

## Chapter 5. Memory

Learning is acquiring new knowledge, behaviors, skills, values, preferences or understanding, and may involve synthesizing different types of information. Memory is an organism's ability to store, retain, and recall information and experiences.

Circuitry in brain: partly genetic and mostly environmental

How it works?

The process of evolving a unique brain

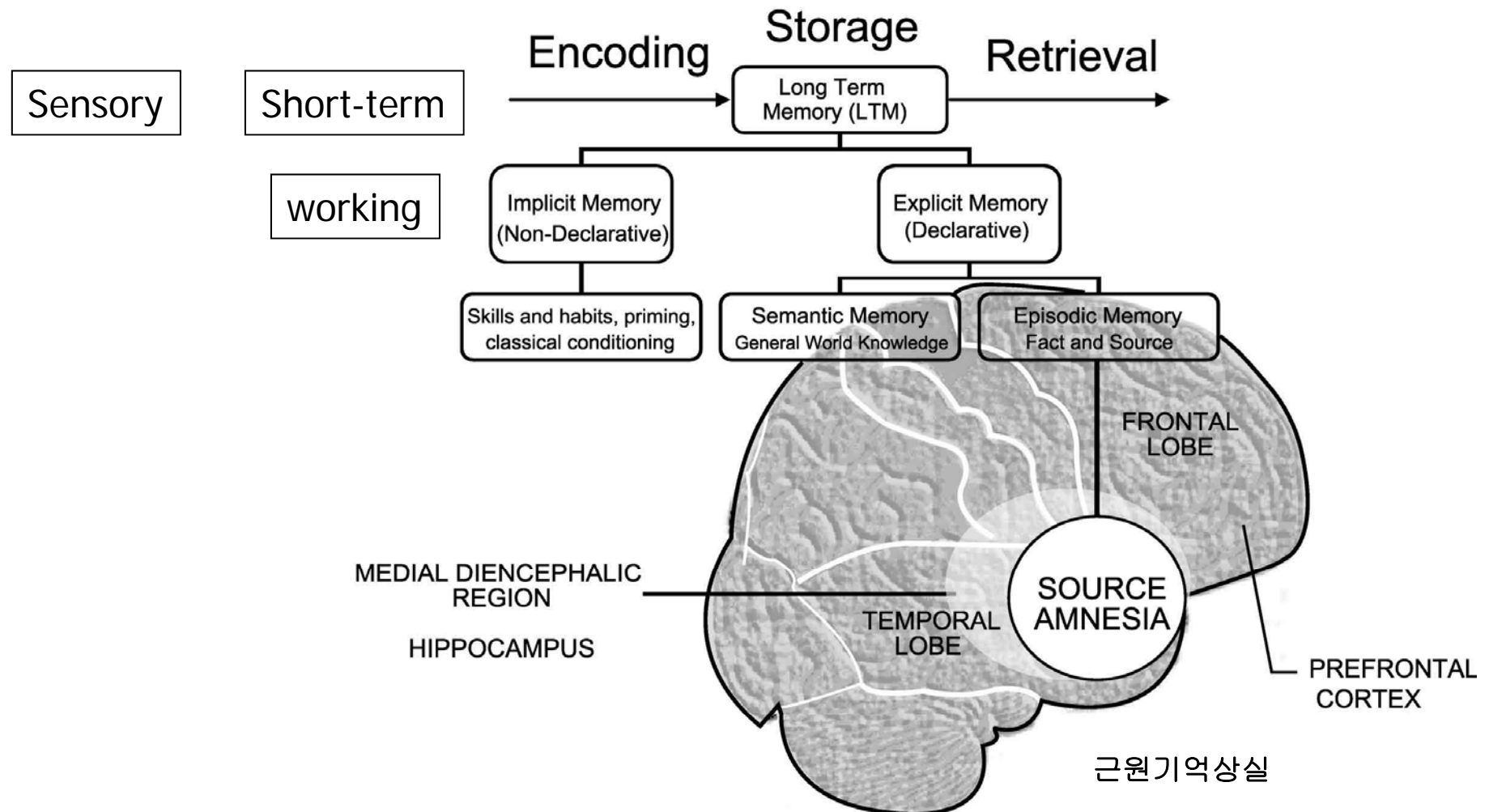
The essence of the individual depends on experience and memory

