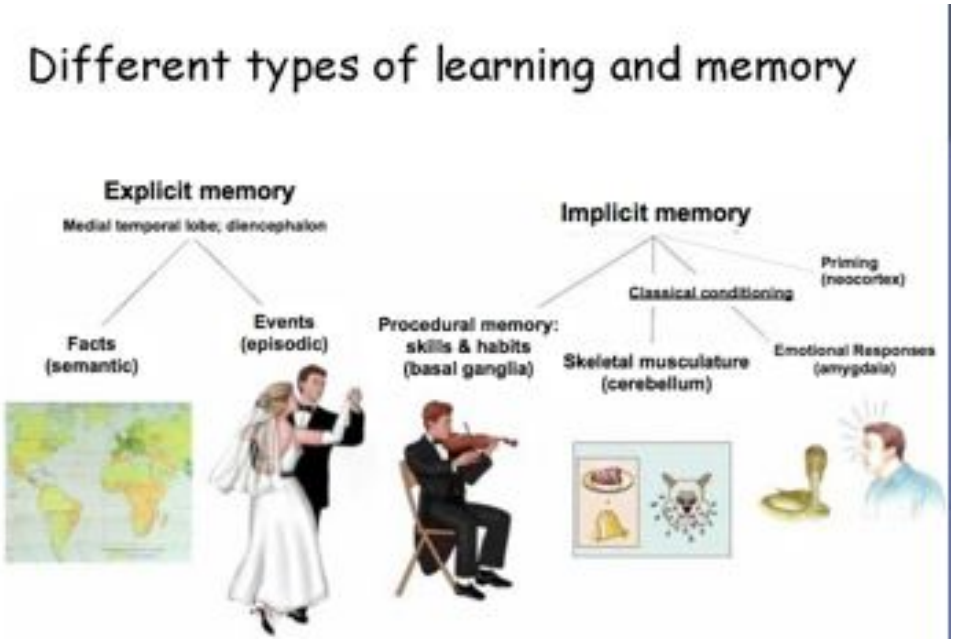
Notes: Cognition 2

Version:
11/18/12 - original version

Memory Classifications



A note on memory classifications

Definitions developed from observing behavior and trying to classify memories accordingly

These definitions could sometimes be fuzzy (e.g. semantic versus episodic)

As we understand more about the brain, can classify according to necessary __brain areas__

_____ memory

Examples: Obama is president, PSYC 2 is in Price Center Theater, my 21st birthday was a disaster

facts (_____), experiences (_____), locations

conscious and explainable (you can be explicit about the memory)

_____ memory

Examples: how to tie a shoe lace, the steps to get from your bed to the bathroom, fear of spiders

skills, routines, emotional memories
subconscious and not easily explained

An experience might lead to both explicit and implicit memories
You might be afraid of spiders and be able to explain when you formed this memory
But the explicit/implicit components of that memory will be handled differently (see below)

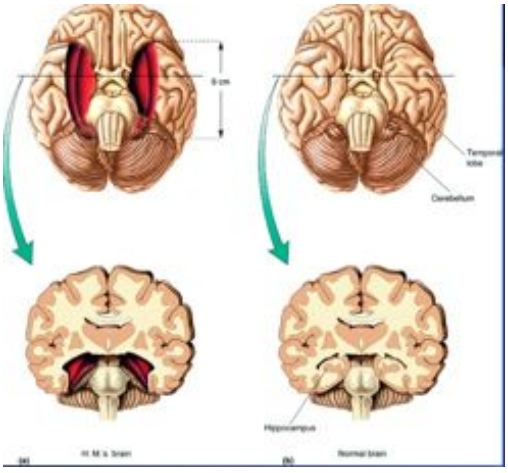
Amnesia Patients

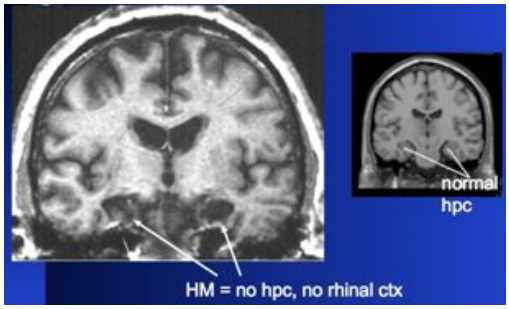
These amnesiac patients have damage to _____ and problems with _____ memory

Patient: H.M.

