Lecture 20. Learning 5- Memory Consolidation and the Hippocampus

Professor Christiane Linster

Pre-lecture preparation

(1) Watch pre-lecture video on Patient H.M.
(2) Read pages 853-857; Figures 24.25
(3) Read text associated with Figure 24.27

Learning Objectives

To understand the model of memory consolidation involving transfer from hippocampus to neo-cortex

(1) Be able to understand how different forms of memory
(2) Be able to explain how memory consolidation is thought to work between hippocampus and neo cortex
(3) Be able to design experiments to test current models of memory consolidation
(4) Be able to apply knowledge of neural disorders to models of memory consolidation

Lecture Outline

(1) Patient H.M's memory deficit strongly suggested that hippocampal structures are needed to create new short term memories but not to recall old memories. This phenomenon only concerned explicit or procedural, but not implicit, memory formation. For example, patient HM could become better at learning a game with practice but have no memory of playing this game (Pages 853-857)
(2) Behavioral experiments in non human primates showed to what extend the idea that short term memories are first stored in the hippocampus holds and suggested a model of memory transfer between hippocampus and neo cortex (Figure 24.25 and associated text).
(3) We will review this model and review experimental evidence in support of this model.
(4) We will discuss how changes in neuromodulators affecting synaptic plasticity such as acetylcholine loss in Alzheimers disease might affect the formation of new memories in this model.

Study Questions

(1) How do molecular mechanisms of synaptic plasticity at different stages of memory relate to the model of memory consolidation we discussed?
(2) Distributed memories are thought to be robust to damage (graceful degradation), explain why this would be ?
(3) What happens to long term memories if a neurological disorder induces loss of synapses?

Lecture 20: Distributed memory and consolidation

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Lectures 16-21: Learning and memory

Lecture 16 NMDA receptor allows to “associate” two events at the level of a synapse

Lecture 17 Learning at the synaptic level: LTP and LTD

Lecture 18 Learning at the network level: how are LTP and LTD involved in changing networks ?

Lecture 19 Learning while behaving: sequences of events and STDP

Lecture 20 **Remembering: Consolidation of what has been learned**

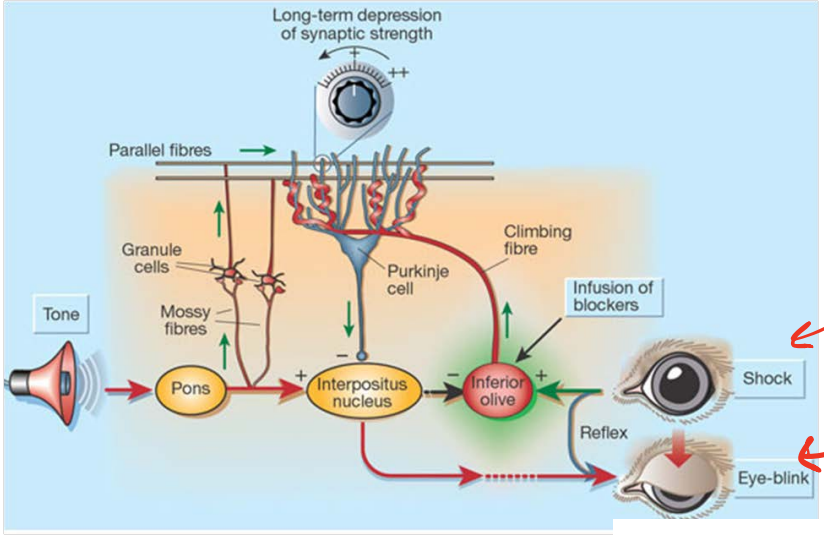
Lecture 21 What is a memory?

Lecture 20: Distributed memory and consolidation

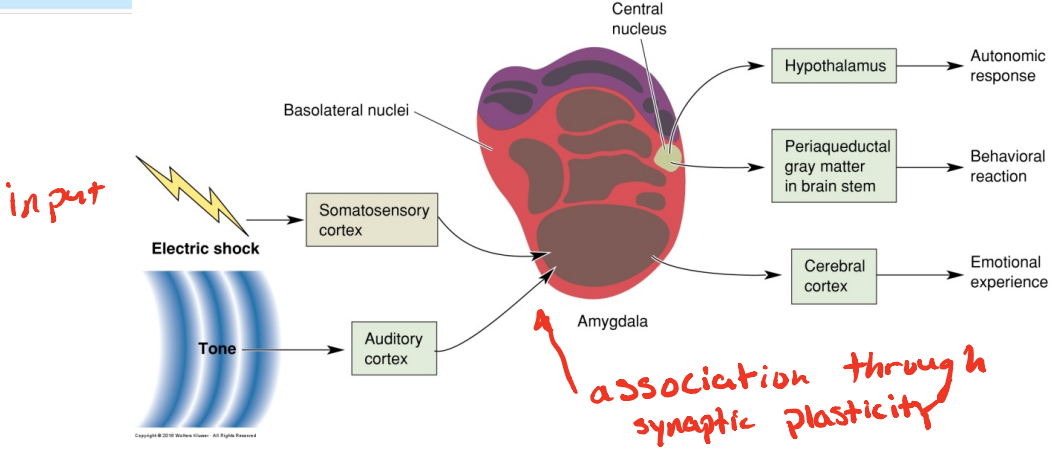
Synaptic plasticity and learning

(1) Be able to explain how memory consolidation is thought to work between hippocampus and neo cortex
(2) Be able to design experiments to test current models of memory consolidation
(3) Be able to apply knowledge of neural disorders to models of memory consolidation

