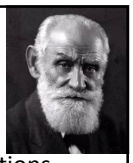
The Biopsychology of Memory

Module 13.1

Different methodologies have been used to try to figure out what regions of the brain are involved in memory functions.

Early Proposal

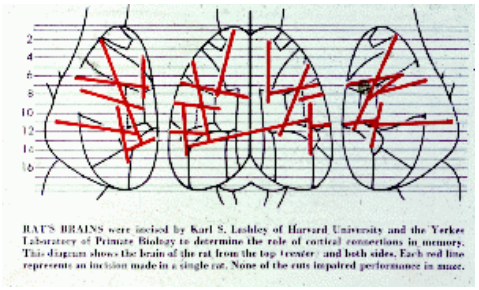


- Pavlov – learning (such as classical conditioning) strengthens the connections between the involved brain areas
- If this is the case, disrupting these connections should impair the learned response

Early Research (1920)

- Karl Lashley – attempted to locate memory "engrams" in rats' cortex by studying the effects of cortical cuts or lesions on memory of various tasks.

Karl Lashley's Cuts in Rat Cortex



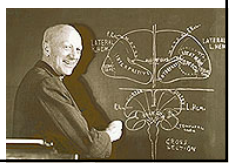
RATS' BRAINS were incised by Karl S. Lashley of Harvard University and the Yerkes Laboratory of Primate Biology to determine the role of cortical connections in memory. This diagram shows the brain of the rat from the top (cerebrum and both sides. Each red line represents an incision made in a single rat. None of the cuts impaired performance in maze.

Early Research

- But it did not seem to matter where the cuts or lesions were. Lashley could not find any single critical "memory area". Concluded that, at least in the rat:
- Law of equipotentiality – all areas of cortex seemed to be equally important to the performance of the learned response
- Law of mass action – degree of impairment was correlated with amount of cortex removed, not the region of the cortex removed
- http://www.learner.org/resources/series142.html#

Neurosurgeon Wilder Penfield

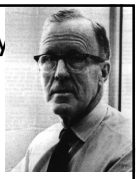
- Found that electrical stimulation of temporal cortex (preceding brain surgery) often triggered memory-like experiences (e.g. "I hear my mother calling me")
- Concluded that episodic memories are localized there
- So it memory localized or not?



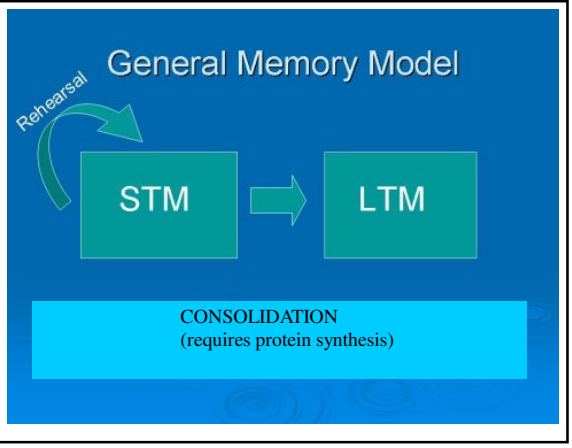
Successful Location of An Engram?

- Richard Thompson (1986) found a nucleus in the cerebellum (LIP – lateral interpositus) essential for the conditioned eyeblink response of rabbits
  - Neurons active in this area during this learning
  - Inactivating these neurons disrupts conditioning
  - These neurons also appear to be active in humans during eyeblink conditioning

Hebb's theory of memory "consolidation" (1949)



- Hebb distinguished between Short Term Memory & Long Term Memory and proposed:
  - STM mediated by temporary patterns of brain activity in "reverberating circuits"
  - This temporary activity is susceptible to disruption
  - LTM depends on lasting structural changes
  - Increased structural connectivity results from repeated activation of the same synapses, causing the "consolidation" of LTMs

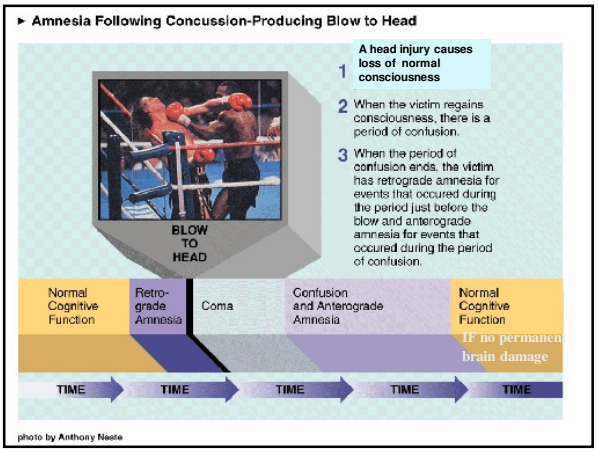


Post-Traumatic Amnesia

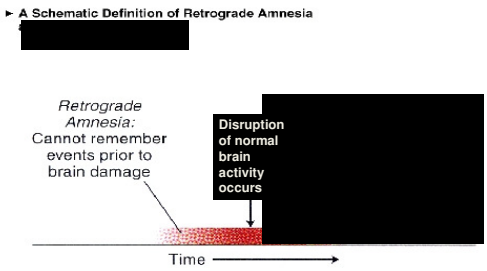
- Some trauma disrupts the functioning of the brain. May be temporary or may be lasting effects if trauma are severe.
- *Retrograde amnesia* for events just *before* the trauma (more severe trauma increases the amount of RA)

