

**NEURONAL BASES OF LEARNING AND MEMORY**  
**PSYCH 558/472, NEUR 461, FALL 2016 (Draft)**

**DR. JANE FLINN**

**AUG 29/31**

TOPICS: OVERVIEW OF THE COURSE; THERE ARE SEVERAL TYPES OF LONG-TERM MEMORY, AND THEY DEPEND ON DIFFERENT BRAIN REGIONS

Memories lost and spared in an amnesic patient, H.M. Two types of long-term memory, declarative and non-declarative, show differential sparing in amnesiacs. Short-term memory is retained. Squire's model of memory. A monkey model of temporal lobe amnesia, Mishkin and Squire's lesion experiments.

Readings:

Introduction and Chapter 1 from Notes.

Ogden and Corkin, (1991) Memories of H.M. In Memory Mechanisms. Eds W.C. Abraham et al., 1991. ( Available in class)

Annese et al., (2014) Postmortem examination of patient H.M.'s brain based on histological sectioning and digital 3D reconstruction. *Nature Communications* 5, Article #3122

**SEP 5,7**

TOPICS: RELATIVE CONTRIBUTIONS OF HIPPOCAMPUS AND OVERLYING CORTEX TO LONG-TERM EPISODIC MEMORY

Memory in children with hippocampal damage. Clive Wearing, a modern H.M. The hippocampus is important in episodic memories but may be less important for semantic memories.

Readings:

Chapter 2, (5) from Notes.

Vargha-Khadem et al., (1997) Differential effects of early hippocampal pathology on episodic and semantic memory. *Science* 277:376-380.

(Squire, L. R, Wixted J. T. The cognitive neuroscience of human memory since H.M. *Ann. Rev. Neurosci.* 2011; 34:259-88)

**SEP 5 IS THE LAST DAY TO ADD**

**SEP 12,14**

TOPICS: THE ROLE OF THE CEREBELLUM AND BASAL GANGLIA IN MEMORY, SEARCH FOR THE ENGRAM

Lashley, Penfield and Thompson's work. Classical conditioning in rabbits and humans. The basal ganglia are needed for habit learning. It may be more important in memory than thought; it communicates with the PFL and may provide a "back up" system.

Readings:

Chapter 4 from Notes :

Clark and Squire, (1998) Classical Conditioning and Brain Systems. *Science* 280:77-81. Snowden

et al., (1997) Brain Infarction and the clinical expression of Alzheimer Disease. The Nun Study. *JAMA* 277:813-817.

## SEP 19,21

### TOPICS: THE HIPPOCAMPUS AND SPATIAL MEMORIES (IMAGING)

The hippocampus is important in spatial memories. Morris water maze. Films of John and of Clive Wearing

#### Readings:

Chapter 5 from Notes.

Maguire et al., (1997) Recalling routes around London: activation of the right hippocampus in taxi drivers. *J. Neurosci.* 17 (18):7103-10.

Maguire et al (2000) Navigation-related structural change in the hippocampi of taxi drivers. *PNAS* 97 (8) 4398–4403

Maguire et al., (2006) London taxi drivers and bus drivers: a structural and neuropsychological analysis. *Hippocampus*, 16(12):1091-1101.

Woollett K. and Maguire E.A. (2009) Navigational expertise may compromise anterograde associative memory. *Neuropsychologia.* 47(4):1088-95.

## SEP 26,28

### TOPICS: EMOTIONAL MEMORIES, ROLE OF THE AMYGDALA, HIPPOCAMPUS AND PREFRONTAL LOBES. WE REMEMBER WHAT IS IMPORTANT TO US.

The amygdala is important in emotional memories. Some memories must be actively extinguished. The prefrontal lobe inhibits the amygdala. (LTP) Reconsolidation. Fear conditioning in animals. Studies using optogenetics show how memories are changed.

#### Readings

Chapter 3 from Notes.

Milad & Quirk, (2002) Neurons in medial prefrontal cortex signal memory for fear extinction. *Nature*, 420 (911):70-74

Quirk G.J., Milad M. R. (2010). Neuroscience: Editing out fear. *Nature*, 463:36-37.

Schiller D. et al (2010) Preventing the return of fear in humans using reconsolidation update mechanisms. *Nature*, 463: p49-54.