Distributed memory processes

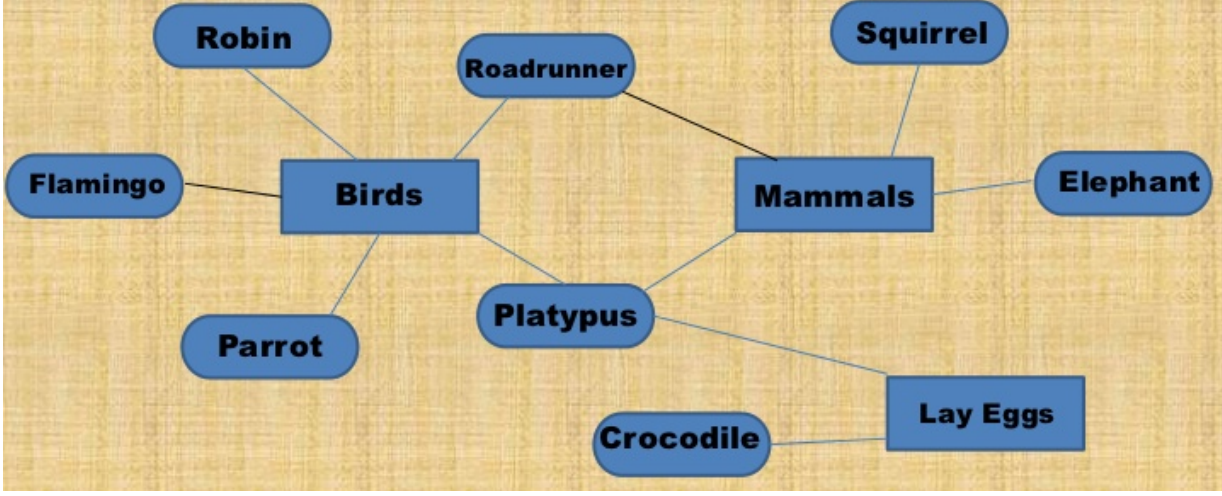


stimulation triggers impulse response

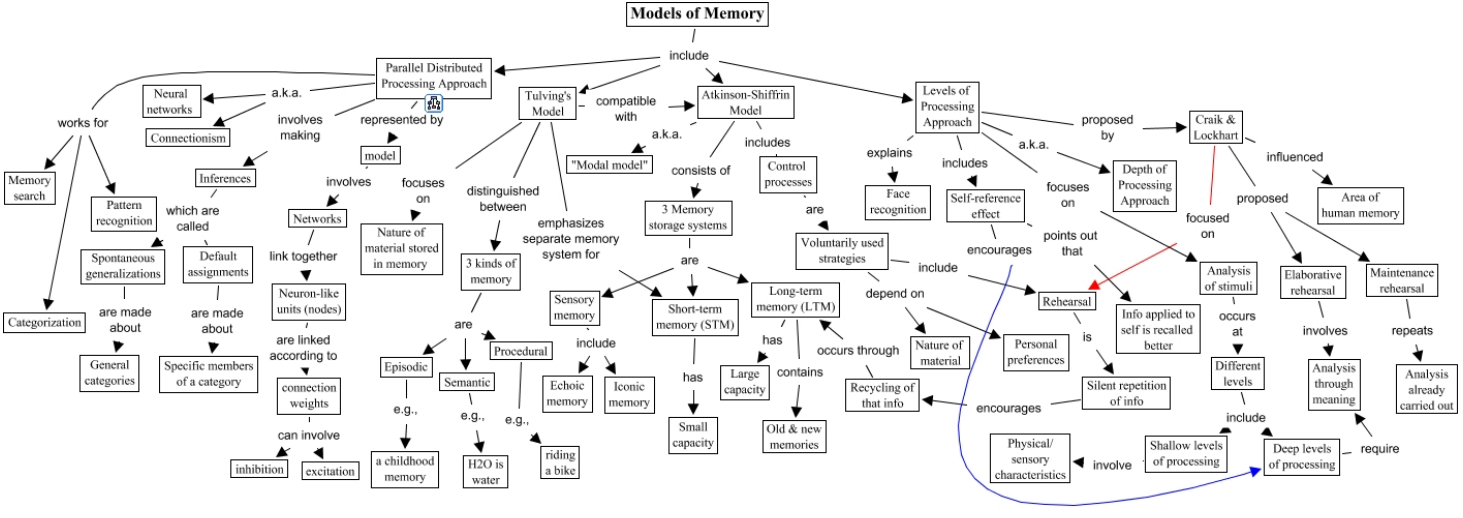


3. Parallel Distributed Processing (PDP)

Memories exist in a "network." New experiences alter this network and change one's knowledge base

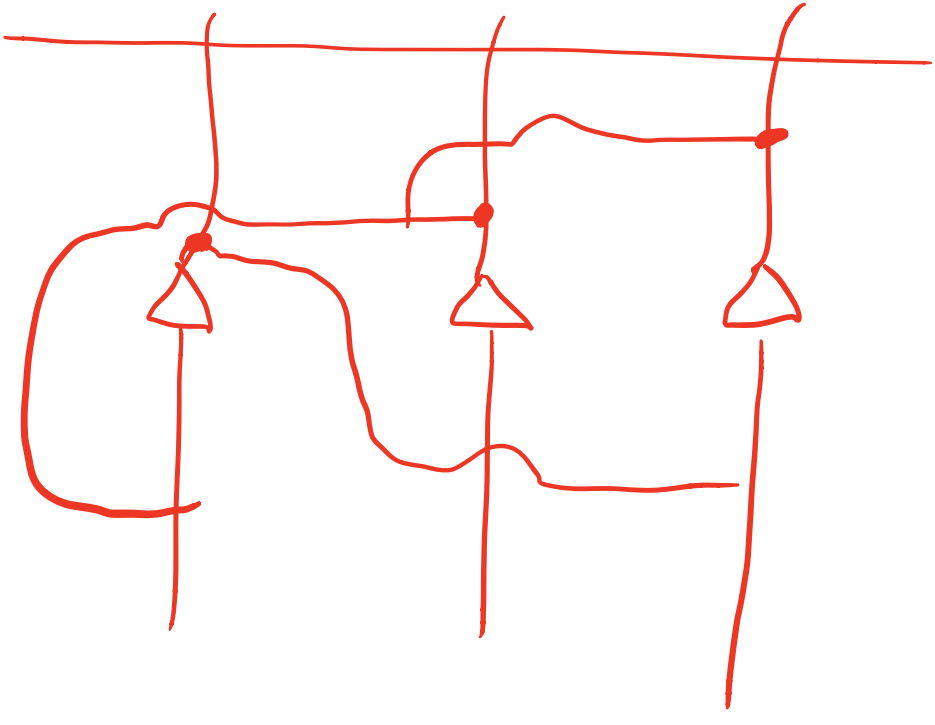


Distributed memory processes



Distributed memory processes

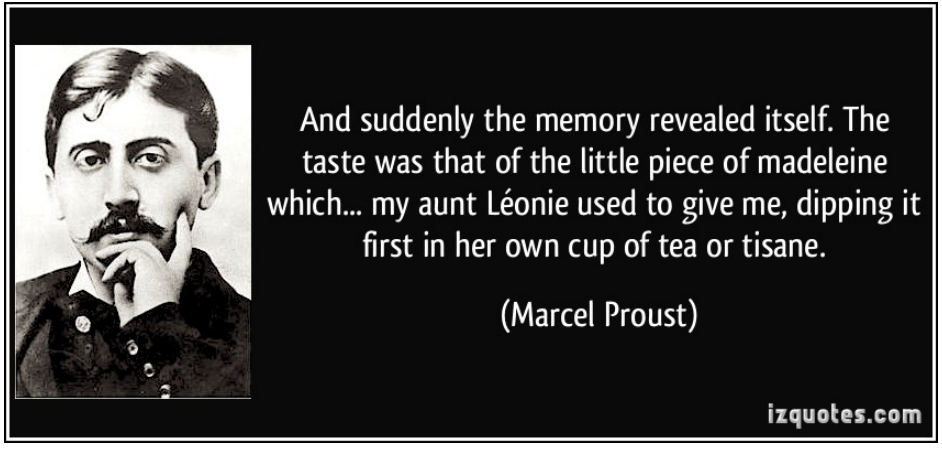
Cortical organization



"it's all connected!"

Associative memory

Associative memory functions.

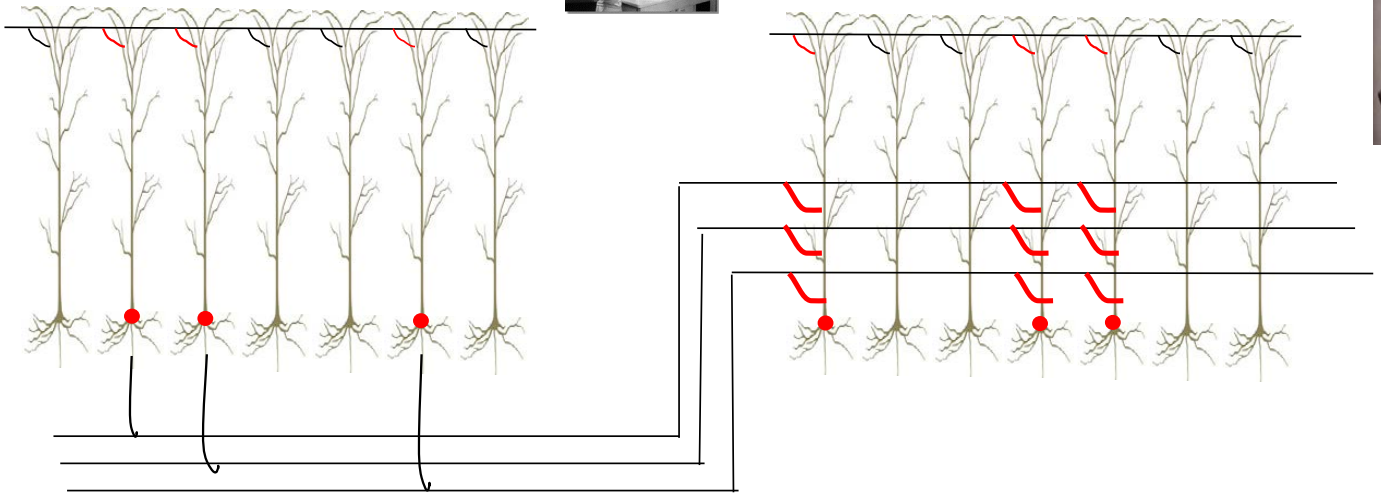


"A la recherche du temps perdu .. "

