THE GOAL OF THIS COURSE IS TO UNDERSTAND THE BIOLOGICAL CAUSES OF ALZHEIMER’S DISEASE, THE BEHAVIORS ASSOCIATED WITH THE DISEASE, AND POSSIBLE THERAPEUTIC APPROACHES.

**SYLLABUS**

**JAN 21, 23. Overview**
History of AD. Different types of memory
AD is characterised by cognitive impairments and the presence of deposits, plaques and tangles, in the brain. There are different forms of memory which depend on different brain regions. Functional anatomy of the brain.
Maurer, 1997, Julia vignettes in Decoding Darkness.

**JAN 28/30. Correlation of brain pathology and behavioural changes in AD.**
Assessment of behavioural changes seen in AD.
Speaking our Minds. Aging with Grace, pp 4-7, 34-35, 140-152.

**FEB 4/6. Stains and Imaging: Localization of brain damage.**
How do you know what brain damage there is and where the amyloid and tau are? Different types of amyloid; cerebral amyloid angiopathy (CAA). Tangles are another marker for AD. Histological studies, Imaging studies. fMRI and PET. AD may begin much earlier than we thought.

**FEB 11/13. Some risk factors for AD.**
My mother has Alzheimer's disease.
Aging with Grace, pp 38-43, 156,

**FEB 18/20. Where does amyloid come from?**
Amyloid is produced from APP. Enzymes involved with APP and the production of amyloid.
The search for the genes underlying AD. There are 2 forms of AD, early-onset and late-onset.

**FEB 24, LAST DAY TO DROP WITHOUT PENALTY OF "F"**

**FEB 25/27. Other factors involved in AD**
The role of tau. APOE4 a late-onset gene. The blood brain barrier may play a role and interact with APOE4.
Decoding Darkness. Aging with Grace, Chapter 8. Yu et al. 2014. (Zlokovic, TBA, )

**MAR 3/5** AD may begin much earlier than we thought. The default network is altered early in AD.
Can Alzheimer's be stopped (Film).
Buckner et al, 2008; Dean et al., 2014

MAR 10/12  SPRING BREAK

MAR 17/19 review, Student presentation/paper topics due, EXAM

MAR 24/26 Animal models: Mice are useful. Soluble versus non-soluble amyloid.
Transgenic mice have been used to model AD. They can be used to assess treatments and understand factors influencing the progress of the disease. Memory loss is seen before plaques appear. This may be due to soluble amyloid. Soluble amyloid precedes tau and causes cognitive impairments in Tg Hsiao, mice. There is synaptic damage. ADDLS, oligomers, etc.
Behavioral measures of memory loss; spatial memory, passive avoidance. LTP. Tg models, 2576, J20 and triple transgenic mice.
Hsiao et al., 1996; Billings et al., (2005); Selkow (2002).

MAR 30/APR 2 Prescription Drugs and other treatments for AD; AChE inhibitors, most AD drugs target acetylcholine degradation. Memantine targets a glutamate receptor. Antibody treatment may be effective. Anti-cholesterol drugs. Blood transfusion.

APR 7/9 Role of metals in AD.
Possible role of the metals in AD. The plaques are high in iron, copper, zinc, and (?) aluminium. Zinc can cause memory loss, but this may be due to an induced copper deficit. Behavioral and histological data in normal and Tg mice. Zinc is prescribed for age-related macular degeneration, but could impact circadian rhythms. Cholesterol with copper may be a risk factor. Iron may be dangerous.
Drugs acting as Metal ionophores; PBT2 is a possible remedy for AD.
Student presentations begin.

APR 14/16 Risk factors
Lack of education, low SES, head injury (inflammation), stroke (smoking) are risk factors.
APOE status may have an interactive effect with other risk factors.
Prescription drugs can cause memory loss.
Aging with Grace. Snowden et al., 1997; Moceri et al., 2001.
Student presentations.

