**UNIVERSITY OF FLORIDA**
**COLLEGE OF MEDICINE SYLLABUS**

# NEUROSCIENCE

## Aging and the Brain: (3 credit hours)

Semester: Fall 2024
Delivery Format: Online

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Preferred Course Communications: Email
Prerequisites: Consent of instructor. This course is designed for graduate students in the Online M.Sc., PhD programs, and Biomedical Neuroscience M.Sc. programs.

### Course Description:

This course will address the primary causes of aging and the history of research on aging. Theories of aging will be applied to the brain and cognitive decline, encompassing biomarkers from biochemistry to physiology, as well as structural changes. Examples will be drawn from recent animal and human research, with a focus on examining cellular and molecular mechanisms. Additionally, differences in the rate of aging due to sex, resilience, compensation, and cognitive reserve, as well as the influence of increased oxidative stress and systemic inflammation on the aging brain, will be discussed. Age-associated changes in synaptic plasticity and their impact on cognitive function will be explained. Finally, therapeutic implications and related topics will be explored.

### Purpose and Outcome:

The purpose of this course is to equip students for research in aging neuroscience. By the end of this course, students should have acquired fundamental knowledge of the aging brain and associated cellular and physiological alterations, as well as their impact on synaptic and cognitive function. Additionally, students will be introduced to basic concepts in slice physiology recorded from hippocampal brain slices. This knowledge will enable you to recognize the significance of questions and emerging findings in this field, empowering you to undertake in-depth studies on specific topics within this domain.

### Course Overview:

This course is organized into 12 modules, each focusing on key aspects of the aging brain, the associated changes, and their functional impact on synaptic plasticity. Each module includes Voice

Thread (VT) lectures and self-check quizzes. This course will address questions of the primary causes of aging and the history of research on aging. Theories of aging will be applied to the brain and cognitive decline and include biomarkers from biochemistry to physiology through structural changes. Examples will be drawn from recent human research involving large populations and cellular and molecular mechanisms examined using animal models whenever possible. Differences in the rate of aging due to sex, resilience, compensation, and cognitive reserve, and the role of aging in disease will be discussed. Finally, therapeutic implications and related topics will be explored.

## Relation to Program Outcomes

This course has been designed to establish an advanced foundation in Aging and the brain for MS and graduate students pursuing a degree in Neuroscience. It is also suitable for students enrolled in the online University of Florida (UF) Biomedical Neuroscience Certificate and Master's Degree programs. Graduate students in other UF colleges and advanced undergraduate students with a background in neuroscience are encouraged to inquire about registration.

## Course Objectives and Goals

Our objective is to facilitate the acquisition of advanced knowledge in the field of the aging brain. This knowledge will enable you to recognize the significance of questions and emerging findings in this field and empower you to undertake in-depth studies on specific topics within this domain. After completing this course, students will be able to:

- Identify the different theories/mechanisms/hallmarks of aging.
- Describe early behavioral measures of cognitive decline in humans and animal models.
- Exemplify measures of biological aging as they relate to the brain.
- Discuss sex differences and reserve/resilience mechanisms that may modulate the trajectory of age-related cognitive decline.
- Explore age-associated Neuroinflammation and Oxidative stress
- Impact of aging on mitochondrial function.
- Therapeutic interventions, antioxidants, social interactions, and physical activity.

## Instructional Methods

This is a 12-week course divided into 12 modules, with one module completed per week. Each module covers specific topics related to Aging and the brain. Each module comprises mostly 2 subunits to enhance accessibility and understanding. The online course offers flexibility in learning, with face-to-face sessions scheduled with instructors as needed.

Each unit comprises a video lecture in VoiceThread (VT) format and a quiz to assess understanding of the material. Each VT lecture lasts approximately 20 minutes and can be viewed slide-by-slide for convenience. You will progress through the 12 modules sequentially, with each module considered complete after taking the unit self-check quizzes.

The self-check quizzes, due each Friday at 11:59 pm, will account for 100% of your grade.

## How to succeed in this online course

First, it is important to recognize that online learning presents unique challenges. With the online classroom accessible 24/7, there is a risk of procrastination, missing deadlines, and not dedicating enough time to studies, which can impact performance on exams and assignments. These challenges are amplified for students who may lack self-motivation or effective time management skills, including the use of reminders.

