Anatomy and psychology of learning and memory

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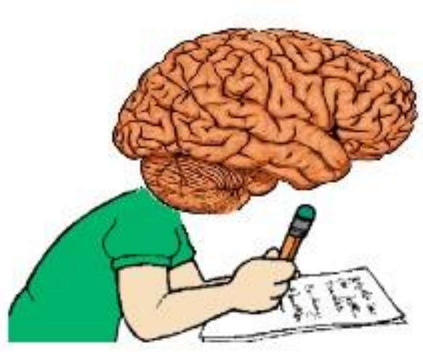
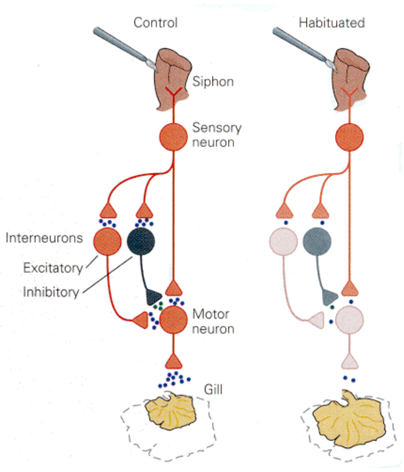
- Nonassociative?



- Associative?

- Nonassociative learning
  - when an animal or a person is exposed once or repeatedly to a single type of stimulus



- Associative learning
  - learning about the relationship of various stimulus or the stimulus and the reaction of organism

NON ASSOCIATIVE LEARNING	ASSOCIATIVE LEARNING
HABITUATION Reaction to the stimulus diminishing When an animal repeatedly encounters a harmless stimulus it learns to habituate to it. **SENZITIZATION** (pseudo conditioning) stronger reaction to the stimulus appearing immediately after the adverse stimulus With a harmful stimulus the animal typically learns to respond more vigorously not only to that stimulus but also to other stimuli, even harmless ones. Defensive reflexes for withdrawal and escape become heightened. *DISHABITUATION	SIMPLE **CLASSIC CONDITIONING-** learning a relationship between two stimuli **OPERANT CONDITIONING–** learning a relationship between the organism's behavior and the consequences of that behavior COMPLEX **Explicit** (declarative) memory **Implicit** (procedural) memory

Nonassociative learning

Habituation

- a decrease in response to a benign stimulus when that stimulus is presented repeatedly

Sensitization (or *pseudoconditioning*)

- an enhanced response to a wide variety of stimuli after the presentation of an intense or noxious stimulus

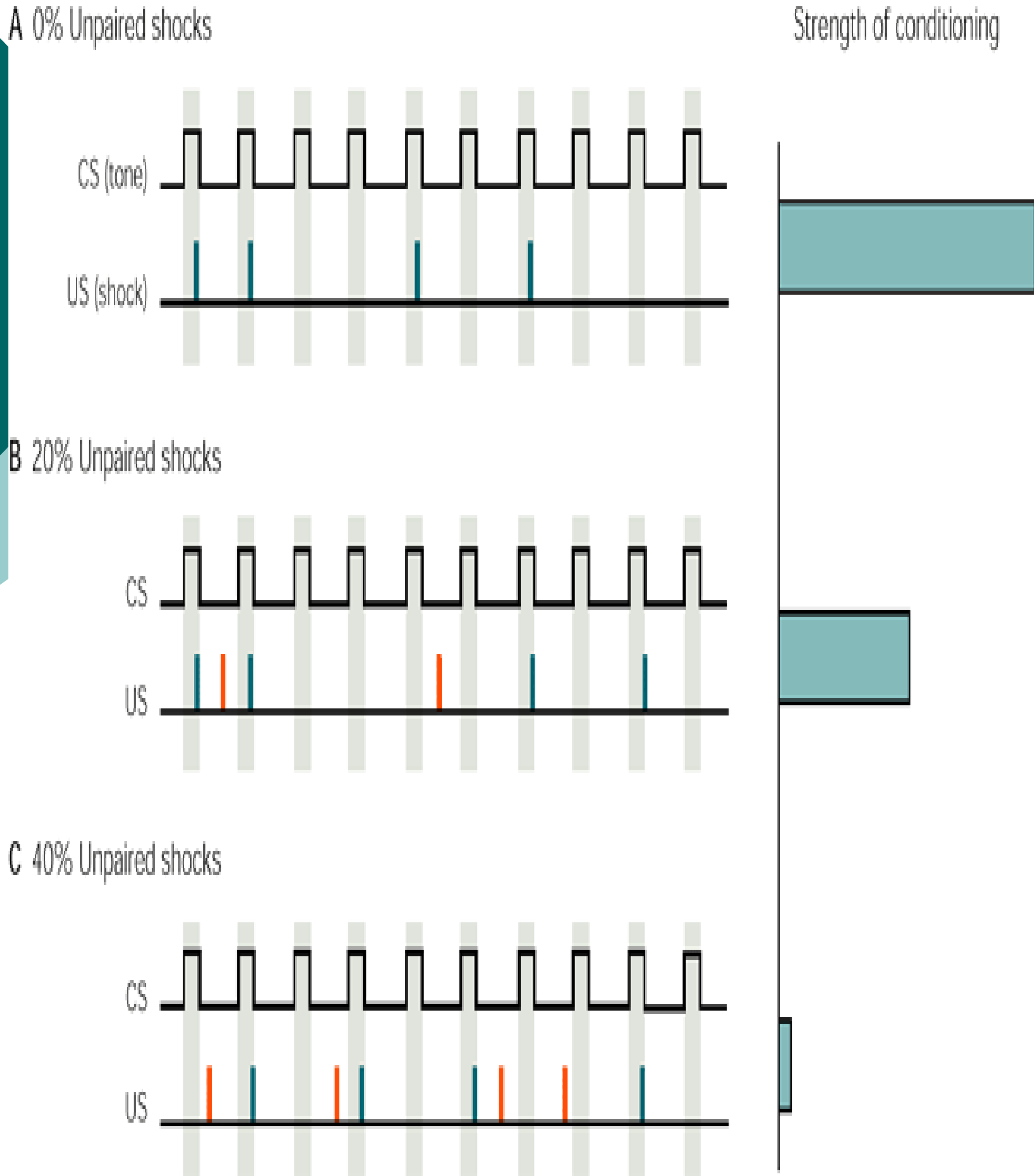
Dishabituation

- a sensitizing stimulus overrides the effects of habituationed
  - For example, after the startle response to a noise has been reduced by habituation, one can restore the intensity of response to the noise by delivering a strong pinch

Classic conditioning - research

- a repeated tone (the CS) paired with an electric shock (the US) in 40% of the trials (**blue vertical lines)**
    - **sometimes the** shock was also presented when the tone was not present (**red vertical lines)**
    - **the percentage of these uncorrelated trials varied for different groups**

- in all three conditions the CS–US pairing was always 40%, but the percentage of US presentation with the absence of the CS pairing varied from 0% to 20% or 40%



- Figure 1
  - **A. US-CS (0%)**
  - **B. US-CS (20%)**
  - **C. US-CS (40%)**

- the degree of conditioning - how effective the tone was in suppressing lever pressing to obtain food

- when the shock occurred without the tone as often as with the tone (40%), little or no conditioning was evident

- some conditioning occurred when the shock occurred 20% of the time without the tone, and maximal conditioning occurred when the shock never occurred without the tone. (Adapted from Rescorla 1968.)

- The capacity for a conditioned stimulus (CS) to produce a classically conditioned response
  - a function of the degree to which the CS and US are correlated

*not a function of the number of times the CS is paired with an unconditioned stimulus (US)

Associative forms of learning – main distinction

CC

- the subject learns that a certain stimulus predicts a subsequent event

OC

- the animal learns to predict the consequences of a behavior

Operant conditioning

- Edgar Thorndike, B. F. Skinner et all.
- operant conditioning involves behaviors that occur either spontaneously or without an identifiable stimulus
  - when a behavior produces favorable changes in the environment (when it is rewarded or leads to the removal of noxious stimuli) the animal tends to repeat the behavior

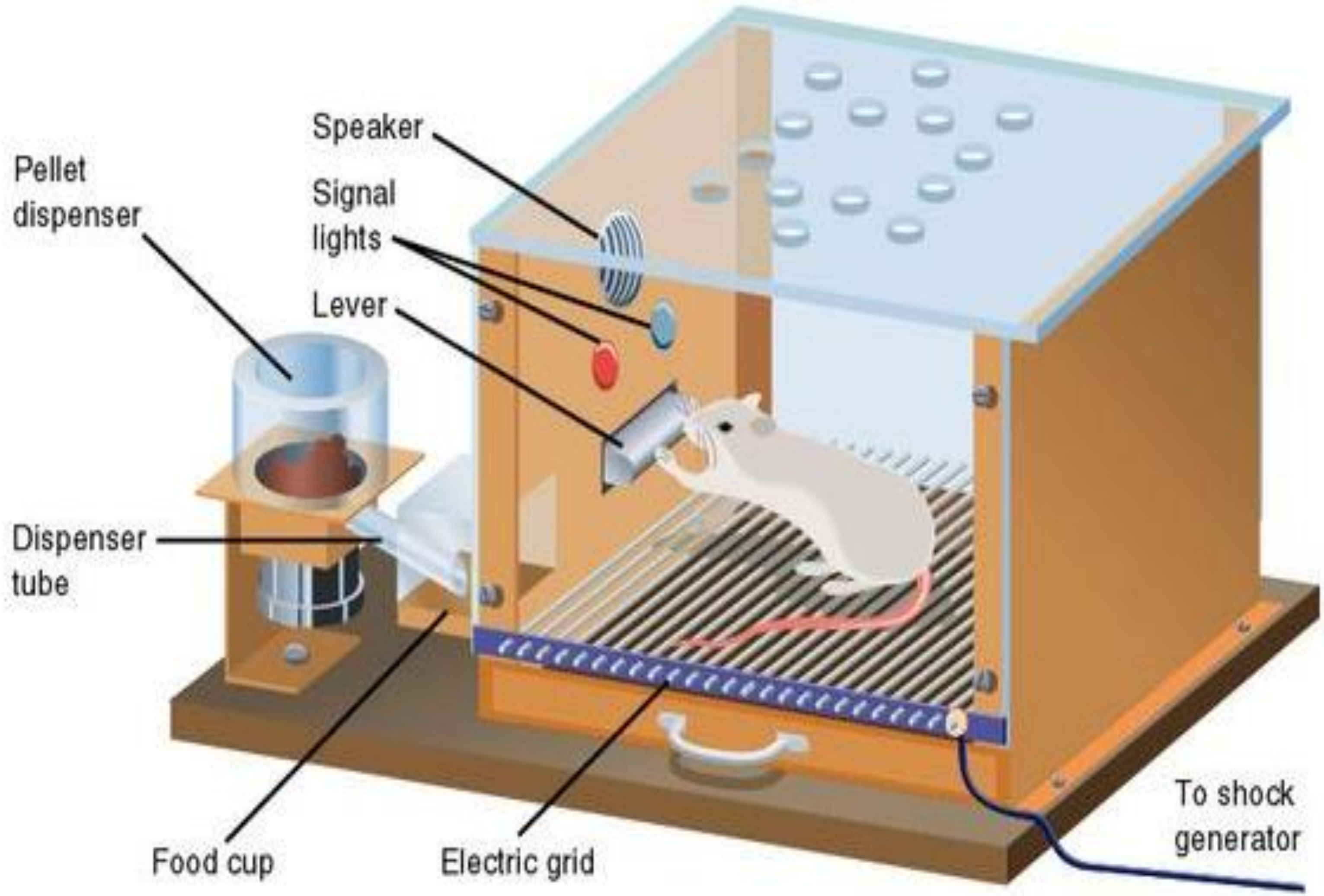


Figure 2. Skinner’s experimental setting

timing - critical for both forms of associative learning

- OC - the reinforcer must closely follow the operant behavior (if it’s delayed too long, only weak conditioning occurs)
  - the optimal interval between behavior and reinforcement depends on the specific task and the species