Associative memory

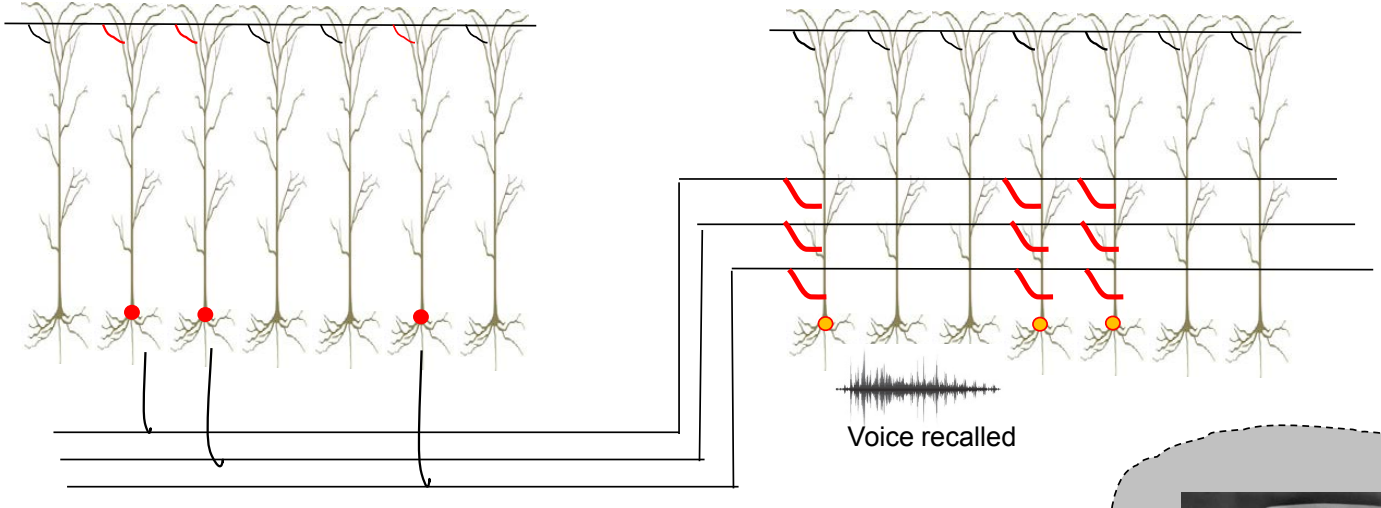
Taste

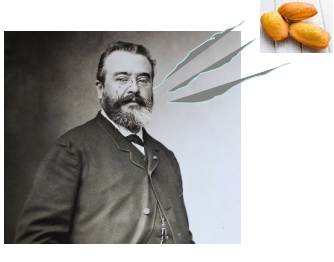
Voice



Synapses between simultaneously activated neurons undergo LTP (“fire together wire together”)

Associative memory





From your text book: Hebb's assemblies and memory formation

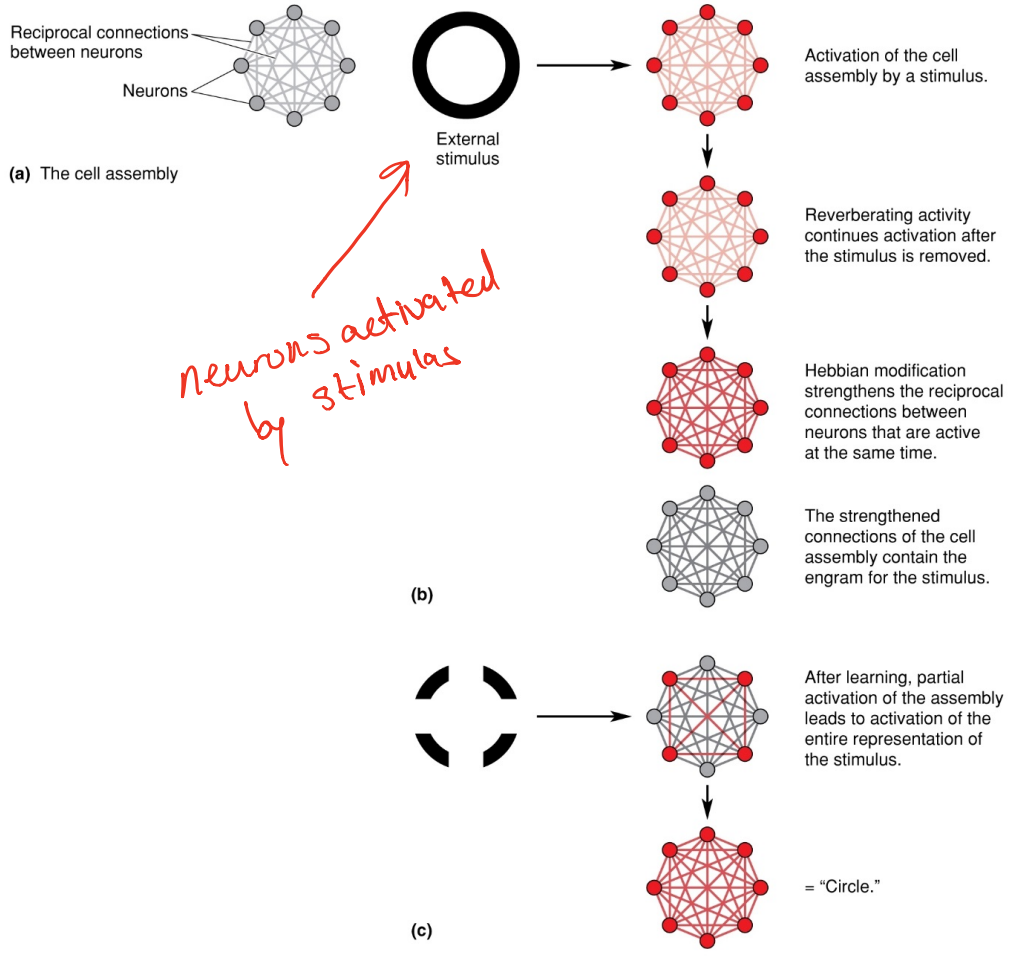
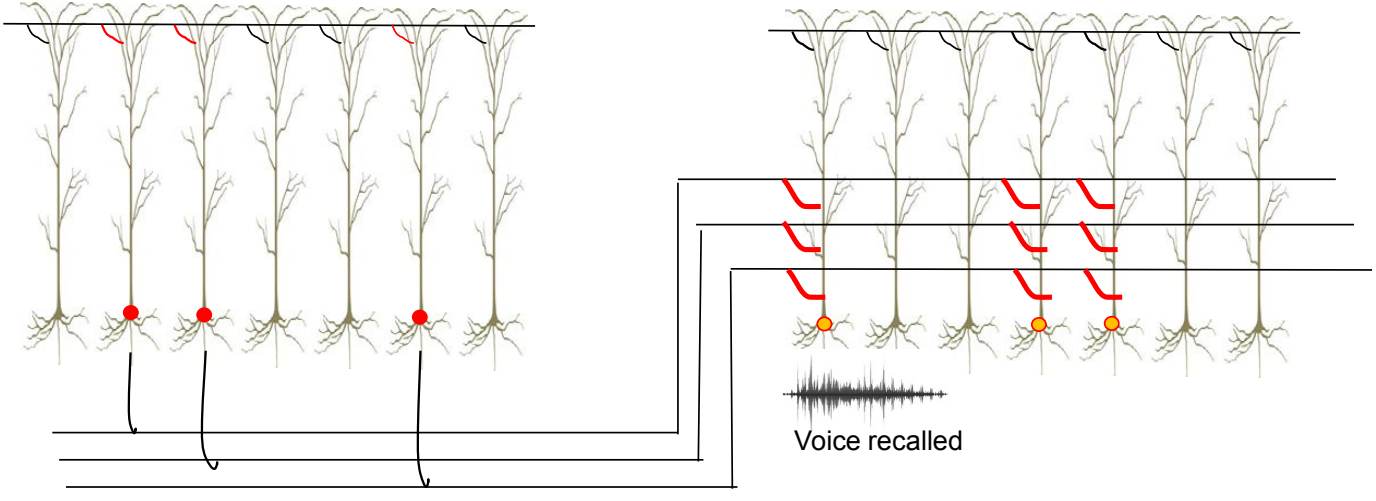


Figure 24.5

Distributed memory

Smell



Distributed memories can “gracefully degrade”. This means that they are robust to a certain amount of loss of neurons and synapses.
In Alzheimers disease for example, loss of neurons can happen long before memory and encoding deficits can be seen.