Unlike traditional instructional settings where students attend the same class, the online setting allows each student to "create" their own class experience. While this approach theoretically accommodates various learning styles, some students may not have identified their optimal learning style yet.

Our observation indicates that poor performance in online courses is often directly tied to inadequate time management, such as attempting to complete a week's worth of work just before the deadline. Rushing to finish assignments before the 11:59 pm deadline is not a reliable strategy for success as it limits the opportunity to seek clarification on unclear material. Asking questions on lecture slides and module discussion boards and receiving prompt responses from instructors are valuable features of online learning. Completing self-check quizzes during the week can help identify areas of confusion. Typically, we aim to address posted questions within 12-24 hours, often much sooner.

You are expected to meet the assignment deadlines as posted; however, it's important to note that the self-check quizzes for each module can be completed at your own pace throughout the week. These quizzes are due on Fridays at 11:59 pm.

## Description of Course Content:

**Module 1: Introduction to Aging, senescence, and longevity**

- What is aging, and why do we age? Is aging programmed in our DNA?
- Chronological age, biological age, and senescence.
- Define Lifespan, Healthspan, and Gerospan.
- Sex is a biological factor in determining the propensity for diseases of aging.
- Aging is a main risk factor for several diseases.

**Module 2: Age-related cognitive decline-episodic memory**

- Which processes decline, and when do they decline?
- Discussion of aging studies and types of carryover effects.
- Animal models and their validity for aging research and challenges.
- Understanding the variability in cognitive aging across individuals.
- Assessing age-associated decline in spatial memory decline.

**Module 3: Age-related cognitive decline-Executive function and the prefrontal cortex**

- Prefrontal cortex, attentional changes, and executive function decline.
- Working memory and aging.
- Testing working memory in rodents and humans.
- Cognitive reserve and associated better cognitive performance.
- Cognitive flexibility and set-shifting tasks.

**Module 4: Hallmarks of Aging and the Chronological Sequence of Aging**

- The hallmarks of aging and the discussion of if there is a chronological sequence of aging.
- Aging hallmarks in the brain.
- Aspects of early versus later biomarkers of aging.
- The concept of resilience and neural network compensation, which can defend against biological aging and hormesis.
- Cellular and molecular mechanisms of aging.
- The concept and studies of caloric restriction and its influence on lifespan.
- Caloric restriction and worm genetics.

**Module 5: Biological Markers of Aging Across Species**

- The biological markers of aging and how to measure these markers.
- Biological age and episodic memory.
- Neuroimaging and cognitive decline.
- Aging-associated decrease in brain volume.
- Hippocampal volume and episodic memory.
- Aging is not associated with neuronal. However, loss of synapses contributes to decreased hippocampal volume.
- Are Inflammation and oxidative stress early markers of aging?
- Impact of aging on prefrontal cortex-dependent executive function.

**Module 6: Evolutionary theories of aging**

- Why does evolution not select healthier individuals that live longer?
- Mutation accumulation theory of aging.
- Familial Alzheimer's disease (AD), in which the genes are deterministic for the disease, and late-onset Alzheimer's disease (LOAD), which does not show a classic Mendelian pattern of inheritance.
- APOE influence on Alzheimer's disease.
- The antagonistic pleiotropic theory of aging.
- Genes for longevity and aging.
- Interaction of genes and environment on cognitive decline with advancing age.
- Somatic mutation theory of aging.
- DNA damage and aged-associated decline in cognitive function.
- Gene sequencing in the brain.
- The aging brain exhibits decreased expression of synaptic genes.
- What might reduce DNA damage associated with an aging brain?

**Module 7: Epigenetics of Aging**

- Epigenetic modifications and gene transcription.

- Influence of environment and the history of experience on epigenetic modifications.
- DNA methylation and gene silencing.
- Closing of the therapeutic window for estrogen with aging.
- Is DNA methylation a good marker for biological aging and a tool for aging research?
- The rate of change in methylation is predictive of lifespan and the decline in cognition function.
- Blood biomarkers for aging research.
- Epigenetics as a marker and mechanism of aging.