- CC - poor if the interval between the conditioned and unconditioned stimuli is too long or if the unconditioned stimulus precedes the conditioned stimulus

ASSOCIATIVE LEARNING – CONSTRAINED BY THE BIOLOGY OF ORGANISM

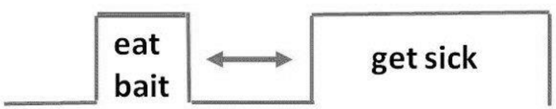
- Traditional view
  - associative learning could be induced simply by pairing any two arbitrarily chosen stimuli or any response and reinforcer

- Research
  - associative learning is constrained by important biological factors

    *animals learn to associate stimuli that are relevant to their survival

Bait shyness

- animals learn to avoid certain foods if a distinctive taste stimulus is followed by a negative reinforcement (eg. nausea)
    - it develops even when the unconditioned response (poison-induced nausea) occurs after a long delay (up to hours) after the CS



REMEMBER

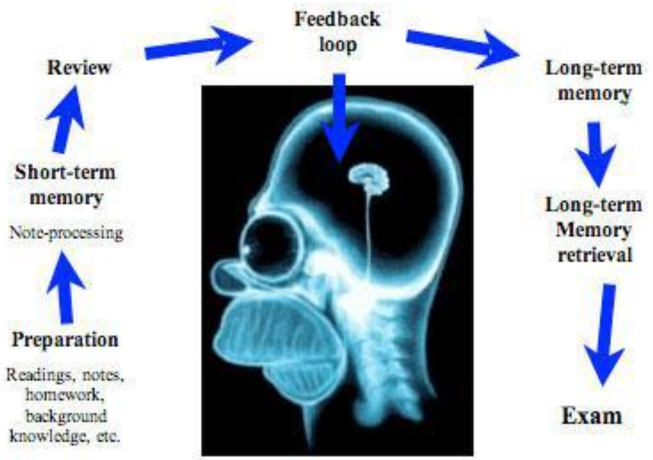
FORGET

food–aversion – only when taste stimuli are associated with subsequent illness, such as nausea and malaise

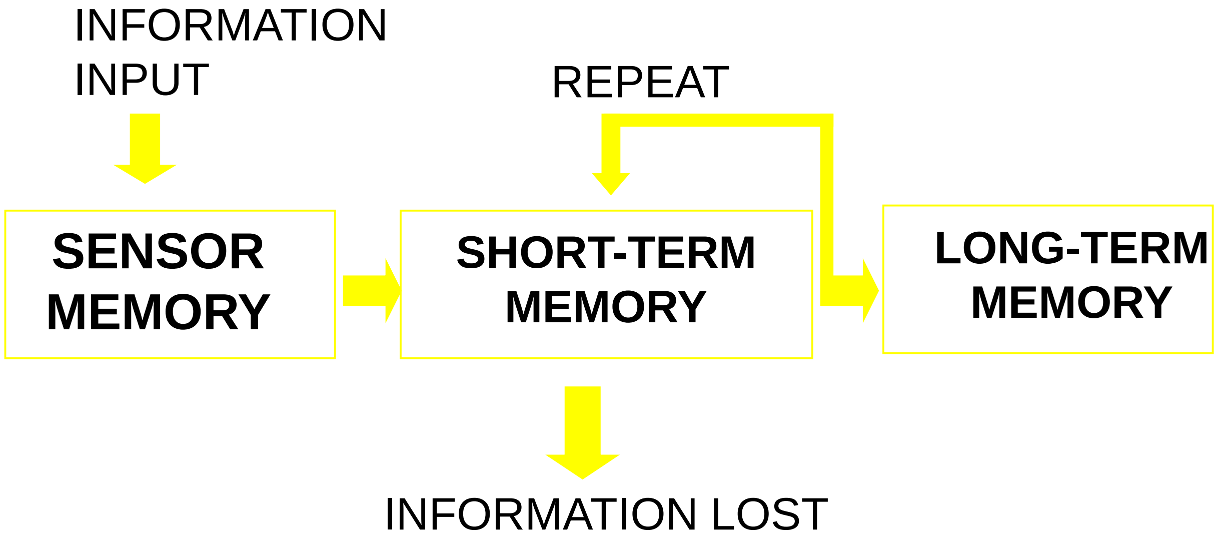
- RARE if followed by a nociceptive, or painful, stimulus that does not produce nausea
- not developed an aversion to a distinctive visual or auditory stimulus that has been paired with nausea

- Evolution
  - different species associate certain stimuli, or a certain stimulus and a behavior, more readily than others

NON ASSOCIATIVE LEARNING MEMORY



Atkinson and Shiffrin model (1968.)



- SPERLING, 1960
  - ICONIC MEMORY (very short term – less than 1 second)
  - ECHO MEMORY – longer, 4 seconds

Iconic memory

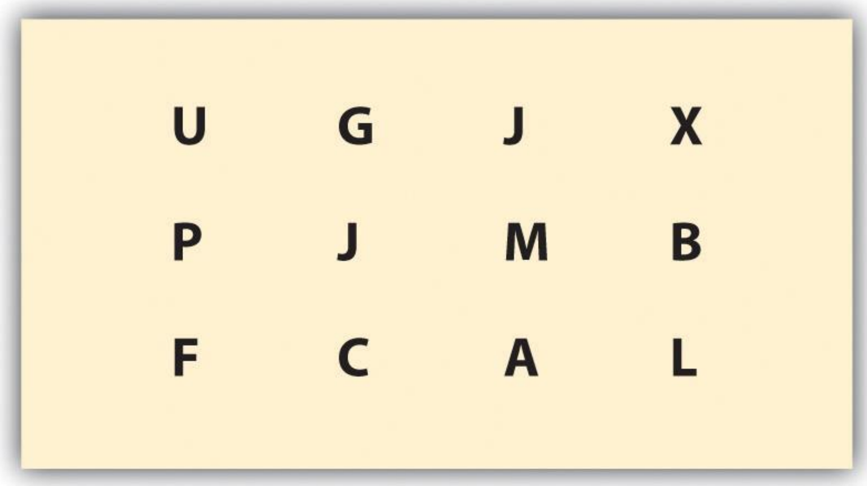


Figure 3. Sperling test

Iconic memory

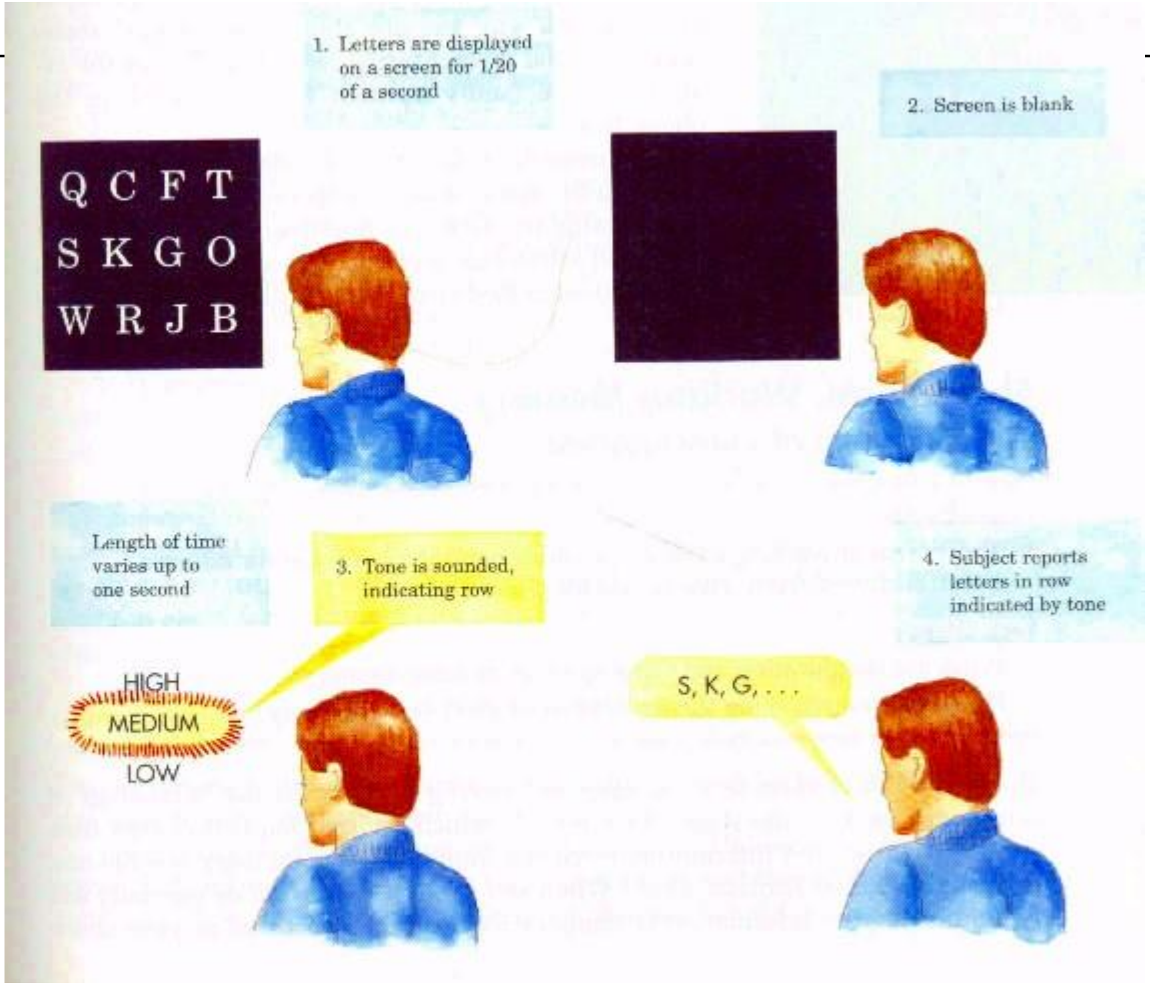


Figure 4. Sperling test

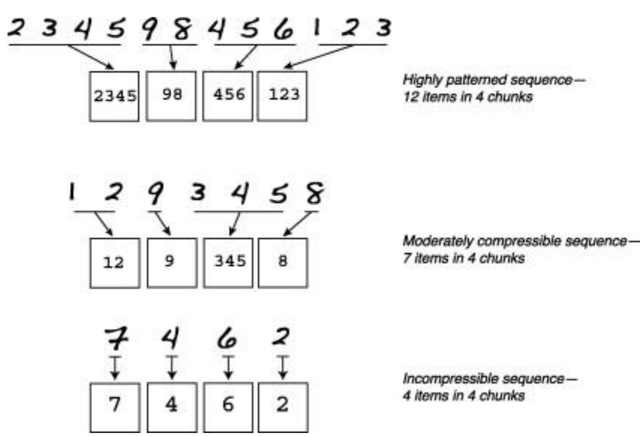
Short term memory

- Limited capacity
- 2 options: lost or connected to long term memory

- MILLER, 1956
  - 5-9 memory capacity

Chunking

- Increases the capacity of short term memory
- The longer the information stays in STM, there is a greater chance for it to be moved to LTM (increases with elaboration, decreases with interference)