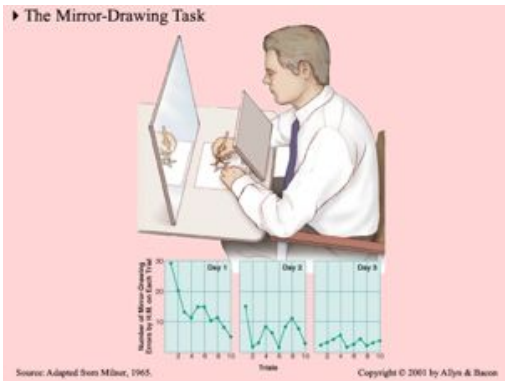
H.M. had bilateral medial temporal lobe lesions for epilepsy in 1953
Studied by Scoville (surgeon) & Brenda Milner (psychologist) in 1957
He was a pivotal case study that changed our understanding of memory
Post surgery:
well-adjusted, sensory & motor intact, high intelligence, short term memory intact
didn't have memories for events up to 2 years before surgery, but older memories intact
could NOT form new memories such as address, why he's in the hospital, people he met
Died in 2008, brain donated to and digitized by UCSD's Brain Observatory

Milner (source)





Intact Learning



Mirror Drawing

Task: trace a shape with a pencil through a reflection in a mirror
Result:
HM initially made many errors (similar to normal subjects)
but improved each day
HM had no memory of the task or his improvement
Summary:
HM was capable of learning a skill without being aware of his ability
(_____ learning)

Lessons from HM

- There are brain areas dedicated to and necessary for memory (_____)
- Long term memory is different than short term memory (more functional segregation)
- Ability to change behavior without being aware of it (explicit versus implicit memory)
(*Pinel, page 272*)

Patient: E.P.

Video (link pending, 14 mins)
Herpes enchephalitis
Charismatic, intelligent, able to reason & problem solve, short term memory (like word lists) intact
Could not permanent store short term memories, remember people, learn address

Patient: Clive Wearing

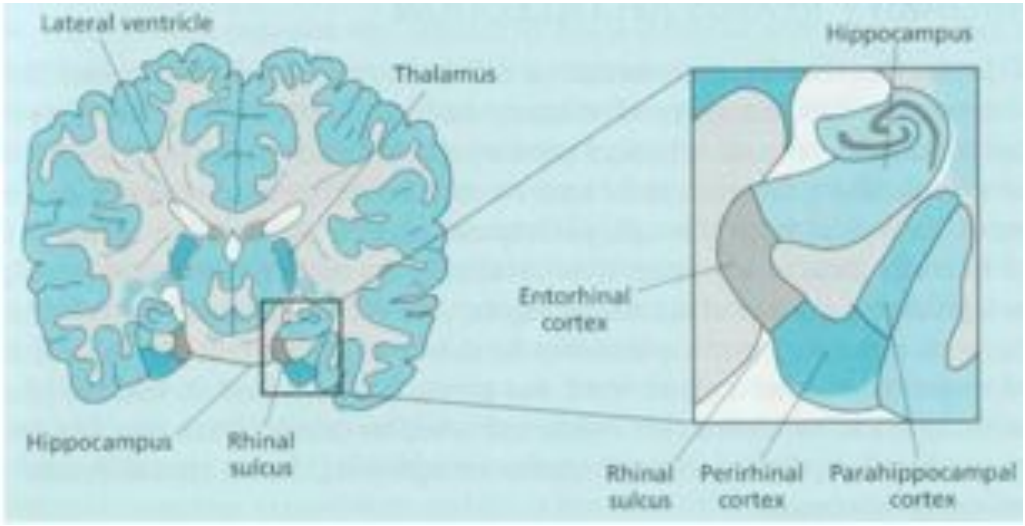
Video (3 mins)
An accomplished symphony conductor
Herpes enchephalitis
Deficits:
Couldn't remember own children's name
Only a few seconds of short term memory
Constant sensation of having just become conscious for the first time in his life
Intact:
Still strongly loved his wife (an emotional memory)
Play piano, conduct symphony, name a few composers, learn habits in his supportive care home