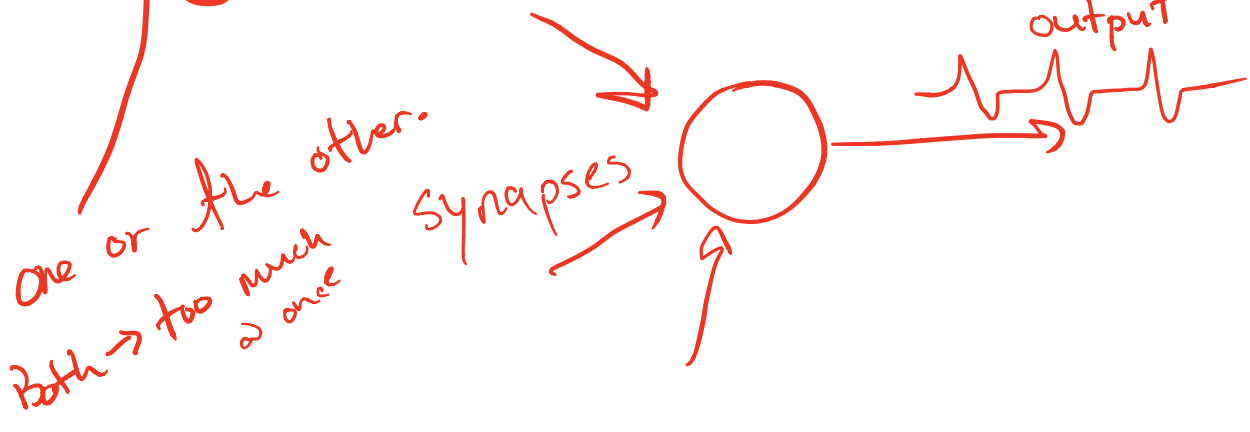
Box 24.3

Clicker question

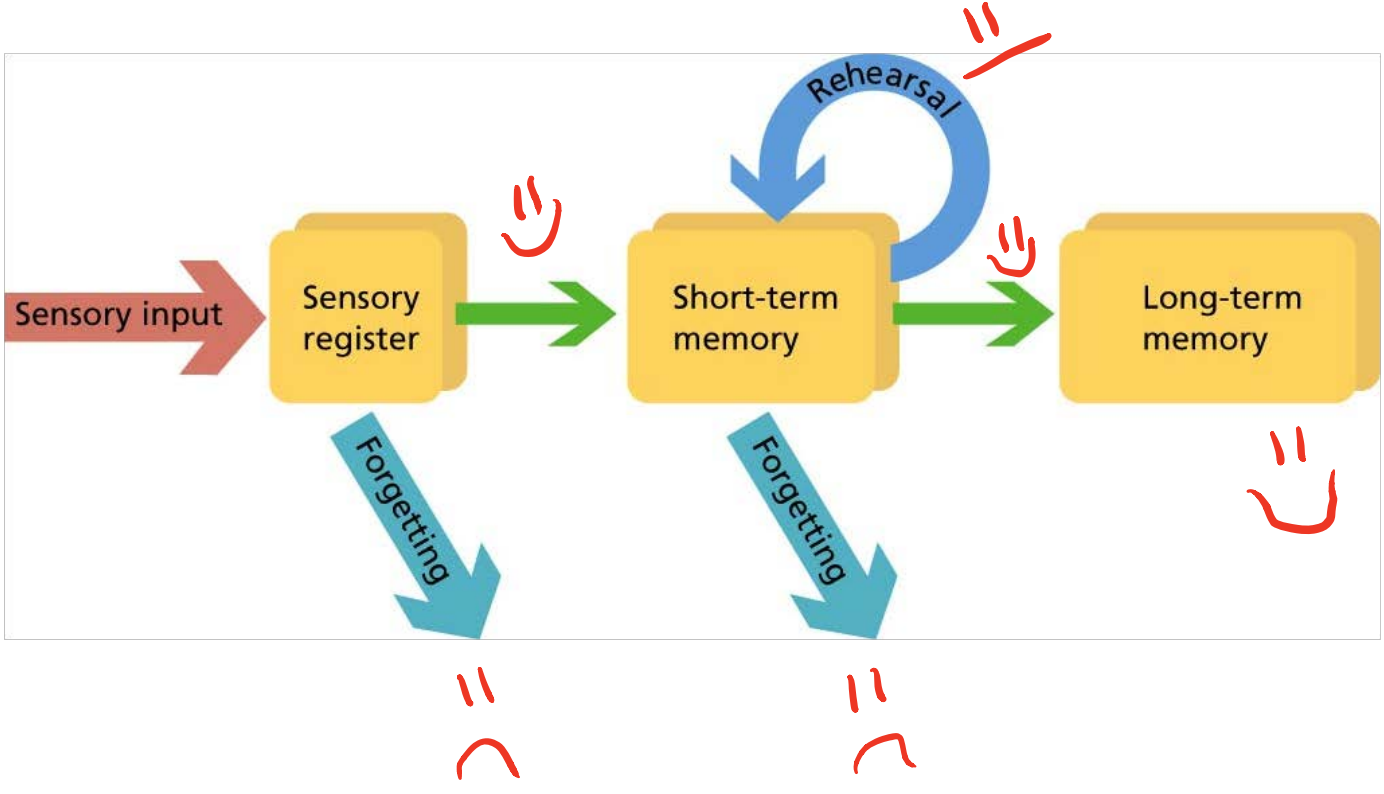
Loss of synapses in dementia could best be counteracted by

A. Lowering of firing thresholds ✓
B. More inhibitory neurons in the network ✗
C. More transmitter release ✓
D. A&B
E. A&C

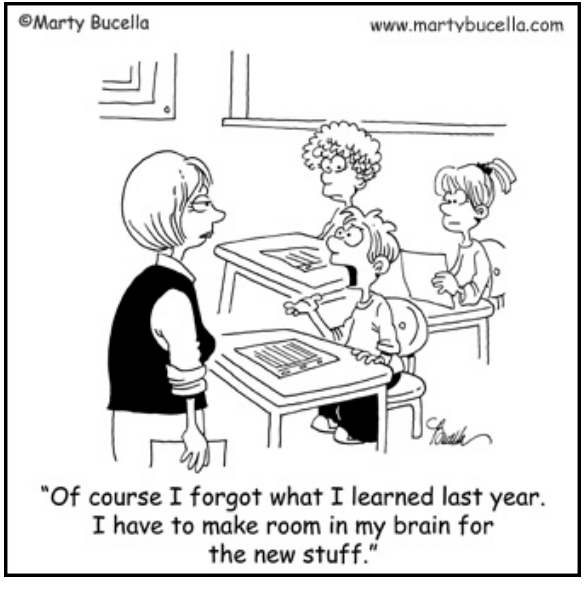
compensate for loss of synapses



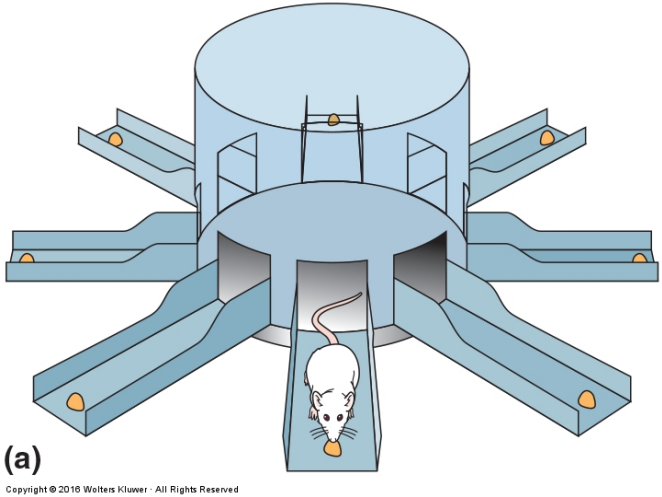
What is memory consolidation?



What is memory consolidation?



Animal models of working and long term memory



https://youtu.be/TPazQm_hvT4

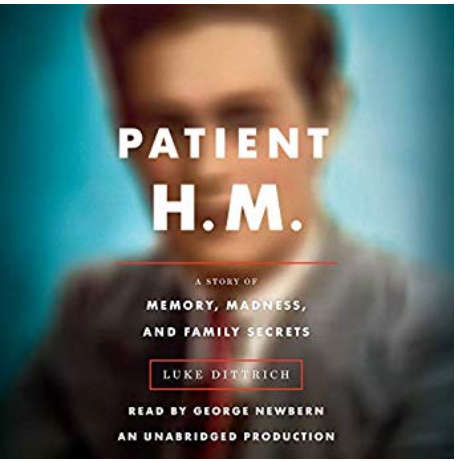
Radial Maze:

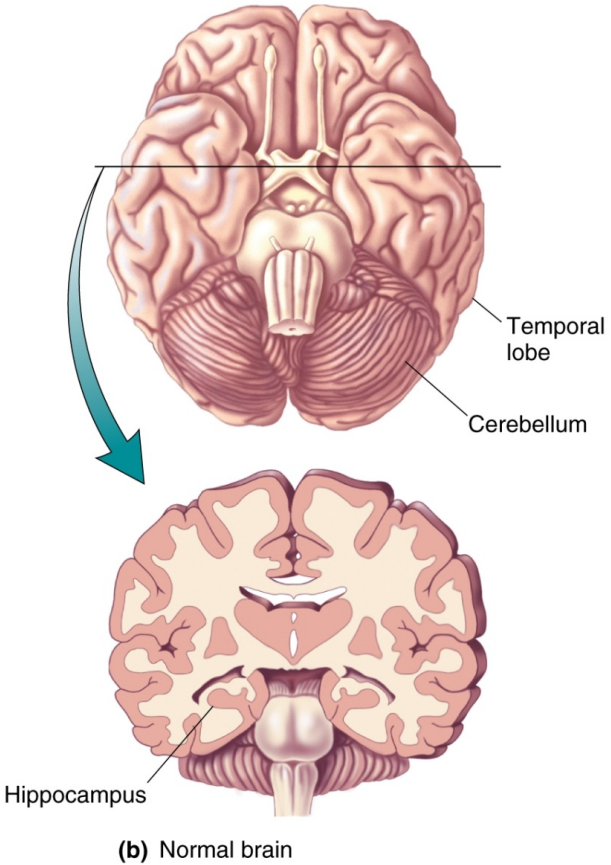
Working memory: Where did I go today?