Retrograde Amnesia by ECS or Other Traumas

- Recent memories most susceptible to disruption
- Rats given ECS 10 secs to 10 mins after learning showed decreased memory for task. ECS 1-3 hrs after learning had no effect.
- More recent memories may continue to be somewhat more susceptible than older memories:
- Humans receiving ECT show decreased recall of TV shows from last 1-3 years, no impairment of memory of shows from 4-17 years ago.



Retrograde Amnesia



Like when a power outage causes you to lose the file you were working on because it hadn't yet been saved. Brain loses what it was working on.

New View of STM

- Now think that "STM" may be the current memory files we "have open" or are still working on – things that we are keeping in mind.
- Now call it "working memory". Depends on prefrontal cortex. Many working memories will never be added to LTM because they concern temporary information.
- This kind of memory has not yet developed in infants & gradually develops into early adulthood.

Different Aspects of Long Term Memory

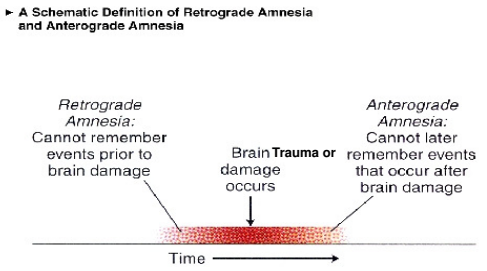
- Terms to refer to types of LTM:
- Declarative memory – memories we can state in words:
  - information ("semantic" memories)
  - life experiences ("episodic" memories)
- Procedural memories – motor skill memories

- Explicit memory – conscious intentional recollections
- Implicit memories – more "unconscious" memories evidenced by improved/altered performance, without conscious recollection of what caused that

Another Type of Post-Traumatic Amnesia

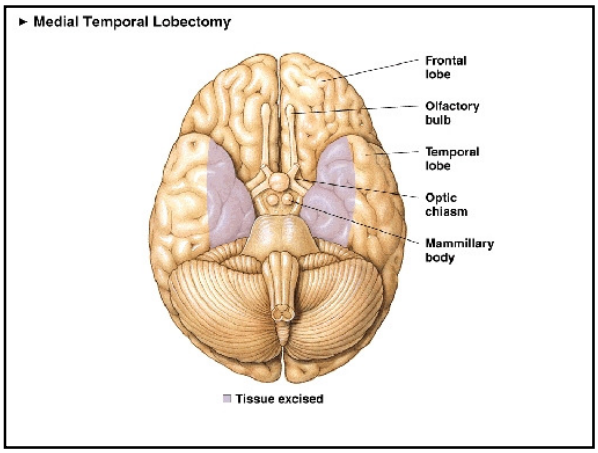
- Anterograde amnesia - impaired storing of memories of events *after* the trauma (more severe damage increases anterograde amnesia)

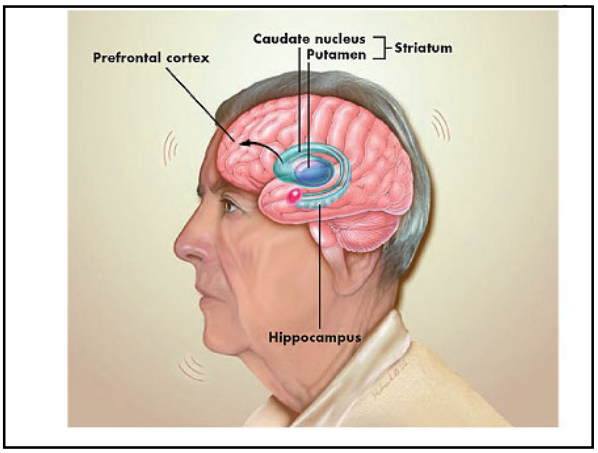
Retrograde vs. Anterograde Loss



The Sad Case of H. M.

- HM suffered a closed head injury when 9→
- Developed post-traumatic focal epilepsy uncontrolled by medication
- EEG revealed seizures were originating in both medial temporal lobes
- Unilateral surgeries had successfully reduced seizures in previous patients
- HM had *bilateral* medial temporal lobectomy





H. M.

- Epilepsy greatly improved but memory severely impaired
- Retrograde amnesia- most severe for things within the 2-3 years before surgery, but older memories and IQ intact
- Severe anterograde amnesia for declarative memories. STM fairly normal but once HM is distracted, those memories are lost

H.M. Also Shows All Memories Not Stored in Same Way

- H.M. has shown evidence of the formation of new procedural & implicit memories
- Finger maze, mirror tracing & reading, rotary pursuit, playing Tetris, classical conditioning

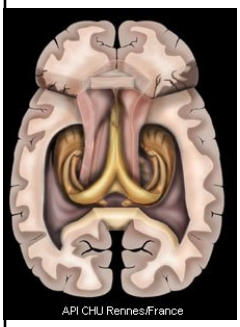
Mirror-Drawing Task

(a)

Clive W.