Tomonori Takeuchi & Richard G. M. Morris, (2014) Neuroscience: Shedding light on a change of mind, *Nature* 513, 323–324

Zimmer, C. Can a Single Neuron Tell Halle Berry From Grandma Esther? A new theory says the brain stores complex pieces of information in "sparse-coding networks." June 2009, *Discover Magazine.* (On line)

Quiroga et al. (2005) Invariant visual representation by single neurons in the human brain. *Nature.* 435(7045):1102-7.

## **Drop date is SEPT 29.**

### Topics for Student presentations/papers due

## OCT 3,5

### TOPICS: ROLE OF THE FRONTAL LOBES.

The frontal lobes are largest in humans. They are responsible for some forms of memory and affect others. Schizophrenia is thought to be associated with impaired working memory and frontal lobe dysfunction

#### Readings

Chapter 6, 7 from Notes.

Goldman-Rakic, Working memory and the mind. *Scientific American* Sep 1992, 111- 117.\*

Davidson D, Chrosniak LD, Wanschura P, Flinn JM. Indications of reduced prefrontal cortical function in chronically homeless adults. *Community Ment Health J.* 2014;50(5):548-52

Ideka et al. (2000) Functional asymmetry of human prefrontal cortex in verbal and non-verbal episodic memory as revealed by fMRI. *Brain Res, Cogn Brain Res* 9(1):73-83.

(Bechara, et al., (1997) Deciding Advantageously Before Knowing the Advantageous Strategy. *Science*, 275:1193-1195.)

Li X, Thermenos HW, Wu Z, Momura Y, Wu K, Keshavan M, Seidman L, DeLisi LE (2016) Abnormal interactions of verbal- and spatial-memory networks in young people at familial high-risk for schizophrenia. *Schizophrenia Res* Jul 29 (e pub ahead of print)

## OCT (11), 13

TOPICS: REVIEW

**Monday Oct 10, is a holiday, Monday classes are held on Tuesday, there will be no class on the 11<sup>th</sup>.**

## OCT 17,19

TOPICS: HUMAN MEMORY DEFICITS, EXAM

Many human illnesses involve memory deficits, alcoholism, schizophrenia, and Alzheimer's disease. Memory impairments in Alzheimer's disease, interaction with stroke. The default network may play a role

### Readings :

Chapter 7 from Notes

Falkenberg I, Chaddock C, Murray RM, McDonald C, Modinos G, Bramon E, Walshe M, Broome M, McGuire P, Allen P (2015) Failure to deactivate medial prefrontal cortex in people at high risk for psychosis. *Eur Psychiatry.* 30(5):633-40.

Mohan A, Roberto AJ, Mohan A, Lorenzo A, Jones K, Carney MJ, Liogier-Weyback L, Hwang S, Lapidus KA (2016) *The Significance of the Default Mode Network (DMN) in Neurological and Neuropsychiatric Disorders: A Review.* *Yale J Biol Med.* 2016 Mar 24;89(1):49-57.

## OCT 24,26

LEARNING IN SIMPLE ANIMALS

Some types of learning can be studied in simple animals. *Aplysia Californica* show habituation dishabituation, sensitization and classical conditioning, which model non-declarative learning in humans.

### Readings:

Chapter 8 from Notes

## OCT 31/NOV 2

TOPICS: LEARNING INVOLVES STRENGTHENING SYNAPTIC CONNECTIONS. LTP, AN INTRODUCTION

Chemical pathways associated with learning and memory were discovered in *A. californica* and *Drosophila*; second messenger systems. Higher order conditioning in invertebrates, *Hermissenda* and *drosophila*. LTP is the major method of memory formation in mammals. Morphological changes are seen with long-term learning,

### Readings:

Chapters 8, (9), 13 from Notes.

Bailey and Chen. (1991) Morphological Bases of Short and Long- Term Memory. In R.G. Lister and H.J. Weingartner Eds. Perspectives on Cognitive Neuroscience.

(Available in class/ on line)

## **NOV 7/9**

**TOPICS: FROM SHORT-TERM TO LONG-TERM MEMORY. CREB, A MASTER SWITCH,**  
Mechanisms of long-term memory are conserved in long term memory across species. The morphological changes seen with long-term learning, require protein synthesis i.e. gene *expression* is changed when long-term memories are formed.

### Readings

Chapters 10, 11, 12 from Notes.

Abel et al. (1998) Memory suppressor genes: inhibitory constraints on the storage of long-term memory. *Science* 279:338-341.