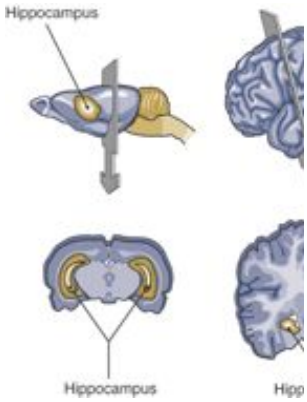
Causes of human amnesia

Damage to hippocampus and surrounding areas

- stroke
- herpes enchephalitis - herpes simplex-1 (cold sores) viral infection of the central nervous system
- Korsakoff's Syndrome - severe alcoholics
- surgery - tumors/epilepsy treatment, bilateral removal of medial temporal lobe are now avoided
- Alzheimer's disease
  - changes throughout the brain that also affect hippocampus
  - made worse by dementia - patients tend to be confused, so memories are less clear to begin with

Temporal Lobe Anatomy





Broad area: medial temporal lobe (MTL)

- Specifically: hippocampus, a critical area within MTL

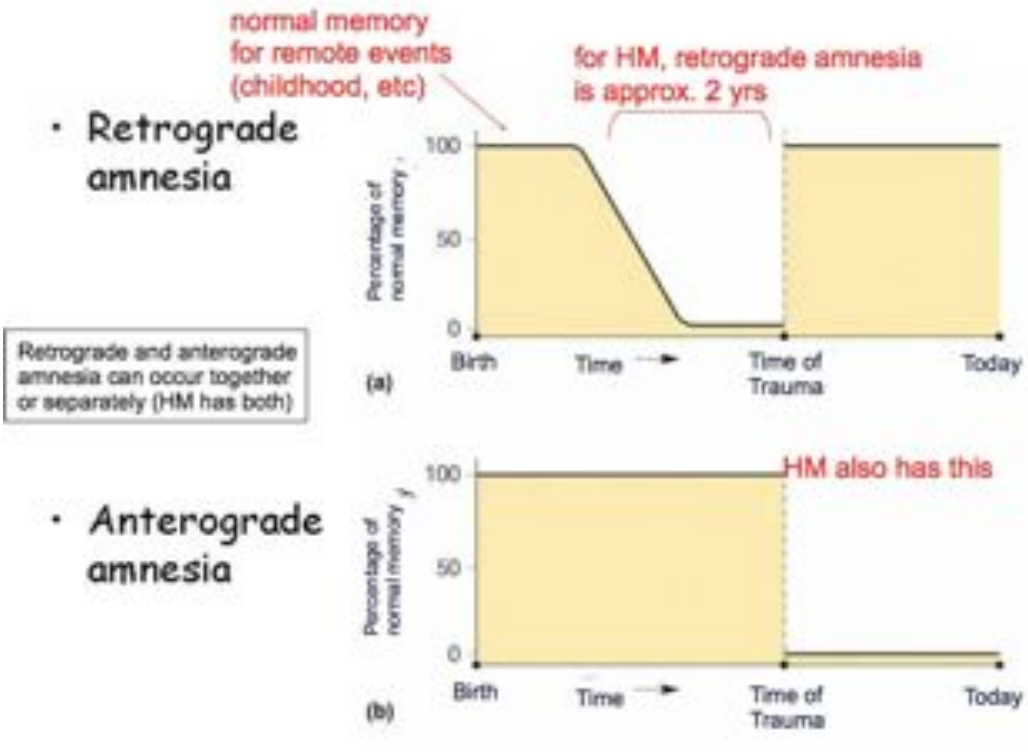
Hippocampus is / is not present across a full range of mammals

