Course Approval Form

For approval of new courses and deletions or modifications to an existing course.

registrar.gmu.edu/facultystaff/curriculum

Action Requested:

- [x] Create new course
- [ ] Inactivate existing course
- [ ] Modify existing course (check all that apply)
  - [ ] Title
  - [ ] Credits,
  - [ ] Repeat Status,
  - [ ] Grade Type,
  - [ ] Prereq/coreq
  - [ ] Schedule Type
  - [ ] Restrictions
  - [ ] Other:

Course Level:

- [x] Undergraduate
- [ ] Graduate

College/School: COS
Department: Neusroscience
Submitted by: Jane Flinn
Ext: 4107
Email: jflinn@gmu.edu

Subject Code: NEUR
Number: 380
(Do not list multiple codes or numbers. Each course proposal must have a separate form.)

Effective Term:

- [x] Fall
- [ ] Spring
- [ ] Summer

Year 2013

Title:
Current
Banner (30 characters max including spaces)
New: Biological Bases of Alzheimer's disease

Credits: (check one)

- [x] Fixed: 3 or
- [ ] Variable: to

Repeat Status: (check one)

- [x] Not Repeatable (NR)
- [ ] Repeatable within degree (RD)
- [ ] Repeatable within term (RT)

Maximum credits allowed: 3

Grade Mode: (check one)

- [x] Regular (A, B, C, etc.)
- [ ] Satisfactory/No Credit
- [ ] Special (A, B C, etc. +IP)

Schedule Type: (check one) LEC can include LAB or RCT

- [x] Lecture (LEC)
- [ ] Lab (LAB)
- [ ] Recitation (RCT)
- [ ] Internship (INT)
- [ ] Independent Study (IND)
- [ ] Seminar (SEM)
- [ ] Studio (STU)

Prerequisite(s):
PSYC 375, 376

Corequisite(s):

Instructional Mode:

- [x] 100% face-to-face
- [ ] Hybrid: ≤ 50% electronically delivered
- [ ] 100% electronically delivered

Restrictions Enforced by System: Major, College, Degree, Program, etc. Include Code.

Are there equivalent course(s)?

- [ ] Yes
- [x] No

If yes, please list

Catalog Copy for NEW Courses Only (Consult University Catalog for models)

Description (No more than 60 words, use verb phrases and present tense)	**Notes** (List additional information for the course)
A survey of the causes, symptoms, drug treatments, risk factors and preventative measures associated with Alzheimer's disease.	

Indicate number of contact hours: Hours of Lecture or Seminar per week: 3 Hours of Lab or Studio:

When Offered: (check all that apply) [ ] Fall [ ] Summer [x] Spring

Approval Signatures

Department Approval — Date: 11/9/12

College/School Approval — Date

If this course includes subject matter currently dealt with by any other units, the originating department must circulate this proposal for review by those units and obtain the necessary signatures prior to submission. Failure to do so will delay action on this proposal.

Unit Name	Unit Approval Name	Unit Approver's Signature	Date

For Graduate Courses Only

Graduate Council Member — Provost Office — Graduate Council Approval Date

For Registrar Office's Use Only: Banner Catalog

revised 11/8/11

Course Proposal Submitted to the Curriculum Committee of the College of Science

1. **COURSE NUMBER AND TITLE: NEUR 380** Biological Bases of Alzheimer's disease

Course Prerequisites:
PSYC 375, 376

Catalog Description:
Survey of the causes, symptoms, drug treatments, risk factors and preventative measures associated with Alzheimer's disease.

2. COURSE JUSTIFICATION:

Course Objectives:
Understanding the many aspects of Alzheimer's disease. These include:
The difference between early-onset and late-onset Alzheimer's disease and the genes associated with these two forms.
The role of amyloid and tau in the development of the disease.
The consequent brain damage and the associated behavioral problems caused by it.
Mode of action of the drugs that have been developed or are in development.
The risk factors associated with Alzheimer's disease.
Preventative measures that may slow down its progression.