**Module 8: Cell senescence and inflammation**

- Cell senescence and inflammatory markers of brain aging.
- The dark and bright side of cell senescence
- Cell damage is due to oxidative stress.
- Cellular senescence increases markers of aging and functional decline.
- Episodic memory decline begins in middle age.
- Senescent cells satisfy the three criteria as biological markers of aging
- What are Senolytic drugs?
- Senolytics and cell senescence.
- Senolytic treatment reduces microglial activation and preserves cognitive and synaptic function.

**Module 9: Systemic Inflammation and aging**

- An early role of systemic inflammation and blood markers of brain aging.
- Severe COVID-19 Induces Molecular Signatures of Aging in the Human Brain.
- Anti-inflammatory cytokines provide resilience against the stressors of aging?
- What is an inflammatory aging (iAge) clock? Is iAge correlated with neurodegenerative diseases?
- Blood-borne inflammatory factors contribute to age-related cognitive decline and satisfy the criterion of biological markers of aging.
- Exosomes and aging.
- Expression of miRNA and age-related decline in cognitive function.
- Blood donation contributing to Anti-aging? Blood markers of aging decline with the replacement of blood plasma.
- Examination and Treatment of Senescent Cells and Systemic Inflammation.

**Module 10-Oxidative Stress and Senescent Physiology**

- Oxidative stress theories (free radical) of aging.
- Dysregulation of calcium signaling in aging.
- Redox-signaling and aging.
- Sources of reactive oxygen species (ROS)
- Measures of oxidative damage.
- Resilience mechanisms limit oxidative damage.
- Calcium regulation and aging.
- How redox signaling contributes to hippocampal senescent neurophysiology.
- Aging and N-methyl D- aspartate (NMDA) receptor

- Age-related altered redox signaling contributes to NMDA receptor hypofunction
- NMDA receptor function and age-associated decline in cognitive function
- Afterhyperpolarization (AHP) and calcium during aging.
- Aging and intracellular calcium stores.

**Module 11- Senescent Physiology Synaptic Plasticity**

- Understand the nature of synaptic potentials, including excitatory postsynaptic potentials.
- Define and differentiate between Long-Term Potentiation (LTP) and Long-Term Depression (LTD).
- Investigate how calcium ions ($Ca^{2+}$) influence synaptic plasticity.
- Comprehend the critical role of synaptic plasticity in learning, memory, and overall brain function.
- Recognize how insights into synaptic plasticity contribute to understanding cognitive processes and neurological disorders.
- Effects of aging on LTP induction and relation to memory.
- Aged-associated oxidative stress and its influence on LTP.
- Is aging associated with increased susceptibility to induction of LTD?
- Influence of calcium release from voltage-dependent calcium channels (VDCC) and intracellular calcium stores (ICS) on induction of LTD during aging.
- How does age-related enhanced susceptibility to LTD induction contribute to episodic memory?

**Module 12- Mitochondrial Dysfunction and Therapeutic Implications**

- Mitochondria and cellular metabolisms.
- How to measure mitochondrial function.
- Aging and mitochondrial dysfunction.
- Mitochondria, oxidative stress, and inflammation.
- Are there differences in the effects of aging on mitochondria?
- Synaptic versus non-synaptic mitochondria.
- Increased oxidative stress with aging.
- Is mitochondria dysfunction a tipping point for neurodegenerative diseases?
- What is “The garbage catastrophe theory of aging?
- Biological mechanisms of aging.
- Therapeutic interventions and lifestyle factors play a significant role in mitigating the effects of aging.
- Caloric restriction.
- The Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy (CALERIE) trials to reduce caloric intake.
- The MIND diet.
- Antioxidants.
- Senolytic treatment.
- Lifestyle factors-physical exercise

## Course Materials and Technology:

**Suggested Reading Material**

Assigned articles

**Required Technology**

- Laptop or desktop computer equipped with a microphone and video camera. A microphone and video camera may be used to post comments to VoiceThread and for online Face-to-face meetings if requested.
    a. There is a Canvas app that can be used to access the course.
    b. There are VoiceThread apps that are available for iOS and Android devices that can be used to view and post comments on VTs. While these portable devices are excellent for watching lectures and asking questions, we strongly recommend that you use a laptop or desktop computer when working on this course.