Temporal Gradient

Anterograde vs Retrograde Amnesia

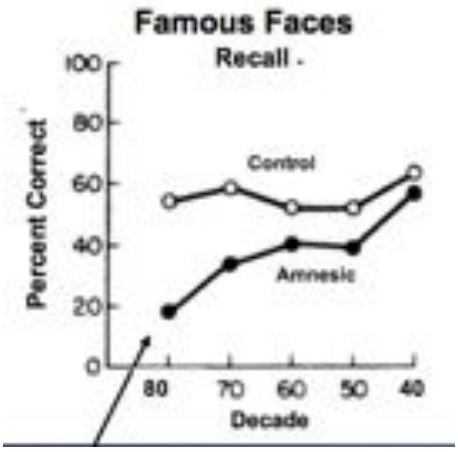
_____ amnesia - can not form memories AFTER the event

_____ amnesia - loss of memories formed BEFORE the event



Experiment: Famous Faces

Source: Haist et al, 2001



Task:

subjects (50+ years old) were healthy and MTL amnesia patients

subjects were shown pictures of famous faces and asked if they can identify them

famous faces belonged to people that reached prominence in many different decades

Results:

healthy patients have comparable memory for faces across all decades

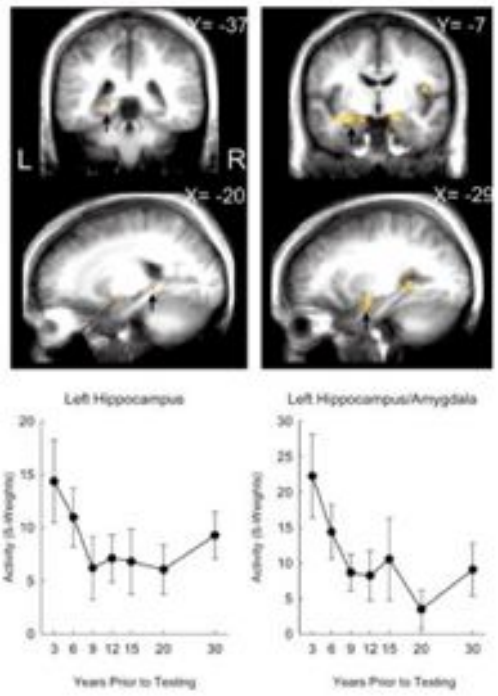
amnesiac patients are particular bad at remembering celebrities from _____ decades

amnesiac patients could/could not remember older memories as well as healthy patients

Summary:

Amnesia is most likely to affect recently formed memories while older memories are intact

Experiment: Famous Faces - fMRI



Source: Smith & Squire, 2009

Task:

Same as above but

All subjects were healthy (no amnesia)

scanned with fMRI during face recall

Result:

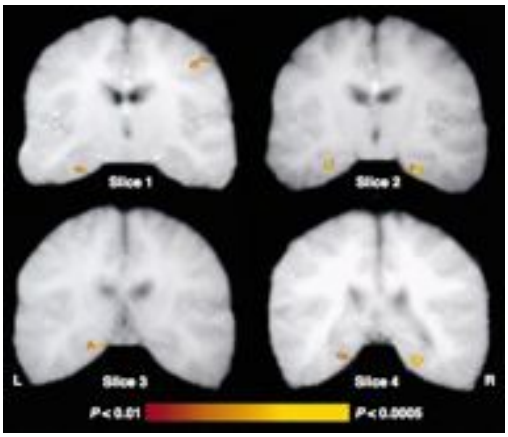
Hippocampus is more active for _____ memories

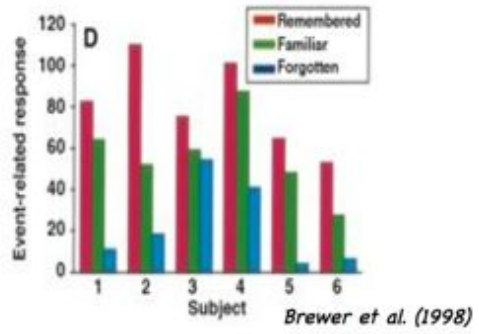
Summary:

Hippocampus activity matches behavioral responses

Encoding

Experiment: Subsequent Memory





Source: Brewer et al, 1998

Task:

Encoding stage:

subjects view photographs while being scanned in fMRI

Testing stage:

after scanning, subjects tested on memory for photographs

Results:

Photographs that were subsequently remembered during the testing stage had produced the greatest activity in the hippocampus during the encoding stage

Summary:

The hippocampus was most active during _____ of photographs that could later be remembered,
and least active for photographs that were later forgotten

The brain does not capture all incoming information equally
Info must be attended to to be encoded and later recalled

Animal Memory: Fear Conditioning

Experiment: Fear Conditioning

Task:

Rat/mouse spends time in a small chamber where it receives an aversive foot shock (training)

Shock is delivered at the same time a tone plays

Days later, animal is returned to chamber to measure about of time that the animal freezes (_____)

Results:

Animal will freeze if returned to identical box (_____ test), even without playing the tone

Animal will freeze if returned to a differently configured box if the tone is played (_____ test)

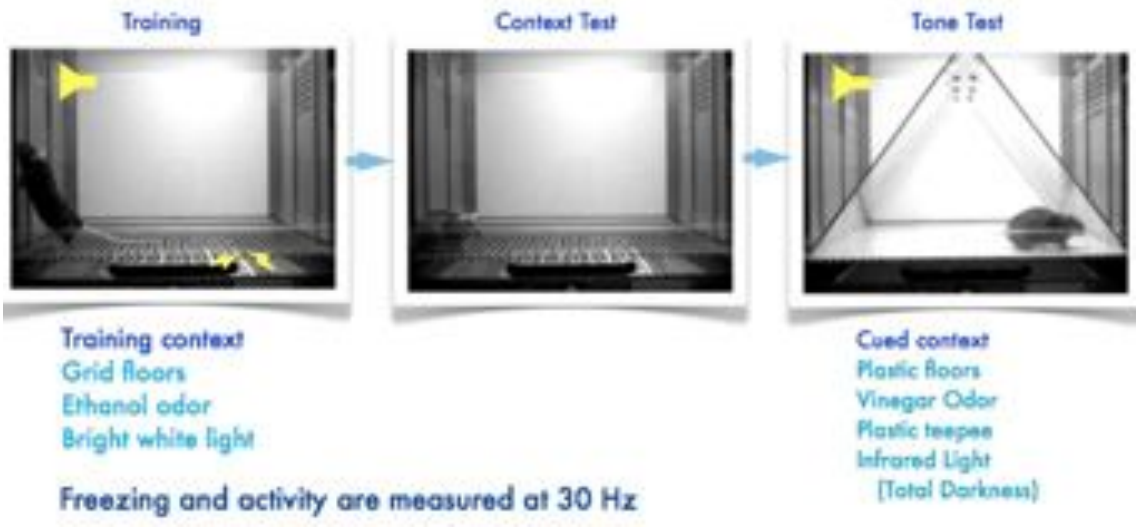
Summary:

Freezing measures fear, which is a form of memory

Memory is simultaneous formed for the place (context) and the tone

This basic memory is formed easily/quickly and animal will remember for its life time

This task can be used to study behavior, but also what is going on in the brain to form this simple memory



Results (below)

Graph: "Acquisition" (training)

Animal does freeze initially (BL=baseline),

but freezes more than 50% of the time after the shocks are delivered

Graph: "Context Fear"

Animal will freeze 75% of the first few minutes when it is returned to chamber

Fear gradually decreases, presumably as animal realizes no more shocks are delivered

Graph: "Tone Fear"

Animal doesn't freeze initially (BL=baseline) because the chamber is configured differently

Once the tone plays (at minute 2), animal suddenly freezes 75% of time

Fear gradually decreases, presumably as animal realizes no more shocks are delivered

Experiment: Fear Conditioning - with lesion to hippocampus

Questions:

Does the context memory depend on the hippocampus?