Course Necessity:
The prevalence of Alzheimer's disease (AD) is growing rapidly as people live to a greater age. It is important that more people understand the factors associated with this disease.

Course Relationship to Existing Programs:

This course will increase the breadth of the Neuroscience program.

Course Relationship to Existing Courses:
The course has been taught as NEUR 461 (Special topics) for several years with good enrollments and evaluations. It has been cross-listed with PSYC 373, Advanced Physiological Psychology. There are too many course being taught as NEUR 461 and many of these should now be listed as stand alone courses.

2. APPROVAL HISTORY:
No previous application has been made.

4. SCHEDULING AND PROPOSED INSTRUCTORS:

Semester of Initial Offering:
Spring 2014.

Proposed Instructors:
Dr Jane Flinn,
5. TENTATIVE SYLLABUS: see attached.

BIOLOGICAL BASES OF ALZHEIMER'S DISEASE,
NEUR 461 SPRING 2012

DR. JANE FLINN

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 24/25. Overview
History of AD.
AD is characterised by cognitive impairments and the presence of amyloid deposits, including plaques and tangles in the brain. Functional anatomy of the brain. There are different forms of memory which depend on different brain regions.
Julia vignettes in Decoding Darkness.
Lage

JAN 31/Feb 2. Correlates of brain pathology in AD and behavioural changes.
Assessment of behavioural changes.
Speaking our Minds. Aging with Grace, Chapter 9 pp 14-152.

FEB 7/9 . Stains and Imaging.
How do you know what brain damage there is and where the amyloid is? Plaques are made of amyloid; there are different types of plaques and different forms of amyloid. Amyloid deposits are also found around blood vessels, cerebral amyloid angiopathy (CAA). Tangles are another marker for AD. Histological studies, Imaging studies. fMRI and PET.
Braak and Braak. Klunk et al.

FEB 14/16. Where does amyloid come from?
Amyloid is produced from APP. There are 2 forms of AD, early-onset and late-onset.
The search for the genes underlying AD.
Decoding Darkness.

FEB 21/23 The Forgetting. (Film)
Presentations of people with Alzheimer's disease. Dr Flinn will be away.

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

FEB 28/MAR 1 Other factors involved in AD
Enzymes involved with APP and amyloid. A late-onset gene. The role of tau.
Decoding Darkness, Aging with Grace, Chapter 8.

MAR 6/8 Animal models: Mice are useful.
Transgenic mice have been used to model AD. They can be used to assess treatments and understand factors influencing the progress of the disease. Behavioral measures of memory loss; spatial memory, passive avoidance. LTP. Hsiao, Westaway and triple transgenic mice. Memory loss is seen before plaques appear. This may be due to soluble amyloid.
Hsiao et al., Billings et al.

MAR 6/8 Soluble versus non-soluble amyloid.
Soluble amyloid may be as dangerous as the aggregated form in plaques, and could be intraneuronal. Soluble amyloid precedes τ and causes cognitive impairments in Tg mice. There is synaptic damage. ADDLS, oligomers, etc.
Billings et al.; Hardy & Selkow. Selkoe
Student presentation topics due.

MAR 12-18 SPRING BREAK

MAR 20/22 review, EXAM

MAR 27/ 29 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 in normal rats and mice, but this may be due to an induced copper deficit. Behavioral and histological data in normal and Tg rats and mice.
Zinc, is prescribed for age-related macular degeneration. Cholesterol with copper may be a risk factor. Iron may be dangerous.
Anti-cholesterol drugs.
Drugs acting as Metal ionophores ,
Bush & Tanzi, 2008; Duce et al, 2010, (see also James 2012 and Duce 2012.)
Sparks & Schreurs.

APR 3/5 Risk factors
Lack of education, low SES, head injury (inflammation), stroke (smoking) are risk factors.
Aging with Grace. Moceri et al.
Student presentations begin.