Long term memory: Where is the food hidden?

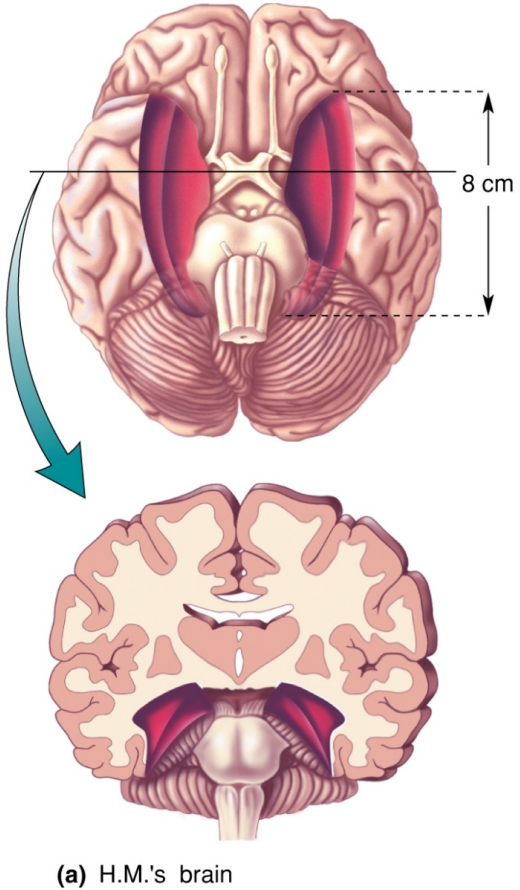
Figure 24.19A

Patient H.M.





(b) Normal brain



(a) H.M.'s brain

Clicker question

Which is NOT an example of procedural (declarative, explicit) memory:

A. How to throw a ball Motor memory
B. Where you last threw a ball Location
C. Whom you threw the ball to Person
D. The color of the ball event

Memory for actions, places, events, names, locations.

Clicker question

Which is an example of implicit memory:

A. How to throw a ball
B. Where you last threw a ball
C. Whom you threw the ball to
D. The color of the ball

Motor Memory

Clicker question

Patient H.M. could get better at playing the piano

A. True
B. False

Clicker question

Patient H.M. could get better at playing the piano

A. True
B. False

Patient H.M. could remember taking piano lessons as a child

A. True
B. False

Clicker question

Patient H.M. could get better at playing the piano

A. True
B. False

Patient H.M. could remember taking piano lessons as a child

A. True
B. False

Clicker question

After his surgery, Patient H.M. could get better at playing the piano

A. True
B. False

Patient H.M. could remember taking piano lessons as a child

A. True
B. False

After his surgery, Patient H.M. could remember taking piano lessons

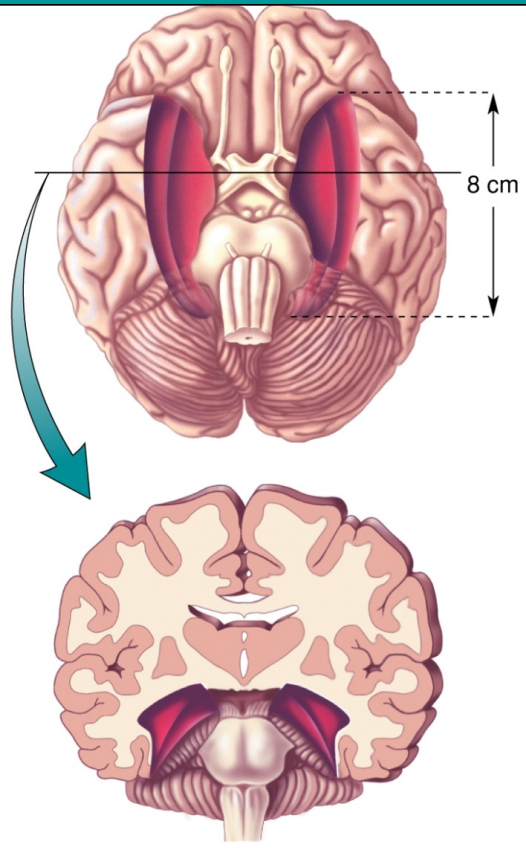
A. True
B. False

Patient H.M.

Unable to form “new” declarative memories

Could recall “old” declarative memories

Able to form “new” non declarative memories



(a) H.M.'s brain

H.M's case suggested that the temporal lobes (hippocampus) are important for storage of information just acquired and for transferring this information into long term storage

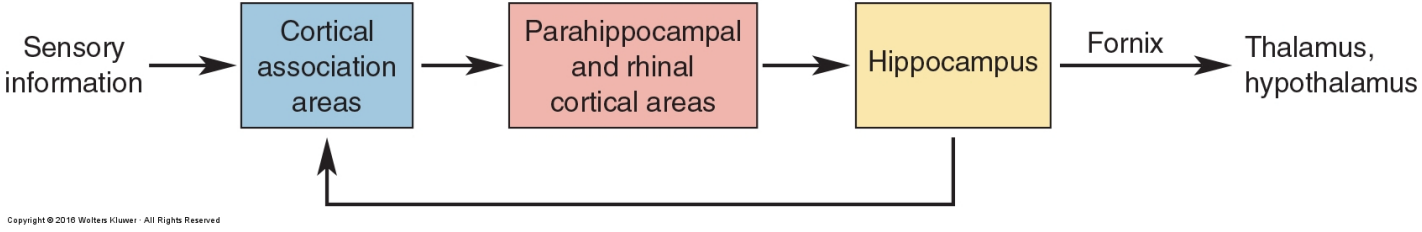


Figure 24.14

Role of the hippocampus in formation of new declarative memories: a theory

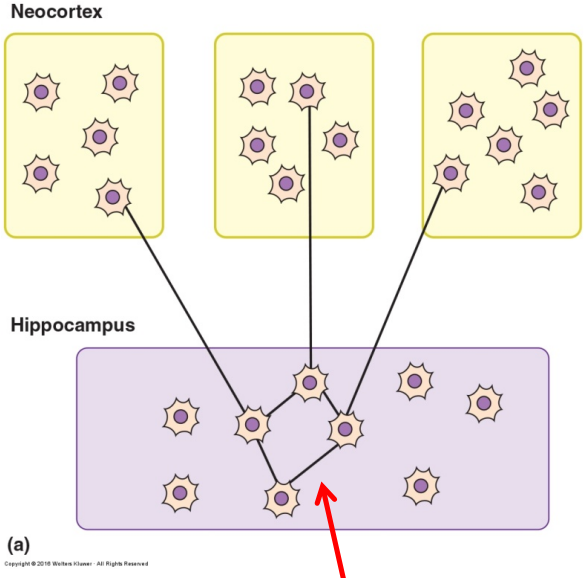
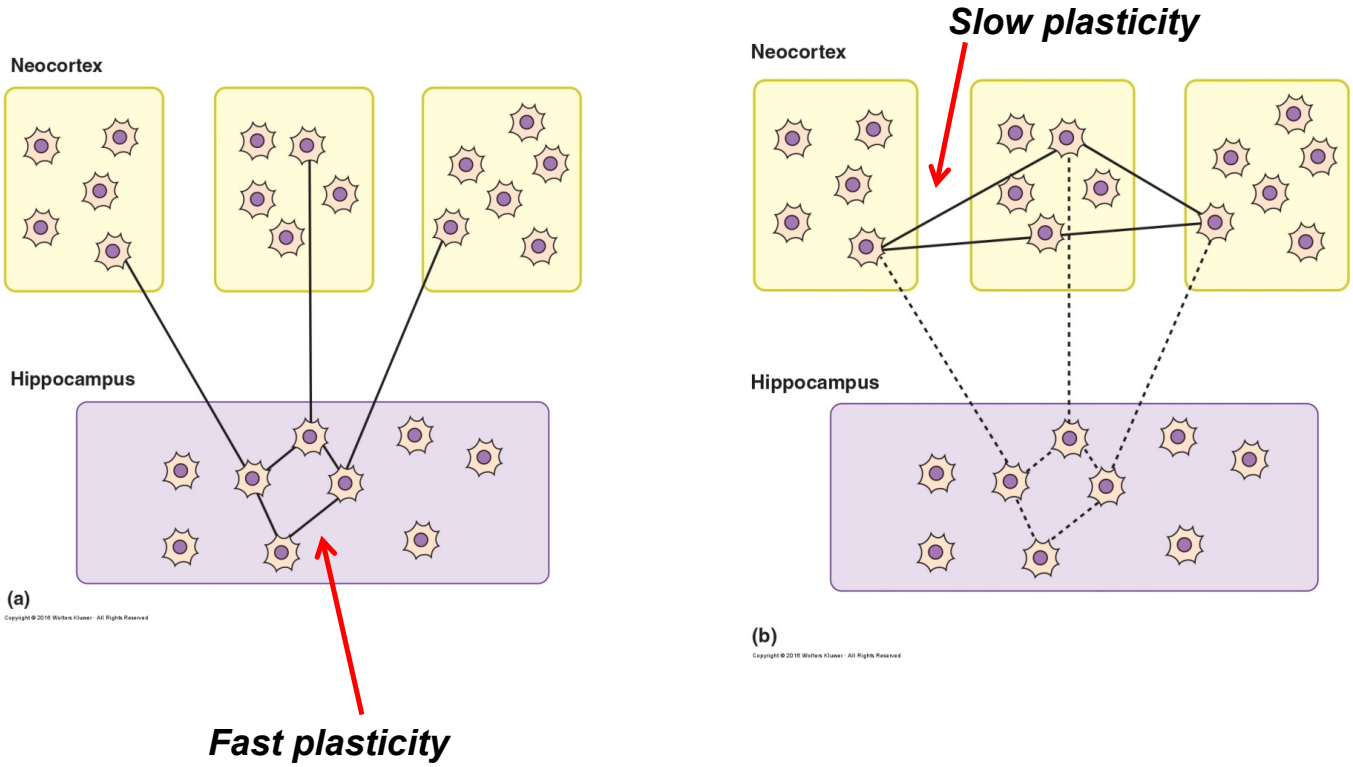