Does this dependence on the hippocampus change with time?

Task:

same as fear conditioning above

4 different treatments

some animals have their dorsal hippocampus (DH) lesioned 1 day after training (Recent)

some animals have a fake lesion procedure (Sham) 1 day after training (Recent)

some animals have their dorsal hippocampus (DH) lesioned 30 days after training (Remote)

some animals have a fake lesion procedure (Sham) 30 days after training (Remote)

Result:

animals given a sham/fake lesion have a good memory for context and freeze about 75%

regardless of when procedure is performed ("Context Summary" graph, yellow line)

this condition is done as a control

if the hippocampus is lesionsed when training is Recent, animal loses memory of training

and doesn't freeze in the context test ("Context Summary" graph, lower right red dot)

if enough time is given after training, hippocampus lesion doesn't affect content memory

("Context Summary", upper left red dot)

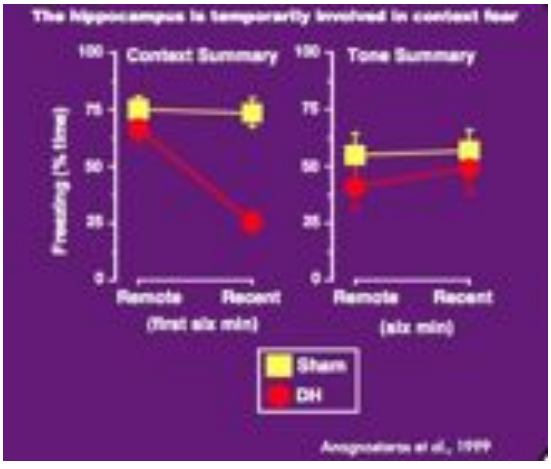
hippocampus lesion does not affect freezing to tone ("Tone Summary" graph)

Summary:

hippocampus is only necessary for remembering the context immediately after training

with time, the memory must _____ on another part of the brain

Strong evidence for the _____ seen in human amnesia



Experiment: Fear Conditioning - inhibition of protein synthesis

Question:

Do you have to make new proteins in order to make (consolidate) a long term memory?

Cell biology background:

Cells make new proteins by assembling amino acids based on DNA

Anisomycin is a drug that interferes with this assembly so that cells temporarily can't make any new proteins

Task:

Same as fear conditioning above

Prior to training, animals are injected with anisomycin to prevent protein synthesis

Result:

Animals injected with anisomycin do/do not freeze during the task training

This is considered short term memory (STM) in the graph below

Animals injected with anisomycin do/do not freeze after an extended delay

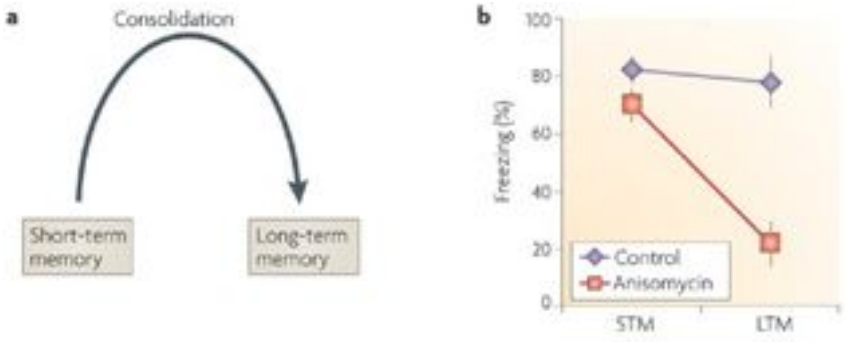
This is considered long term memory (LTM) in the graph below

Summary:

Animals can learn and form a short term memory even if anisomycin is injected.