APR 10/12 Preventative factors.
Exercise and education are helpful.
Diet can include foods that act as anti oxidants: blueberries, curcumin, pomegranates and folic acid.
Adlard et al.

APR 17/19 Drugs
AChE inhibitors; most AD drugs target target acetylcholine degradation.
Memantine targets a glutamate receptors. Antibody treatment may be effective.

Parsons et al..

APRIL 24/26
Student presentations.

May 1/3 Summary, Student presentations.

PAPERS DUE MAY 3TH
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!) Undergraduates should be 12- 15 minutes. Undergraduates may present as pairs.

GRADING
QUIZZES, 10%
IN CLASS PRESENTATIONS 15%
WRITE UP 15%
MID-TERM EXAM, 30%
FINAL EXAM 30%

OFFICE HOURS
TH 4:30-5:30
AND BY APPOINTMENT.

PHONE, 993-4107
OFFICE, DKH 2022
E-MAIL jflinn@gmu.edu

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.

Decoding Darkness, R. Tanzi & A. Parsons. A history of the search for genes underlying Alzheimer's disease.

Required Papers
P.A. Adlard, V.M. Perreau, V. Pop and C.W. Cotman, Voluntary exercise decreases amyloid load in a transgenic model of Alzheimer's disease, *J Neurosci* **25** (2005), 4217-4221.

Ballard C.G., Greig N.H., Guillozet-Bongaarts A.L., Enz A. & Darvesh S. (2005) Cholinesterases: roles in the brain during health and disease. Curr. Alzheimer res. 2(3):307-18

Billings L.M., Oddo S., Green K.N., McGaugh J.L. & LaFerla M. (2005) Intraneuronal Aβ Causes the onset of early Alzheimer's disease-related cognitive deficits in transgenic mice. Neuron. Mar 3;45(5):675-88

Braak H. & Braak E. (1991) Neuropathalogical staging of Alzheimer-related changes. Acta Neuropath 82:239-159.)

Bush A.I. & Tanzi R. (2008). Therapeutics for Alzheimer's disease based on the metal hypothesis. Neurotherapeutics5:421-432.

Duce et al. (2010) Iron-export ferroxidase activity of β-amyloid precursor protein is inhibited by zinc in Alzheimer's disease. Cell. 142(6):857-67.

Hardy J. and Selkow D. 2002. The amyloid hypothesis of Alzheimer's disease: progress and problems on the road to therapeutics. Science 297(5580): 353-356.

Hsiao K. Chapman, P., Nilsen S., Eckman C., Harigaya Y., Younkin S., Yang F., and Cole G. (1996) Correlative memory deficits, Abeta elevation, and amyloid plaques in transgenic mice. Science 274:99-102.

Klunk W.E., Engler H., Nordberg A., Wang Y/Daniele S., Blomquist G. et al. (2004) Imaging brain amyloid in Alzheimer's disease with Pittsburgh compound-B. Ann. Neurol. 55:306-319.

Lage, J.M.M. (2006) 100 years of Alzheimer's disease (1906-2006). J.Alz. Dis 9:15-26. (supplement 3)

Moceri VM, et al. (2001) Using census data and birth certificates to reconstruct the early-life socioeconomic environment and the relation to the development of Alzheimer's disease. Epidemiology. 12(4):383-9.

Parsons, C.G., Sto¨ffler, 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

Selkoe D.J. Alzheimer's disease is a synaptic failure. (2003?) Science 298:789-791.
Snowden et al. Brain Infarction and the clinical expression of Alzheimer Disease. The Nun Study. JAMA 277:813-817. 1997

Sparks D.L. & Schreurs B.G. Trace amounts of copper in water induce beta-amyloid plaques and learning deficits in a rabbit model of Alzheimer's disease. P.N.A.S. (2003) 100(19) :11065-9.*

Tanzi R. (2005) The synaptic Aβ hypothesis of Alzheimer disease. Nature Neuroscience 8: 977-979. (?)