APR 21/23/ Preventative factors.
Exercise, education, and music, etc. are helpful.
Diet can include foods with folic acid, caffeine and those that act as anti oxidants: dark chocolate, spinach, blueberries, curcumin, pomegranates. Brushing your teeth is important! The rate of dementia might be going down.
Student presentations

APR 28/30/  Summary
Student presentations.

PAPERS DUE MAY 3
FINAL EXAM  DUE MAY10TH (take home)
There will be a take home quiz most weeks on an assigned paper. The exams will be essay exams. Graduate student presentations should be ~ 20 mins (- points for going over!)

OFFICE HOURS, TU/ TH 4:30-5  DKH
AND BY APPOINTMENT
PHONE, 993-4107, E-MAIL  jflinn@gmu.edu

GRADING
QUIZZES, UNDERGRADUATE, INCLUDING IN-CLASS QUESTIONS, 20%
QUIZZES, GRADUATE, INCLUDING IN-CLASS QUESTIONS, 15%
UNDERGRADUATE, 10 MIN GROUP PRESENTATION, 7%; WRITE UP 8%, (15%)
GRADUATE, 15 MIN INDIVIDUAL PRESENTATIONS 10%; WRITE UP 10%, (20%)
MID-TERM EXAM, 30%
FINAL EXAM, 30%  (take home)

Since the total is 95 points for both the undergraduates the total score will be divided by 95 and multiplied by 100 to give the % grade. There will be an additional; question on the exams for the graduate students.

Books
Aging With Grace, D. Snowden. Describes the School  Sisters of Notre Dame study in which risk factors for Alzheimer’s disease are studied.

Speaking Our Minds L. Snyder. Personal reflections from individuals with Alzheimer’s disease.


Required Papers


Björklund NL, Reese LC, Sadagoparamanujam VM, Ghirardi V, Woltjer RL, Taglialatela G. (2012) Absence of amyloid β oligomers at the postsynapse and regulated synaptic Zn2+ in cognitively intact aged individuals with Alzheimer's disease neuropathology. Mol Neurodegener. 7:23 (Find on google)


Hernandez et al., submitted to J. Alz Dis.


Lippi et al., submitted to Frontiers in Neuroscience.


Parsons, C.G., Stoﬄer, A., Danysz, W. Memantine: a NMDA receptor antagonist that improves memory by restoration of homeostasis in the glutamatergic system - too little activation is bad, too much is even worse. Neuropharmacology 53 (2007) 699e723


Tergesen, A.,. What Science tells us about preventing dementia. Wall St J. 11/17/19


Reference papers


If you are a student with a disability and you need academic accommodations, please see me and contact the Disability Resource Center (DRC) at 703-993-2474. All academic accommodations must be arranged through that office.

Honor Code
George Mason University has an Honor Code, which requires all members of this community to maintain the highest standards of academic honesty and integrity. Cheating, plagiarism, lying, and stealing are all prohibited. It is every student’s responsibility to familiarize himself or herself with the Honor Code. The Honor Code is available at: http://oai.gmu.edu/the-mason-honor-code-2/ All violations of the Honor Code will be reported to the Honor Committee.

Communications via GMU E-mail:
Mason uses electronic mail to provide official information to students. Examples include communications from course instructors, notices from the library, notices about academic standing, financial aid information, class materials, assignments, questions, and instructor feedback. Students are responsible for the content of university communication sent to their Mason e-mail account and are required to activate that account and check it regularly.

Technology
Quizzes will be posted on Blackboard. Dr Flinn and the TA will also communicate with students in the class via e mail.
Cell phones may not be used in class. Students may use computers to take class notes but for no other purpose. I may ask to see your notes at the end of class, those using the computer for other reasons than note taking can get a zero on the next quiz.

Class Cancellation
If class has to be cancelled, e.g. for weather, an e mail will be sent to the class. In such cases the class will be rescheduled during the snow day.
Add/Drop deadlines
2/5 last day to add/drop with no tuition penalty, 2/24 last day to drop.