You have 15 seconds to memorize these letters:

BGI TAE LTE GDO HTE

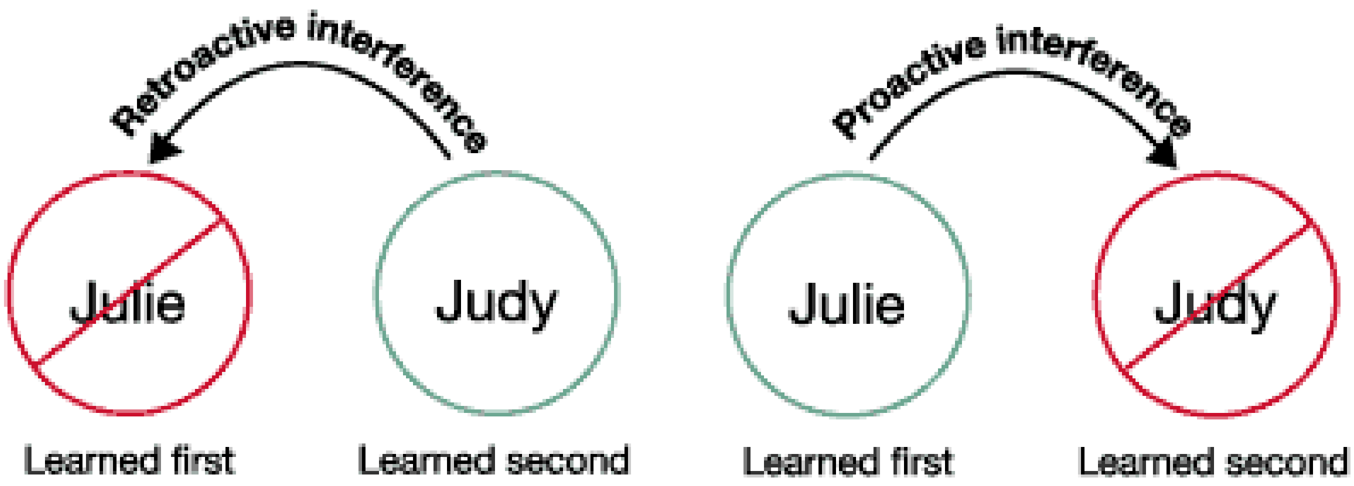
Would it be easier to remember this?

BIG EAT LET DOG THE

And easier still to remember this?

LET THE BIG DOG EAT

- Why do we loose information from LTM?


Retroactive interference
Proactive interference
Julie
Judy
Julie
Judy
Learned first
Learned second
Learned first
Learned second

<u>implicit memory (or nondeclarative memory)</u>

- a memory that is recalled unconsciously – how to perform something
- involved in training reflexive motor or perceptual skills
- rigid and tightly connected to the original stimulus conditions under which the learning occurred

<u>explicit memory (or declarative memory)</u>

- factual knowledge of people, places, and things, and what these facts mean
- conscious
- flexible
- involves the association of multiple bits and pieces of information

Endel Tulving

- explicit memory : ***episodic*** or ***semantic***

<table>
<tr><th>explicit memory</th><th>implicit memory</th></tr>
<tr><td>Episodic
• a memory for events and personal experience</td><td rowspan="2">•recalled unconsciously
•Includes training reflexive motor or perceptual skills</td></tr>
<tr><td>Semantic
• a memory for facts
• used to store and recall objective knowledge, the kind of knowledge we learn in school and from books
•includes the naming of objects, the definitions of spoken words, and verbal fluency</td></tr>
</table>

- Explicit memory storage?

1. SEMANTIC KNOWLEDGE – no storage

through experience a visual image becomes associated with other forms of knowledge

- **The more associations** to the image – **the better we *encode* that image** – the **better we can recall** the features of an image at a future time

- damage to the posterior parietal cortex
  - ***associative visual agnosia***
    - patients cannot *name* objects but they can *identify* objects by selecting the correct drawing and can faithfully reproduce detailed drawings of the object

- damage to the occipital lobes and surrounding region
  - ***apperceptive visual agnosia***
    - patients are unable to draw objects but they can name them if appropriate perceptual cues are available

- lesions in the inferotemporal cortex
  - ***prosopagnosia***
    - the inability to recognize familiar faces or learn new faces
    - all other aspects of visual recognition intact

PET studies
  - object recognition activates the left occipitotemporal cortex
    - not the areas in the right hemisphere associated with face recognition
    - not all of our visual knowledge is represented in the same locus in the occipitotemporal cortex

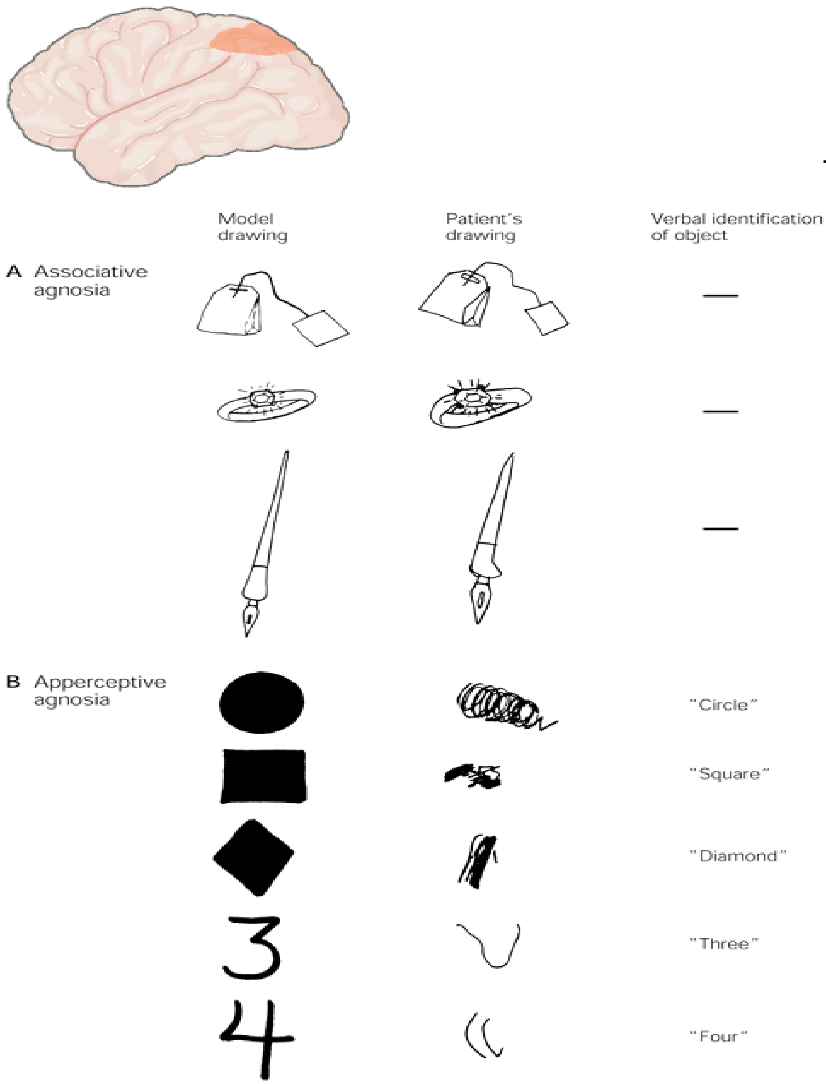


Figure 6.

•damage to the posterior parietal cortex
-associative visual agnosia

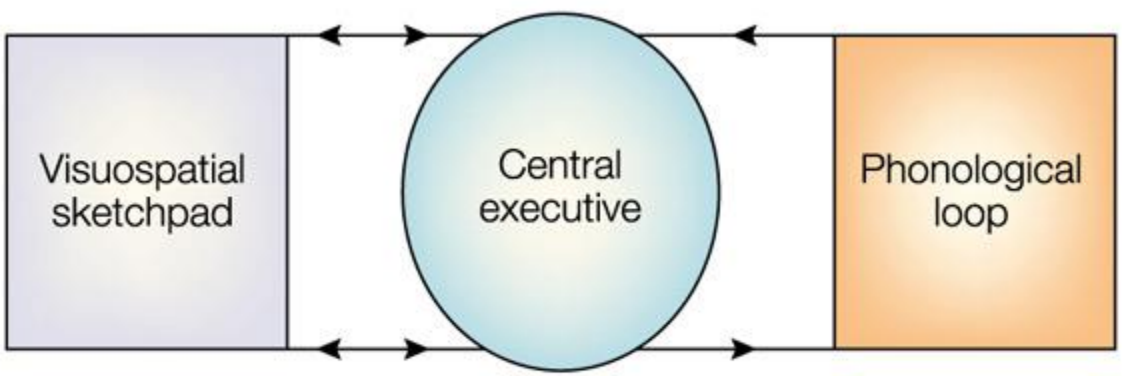
•damage to the occipital lobes and surrounding region
-apperceptive visual agnosia

2. EPISODIC KNOWLEDGE – prefrontal cortex

- patients with loss of episodic memory have the ability to recall vast stores of **factual (semantic**) knowledge
  - long-term storage of <u>episodic</u> knowledge – the association areas of the **frontal lobe** (work with other areas of the neocortex to allow recollection of when and where a past event occurred)
- ***source amnesia***
  - how information was acquired
- the ability to associate a piece of information with the time and place it was acquired – **the core of how accurately we remember**

- a temporary storing of information used to guide future actions - the active maintenance of information relevant to an ongoing behavior – prefrontal association area

