathology and treatments
    d) Overview of the auditory system
    e) Changes in structure and function of the auditory system with aging
    f) Four types of presbycusis with aging – pathology and treatments
7) Neuroendocrine Control of Stress Responses
    a) The hypothalamic-pituitary-adrenal axis' role in stress responses
    b) Other neural-hormonal responses to stress
    c) Changes in stress responses with aging
    d) Link between chronic stress and accelerated aging

Accommodations: It is the policy of William & Mary to accommodate students with disabilities and qualifying diagnosed conditions in accordance with federal and state laws. Any student who feels s/he may need an accommodation based on the impact of a learning, psychiatric, physical, or chronic health diagnosis should contact Student Accessibility Services staff at 757-221-2512 or at sas@wm.edu to determine if accommodations are warranted and to obtain an official letter of accommodation. For more information, please visit www.wm.edu/sas.

Schedule

Wed., Jan. 26	Lecture #1: Introduction to the Science of Aging/Longevity	
Mon., Jan. 31	Paper #1 and general information about scientific journals	
Wed., Feb. 2	Lecture #2: Changes in Nervous System with Aging, Learning/Memory	
Mon., Feb. 7	Lecture #3: Dementias & Alzheimer's Disease	
Wed., Feb. 9	Paper #2	[Topic Idea Due]
Mon., Feb. 14	Paper #3	
Wed, Feb. 16	Lecture #4: Motor Control, Parkinson's Disease	
Mon., Feb. 21	Paper #4	
Wed., Feb. 23	Lecture #5: Sleep and Circadian Rhythms	[Abstract & References Due]
Mon., Feb. 28	Paper #5	
Wed., Mar. 2	**Quiz #1**	
Mon., Mar. 7	Paper #6	
Wed. Mar. 9	Lecture #6: Vision and Hearing	[First Draft Due, Mon., Mar. 22, 5:00 PM]
SPRING BREAK		
Mon., Mar. 21	Lecture #7: Neuroendocrine Control of Stress Responses	
Wed., Mar. 23	Paper #7	
Mon., Mar. 28	Paper #8	
Wed., Mar. 30	Lecture #8: Anti-aging Interventions	
Mon., Apr. 4	Paper #9	
Wed., Apr. 6	TBA	
Mon., Apr. 11	**Quiz #2**	
Wed., Apr. 13	Sample Presentation	[Small group discussion of project abstracts]
Mon., Apr. 18	Student Presentations	
Wed., Apr. 20	Student Presentations	
Mon., Apr. 25	Student Presentations	
Wed., Apr. 27	Student Presentations	
Mon., May. 2	Student Presentations	
Wed., May 4	Student Presentations	[Final Draft Due, 5:00 PM]

Mon., May 11 Final Presentation Powerpoint Due by 2:00 PM Sharp

Discussion Papers:

1) Xu, et al. Senolytics improve physical function and increase life span in old age. Nature Medicine 24:1246-56, 2018.

2) Dominy, et al. Porphyromonas gingivalis in Alzheimer's disease brains: Evidence for the disease causation and treatment with small-molecule inhibitors. Science Advances 5:eaau3333, 2019.

3) Choi, et al. Combined adult neurogenesis and BDNF mimic exercise effects on cognition in an Alzheimer's mouse model. Science 361:eaan8821, 2018.

4) Horowitz, et al. Blood factors transfer beneficial effects of exercise on neurogenesis and cognition in the aged brain. Science 367-173, 2020.

5) Martorell, et al. Multi-sensory gamma stimulation ameliorates Alzheimer's-associated pathology and improves cognition. Cell 177:256-271, 2019.

6) Student's Choice (by vote):

    a) De Miguel, et al. Exercise plasma boosts memory and dampens brain inflammation via clusterin. Nature 600:494-499, 2021.

    or

    b) Hou, et al. NAD+ supplementation reduces neuroinflammation and cell senescence in a transgenic mouse model of Alzheimer's disease via cGAS-STING. Proceedings of the National Academy of Sciences 118:e2011226118.

7) Holth, et al. The sleep-wake cycle regulates brain interstitial fluid tau in mice and CSF in humans. Science 363:880-84, 2019.

8) Kam, et al. Poly(ADP-ribose) drives pathologic α-synuclein neurodegeneration in Parkinson's disease. Science 362:eaat8407, 2018.

9) Lu, et al. Reprogramming to recover youthful epigenetic information and restore vision. Nature 588:124-129, 2020.