NEURONAL BASES OF LEARNING AND MEMORY
PSYCH 558/472, NEUR 461, FALL 2012 (Draft)

DR. JANE FLINN

AUG 28,30

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, procedural and 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.

(Milner, Squire, Kandel, 1998)

On the web please download H.M's brain… (NPR), Brain of the most studied… (SD), H.M. an unforgettable Amnesiac (NY Times).

SEP 4,6

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

Memory in children with hippocampal damage.

Clive Wearing, a modern H.M.

The hippocampus is important in episodic 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, LR, Wixted JT. The cognitive neuroscience of human memory since H.M. Ann. Rev. Neurosci. 2011; 34;259-88

SEP 11,13

THE HIPPOCAMPUS AND SPATIAL MEMORIES

IMAGING

The hippocampus is important in spatial memories. Morris water maze (?)

Films of John and Clive Wearing

Readings:

Chapter 5: MM Ch 2.II; Ch 6.

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 18, 20

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

Lashley's and Penfield's work.
Classical conditioning in rabbits and humans.
The basal ganglia may provide a "back up" system.
Readings:
Chapter 4: MM Ch2.III
Clark and Squire, (1998) Classical Conditioning and Brain Systems. Science 280:77-81.
(Snowden et al, 1997)
Topics for Student presentations due

SEP 25, 27

EMOTIONAL MEMORIES, ROLE OF THE AMYGDALA & HIPPOCAMPUS. METHODS OF ANIMAL RESEARCH

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.
The Morris Water maze, Place cells, Novel Object recognition, Fear conditioning, etc.
Readings
Chapter 3: MM Ch 4; 5. II
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
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.
Calendar for student presentations

OCT 2, 4

ROLE OF THE FRONTAL LOBES

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

Readings:

Chapter 6: MM Ch 1.II B, C

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

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

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.

OCT 11

Monday Oct 8, is a holiday, Monday classes are held on Tuesday, there will be no class on the 11th.

STRESS MAY IMPAIR MEMORY PROCESSES

Readings

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

. Sapolsky,Why Zebras Don't get Ulcers, chap 10, 1998.

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

OCT 16,18 **SFN**

HUMAN MEMORY DEFICITS

Readings Chapter 7.

Oct 16, no class.

Oct 18, Memory impairments in alcoholism, Michael Anderson, guest lecturer.

OCT 23, 25 HUMAN MEMORY DEFICITS, REVIEW

Alzheimer's disease, interaction with stroke

Readings:

Chapter 7: MM Ch12.

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

OCT 30, NOV 1

EXAM OCT 30 th

LEARNING INVOLVES STRENGTHENING SYNAPTIC CONNECTIONS.

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.

Higher order conditioning in invertebrates, *Hermissenda* and *drosphila.*

Readings:

Chapters 8, (9): MM Ch 3.III

NOV 6, 8

SHORT-TERM MEMORY.FROM SHORT-TERM TO LONG-TERM MEMORY.

Chemical pathways associated with learning and memory were discovered in *A. californica* and *Drosophila*; second messenger systems. Morphological changes are seen with long-term learning, which requires protein synthesis i.e. gene *expression* is changed when long-term memories are formed.

Readings:

Chapter 10, 11: MM Ch 3, IV,V,VI

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.

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

Student presentations begin

NOV 13, 15

FROM SHORT-TERM TO LONG-TERM MEMORY, CREB, A MASTER SWITCH, LEARNING IN DROSOPHILA

Mechanisms of long-term memory are conserved in long term memory across species.

Readings

Chapters 11, 12, MM Ch 10.LLL.

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

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

Time, Love Memory; Weiner, 1999. (Chapters 10, 16)

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

NOV 20

NEURONAL CHANGES ASSOCIATED WITH LEARNING IN THE MAMMALIAN BRAIN.

Long term potentiation (LTP) in the hippocampus, a Hebbian synapse. Role of the different glutamate receptors.

Hebbian synapses in *Aplysia*

Readings:

Chapter 13: MM Ch 7, 8, 9, 10.II

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 27, 29

DUMB FLIES AND SMART MICE
DO DEVELOPMENT AND LEARNING SHARE THE SAME MECHANISMS?
Genetic manipulations can change how animals learn, drosophila and knock-out mice. The environment interacts with the genome. Implications for human memory. The brain is most plastic during neo-natal sensitive periods in order to fine-tune the brain. However, neurogenesis also takes place in the adult mammalian brain.

Readings:

Chapter 13,14. MM Ch 10 .IV

(Weiner, Time, Love, Memory. 1999 (Chapters 10,16))

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.

DEC 6, 8

NEUROGENESIS AND LEARNING,

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

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

DEC 11 PAPERS DUE

DEC 14

TAKE HOME FINAL DUE.

Grading Policy:

35% midterm exam
35% final exam
7% presentation
8% paper (on the same topic as the presentation)
10% quizzes
5% recent paper

Office Hours: Tu 3-4, TH 4:30-5 DKH 2022
Call 993-4107 or 370-1406 for an appointment at other times.

E-MAIL jflinn@gmu.edu

Each 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. Undergraduate students should preferentially work in pairs (due to class size).

Graduate students should select 2 recent papers and undergraduates should select one paper (2011 or 2012) that presents recent work on a topic discussed in class. Please choose a topic after the 1st class. If you do not select topics, I will assign them.

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. This is covered extensively in the text Memory Mechanisms.

Students with disabilities should present documentation to me and appropriate arrangements will be made.

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

Strongly recommended for Graduate students, Memory mechanisms, D. Sweatt.

Recommended (Get on Amazon)
Time, Love, Memory, by J. Weiner. Describes the early work on genetics and discusses the genetic bases of memory.
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. At least 2 copies will be on reserve in the library.

Each of the last three books are worth reading in full and not expensive.
Students are expected to follow the GMU Honor code.

Supplementary Readings:
Benton, The prefrontal region, its early history. In Levin et al. Frontal lobe function and dysfunction. (E reserves)

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.

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

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 paper

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.

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

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