NEURONAL BASES OF LEARNING AND MEMORY
PSYCH 558/472, NEUR 480, FALL 2022

DR. JANE FLINN

SFN has a conference from Nov 12 - Nov 16th in San Diego which I will attend.

AUG 23/25
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:

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

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.

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

AUG 29 IS THE LAST DAY TO ADD,

AUG 30/SEP1
TOPICS: RELATIVE CONTRIBUTIONS OF HIPPOCAMPUS AND OVERLYING CORTEX TO LONG-TERM EPISODIC MEMORY.
IMAGING ;
Memory in children with hippocampal damage. 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.

SEP 6 IS THE FINAL DROP DATE FOR 100% REIMBURSEMENT.

SEP 6/8
TOPICS: THE HIPPOCAMPUS AND SPATIAL MEMORIES
The hippocampus is important in spatial memories. Morris water maze. Films of John and of Clive Wearing
Readings:

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.
Sharon, Being Permanently Lost. From Unthinkable, by H.Thomson, pp 45-72.

SEP 13/15
TOPICS: THE DEFAULT NETWORK.
THE ROLE BASAL GANGLIA IN MEMORY,
The default network is active when we are not doing a task.
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. Lashley, Penfield and Thompson's work. Classical conditioning in rabbits and humans.
Clive Wearing, a modern H.M.
Clive Wearing Video
Readings:
Buckner, R.L., Andrews-Hanna, J.R., Schacter D.L.(2008) The Brain's Default Network Anatomy, Function, and Relevance to Disease. Ann N Y Acad Sci. 1124:1-38. doi: 10.1196/annals.1440.011. Review.**.**
doi:10.1016/j.nlm.2012.05.002.
Snowden et al., (1997) Brain Infarction and the clinical expression of Alzheimer Disease. The Nun Study. *JAMA* 277:813-817.

SEP13 IS THE FINAL DROP DATE FOR 50% REIMBURSEMENT

SEP 20/22
TOPICS: THE CEREBELLUM.
EMOTIONAL MEMORIES, ROLE OF THE AMYGDALA, PRE-FRONTAL LOBE. (HIPPOCAMPUS);
The amygdala is important in emotional memories.. The prefrontal lobe inhibits the amygdala. Fear conditioning in animals. Some memories must be actively extinguished.

Readings
Clark and Squire, (1998) Classical Conditioning and Brain Systems. *Science* 280:77-81
Milad & Quirk, (2002) Neurons in medial prefrontal cortex signal memory for fear extinction. *Nature*, 420 (911):70-74.

SEP 27/29
TOPICS: EXTINCTION, AND RECONSOLIDATION.
WE REMEMBER WHAT IS IMPORTANT TO US. CONCEPT CELLS.
Reconsolidation.
(LTP)
Readings:
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.

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

Quiroga (2012) Concept cells: the building blocks of declarative memory functions. NATURE REVIEWS | NEUROSCIENCE, VOLUME 13 | AUGUST 2012 | **587-597**

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)

OCT 4/6

TOPICS: OPTOGENETICS A NEW TECHNIQUE. ROLE OF THE FRONTAL LOBES.

Studies using optogenetics show how memories are changed.

The frontal lobes are largest in humans. They are responsible for some forms of memory and affect others.

Readings

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

Redondo, R.L., Kim, J., Arons, A.L., Ramirez, S., Liu, X., Tonegawa, S. (2014). Bidirectional switch of the valence associated with a hippocampal contextual memory engram. Nature 513:(7518) 426- 430. doi:10.1038/nature13725.

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.* 201450(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.

TBA

Topics for Student presentations/papers due

OCT 11/13

Monday Oct 10, is a holiday, Monday classes are held on Tuesday, there will be no class on Tue the 11th.

TH ; REVIEW FOR EXAM. (HUMAN MEMORY DEFICITS),

OCT 18/20 TOPICS: HUMAN MEMORY DEFICITS,

TU

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

THURSDAY, EXAM

Readings :

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.

TBA

OCT 25/27

LEARNING IN SIMPLE ANIMALS; LEARNING INVOLVES STRENGTHENING SYNAPTIC CONNECTIONS. NEURONAL CONDUCTION.

TOPICS: LEARNING INVOLVES STRENGTHENING SYNAPTIC CONNECTIONS:FROM SHORT-TERM TO LONG-TERM MEMORY. CREB, A MASTER SWITCH.