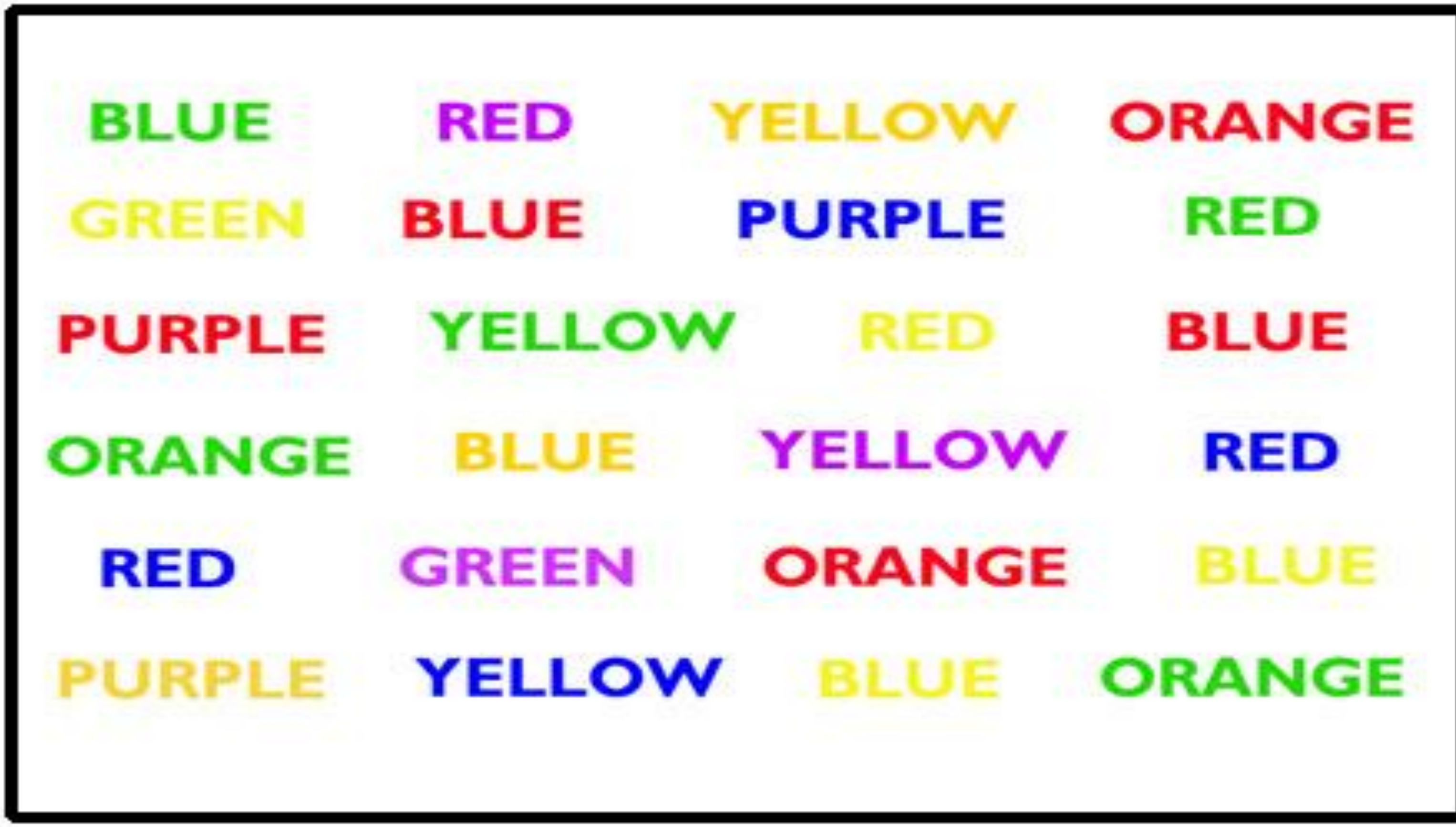
<u>Three distinct components</u>



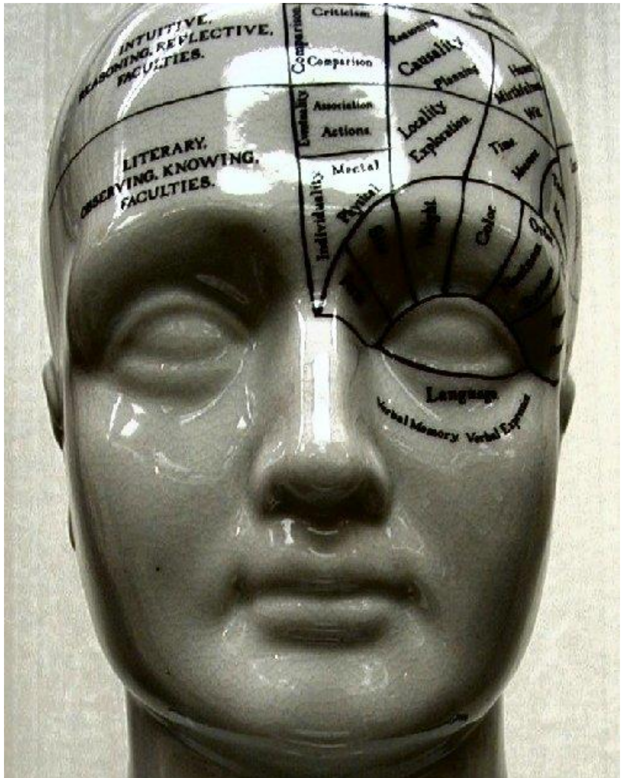
CENTRAL EXECUTIVE

- Function of the central executive – to recognize the words and to recognize the colour
- Due to previous experience – reading is dominant to recognition of colour, and consequently faster

Figure 8. Stroop test


BLUE RED YELLOW ORANGE
GREEN BLUE PURPLE RED
PURPLE YELLOW RED BLUE
ORANGE BLUE YELLOW RED
RED GREEN ORANGE BLUE
PURPLE YELLOW BLUE ORANGE

- “Our attention is not drawn to by the damage itself, but the fact that, through damage or disease, a function can be revealed’’
    - (Sir Henry Head - neurologist, 20th century)



WILDER PENFIELD – mapping the functions of the cortex

- electrical stimulation to map the motor, sensory, and language functions in the cerebral cortex

- electrical stimulation of the temporal lobes produced an ***experiential response*** —a coherent recollection of an earlier experience (8%)

- patients
  - epileptic seizure center in the temporal lobe – the sites most effective in eliciting experiential responses were near those regions – the responses might have been the result of localized seizure activity

- TEMPORAL LOBE – MEMORY

BRENDA MILNER AND WILLIAM SCOVILLE - H.M.

Henry Gustav Molaison

27-year-old man – suffered for over 10 years from untreatable bilateral temporal lobe seizures

- the hippocampal formation, the amygdala, and parts of the multimodal association area of the temporal cortex removed bilaterally

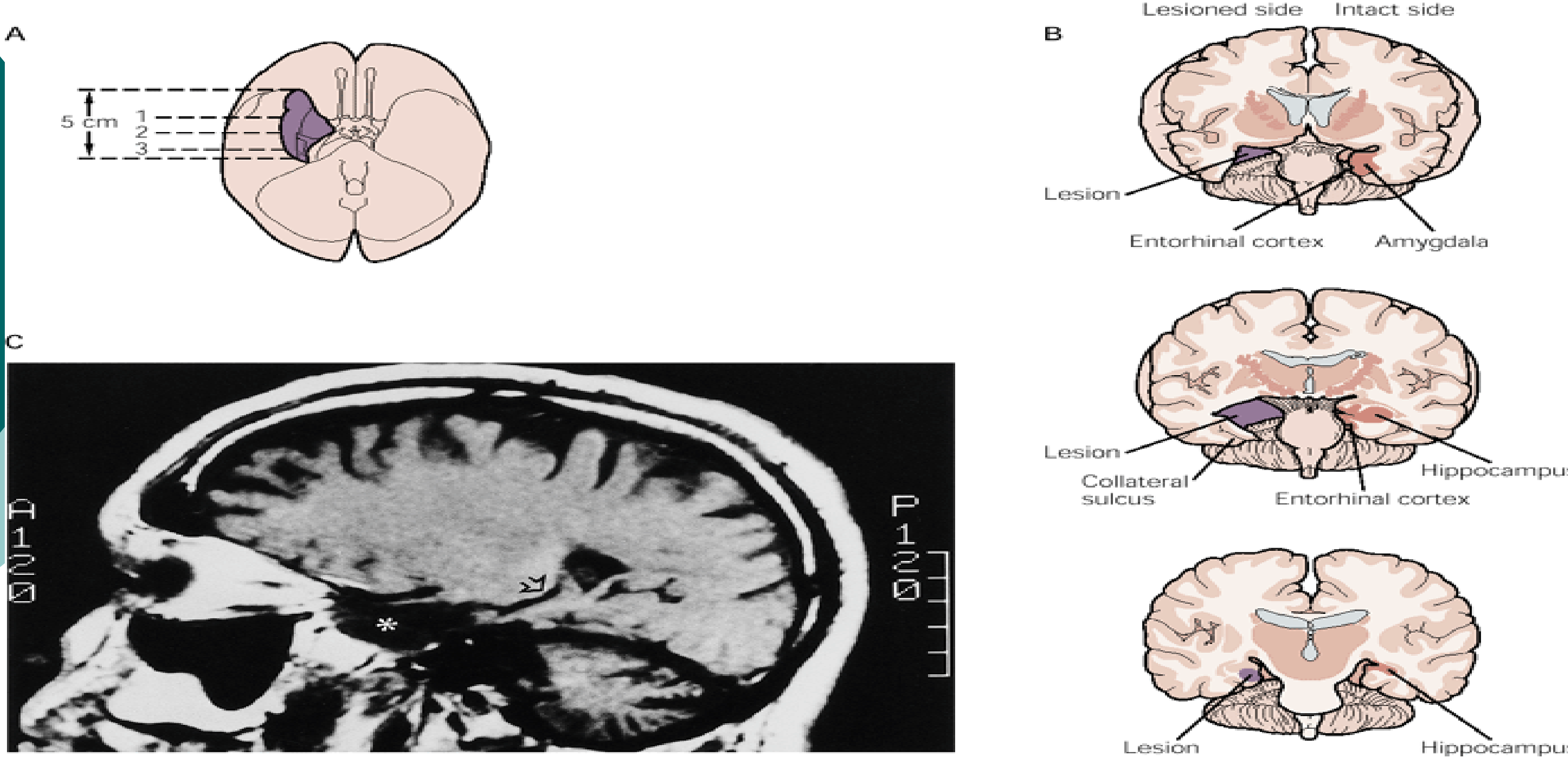


Figure 9. The medial temporal lobe and memory storage

A. The longitudinal extent of the temporal lobe lesion in the patient known as H.M. in a ventral view of the brain.

B. Cross sections showing the estimated extent of surgical removal of areas of the brain in the patient

C. Magnetic resonance image (MRI) scan of a parasagittal section from the left side of H.M.'s brain. (From Corkin et al. 1997.)

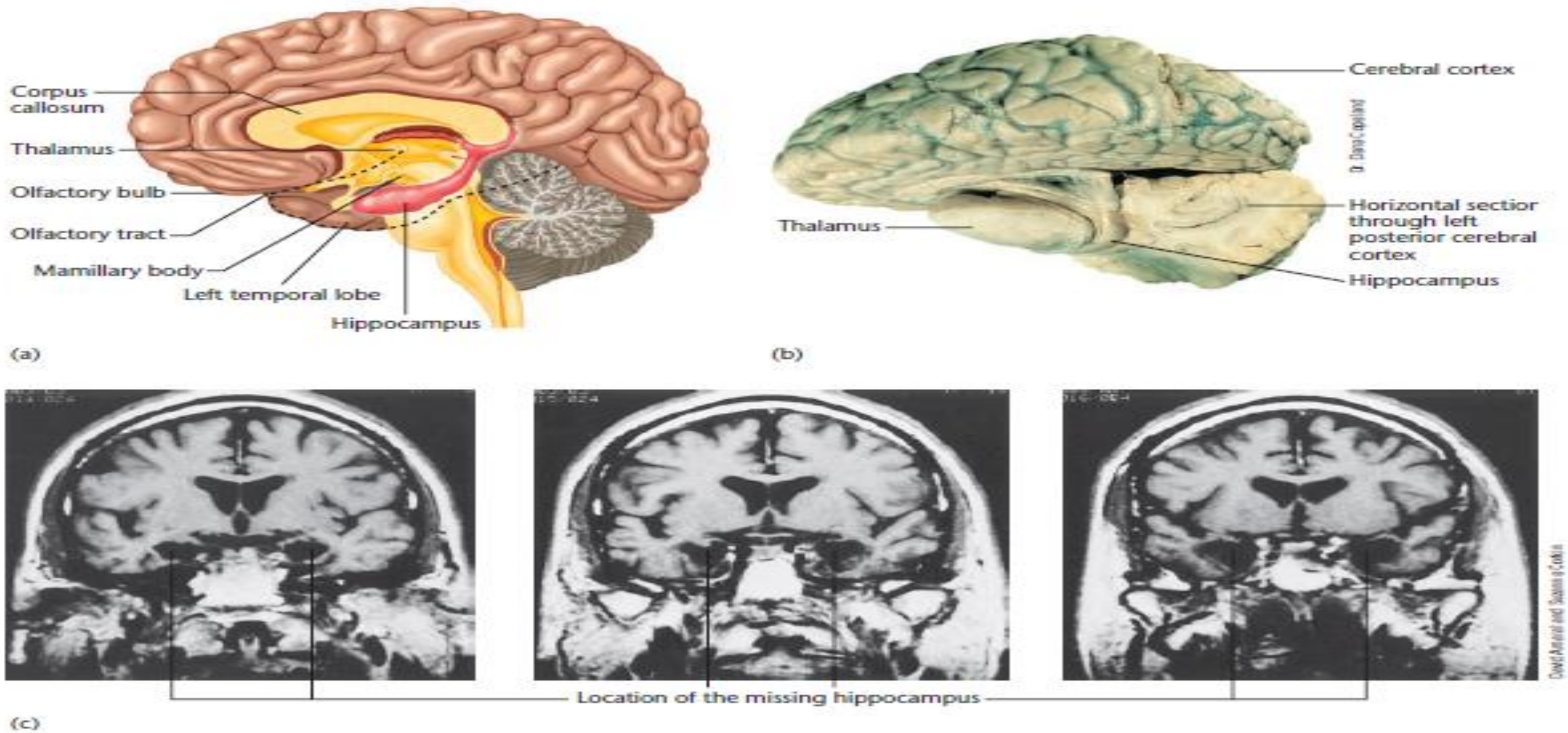


Figure 10. Hippocampus lesion – H.M.