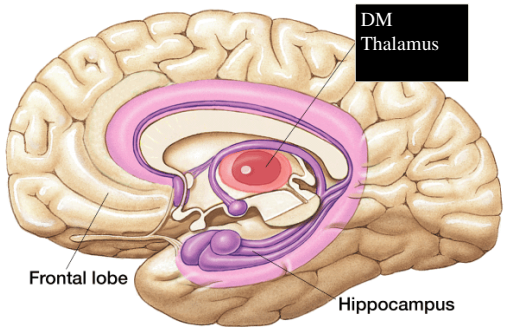
- Suffered damage to hippocampus and frontal cortex during a bout of encephalitis
- Extreme anterograde amnesia similar to H.M.'s; old LTM s are fine – some additional dyscontrol of emotion because of frontal lobe damage.

Role of Hippocampus Within Medial Temporal Lobe



- Seems to be involved in the *process of memory storage ("consolidation")* but is **not** the final "memory bank"
- (we'll come back to the "memory bank" in a minute)

How About Other Limbic Areas?



Amnesia Due to Thalamus/Hypothalamus Damage

- Korsakoff's Syndrome - serious anterograde AND increasing retrograde amnesia . Tendency to **confabulate as their episodic memories deteriorate.**
- Once again implicit memories are better preserved.
- Due to thiamine deficiency, most often in alcoholics, which impairs the supply of energy (glucose) to the brain
- Widespread loss of neurons; most concentrated damage in DM thalamus & mammillary bodies of hypothalamus, and cortex

Other Diencephalic Cases

- N.A. & his fencing foil
- mild retrograde + more serious anterograde amnesia
- 1970 CAT scan revealed left DM thalamus lesion
- More recent MRI scan showed additional damage to mammillary bodies.

Memory Role of Other Areas

- Amygdala - emotional significance
- Frontal lobe – working memory; memory for consequences
- Cerebellum & Basal Ganglia- implicit, procedural memories
- **Long-term memories** - stored in the secondary & association cortex areas involved in the original stimulus perception/processing
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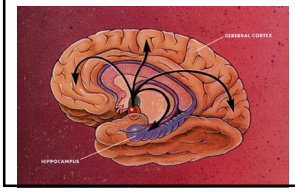
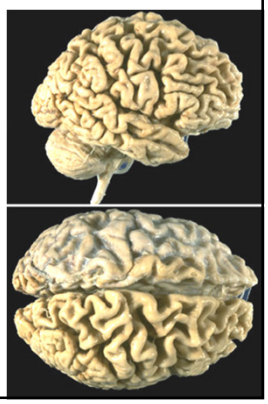
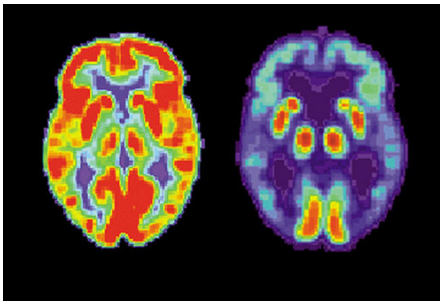
Alzheimer's Disease

Widespread degeneration in cortex (especially association areas), hippocampus, amygdala, as well as a critical source of ACh -nucleus basalis. Cortical & hippocampal changes can be seen on MRI as disease advances.



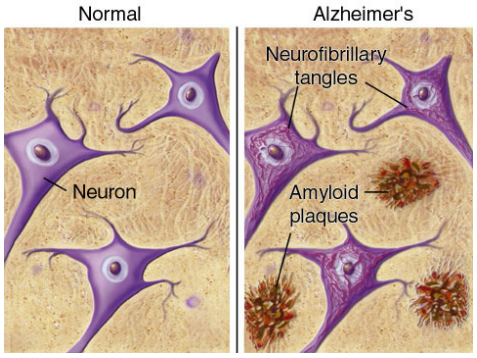


PET Scan of Decreased Brain Activity in Severe AD



Alzheimer's Disease

- Runs in families; genes on at least 4 different chromosomes have been linked to early AD and others are linked (but less strongly) to the more common late-occurring variety
- Several pathological changes in brain
  - Production of **abnormal amyloid protein** which damages neurons, causing distinctive **plaques** of neural debris
  - Production of **abnormal tau protein** which produces abnormal **neurofibrillary tangles** within neurons. Interfere with neuron function & may cause toxic levels of glutamate to be released, causing cell death.



- Currently: drugs to boost ACh by preventing its breakdown (Aricept, Cognex, Exelon, Reminyl) provide some improvement in the early stages.
- One new med to try to block toxic effects of glutamate (Namenda)
- Researchers investigating potential genetic, stem cell, and insulin related treatments as well as a possible amyloid 42 vaccine.