However, because they can't make proteins, they can't _____ a permament memory

Protein synthesis is necessary for forming long term memories



Source: Nader & Hardt, Nature Reviews Neuroscience, 2009

Experiment: Fear Conditioning - Reconsolidation

Question:

Once learned, are memories stable? Can they be unlearned?

Task

Same as fear conditioning above (no injection of anisomycin yet)

After training, the memory is reactivated by re-exposing the animal to the context

Some animals have anisomycin injected prior to re-exposure

Days later, animals are returned a 3rd time (1st for training, 2nd for re-exposure, 3rd for testing)

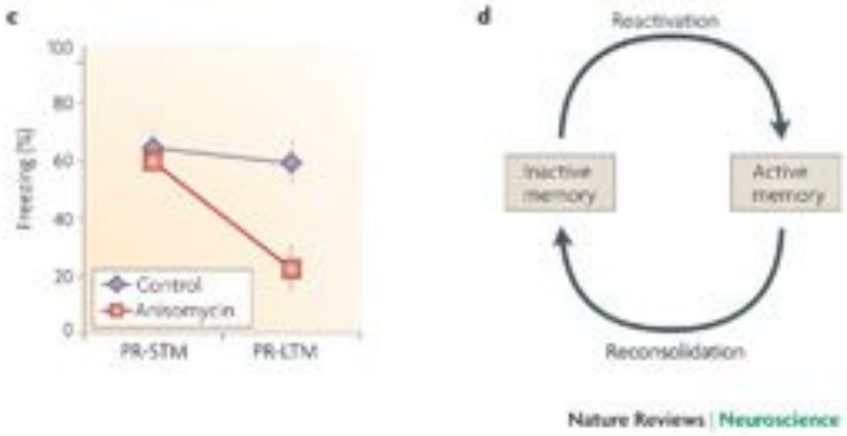
Results:

All animals freeze the same during the re-activation (PR-STM = post reactivation short term memory)

Animals that had anisomycin during the reactivation had their memory destroyed (PR-LTM)

Summary:

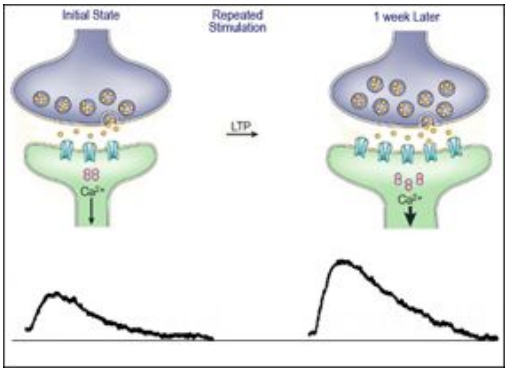
A reactivated memory requires another round of protein synthesis to _____ it, or the memory will be lost



Source: Nader & Hardt, Nature Reviews Neuroscience, 2009

Memory Consolidation

Molecular Consolidation



this is the process by which memories are formed at the level of the neuron/synapse

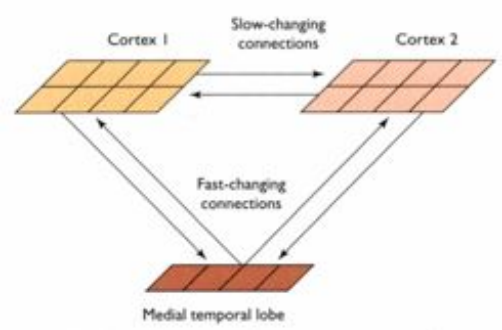
also called "Cellular Consolidation"

Strengthening existing synapses (new receptors) and creating new synapses (new neuron structures)

requires _____

Takes place over a time scale of minutes to hours

Systems consolidation



A model of how the storage of long-term memory might work. Each unit in each of the areas (four in the medial temporal lobe and eight in the two areas of cortex) is reciprocally connected to each unit in the other areas.