Bourtchuladze et al., (1994). Deficient Long term memory in mice with a targeted mutation of the cAMP-responsive element binding protein. *Cell* 79:56-68

Suzuki et al (2011) Upregulation of CREB-mediated transcription enhances both short and long-term memory. *J Neurosci.* 31(24):8766-802

Jieun K. et al., (2014) Memory recall and modifications by activating neurons with elevated CREB. *Nature Neuroscience* 17,65–72

(The Pursuit of Memory, Kandel, 2007, (chaps 16-18) Chap 19)

(Kandel, E.R. The Molecular Biology of Memory Storage. (2001) *Science* 294: 1030- (Nobel lecture).

Frank and Greenberg. CREB: a mediator of long-term memory from mollusks to mammals. *Cell.* 79:5-8. 1994

**Student presentations begin**

## **NOV 15, 17 SFN, Dr Flinn will be off campus on Tue.**

### **TOPIC: VIDEOS**

"A Murder of Crows", Crows show sophisticated learning and memory abilities.

"Stress, Portrait of a Killer"; "League of Denial", 1st part shows the effect of continued blows to the brain on behavior

All films available on You Tube. Choose 1.

**Student presentations**

## **NOV 22, 24 THANKSGIVING,**

### **TOPICS: LTP CONTINUED.**

Role of the different glutamate receptors. (Hebbian synapses in *Aplysia*)

### Readings:

Chapter 13 from Notes.

Baer et al., Discovering LTP. In Neuroscience. ( Available in class.)

Bear. (1997) How do memories leave their mark? *Nature* 385:481-482.

(Frey & Morris. (1997) Synaptic tagging and long term potentiation. *Nature* 385 (6616) 53

**Presentations**

## **NOV 29, DEC 1**

**TOPICS: GENETIC MANIPULATIONS AND THE ENVIRONMENT BOTH AFFECT LEARNING:**

## YOUNG BLOOD IS GOOD.

Genetic manipulations can change how animals learn, drosophila and knock-out mice. The environment interacts with the genome. The brain is most plastic during neo-natal sensitive periods in order to fine-tune the brain. Implications for human memory. Stress affects memory through the glucocorticoid system.

### Readings:

Chapters 10, 13, 14 from Notes.

Elbert et al, Increased cortical representation of the left hand of string players. *Science*, 270:305-309.

Tang et al. Genetic enhancement of learning and memory in mice. (1999) *Nature* 401:63-69.

Tang et al. Differential effects of enrichment on learning and memory in NR2B transgenic mice. *Neuropharmacology* 41:779-90. 2001

Cao X, Cui Z, Feng R, Tang YP, Qin Z, Mei B, Tsien JZ. (2007) Maintenance of superior learning and memory function in NR2B transgenic mice during ageing. *Eur J Neurosci*. 25(6):1815-22.

Villeda, S.A. et al., (2014) Young blood reverses age-related impairments in cognitive function and synaptic plasticity in mice. *Nature Medicine* 20,659–663

### **Presentations**

## **DEC 6, 8**

TOPICS: ENVIRONMENTAL EFFECTS, NEUROGENESIS AND LEARNING, STRESS MAY IMPAIR MEMORY PROCESSES,

The environment can affect brain function. Neurogenesis also takes place in the adult mammalian brain.

### Readings:

Sapolsky, (1997) The importance of the well groomed child. *Science* 277:1620-1621.

Liu et al. Maternal care, hippocampal glucocorticoid receptors and hypothalamic-pituitary adrenal responses to stress. (1997) *Science* 277:1659-1662.

Moshe S. (2014) Lamarck revisited: epigenetic inheritance of ancestral odor fear conditioning. *Nature Neuroscience* 17 (1) 2-4. (Commentary on Dias & Kessler)

Dias BG, Ressler KJ. Parental olfactory experience influences behavior and neural structure in subsequent generations. *Nat Neurosci*. 2014 Jan;17(1):89-96.

Gould et al. (1999) Learning enhances adult neurogenesis in the hippocampal formation. *Nature Neuroscience* 2:260-265.

Shors T., Saving new brain cells. (2009). *Sc Am*. 300(3): 46-52.

### **Presentations**

**DEC 8**

**PAPERS DUE**

**DEC 15**

**TAKE HOME FINAL DUE.**

**Grading Policy:**

- 35% midterm exam
- 30% final exam (take home)
- 5% class participation, including in-class quizzes.
- 15% quizzes,
- 15 % presentation and paper, (8% for paper, on the same topic as the presentation (7%)).