Figure 24.25A

Memory consolidation as a distributed process



Short term memories are stored in Hippocampus first and later in Neocortex because of different time scales of plasticity

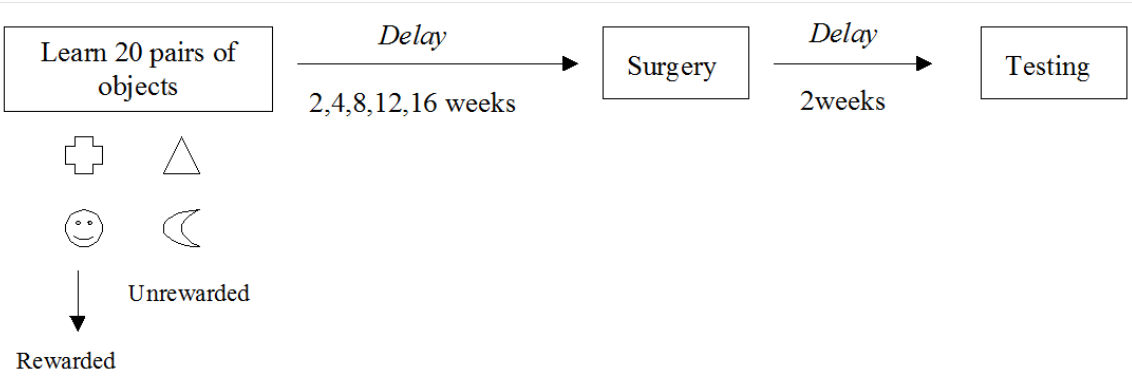
Figure 24.25A&B

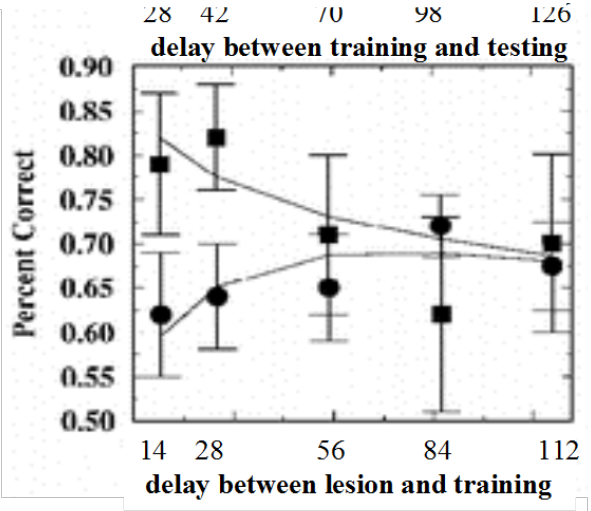
Experimental evidence for this model

(1) Patient H.M and others

(2) Long term memory formation impaired with MT lesions in non-human primates

Experimental evidence





Controls

Lesions

Controls exhibit normal forgetting

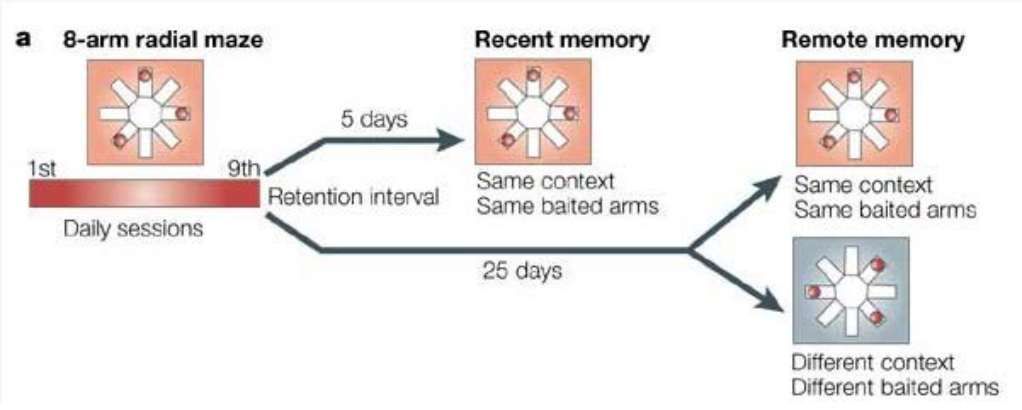
Hippocampal lesions impair memory formation only when they occur < 30 days after learning occured

Larry Squire and colleagues

Experimental evidence for this model

(1) Patient H.M and others
(2) Long term memory formation impaired with MTL lesions
(3) Neural activity in MTL represents more recently learned events than that in neocortex

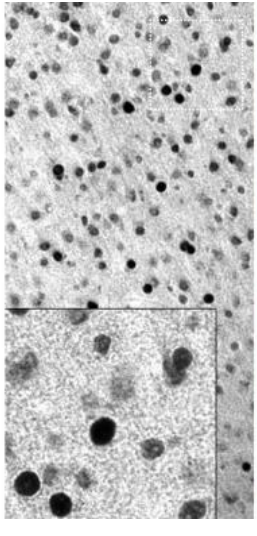
Short and long term memory processes in rodents



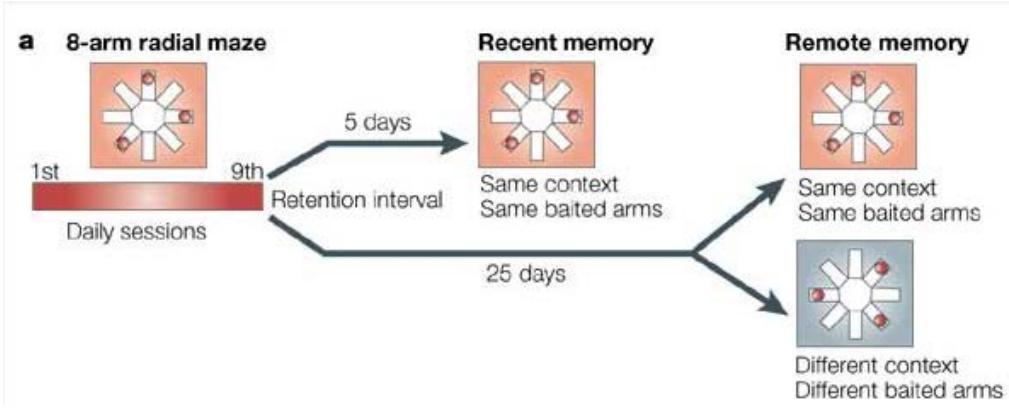
Activity mapping via IEGs

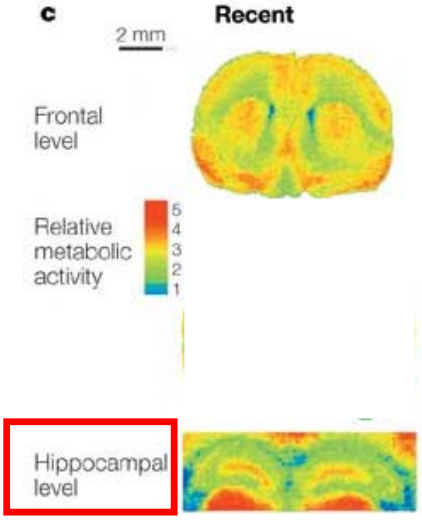
Immediate early genes such as c-fos are activated in response to stimuli, contexts