Theory:

Hippocampus has _____, adaptive connections to learn quickly

Cortex has _____ changing connections to maintain knowledge

The hippocampus _____ the cortex over time if information is useful or frequently encountered

Summary:

memory is initially in hippocampus (or hipp. points to memory)

gradually strengthens in the cortex until hipp. no longer needed

Takes place over a time scale of days to years

Hippocampus & Spatial Memory

Experiment: Morris Water Maze

Task:

Mice learn to swim around a tub of water to find a hidden platform

After training, some animals have cortex lesions, some have hippocampus lesions

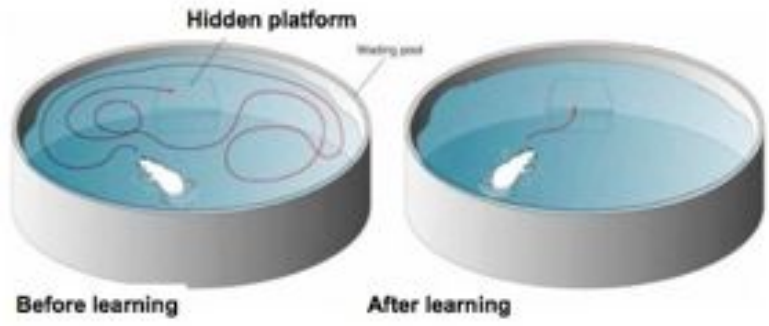
Results:

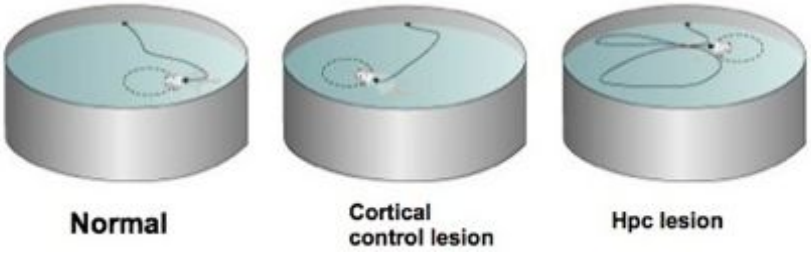
With training, animals learn to swim directly to the location of the hidden platform

With enough time to consolidate, animals with hippocampus lesions can/can not do the task

Summary/Theory:

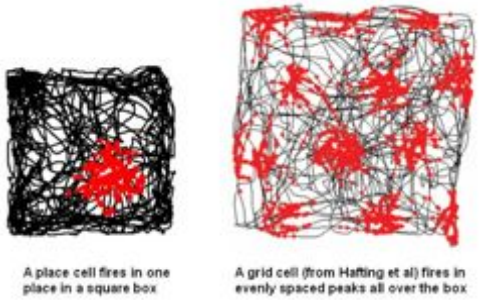
Hippocampus is strongly involved in _____ memories and always necessary for _____





Experiment: Place Cells

Source: Nakazawa... & Tonegawa, 2004



Source: www.ucl.ac.uk/jefferylab/research

Task:

Rodents have electrodes implanted to measure from hippocampus

Rodents are allowed to freely roam in an enclosed area

Results:

Some neurons in the hippocampus reliably fire whenever the animal is in a certain location (_____ cells)

Other neurons respond in many, grid like locations (_____ cells)

Summary:

Individual hippocampus neurons "lock on to" or represent specific locations

Together, these neurons make-up a _____ of space

Review

- Explicit memories depend on the medial temporal lobe (MTL), specifically the hippocampus
- The importance of hippocampus was revealed by human amnesiacs with a deficit in creating new memories
- Contextual fear condition is a popular memory experiment because it is easy to train, depends on a natural behavior, is long lasting and involves the hippocampus
- Molecular consolidation - forming new memories requires making new proteins to change synaptic strength
- Systems consolidation - memories are initially dependent on the hippocampus but transition over time, likely to the cortex
- Reconsolidation - memories can become vulnerable once they are reactivated
- The hippocampus is heavily involved in spatial tasks:
  - the hippocampus is always required for successful navigation in the water maze task
  - the hippocampus has place cells - neurons that reliably fire when an animal is in a specific location