(a) Location of the hippocampus in the human brain. The hippocampus is in the interior of the temporal lobe. The dashed line marks the location of the temporal lobe, which is not visible in the midline.

(b) Photo of a human brain from above. The right hemisphere is intact. The top part of the left hemisphere has been cut away to show how the hippocampus loops over (dorsal to) the thalamus, posterior to it, and then ventral to it.

(c) MRI scan of the brain of H. M., showing absence of the hippocampus. Note the large size of this lesion. Anterior to posterior.

H.M.

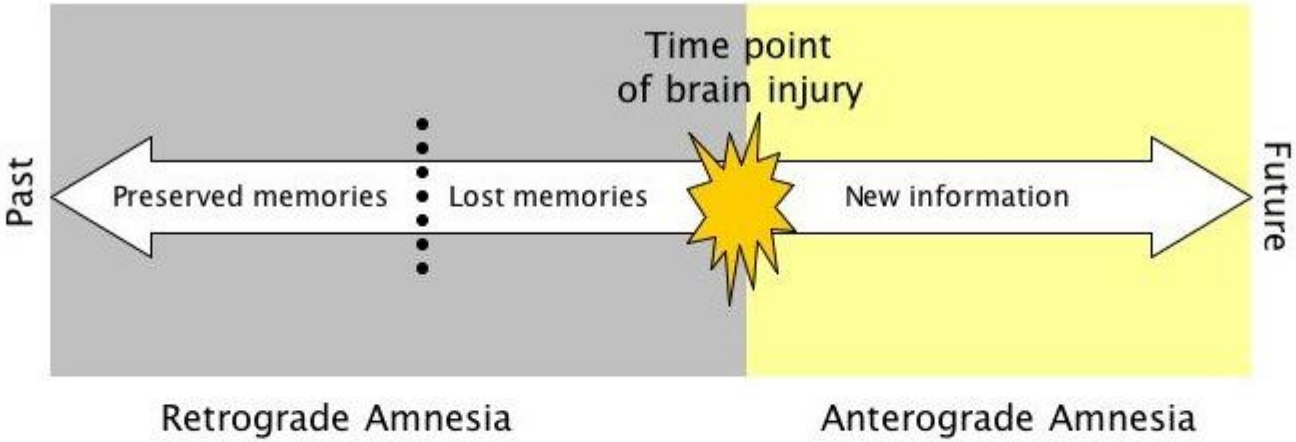
- The surgical lesion of H.M.'s temporal lobe – a number of regions
  - the temporal pole, the ventral and medial temporal cortex, the amygdala, and the hippocampal formation (which includes the hippocampus proper, the subiculum, and the dentate gyrus) and the surrounding entorhinal, perirhinal, and parahippocampal cortices

CONSEQUENCES:

- <u>seizures were much better controlled after surgery</u>
- devastating memory deficit

AMNESIA

RETROGRADE VS. ANTEROGRADE



H.M.

- a perfectly good long term memory for events that had occurred before the operation
- he remembered his name and the job he held, and he vividly remembered childhood events
- some evidence of a retrograde amnesia for information acquired in the years just before surgery
- a perfectly good command of language
- normally varied vocabulary

H.M.

- **inability to transfer new short-term memory into long-term memory**
  - he was unable to retain for more than a minute information about people, places, or objects
  - when asked to remember a number such as 8414317, H.M. could repeat it immediately for many minutes, because of his good short-term memory
    - when distracted, even briefly, he forgot the number
- H.M. could not recognize people he met after surgery
- profound difficulty with spatial orientation
- patients with extensive bilateral lesions of the limbic association areas of the medial temporal lobe - similar memory deficits

H.M.

- social skills and sense of humour – intacted
- rembered the old adress, not the new one
- didn’t remeber meals eaten half an hour before
- IQ=112
- abstract reasoning and perceptive motor abilities intacted
- Explicit memory −
- Implicit memory +

H.M.

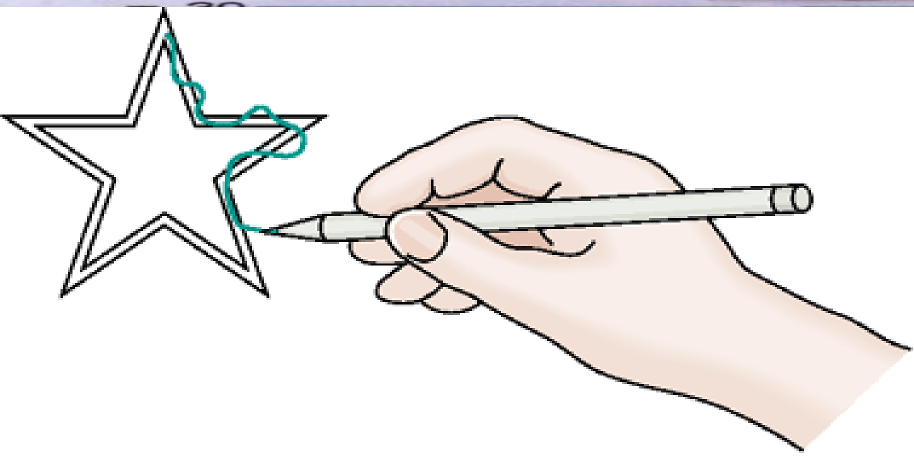
Intact Short-term Memory

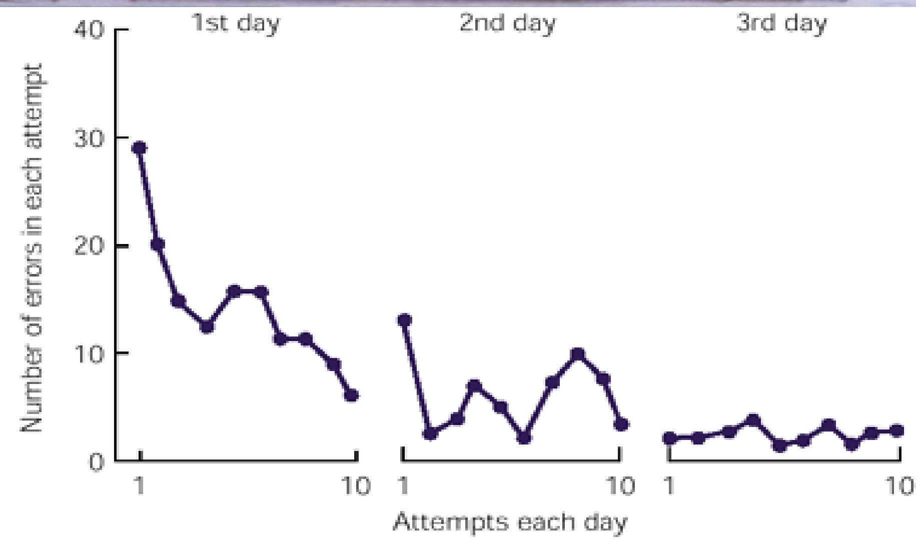
- Brenda Milner (1959) asked him to remember the number 584. After a 15-minute delay without distractions, he recalled it correctly, explaining:

"It's easy. You just remember 8. You see, 5, 8, and 4 add to 17. You remember 8, subtract it from 17, and it leaves 9. Divide 9 in half and you get 5 and 4, and there you are, 584. Easy."

- A moment later, after his attention had shifted to another subject, he had forgotten both the number and the complicated line of thought he had associated with it.
- Most patients with severe amnesia also show normal short-term or working memory (Shrager, Levy, Hopkins, & Squire, 2008).

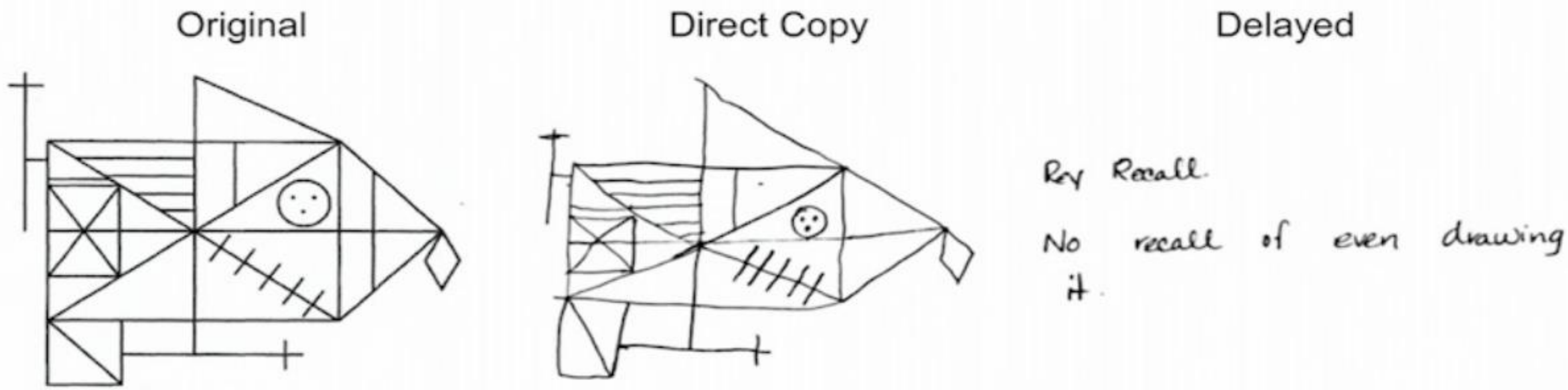
- able to learn **certain types of tasks and retain** this learning for as long as normal subjects
- the spared component of memory - H.M. could learn **new motor skills** at a normal rate