Expression of c-fos can be an indirect marker of neural activity because it is often expressed when neurons fire action potentials. Upregulation of c-fos mRNA indicates recent activity

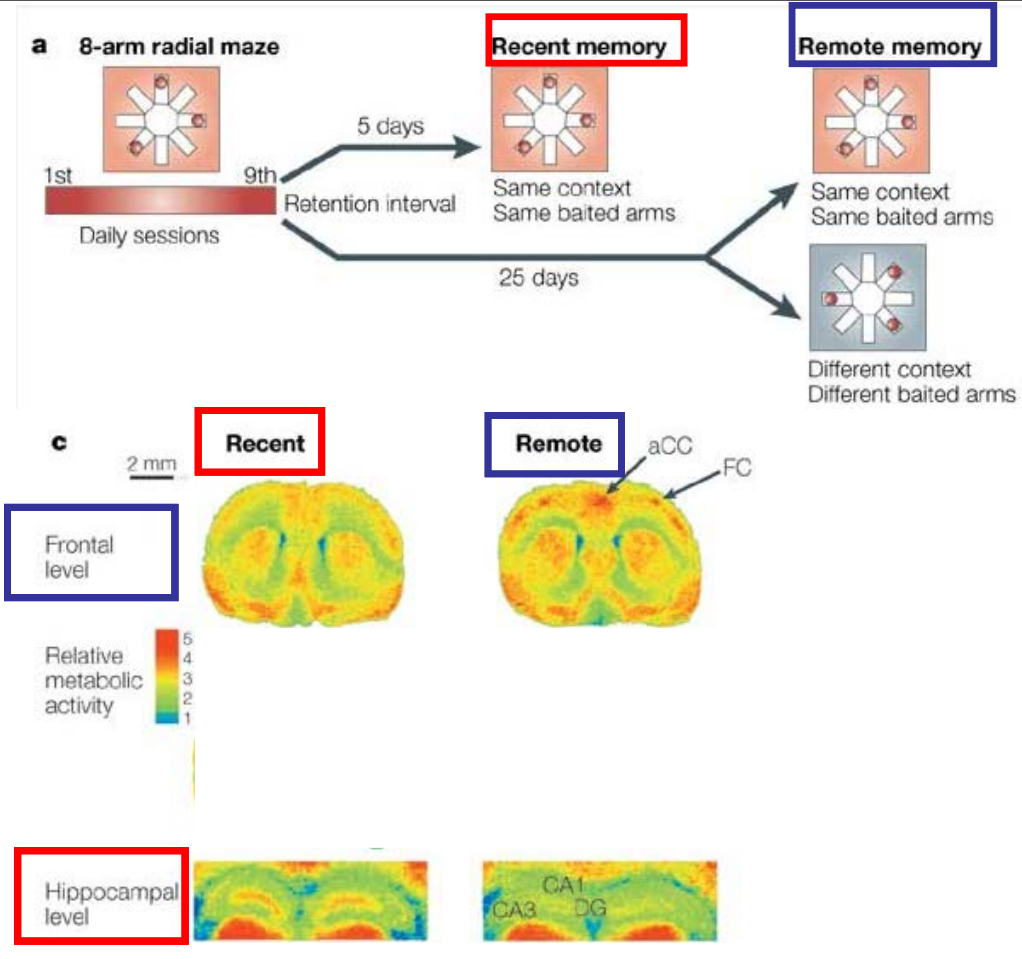


Activation of hippocampal neurons during recall of recent memories

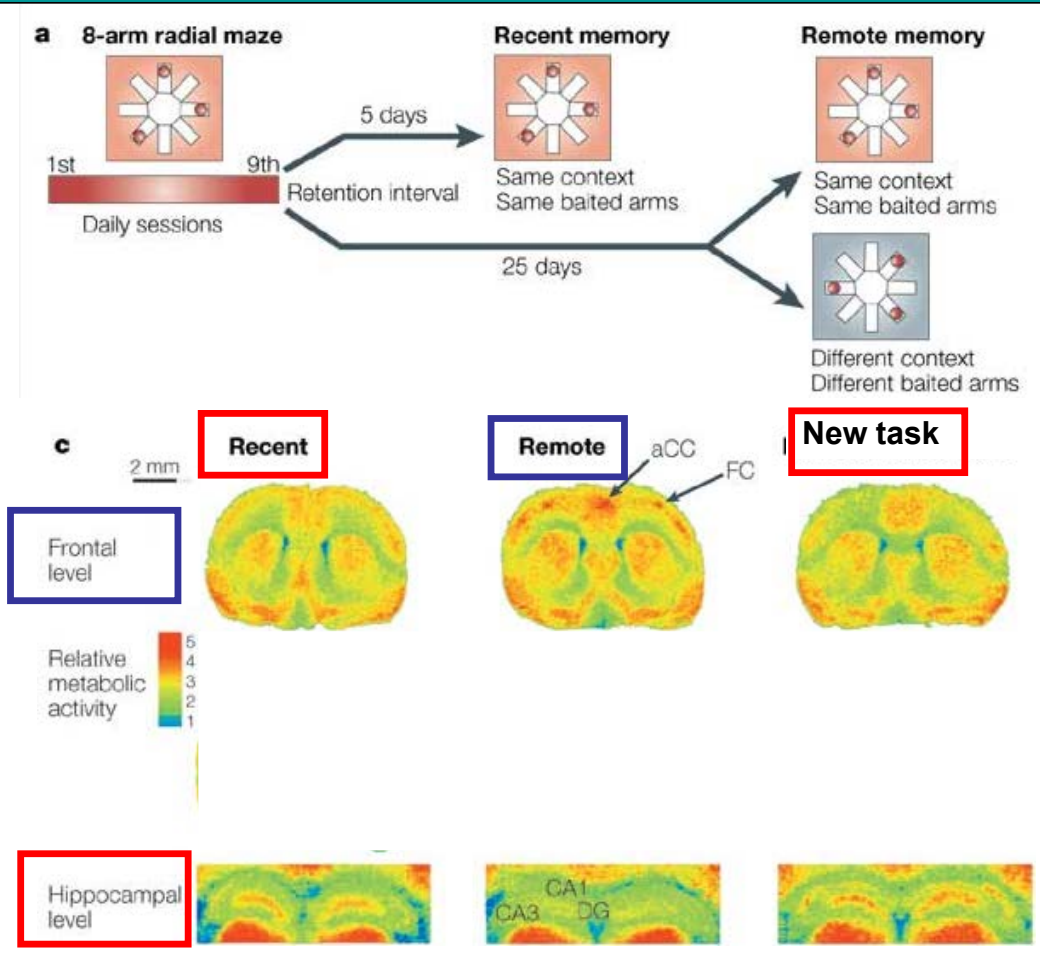




Activation of cortical neurons during recall of remote memories



Activation of cortical neurons during formation of new memories

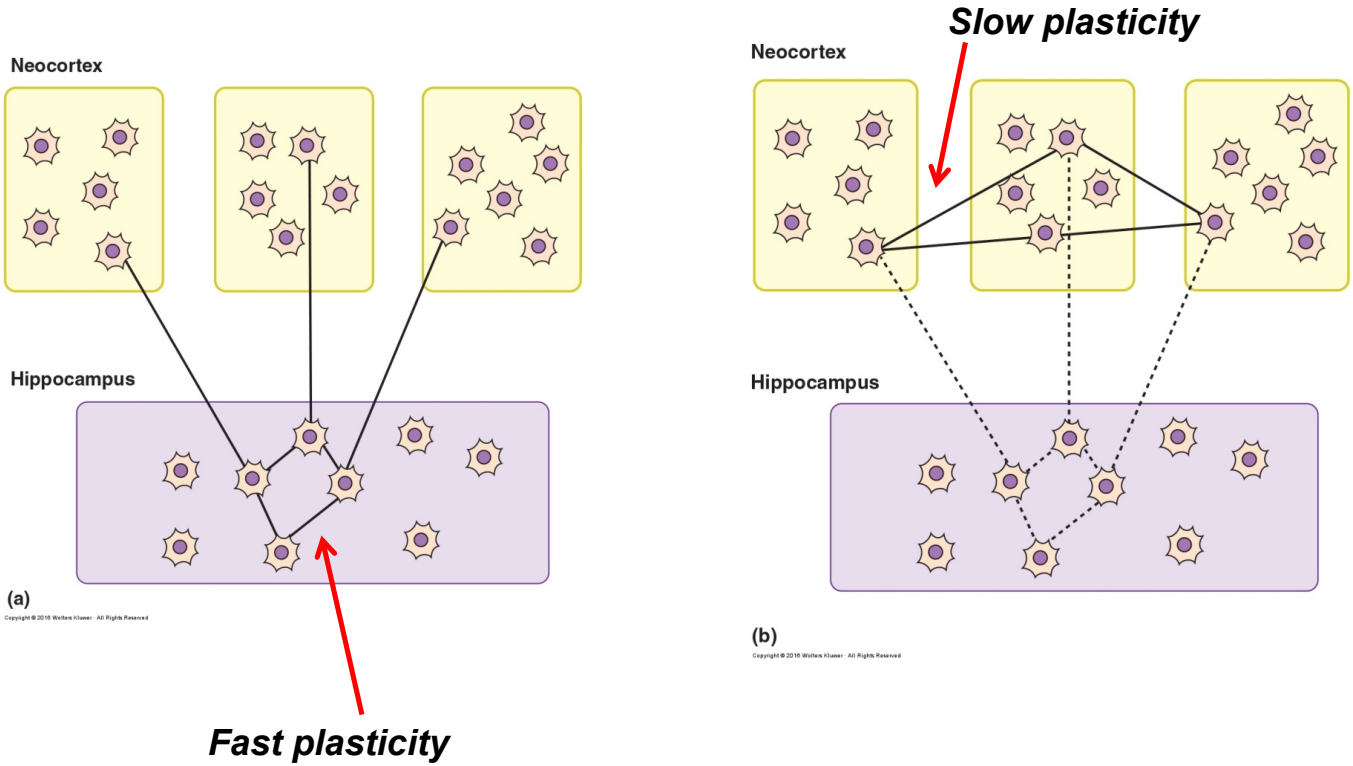


(1) Hippocampal structures were active during recall of recent memories

(2) Neocortical structures were active during recall of remote memories

(3) Hippocampal structures were active during learning of new memories

Memory consolidation as a distributed process



Hippocampal activity needs to be "reactivated" during sleep to allow for successful transfer to neo cortex

Figure 24.25A&B

Experimental evidence for this model

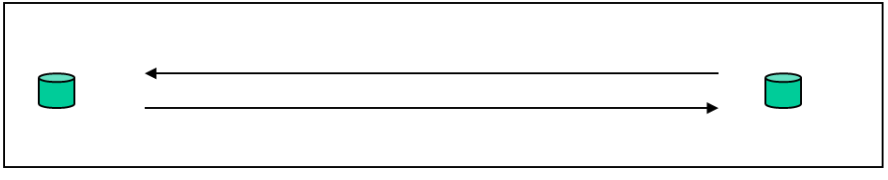
(1) Patient H.M and others
(2) Long term memory formation impaired with MTL lesions
(3) Neural activity in MTL represents more recently learned events than that in neocortex
(5) **Hippocampal place cells “replay” information during sleep**

Hippocampal replay during sleep

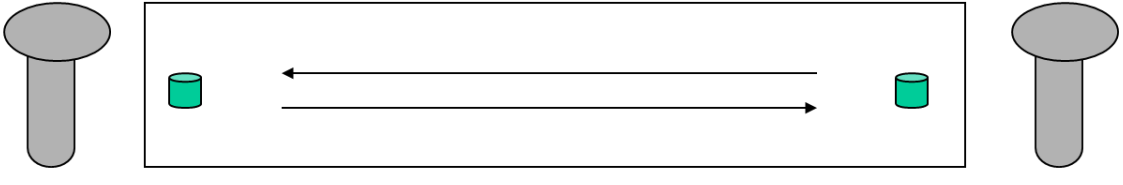
Random activation during consolidation:

Some researchers believe that neurons in the hippocampus "replay" events that have been lived during the day during REM sleep. Some evidence for this idea exists.

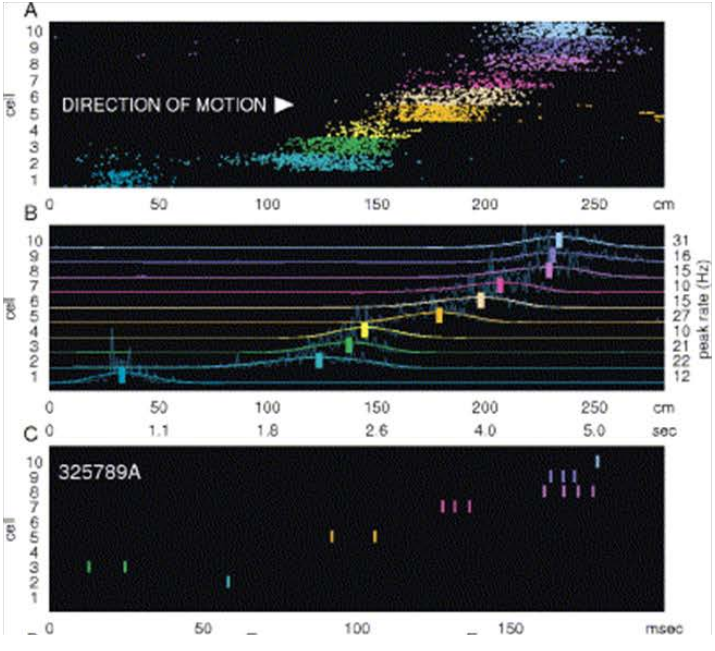