Reference papers

Barnes P. & Good M. (2005) Impaired Pavlovian cued fear conditioning in Tg 2576 mice expressing a human mutant amyloid precursor protein gene. Behav. Brain Res. 157(1) 107-117.

Bishop G.M., Robinson S.R., Liu Q., Perry G., Atwood C.S., & Smith M.A.. (2002). Iron: A pathological marker of Alzheimer Disease? Developmental Neuroscience, 24:184-187.

Bjorklund NL, Sadagoparamanujam VM, Taglialatela G. (2012) Selective, quantitative measurement of releasable synaptic zinc in human autopsy hippocampal brain tissue from Alzheimer's disease patients. J. Neurosci Methods. 203(1):146-51.

Braak, H., Rub, U., Schuktz, C., Del Tredict, K. (2006). Vulnerability of cortical neurons to Alzheimer's and Parkinson's diseases. J.Alz Dis, 9:35-44.

Brendza R.P., Bacskai B.J., Cirrito J.R., Simmons K.A., Skoch J.M., Klunk W.E., Mathis C.A., Bales K.R.,

Paul S.M., Hyman B.T., and Holtzman D.M. 2005. Anti-Aβ antibody treatment promotes the rapid recovery of amyloid-associated neuritic dystrophy in PDAPP transgenic mice. J.Clin. Invest. 115(2):428-433.

Bush A.I. & Tanzi R. (2002). The galvanization of β-amyloid in Alzheimer's disease. PNAS. 99:7317-7319.

Bush A.I. Masters C.L. & Tanzi R.E. (2003) Copper, beta –amyloid, and Alzheimer's disease: tapping a sensitive connection. P.N.A.S. 100(20):11816 Comment on Sparks and Schreurs.

Dickerson B.C. & Sperling R.A. (2005) Neuroimaging biomarkers for clinical trials of disease- modifying therapies in Alzheimer's disease. NeuroRx. 2:348-360.

House E., Collingwood J., Khan A., Korchazkina O., Berthon G., and Exley C. (2004) Aluminum, iron, zinc and copper influence the *in vitro* formation of amyloid fibrils of $A\beta_{42}$ in a manner which may have consequences for metal chelation therapy in Alzheimer's disease. J. Alz. Dis. 6:291-301.

*James SA, Volitakis I, Adlard PA, Duce JA, Masters CL, Cherny RA, Bush AI. (2012) Elevated labile Cu is associated with oxidative pathology in Alzheimer disease. Free Radic Biol Med. 2(2):298-302

Linkous, D. H.. Adlard P.A., Wanschura P.B., Conko K.M., Flinn J.M. (2009) The effects of enhanced zinc on spatial memory and plaque formation in transgenic mice. J. Alzheimer's Disease. 18(3) 541-551.

Maurer, K., Volk S., Gerbaldo H. (1997). Auguste D. and Alzheimer's disease. Lancet, 349:1546-49.

Ognibene E., Middei S., Daniele S., Adriani W., Ghirardi O., et al. (2005) Aspects of spatial memory and behavioral disinhibition in Tg2576 transgenic mice as a model of Alzheimer's disease. Behav. Brain Res. 2005:225-232.

Roberts BR, Ryan TM, Bush AI, Masters CL, Duce JA. (2012) The role of metallobiology and amyloid-β peptides in Alzheimer's disease. Neurochem. 2012 Jan;120 Suppl 1:149-66. *

Sparks L.D. (2004) Cholesterol, copper, and accumulation of thioflavine S-reactive Alzheimer's like amyloid beta in rabbit brain. J. Mol. Neurosci. 24 (1): 97-104

Reference Books

Mace N.L. & Rabins, P.V. (2006). The 36 hour day. Johns Hopkins. A guide for family members or caretakers of those with AD.

Perry et al. Alzheimer's Disease (2006). IOS (papers from the J. Alz. Dis. commemorating the 100 year "anniversary" of AD.

Thorndike J. The Last of His Mind. Swallow Press.

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.

Students are expected to be familiar with and to uphold the honor code.