- High-speed, broadband internet connection such as DSL or cable. We highly recommend that you use a broadband, stable Internet connection when taking exams.
    c. SPECIAL NOTE: Some users with satellite Internet service may find their online courses do not load quickly or consistently due to satellite network issues.

- It is highly recommended that you work with Canvas and VT through **Firefox or Chrome Browsers.** For specific questions about browser compatibilities and general questions about e-learning at UF please visit https://wiki.helpdesk.ufl.edu/FAQs/E-Learning.

- You should also make sure you have the **most recent version of Adobe Flash player** installed on your computer. Adobe Flash player can be downloaded from this website.

For additional technical support for this class, please contact the UF Help Desk at:

- Learning-support@ufl.edu
- (352) 392-HELP - select option 2
- UF eLearning

## Academic Requirements and Grading

**Assignments and Grading**

Students will complete a self-check module quiz for each of the 12 modules. Self-check quizzes are due each Friday by 11:59 p.m.

The scores from the self-check quizzes will be weighted to represent 100% of your grade. You will be given grading rubrics for these assignments so that you will understand what is required to complete these assignments and how they will be evaluated.

**Weighting of course assignments (% of final grade)**

Unit Self-check Quizzes: 100% Grade

***Assignments, quizzes, and tests will not be accepted late.***

All self-check quizzes for a module are due Fridays at 11:59 p.m. You will be able to view the correct answers for all quizzes that you submit for 24 hours starting at 12:01 a.m. on the Saturday following the Friday on which they are due. Self-check quizzes not completed by the Friday 11:59 deadline will result in zeros.

As a rule, unless you have a medical excuse or a confirmed family emergency with appropriate documentation, we will not accept late assignments, quizzes, and tests. We recognize that personal circumstances arise that may interfere with your ability to meet a deadline. If this occurs, please let us know as soon as you know- preferably a minimum of 24 hours before the deadline. We will not be receptive to retrospective requests for deadline extensions. Your emails will be responded to within 24 business hours (typically sooner).

If you encounter computer technical difficulties, be sure to include a UF helpdesk ticket number in your request for a deadline extension if you plan to request one. The extension request MUST be submitted within 24 hours of the technical difficulty.

**Grading scale**

A letter grade will be given at the end of the course that will reflect the weighted percentages of the points you have earned:

93-100% = A

90-92%= A-

87-89% = B+

83-86% = B

80-82% = B-

77-79% = C+

73-76% = C

70-72% = C-

67-69% = D+

63-66% = D

<63% =E

## Grading Policy:

Students will be expected to complete all requirements for one module each week. There will be no deadline extensions for the completion of a module unless granted by the course directors before the scheduled completion date. You will receive zeros for failure to submit module self-check quizzes or assignments by their deadlines in the absence of an approved excuse.

More information on UF grading policy may be found at:

http://gradcatalog.ufl.edu/content.php?catoid=10&navoid=2020#grades

## Policy Related to Required Class Attendance:

This course is entirely online and is asynchronous. Thus, there is no formal class attendance policy. Requirements for make-up quizzes, assignments, and other work in this course are consistent with university policies that can be found at:
https://catalog.ufl.edu/ugrad/current/regulations/info/attendance.aspx

Excused absences must be consistent with university policies in the Graduate Catalog (http://gradcatalog.ufl.edu/content.php?catoid=10&navoid=2020#attendance).

Additional information can be found here:
https://catalog.ufl.edu/ugrad/current/regulations/info/attendance.aspx

## Expectations Regarding Course Behavior:

**Communication Guidelines**

**WHEN DO I CONTACT THE UF HELPDESK?**
If you have **technical difficulties with E-learning**, please contact the UF helpdesk at learning-support@ufl.edu, or (352) 392-4357 - select option 2. If your technical difficulties will cause you to miss a due date, you MUST report the problem to E-learning. Include the ticket number that you are given in an e-mail to the instructor to explain the late assignment/quiz/test.