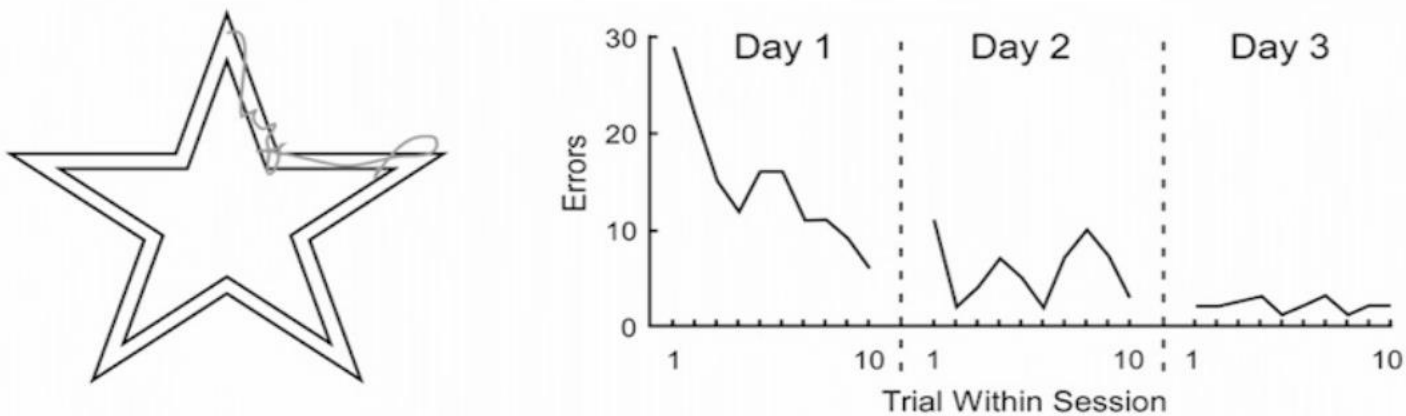




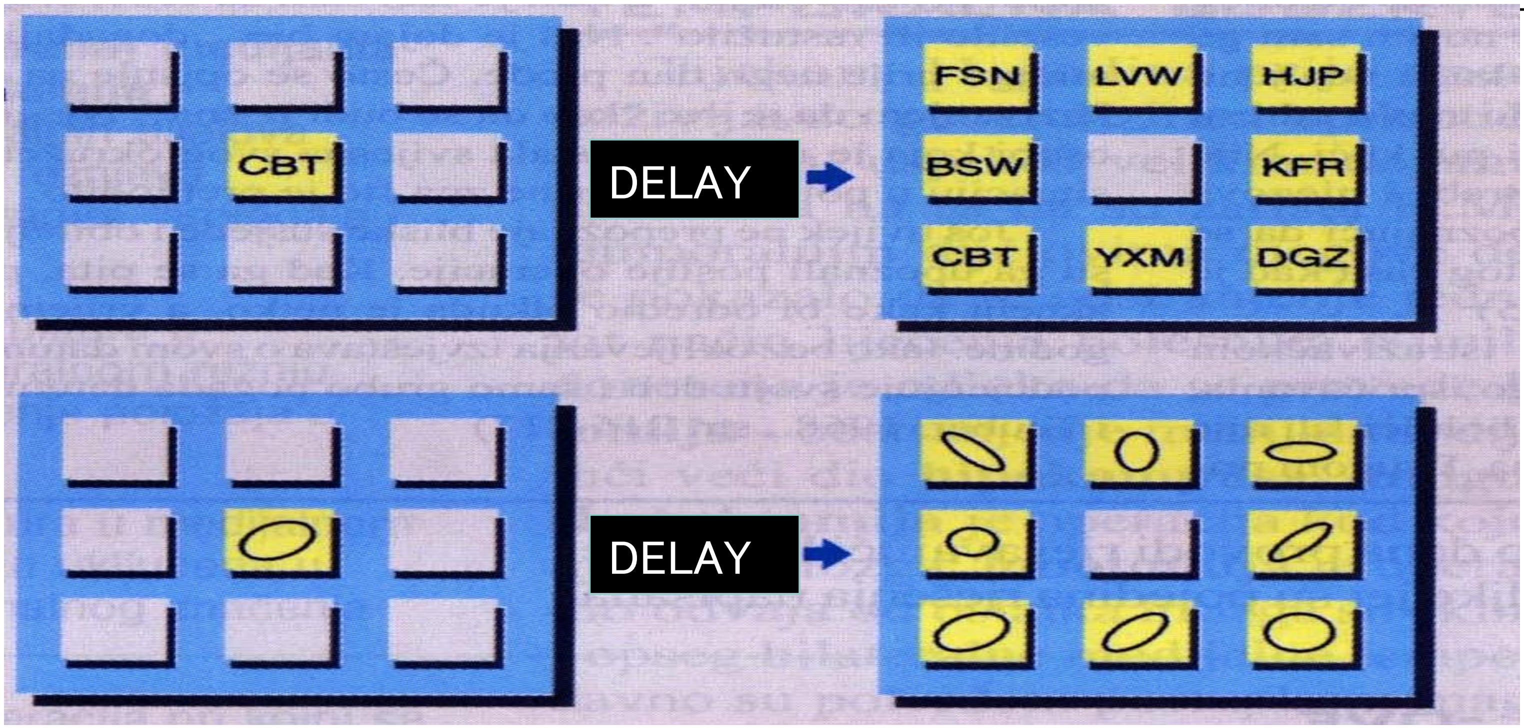
- **Figure 11.**
- **H.M.** showed improvement in any task involving learning skilled movements. He was taught to trace between two outlines of a star while viewing his hand in a mirror, improving considerably with each fresh test, although he had no recollection that he had ever done the task before. The graph plots the number of times, in each trial, that he strayed outside the outlines as he drew the star. (From Blakemore 1977.)

Patient HM: Impaired memory and intact memory





H.M.



- Figure 12. Sidman, Stoddard i Mohr (1968.) verbal and non verbal *match*–to–*sample test* , applied with H.M.
- Correct answer for the verbal form when the retention time was less than 40 sec
- Correct answer for the non verbal form when the retention time was less than 5 sec

Larry Squire et all.

- **the memory capacities of H.M. and other patients with bilateral medial temporal lobe lesions are not limited to motor skills**

- capable of various forms of **simple** reflexive learning
  - habituation, sensitization, classical conditioning, and operant conditioning
    - they are able to improve their performance on certain perceptual tasks

- they do well with **priming**
  - the recall of words or objects is improved by prior exposure to the words or object
    - *no conscious memory of having seen the word before*

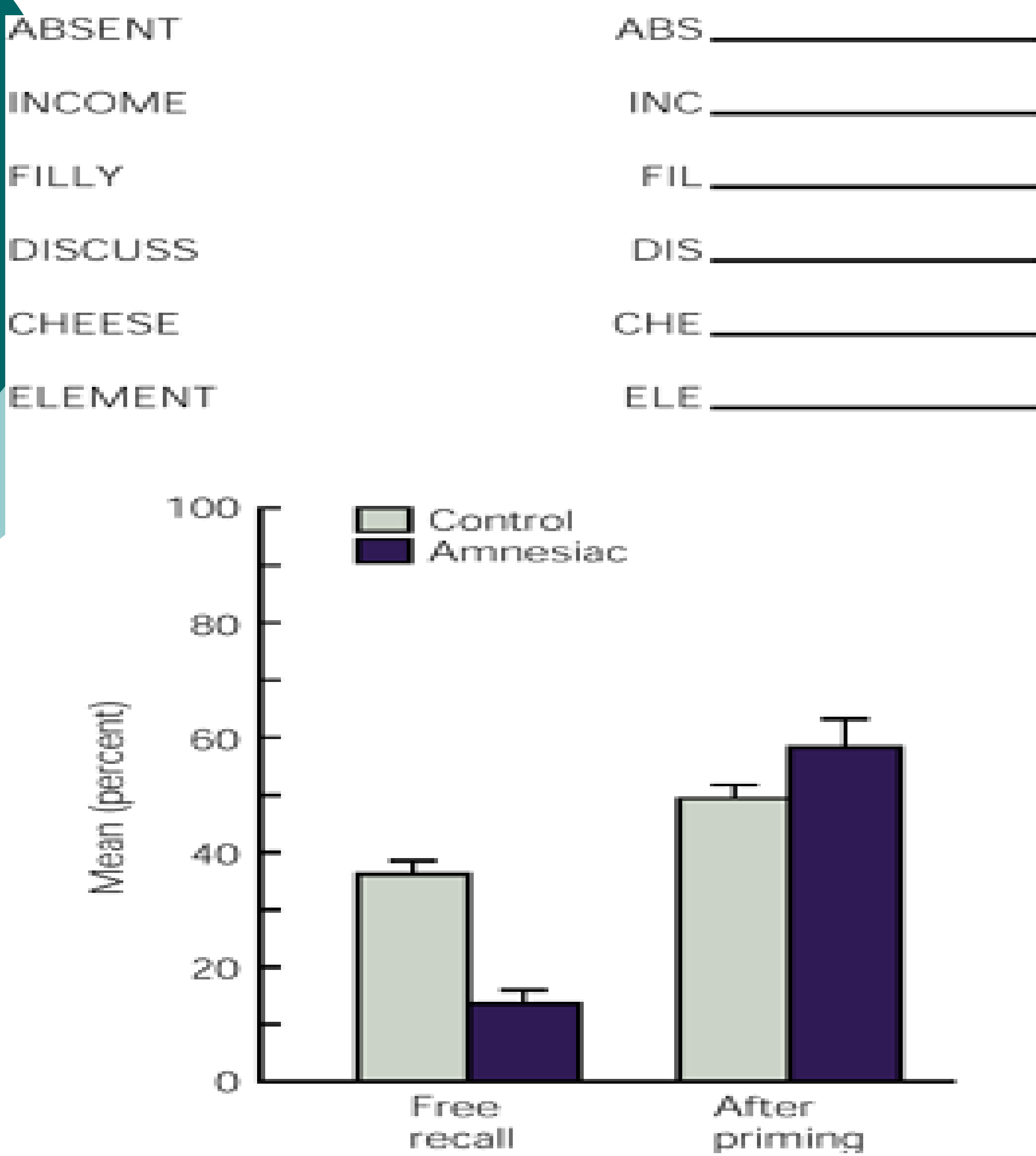
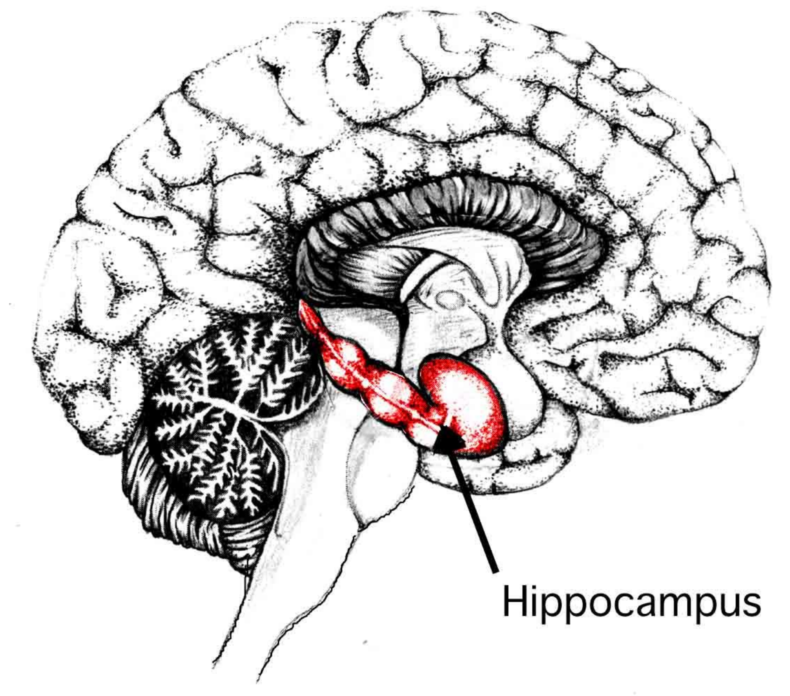


Figure 13.

In a study of recall of words, amnesiacs and normal control subjects were tested under two conditions. (From Squire 1987.)

- HIPPOCAMPUS AND MEMORY ?