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. Morphological changes are seen with long-term learning.

Readings:

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.

Chemical pathways associated with learning and memory were discovered in *A. californica* and *Drosophila*; second messenger systems. (Higher order conditioning in invertebrates, *Hermissenda* and *drosphila.*)

Readings:

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

NOV 1/3

Student presentations begin

TOPICS:FROM SHORT-TERM TO LONG-TERM MEMORY. CREB, A MASTER SWITCH; THERE ARE 2 FORMS OF CREB. 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 (may be changed)

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

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

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

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

NOV 9/11

TOPICS: Long term potentiation (LTP) is the basis of memory formation at the synapse.

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

Readings:

Baer et al., Discovering LTP. In Neuroscience.
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)

NOV 15/17 Dr Flinn will be away at SFN on the 15th and 17th .
TOPICS: GENETIC MANIPULATIONS AND THE ENVIRONMENT BOTH AFFECT LEARNING:
Genetic manipulations can change how animals learn. 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 glutocorticoid system.
Readings:

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.
Sapolsky, (1997) The importance of the well groomed child. Science 277:1620-1621.
Liu et al. Maternal care, hippocampal glutocorticoid receptors and hypothalamic-pituitary adrenal responses to stress. (1997) *Science* 277:1659-1662.
Presentations

NOV **22/24 (THANKSGIVING)**
YOUNG BLOOD IS GOOD. SLEEP, THE BRAIN'S HOUSEKEEEPER. (MAY BE COVERED NEXT WEEK.)

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.
Xie et al., 2013,. Sleep Drives Metabolite Clearance from the Adult Brain. Science 342, p 373 (Nedergaard is the senior author.)
Underwood, Sleep the Brain's Housekeeper (a commentary). 2013; Science 342, p 301.

NOV 29/ DEC1 TOPICS: ENVIRONMENTAL EFFECTS, NEUROGENESIS AND LEARNING.
Neurogenesis also takes place in the adult mammalian brain.
The environment can affect brain function. New evidence suggests that memory can be transferred from one animal to another via RNA. But there are other ways to enhance your brain

Readings:

Shors T., Saving new brain cells. (2009). *Sc Am*. 300(3): 46-52.
Gould et al. (1999) Learning enhances adult neurogenesis in the hippocampal formation. *Nature Neuroscience* 2:260-265.
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.

Carney, R.S.E., (2018) An Emerging Role for RNA in a Memory-Like Behavioral Effect in *Aplysia* , eNeuro. 2018 May-Jun; 5(3): ENEURO.0193-18.2018.

Bédécarrats A, Chen S, Pearce K, Cai D, Glanzman DL. (2018). RNA from Trained *Aplysia* Can Induce an Epigenetic Engram for Long-Term Sensitization in Untrained *Aplysia*. eNeuro. 2018 May 21;5(3). ENEURO.0038-18.2018.

DEC 5 **PAPERS DUE**

DEC 9 **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%)).
There will be an additional question on the exams for the graduate students.

Office Hours: Tu/Th 4:30 to 5 and by appointment , DKH 2022
Call 993-4107 or send an e mail for an appointment at other times. E-MAIL jflinn@gmu.edu

- Each PhD 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.
- MA and 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 and how these may be modified.
- 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 I may ask to see your notes at the end of class or ask you to send me a copy of your notes. 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 assigned readings. Additional/alternative research articles may be assigned.
Recommended Books (Get online)

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

Aurora et al. (2012). Behavioral and neuroanatomical investigation of Highly Superior Autobiographical Memory (HSAM) Neurobiol Learn Mem. 2012 July ; 98(1): 78–92.

(Bechara, et al., (1997) Deciding Advantageously Before Knowing the Advantageous Strategy. *Science*, 275193-1295.)

Deng W, Almone 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

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*

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

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

(Kandel, E.R. The Molecular Biology of Memory Storage. (2001) *Science* 294: 1030- (Nobel lecture).
Chen, et al. (2017). Are There Multiple Kinds of Episodic Memory? An fMRI Investigation Comparing Autobiographical and Recognition Memory Tasks. J. Neurosci. 37(10):2764 –2775. (default network)

Ramanan S. (2017) Distinct Neural Networks Support Autobiographical and Episodic Remembering. J Neurosci. 37(23):5591-5593. doi: 10.1523/JNEUROSCI.0863-17.2017. Commentary on Chen et al..