**Office Hours:** Tu/Th 4:30-5:30, DKH 2022

Call 993-4107 or send an e mail for an appointment at other times. E-MAIL [jflinn@gmu.edu](mailto:jflinn@gmu.edu)

- Each graduate student needs give a presentation on topic related to the field of learning and memory and to write a paper on the same topic. This should not be *narrowly* your MA/ PhD topic. Please have the topic approved first.
- Undergraduate students will also make presentations, but can work in groups of 2/3 due to time limitations. The papers should be individually written.
- There will be a quiz most weeks on one of the assigned papers.
- The goal of this course is to examine the tremendous strides that have been made in understanding the biological bases of memory in the last 50 years. The first part of the course examines the role of various structures in the mammalian brain in memory formation and retention. The second part of the course describes the basic neuronal mechanisms that underlie learning and the formation of memories.
- Students with disabilities should present documentation to me and appropriate arrangements will be made.
- The George Mason Honor code will be followed.
- Class cancellation policy: Since the class is in the afternoon, Mason will probably have made an announcement, however, I will also e mail the class the class to give the status.
- Cell phones may not be used in class; If you are using your computer please send me a copy of your notes after class. A zero may be given for the following quiz if the computer is being used for other purposes than taking notes.
- Official 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.

Readings are from class notes, and from assigned readings. Additional/alternative research articles may be assigned.

How We Remember, by Flinn, (Notes)

Recommended (Get on Amazon)

Time, Love, Memory, by J. Weiner. 1999. Describes the early work on genetics and discusses the genetic bases of memory. (Chapters 10,16))

The Pursuit of Memory, E. Kandel. Kandel won the Nobel prize for his work on memory. This is his autobiography.

Forever Today. Wearing, D. (2005) The first few chapters read like a “true Romance” paperback. However, this book does make very clear the devastating consequences of damage to the hippocampus.

Unfortunately the Mason bookstore cannot order it due to copyright issues, however you may obtain it via Amazon etc.

Patient H.M. (2016) A rather dark book written by the grandson of William Scoville who operated on H.M. which also discusses the final brain dissection. (General interest.)

Each of the first three books are worth reading in full and are not expensive.

### Supplementary Readings:

Augustinack JC, van der Kouwe AJ, Salat DH, Benner T, Stevens AA, Annese J, Fischl B, Frosch MP, Corkin S. (2014) H.M.'s contributions to neuroscience: a review and autopsy studies. *Hippocampus*. 24(11):1267-86

Deng W, Almqvist JB, Gage FH. (2010) New neurons and new memories: how does adult hippocampal neurogenesis affect learning and memory? *Nat Rev Neurosci* 11(5): 339-50.

Gauthier, I., Skudlarski, P., Gore J.C., Anderson, A.W. (2000) Expertise for cars and birds recruits brain areas involved in face recognition. *Nature Neuroscience*. 3 (2)191-197.

Hugdahl K, Raichle ME, Mitra A, Specht K. (2015) On the existence of a generalized non-specific task-dependent network. *Front Hum Neurosci*. 2015 Aug 6;9:430

Malenka & Bear, LTP and LTD: an embarrassment of riches. (2004) *Neuron* 44(1): 5-21.

Milner. B., Squire L.R., Kandel, ER. (1998) *Cognitive Neuroscience and the Study of Memory*. *Neuron* 20:445-468.

Mumby et al., (2002) Hippocampal damage and exploratory preferences in rats: memory for objects, places and contexts. *Learning and Memory*. 9(2):49-57.

Raichle (several), e.g. Petersen SE, Fox PT, Posner MI, Mintun M, Raichle ME. (1988) Positron emission tomographic studies of the cortical anatomy of single-word processing. *Nature*. 331(6157):585-9

Posner MI, Petersen SE, Fox PT, Raichle ME. (1988) Localization of cognitive operations in the human brain. *Science*. 240(4859):1627-31

Raichle M. E (2015) The brain's default mode network. *Annu Rev Neurosci*. 2015 38:433-47

Sah, (2002). Never Fear Cannaboids are here. *Nature* 418:488-499. 2002.

Shors TJ, et al. (2002) Neurogenesis may relate to some but not all types of hippocampal-dependent learning. *Hippocampus*. 12(5):578-84.

Sotres-Bayon F. Quirk GJ, (2010) Prefrontal control of fear: more than just extinction. *Current Opinion in Neurobiology* 20: 231-235.

Squire (2009) The Legacy of Patient HM for Neuroscience. *Neuron* 61(1): 6-9

Leslie G. Ungerleider, (1995) Functional Brain Imaging Studies of Cortical Mechanisms for Memory. *Science* 270: 769-775