HIPPOCAMPUS AND MEMORY

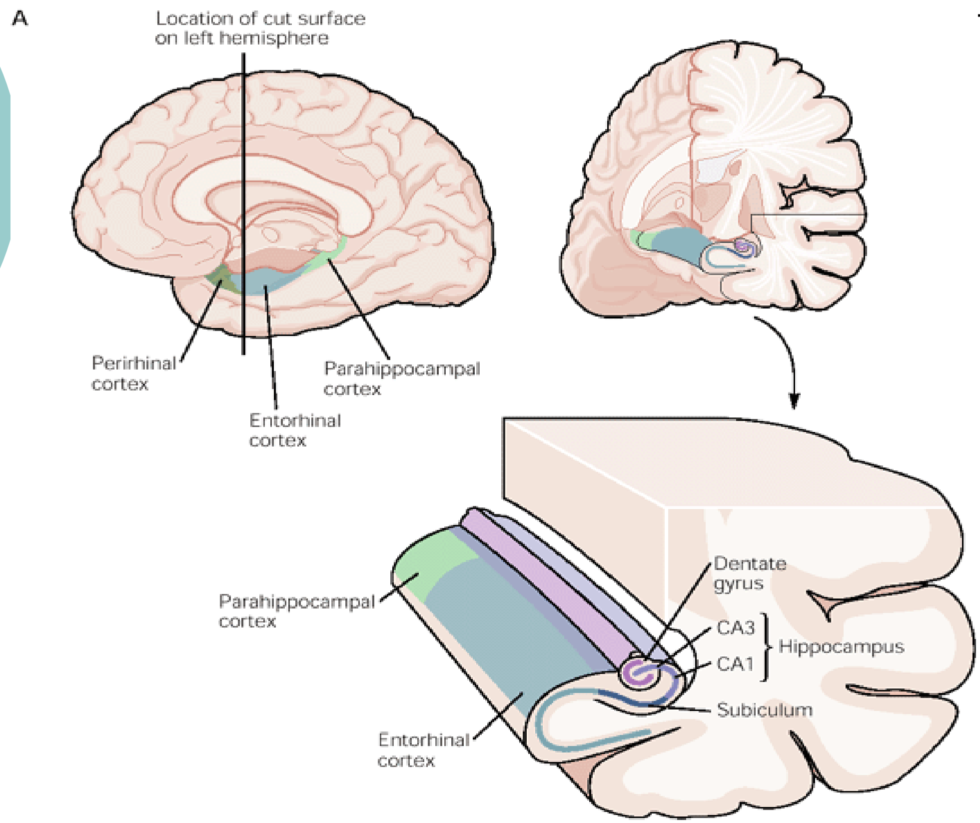


Figure 14.

- **The anatomical organization of the hippocampal formation.**

  The key components of the medial temporal lobe important for memory storage can be seen in the medial (**left**) and ventral (**right**) surface of the cerebral hemisphere.

Mortimer Mishkin and Larry Squire – animal studies

- produced lesions in monkeys identical to those reported for H.M.
  - defects in explicit memory for places and objects similar to those observed in H.M.

- *selective damage* to the hippocampus or the polymodal association areas in the temporal cortex with which the hippocampus connects—the perirhinal and parahippocampal cortices—produces clear impairment of explicit memory

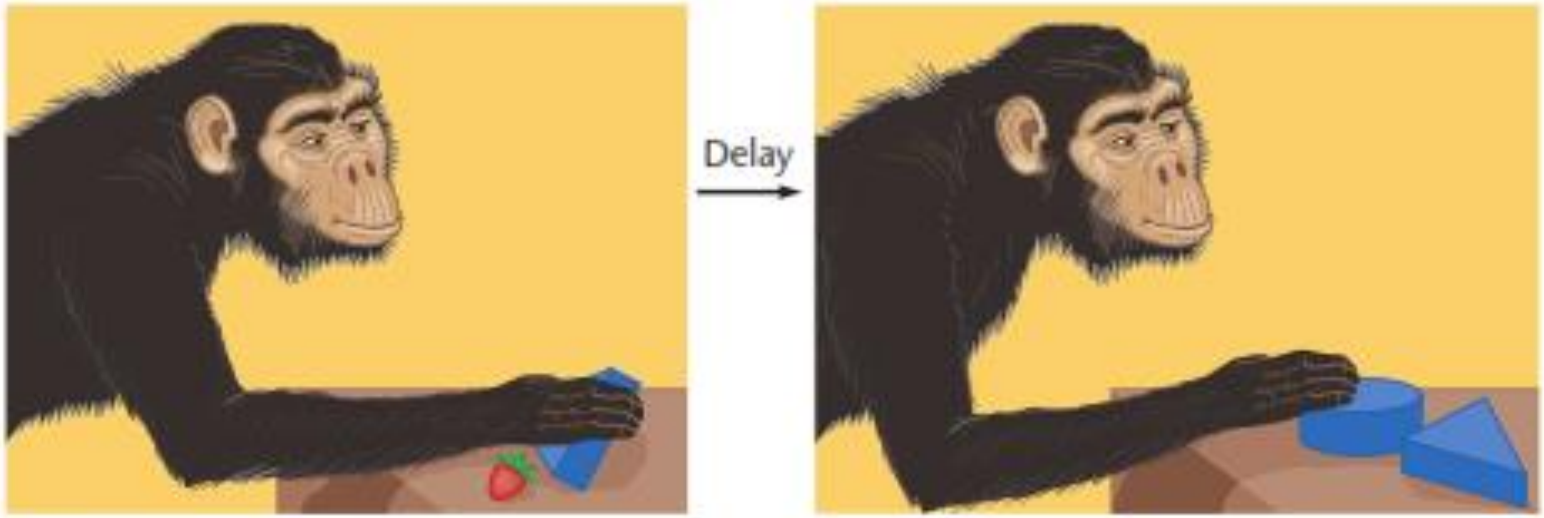


Figure 13.7 **Procedure for delayed nonmatching-to-sample task**

Figure 15. Memory tests on monkeys

- RESEARCH CONCLUSIONS?

Zola-Morgan S, Squire LR, Clower RP, Rempel NL (1993) Damage to the perirhinal cortex exacerbates memory impairment following lesions to the hippocampal formation. J Neurosci 13:251–265.

Mishkin, M.; Squire, L.; Zola Morgan, S.; Amaral, D.;

- **H+A+ lesion**
  - medial temporal lobe lesion – includes the hippocampal formation (i.e., the hippocampus proper, the dentate gyrus, the subicular complex), the amygdala, as well as adjacent cortical regions that are necessarily damaged when the hippocampus and amygdala are removed using a direct surgical approach (the surrounding entorhinal, perirhinal, and parahippocampal cortices) – severe memory impairment

- **H+ lesion**
  - bilateral lesions that damaged the hippocampal formation and the parahippocampal cortex – less severe impairment

  (cornu ammonis, dentate gyrus, subiculum, and parahippocampal cortices)

Zola-Morgan S, Squire LR, Clower RP, Rempel NL (1993) Damage to the perirhinal cortex exacerbates memory impairment following lesions to the hippocampal formation. J Neurosci 13:251–265.

Mishkin, M.; Squire, L.; Zola Morgan, S.; Amaral, D.;

- **A+ lesion**
  - Amygdala – no memory impairment
  - Stores just components of memory concerned with emotion, **not factual information**

- **H++ lesion**
  - **H+ lesion with complete** perirhinal cortex
  - **Memory impairment more severe than with** H+ or H+A+ lesion

Zola-Morgan S, Squire LR, Clower RP, Rempel NL (1993) Damage to the perirhinal cortex exacerbates memory impairment following lesions to the hippocampal formation. J Neurosci 13:251–265.

- the perirhinal cortex and parahippocampal cortex provide the major source of cortical inputs to the entorhinal cortex
- the perirhinal cortex provide the major route through which the hippocampal formation can influence other cortical regions
- entorhinal cortex is the main source of projections to the hippocampus

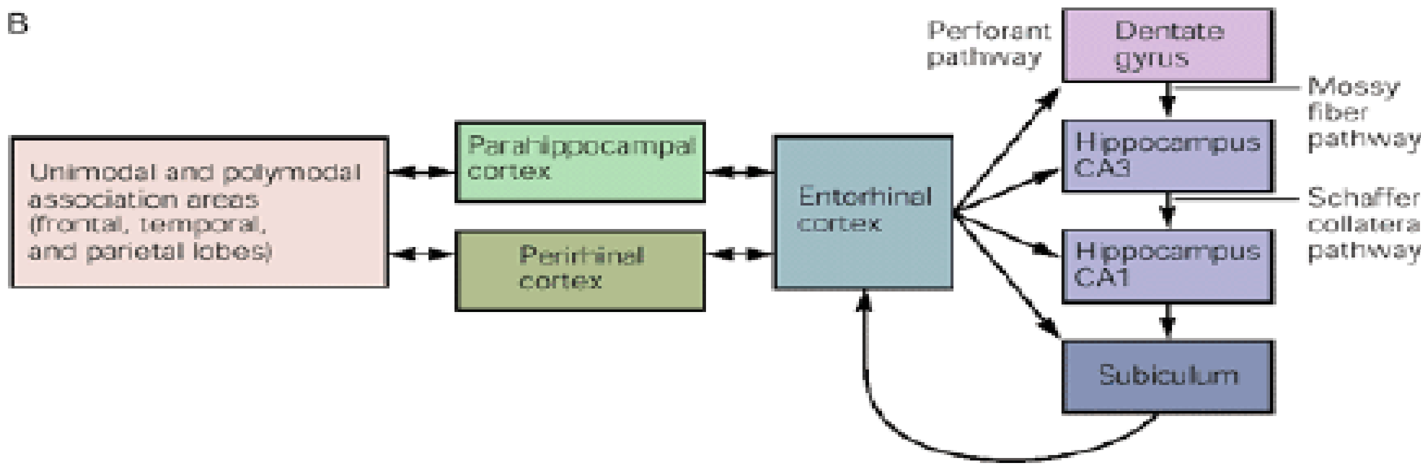
Zola-Morgan S, Squire LR, Clower RP, Rempel NL (1993) Damage to the perirhinal cortex exacerbates memory impairment following lesions to the hippocampal formation. J Neurosci 13:251–265.

