

NEURONAL BASES OF LEARNING AND MEMORY
PSYCH 558/472, NEUR 461 FALL 2011

DR. JANE FLINN

AUG 30, SEP 1

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.

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. (In library)

(Milner, Squire, Kandel, 1998)

Wearing, D. (2005) Forever Today, read sections throughout the semester.

On the web please download H.M.'s brain... (NPR), Brain of the most studied... (SD), H.M. an unforgettable Amnesiac (NY Times). Use H.M. amnesia to search. for abstracts you could use, in pubmed, or Corkin H.M.

SEP 6, 8

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

A monkey model of temporal lobe amnesia, Mishkin and Squire's lesion experiments.

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.

(Murray and Wise, 2010)

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

SEP (13), 15

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

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., (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 20, 22

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:

Chapters 4, from Notes.

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

(Snowden et al, 1997)

Topics for Student presentations due

SEP 27, 29

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, from Notes

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 4, 6

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 from Notes.

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, 275:1193-1195.

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 13

Monday Oct 10, 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 glucocorticoid receptors and hypothalamic-pituitary adrenal responses to stress. (1997) Science 277:1659-1662.

OCT 18, 20

HUMAN MEMORY DEFICITS, REVIEW

Amnesias following cortical damage due to stroke etc. Effect of Alzheimer's disease, Korsakoff's syndrome on different forms of memory.

Readings:

Chapters 7, from Notes.

(Aging with Grace; Snowden. 2002)

EXAM OCT 20 th

OCT 25, 27

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 *drosophila*.

Readings:

Chapters 8, 9, 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.

Student presentations begin

NOV 1,3

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, from Notes.

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

NOV 8, 10

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, from Notes.

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 15, 17

NO CLASSES, SFN NOV 15th

Discussion of SFN presentations.

NOV 22

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 from Notes.

Baer et al., Discovering LTP. In Neuroscience.

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

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 29, DEC 1

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 from Notes.

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.

For abstracts look under neurogenesis and Shors, Gould or Gage.

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 13 PAPERS DUE

DEC 16

TAKE HOME FINAL DUE.

Grading Policy:

35% for midterm exam

35% for final exam

7% for presentation

8% for paper (on the same topic as the presentation)

10% for abstracts

5% abstract discussion

Office Hours: Tu/Th 3-3:30 DKH 2022

Call 993-4107 or 370-1406 for an appointment at other times.

E-MAIL jflinn@gmu.edu

In most weeks, in each class I will ask 4 students to present an abstract of a recent paper

relevant to the papers discussed in class of the previous week. I will go in rotation on the class list. These presentations should last 2-3 minutes only. i.e. ~10 mins total. Please send the abstract you choose to the rest of the class ahead of time to avoid overlaps and so people can see the abstract.

Each student needs make a presentation related to the field of learning and memory and to write a paper on this topic. This should not be *narrowly* your MA/ PhD topic.

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.

Readings are from class notes, from How We Remember and from assigned readings, including book chapters. The latter will be on e-reserves in the library. Additional/alternative research articles may be assigned.

Forever Today, by D. Wearing. 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. Selected parts will be made available. At least 2 copies will be on reserve in the library.

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.

Relevant chapters from each of these books will be on reserve in the library, but they are worth reading in full and not expensive.

Supplementary Readings:

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

Deng W, Almon 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.

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.

Murray EA & Wise SP (2010) What, if anything, can monkeys tell us about human amnesia when they can't say anything at all? *Neuropsychologia* 48(8): 2385-405.

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.