Types of questions that should be directed to the Help Desk:

1. I can't log into E-learning
2. I have clicked on the "submit" button for my quiz and nothing is happening
3. I can't upload an assignment (be sure that you have reviewed the tutorial on how to do this BEFORE you contact the Help Desk)

4. E-learning has given me an error message and I can't submit my assignment.

***NOTE:*** *Late work that involves technical difficulties with E-learning MUST be accompanied by a ticket number from the Help Desk.*

***ALSO*** *- Be sure to be familiar with the hours of operation for the UF help desk since they are oftentimes not available after 10:30pm on workdays and after 8:00 pm on weekends. There hours are posted at http://helpdesk.ufl.edu/about/business-hours/*

**WHEN DO I POST QUESTIONS TO THE COURSE QUESTIONS DISCUSSION BOARD?**

Questions that deal with the course itself should be submitted to the Course Questions board. Posted questions should NOT be about grades or a private matter. Do not post personal grade questions on the Course Questions discussion board.

Before posting a question, check those already posted to be sure that you are not duplicating a question. These should be things that other students in the class might have trouble with. For example:

1. I am unable to post comments to VoiceThread.
2. The link to specific VoiceThread is not working.
3. One of the quiz questions did not display properly.

Posting on the Course questions board is the fastest way to get an answer to your question. Be sure to give it a meaningful heading!

**Questions of a private nature should be e-mailed to the course instructor** (see below on how to e-mail within E-learning). In all cases, please allow 24 hours for a response. Every effort will be made to answer questions posted over the weekend within 24 hours. If not addressed, they will be addressed on the following Monday.

**WHEN DO I EMAIL MY INSTRUCTOR?**

Questions about the course should be e-mailed to the instructor through the e-mail tool in E-learning.

Examples of e-mail questions for the instructor to get clear, concise responses:

1. I think there is an error in my grade for the assignment in module 3 (be sure to explain exactly why you think there is an error and provide documentation)
2. I am behind in the course, and I would like to know how I may catch up (in such a case, your instructor may ask you to set up a Skype meeting or a time to call on the telephone)

If you have questions about the course itself, please reread the syllabus before asking a question. If the answer is not in the syllabus, check the Course Questions discussion board (this discussion board can be located by clicking on the discussions menu tab on the left of the course home page). If the answer to your question is not there, please post the question on the Course Questions discussion board.

DO NOT e-mail the instructor with general course questions. If your question is personal, e-mail your instructor from within the e-learning system using the instructions below.
Late work that involves technical difficulties with E-learning MUST be accompanied by a ticket number from the Help Desk.

**HOW TO EMAIL YOUR INSTRUCTOR**
When emailing your instructor, please do so through Canvas.
To send an e-mail from the course:

1. Click on the mail icon that is located on the left side of your screen.
2. Click the "Compose Message" button.
3. "To window" will display.
4. Locate your instructor's name.
5. Always include a description in your subject line
6. Type your message and add any necessary attachments. Be sure that your subject line is meaningful.
7. Click "send."

## Academic Integrity:

***PLAGIARISM***
Weekly assignments involve the review of the primary literature to formulate their essay for each topic. Students must understand what plagiarism is and must not engage in this behavior when completing assignments in this course. The University of Florida Student Honor Code states that plagiarism includes but is not limited to:

1. Quoting oral or written materials, including but not limited to those found on the internet, whether published or unpublished, without proper attribution.
2. Submitting a document or assignment that is identical or substantially identical to a document or assignment not authored by the student in whole or in part.

Students whose assignments/tests exhibit evidence of plagiarism will receive zeros for those assignments and tests for the first offense and will receive a warning. Students who continue to engage in this behavior after the first warning will be reported to the UF Dean of Students Office.

***PROHIBITED COLLABORATION OR CONSULTATION***
Students found to be involved in sharing answers and/or collaborating on assignments will receive zeros for those exams and assignments. Students who continue to engage in this behavior after the first warning will be reported to the UF Dean of Students Office.

Students are expected to act by the University of Florida policy on academic integrity. As a student at the University of Florida, you have committed yourself to uphold the Honor Code, which includes the following pledge:

"**We, the members of the University of Florida community, pledge to hold ourselves and our peers to the highest standards of honesty and integrity**."

