LEARNING AND MEMORY (p.1)
You are your learning and memory! (see movie *Total Recall*)

L&M, two sides of the same coin
"**learning**" – refers more to the **acquisition** of new information & brain circuits (**storage**)
"**memory**" – refers more to the ability **to access** the above (**retrieval**)

1. <u>Synaptic Mechanisms of L&M</u>
We have long-assumed a chemical/electrical event --- a structural change in NS
What do we really observe?
Pre- and post-synaptic membranes getting thicker
Area of contact between pre- and post-synaptic membranes enlarging
More pre-synaptic axon terminals making synaptic contacts on a post-synaptic area
More dendritic spines, changes in shapes of dendritic spines
More NT released by presynaptic membrane

Long-Term Potentiation
If high-frequency electrical stimulation is applied to a presynaptic neuron --- it then fires more when it is next stimulated (its response has been amplified/facilitated)

Much of this research has been done on neurons in **hippocampal system**
1st single, low-intensity electrical pulse is delivered to **perforant path** (major input to dentate gyrus)
2nd output response is measured in the **granule cells** of the **dentate gyrus** (perforant path neurons synapse on granule cells) to get a "baseline" response from the granule cells
3rd a high-intensity, high-frequency electrical pulse lasting 10 seconds is delivered to the perforant path neurons (to produce LTP)
4th single, low-intensity electrical pulse is again delivered to perforant path and response in granule cells is again measured
The response is now greatly amplified, indicating LTP has occurred.
Can even delay one week between steps #3 and #4 and see LTP!

LEARNING AND MEMORY (cont., p.2)

1.**Synaptic Mechanisms** (cont.)

Long-Term Potentiation (cont.)

Further study of LTP on neurons in dentate gyrus

How do these synapses work?

Use **NMDA post-synaptic receptors** (N-methyl-D-aspartate)

NMDA receptor must have two events occur simultaneously:

Glutamate must bind to receptor

+**Postsynaptic neuron must already be partially depolarized**

which leads to more **Ca++** entering the neuron

so for LTP to occur, a neuron must already be "primed" (depolarized) when the second signal comes in (glutamate is released) --- LTP

Also know that LTP depends on protein kinases (in potentiated neuron)

Drugs that block protein kinases --- no LTP

A "primed" postsynaptic neurons most likely sends a signal back to its inputting presynaptic neuron by way of sending **nitric oxide** back to that presynaptic neuron

Note: LTP occurs not just in hippocampal neurons, but in other areas of the brain as well. Also, non-glutamate (non-NMDA) systems are being discovered.

LEARNING AND MEMORY (cont., p3)

2. Memory

a. The Case of H.M.

What was known in 1953 about the hippocampus when his bilateral medial temporal lobectomy was performed?
…hyperactive rats…
But H.M. had mild **retrograde amnesia** (up to 2 years) and severe **anterograde amnesia** (from then on)
Along with normal **short-term memory** (7 items + or – 2)

Poor memory for stimuli presented in any sensory system (visual, aud, etc)
Showed improvement on mirror-drawing test (but no recall of doing test)
Showed improvement on rotary-pursuit test (but no recall of doing test)
Showed improvement on incomplete-pictures test (but no recall of doing)
Could learn via classical conditioning (eye blink) (but no recall of doing)

So…H.M. cannot consolidate STM into LTM
Does have **good implicit memory** (improved performance w/o conscious memory for events); does not know that he knows…
Does not have good explicit memory (conscious memory of doing/ knowing something)

Note: H.M. must now be in his mid-70s…but thinks he is 27…
What must this be like?….

b. Other persons with partial hippocampal (temporal lobe) damage

Difficulty forming explicit LTMs, but may not completely be unable to do so
Often **recall general facts/information** ("semantic" or **reference memory**) but have **difficulty with explicit memories for particular events or experiences** ("episodic" or **working memory**)

LEARNING AND MEMORY (cont., p.4)

Note: Probably unconscious/implicit memory evolved first, and then conscious/explicit memory later on…
Evidently, must have explicit memory in order to use/transfer that memory/skill to a new situation

c. Cerebral Ischemia and Hippocampal Damage
Interruption of blood supply --- hippocampal damage
e.g. from failed heart/lung machine (case of R.B.)
e.g. from carbon monoxide poisoning
often damages pyramidal cell layer of CA1 subfield in hippocampus

d. Amnesia in **Korsakoff's Syndrome**
Usually from long-term, chronic abuse of alcohol
Specific cause:
Symptoms: extreme confusion, personality changes, "**confabulation**"
Seeming lack of awareness of deficit
Damage to neocortex & cerebellum, to **medial diencephalon** (both thalamus and hypothalamus)
Initially shows anterograde amnesia for explicit episodic/working memory
Later on shows severe retrograde amnesia for explicit episodic/working and semantic/reference memory as well
Failure to store new memory vs. failure to retrieve stored memories?

May be somewhat similar to **case of N.A.** who had severe damage to the medial diencephalic areas (incl. mediodorsal nucleus of thalamus) and mammillary bodies

e. Amnesia in Alzheimer's Disease
Mild deterioration of memory --- severe dementia (severe amnesia) --- terminal
Show more **global, general memory deficits** than those above
Initial problems with STM & some types of implicit memory
Later on LTM and explicit material is lost too

LEARNING AND MEMORY (cont., p5)

f. **Amnesia in Alzheimer's Disease** (cont.)
Widespread loss of ACh neurons, esp. in **basal forebrain** (which is brain's main source of ACh axons)
Note: CVAs in basal forebrain can --- amnesias
ACh neurons in hippocampus are dying too…
Note: very early sign of Alzheimer's (prior to onset of memory problems) is a problem with memory for olfactory stimuli, **what is that smell**?

g. Post-Concussion Amnesia
Anything that interrupts the process of memory storage (consolidation) will result in complete or partial amnesia for that memory
e.g. sudden blow to the head (concussion)
electric shock
even strong startle/fear/ trauma
can have both retrograde (usually shorter) and anterograde (usually longer) effects on memory
retrograde amnesia may show "swiss cheese" effects (islands of preserved memory within the amnesia)

Initial research showed that could disrupt consolidation for minutes to an hour after the event to be remembered had occurred…but now we think that **memory consolidation may go on for months/years after the event**

Retained memories become increasingly more resistant to forgetting the more often they are recalled ("practiced")
The more often a memory is recalled and the more other memories are linked to that first memory, the easier the first memory is to recall
Thus, "**over-learning**" works (studying again what you already know)
Increased ease of recall, decreased retrieval problems