1) Rats were trained to run back and forth on various linear tracks



2) During the experiment, rats were first moved onto a circular platform on which movement was restricted (PRE). They then ran on a linear track (RUN) and were returned to the platform immediatly after (POST)



Hippocampal replay during sleep



A: Firing raster of cells during running on linear track

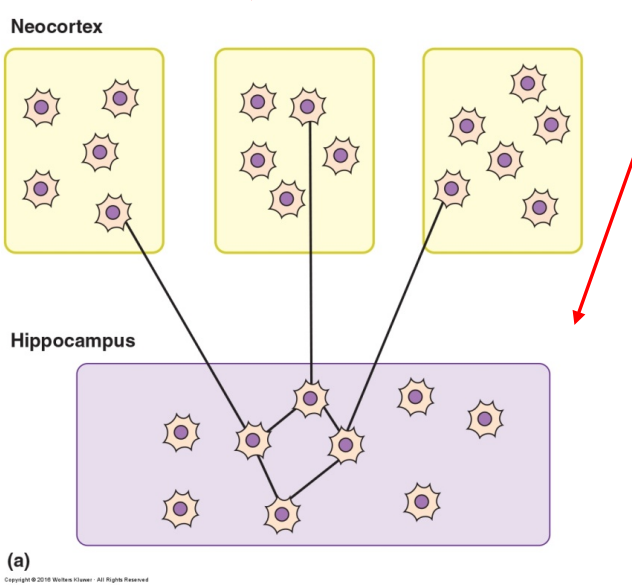
B: Place fields of recorded cells on linear track

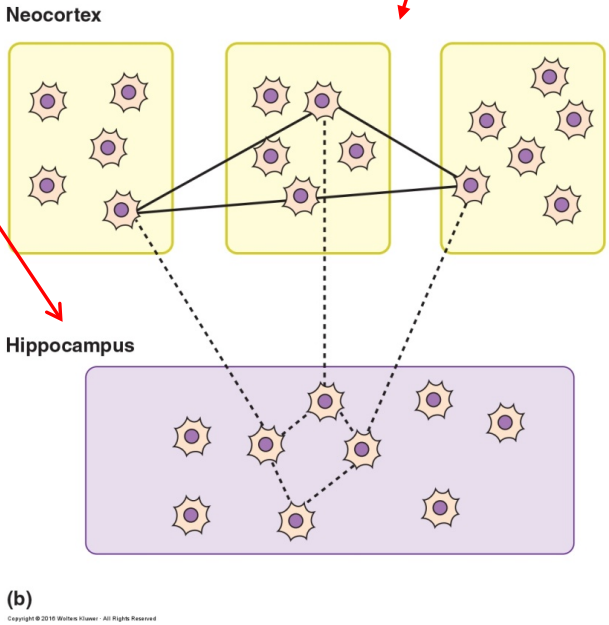
C: Cells recorded during sleep firing in the same sequence than on the linear track

Hippocampal areas more activated during new memory formation and recall of recent memories (Gage lab)

Cortical areas more activated during recall of remote memories

"Hippocampal replay during sleep (Wilson lab)





Hippocampal lesions impair recall only after a short time (Squire lab)

Summary and what you should remember

- Difference between explicit and implicit memories
- Associative memory
  - Process of forming associations between stimuli and/or situations by strengthening synapses between simultaneously active neurons
- Hebbian assemblies
  - Assemblies of neurons encoding or representing a memory formed via synaptic plasticity rules.
- Loss of neurons
  - Distributed representations of information can gracefully degrade when neurons or synapses are lost
- Patient H.M. history and symptoms
- Memory consolidation
  - One theory of memory consolidation involves shorter term storage in the HC, longer term storage in cortex and reactivation of memories to enable consolidation