You are expected to exhibit behavior consistent with this commitment to the UF academic community, and on all work submitted for credit at the University of Florida, the following pledge is either required or implied:

**"On my honor, I have neither given nor received unauthorized aid in doing this assignment."**

It is your responsibility to know and comply with all university policies and procedures regarding academic integrity and the Student Honor Code. Violations of the Honor Code at the University of Florida will not be tolerated. Violations will be reported to the Dean of Students Office for consideration of disciplinary action. For additional information regarding Academic Integrity, please see Student Conduct and Honor Code or the Graduate Student Website for additional details:
https://www.dso.ufl.edu/sccr/process/student-conduct-honor-code/
http://gradschool.ufl.edu/students/introduction.html

Please also review the use of copyrighted materials, which can be found on the Health Science

Center Library's web page:

http://www.library.health.ufl.edu/services/copyright.htm

**Please remember cheating, lying, misrepresentation, or plagiarism in any form is unacceptable and inexcusable behavior.**

## Online Faculty Course Evaluation Process:

Students are **expected** to provide professional and respectful feedback on the quality of instruction in this course by completing course evaluations online via GatorEvals. Guidance on how to give feedback professionally and respectfully is available at

https://gatorevals.aa.ufl.edu/students/ . Students will be notified when the evaluation period opens and can complete evaluations through the email they receive from GatorEvals, in their Canvas course menu under GatorEvals, or via https://ufl.bluera.com/ufl/. Summaries of course evaluation results are available to students at https://gatorevals.aa.ufl.edu/public-results/.

## Support Services:

**Accommodations for Students with Disabilities:**

Students with disabilities who experience learning barriers and would like to request academic accommodations should connect with the Disability Resource Center by visiting https://disability.ufl.edu/students/get-started/. Students need to share their accommodation letter with their instructor and discuss their access needs, as early as possible in the semester. The College is committed to providing reasonable accommodations to assist students in their coursework.

### Counseling and Student Health:

Students sometimes experience stress from academic expectations and/or personal and interpersonal issues that may interfere with their academic performance. If you find yourself facing issues that have the potential to or are already negatively affecting your coursework, you are encouraged to talk with an instructor and/or seek help through University resources available to you.

- The Counseling and Wellness Center 352-392-1575 offers a variety of support services such as psychological assessment and intervention and assistance for math and test anxiety. Visit their web site for more information: http://www.counseling.ufl.edu. On line and in person assistance is available.

- You Matter We Care website: http://www.umatter.ufl.edu/. If you are feeling overwhelmed or stressed, you can reach out for help through the You Matter We Care website, which is staffed by Dean of Students and Counseling Center personnel.

- The Student Health Care Center at UF Health is a satellite clinic of the main Student Health Care Center located on Fletcher Drive on campus. Student Health at UF Health offers a variety of clinical services. The clinic is located on the second floor of the Dental Tower in the Health Science Center. For more information, contact the clinic at 392-0627 or check out the website at: https://shcc.ufl.edu/

- UF Health Emergency Room / Trauma Center: For immediate medical care call 352-733-0111 or go to the emergency room at 1515 SW Archer Road, Gainesville, FL 32698, ufhealth.org/emergency-room-trauma-center.

- University Police Department: Visit police.ufl.edu/ or call 352-392-1111 (or 9-1-1 for emergencies).

- Crisis intervention is always available 24/7 from:

Alachua County Crisis Center:
(352) 264-6789

http://www.alachuacounty.us/DEPTS/CSS/CRISISCENTER/Pages/CrisisCenter.aspx

Do not wait until you reach a crisis to come in and talk with us. We have helped many students through stressful situations impacting their academic performance. You are not alone so do not be afraid to ask for assistance.

## Academic Resources

**E-learning technical support**: Contact the UF Computing Help Desk at 352-392-4357 or via e-mail at helpdesk@ufl.edu.

**Career Connections Center**: Reitz Union Suite 1300, 352-392-1601. Career assistance and counseling services career.ufl.edu/.

**Library Support:** cms.uflib.ufl.edu/ ask various ways to receive assistance with respect to using the libraries or finding resources.

**Teaching Center**: Broward Hall 352-392-2010 or to make an appointment 352 392-6420. General study skills and tutoring. teachingcenter.ufl.edu/

**Writing Studio**: 2215 Turlington Hall, 352-846-1138. Help brainstorming, formatting, and writing papers. writing.ufl.edu/writing-studio/

**Student Complaints On-Campus**: sccr.dso.ufl.edu/policies/student-honor-code-student-conduct-code/

**On-Line Students Complaints**: distance.ufl.edu/student-complaint-process