Explicit memory

- acquired through processing in one or more of the three **polymodal association cortices** (the prefrontal, limbic, and parieto-occipital-temporal cortices)

- synthesize visual, auditory, and somatic information

- than the information is conveyed to the parahippocampal and perirhinal cortices, the entorhinal cortex, the dentate gyrus, the hippocampus, the subiculum, and back to the entorhinal cortex


B
Unimodal and polymodal association areas (frontal, temporal, and parietal lobes)
Parahippocampal cortex
Perirhinal cortex
Entorhinal cortex
Perforant pathway
Dentate gyrus
Mossy fiber pathway
Hippocampus CA3
Schaffer collateral pathway
Hippocampus CA1
Subiculum

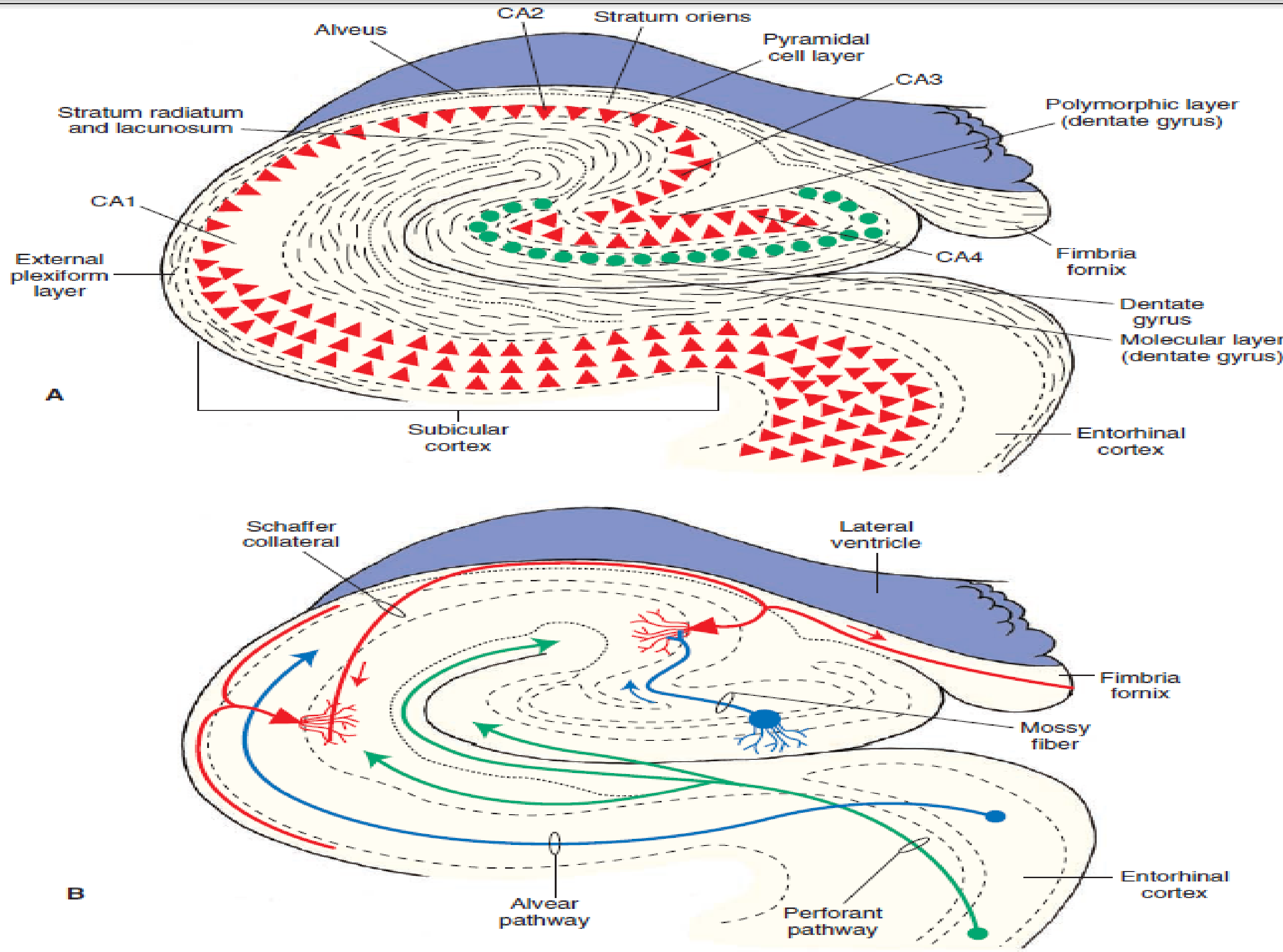


FIGURE 25–2 Hippocampal anatomy and internal circuitry. (A) Diagram illustrates the histological appearance of the cell layers within the hippocampus and loci of the hippocampal fields, dentate gyrus, and subicular cortex. (B) Semischematic diagram illustrates: (1) inputs from the entorhinal region, which include the perforant and alvear pathways; (2) internal circuitry, which includes the connections of the mossy fibers and Schaffer collaterals; and (3) efferent projections of the hippocampal formation through the fimbria-fornix system of fibers. CA1–CA4 denote the four sectors of the hippocampus.

Damage Restricted to Specific Subregions of the Hippocampus Is Sufficient to Impair Explicit Memory Storage

- a lesion restricted to *any* of the major components of the hippocampus can have a significant effect on memory storage

Larry Squire, David Amaral, et all. (1986) – the patient R.B.

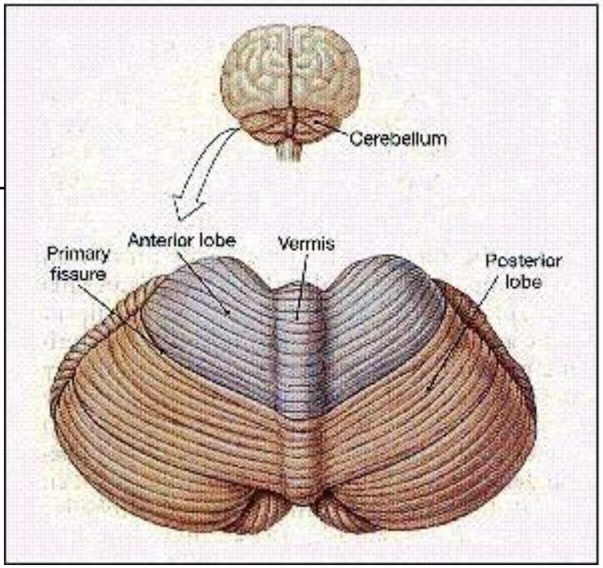
- R.B. – a destruction of the pyramidal cells in the CA1 region of the hippocampus
- a deficit in explicit memory – qualitatively similar to that of H.M., quantitatively milder

Implicit Memory and the Cerebellum

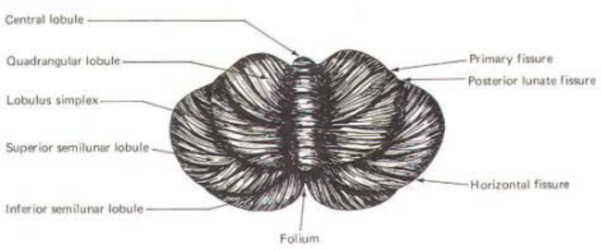
- classical conditioning of the protective eyeblink reflex in **rabbits** (Richard Thompson et all.)
  - a specific form of motor learning
  - conditioned eyeblink – established by pairing an auditory stimulus with a puff of air to the eye
- conditioned response (eyeblink in response to a tone) can be abolished by a lesion at either of two sites

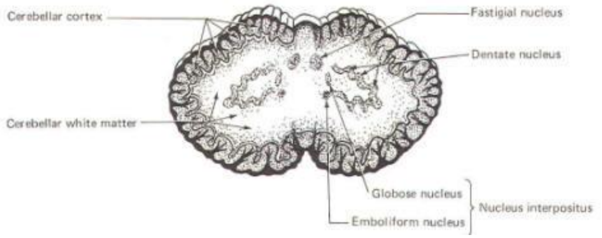
the vermis of the cerebellum

- lesion abolishes the conditioned response
- does not affect the unconditioned response



- a lesion in *the interpositus nucleus* (a deep cerebellar nucleus)
  - abolishes the conditioned eyeblink

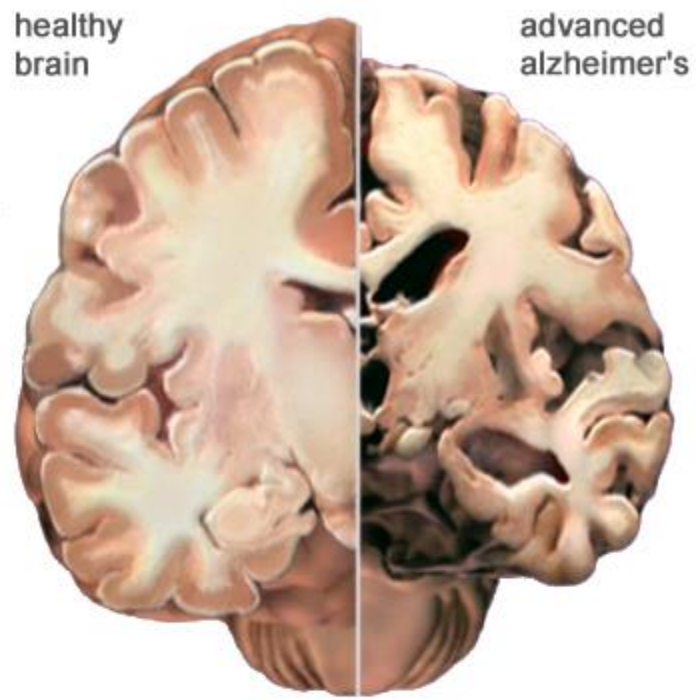





Facts about
dementia
100
there are over 100
types of dementia
alzheimer's
the most common type
accounting to 60%-70% of
all dementia cases
36.5million
number of people living
with dementia in 2011
1 new dementia
case per 4
seconds
65.7 million
115.4 million
2011
2030
2050
prevention
countering risk factors for
vascular disease, such as
diabetes, midlife hypertension,
midlife obesity, smoking, &
physical inactivity.
challenges
(1) NO TREATMENT
currently available to
cure dementia or alter
its progressive course
(2) Research
identifying modifiable
risk factors of dementia
is very limited
$604
billion
(in 2010)
estimated
worldwide
cost of
dementia
3 Main
symptoms:
COGNITIVE,
FUNCTIONAL,
& MOOD
CHANGES
Dementia
in a nutshell

Alzheimer's disease

- neuronal **degeneration** triggered by the accumulation of the amyloid-β peptide (Aβ)
- **Senile plaques** – polymorphous beta-**amyloid** protein deposits found in the brain
- deficiency in the brain neurotransmitter **acetylcholine**
- 1- 3 % prevalence
- most common in the 5th and 6th decade of lifetime
- 5 years – severe dementia

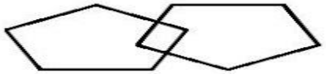


Category
Orientation to time
Orientation to place
Registration
Attention and calculation
Recall
Language
Repetition
Complex commands

Mini-Mental State Examination (MMSE)

Patient's Name: ______________________________ Date: ______________

Instructions: Score one point for each correct response within each question or activity.

Maximum Score	Patient's Score	Questions
5		"What is the year? Season? Date? Day? Month?"
5		"Where are we now? State? County? Town/city? Hospital? Floor?"
3		The examiner names three unrelated objects clearly and slowly, then the instructor asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible.
5		"I would like you to count backward from 100 by sevens." (93, 86, 79, 72, 65, …) Alternative: "Spell WORLD backwards." (D-L-R-O-W)
3		"Earlier I told you the names of three things. Can you tell me what those were?"
2		Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them.
1		"Repeat the phrase: 'No ifs, ands, or buts.'"
3		"Take the paper in your right hand, fold it in half, and put it on the floor." (The examiner gives the patient a piece of blank paper.)
1		"Please read this and do what it says." (Written instruction is "Close your eyes.")
1		"Make up and write a sentence about anything." (This sentence must contain a noun and a verb.)
1		"Please copy this picture." (The examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.) 
30		TOTAL

Korsakoff's syndrome

- Six symptoms:
  - anterograde amnesia
  - retrograde amnesia, severe memory loss
  - confabulation, that is, invented memories which are then taken as true due to gaps in memory sometimes associated with blackouts
  - meager content in conversation
  - lack of insight
  - apathy – the patients lose interest in things quickly and generally appear indifferent to change.

- Dorsomedial nucleus of thalamus
- Frontal cortex
- ***Mamillary bodies***
- Amygdala
    - thiamine **deficiency**
        - Used in the biosynthesis of the acetylcholine and GABA

- Kandel ER, Schwartz JH, Jessell TM 2000. *Principles of Neural Science, 4th ed.* McGraw-Hill, New York.
- Chapter 62.