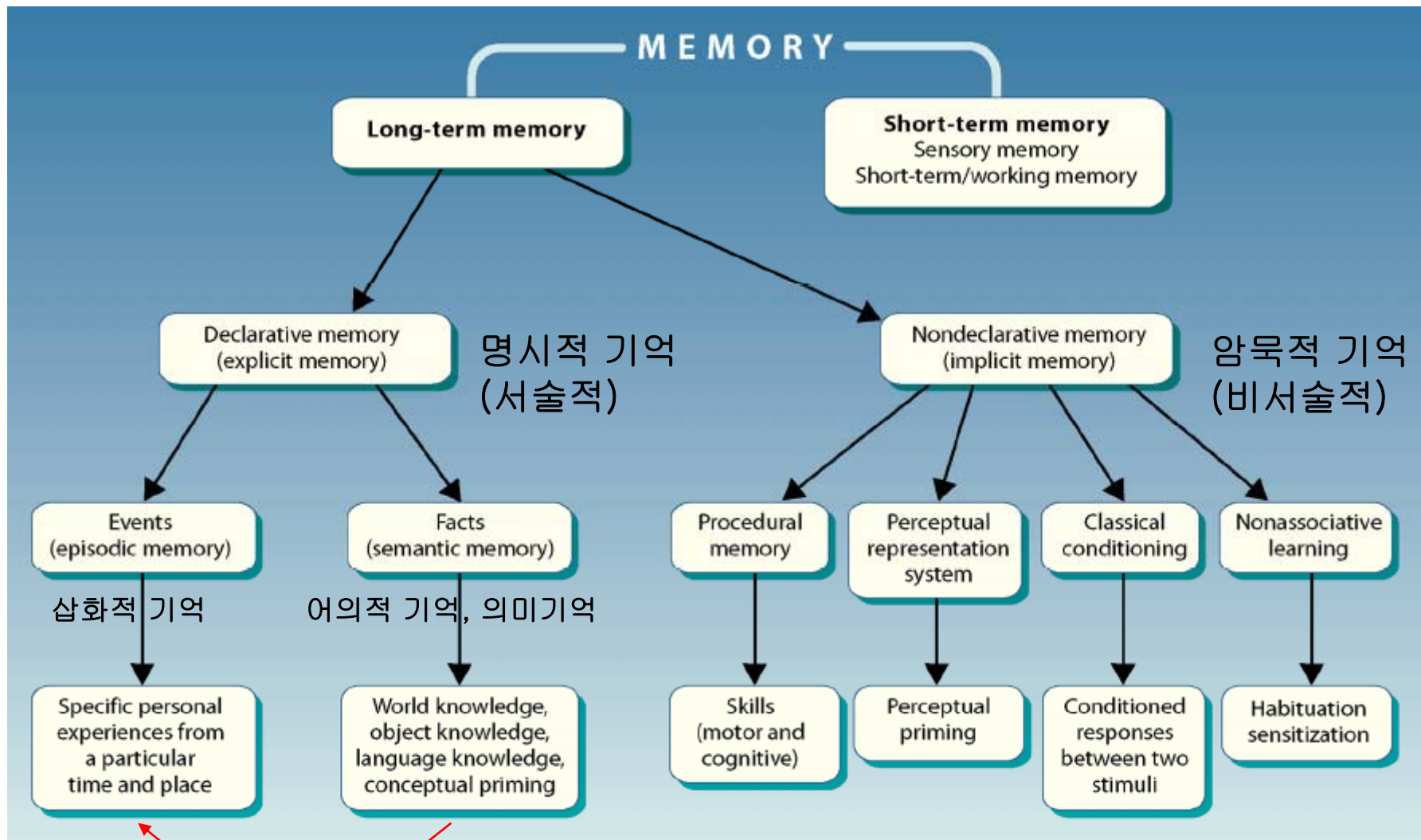
# Memory

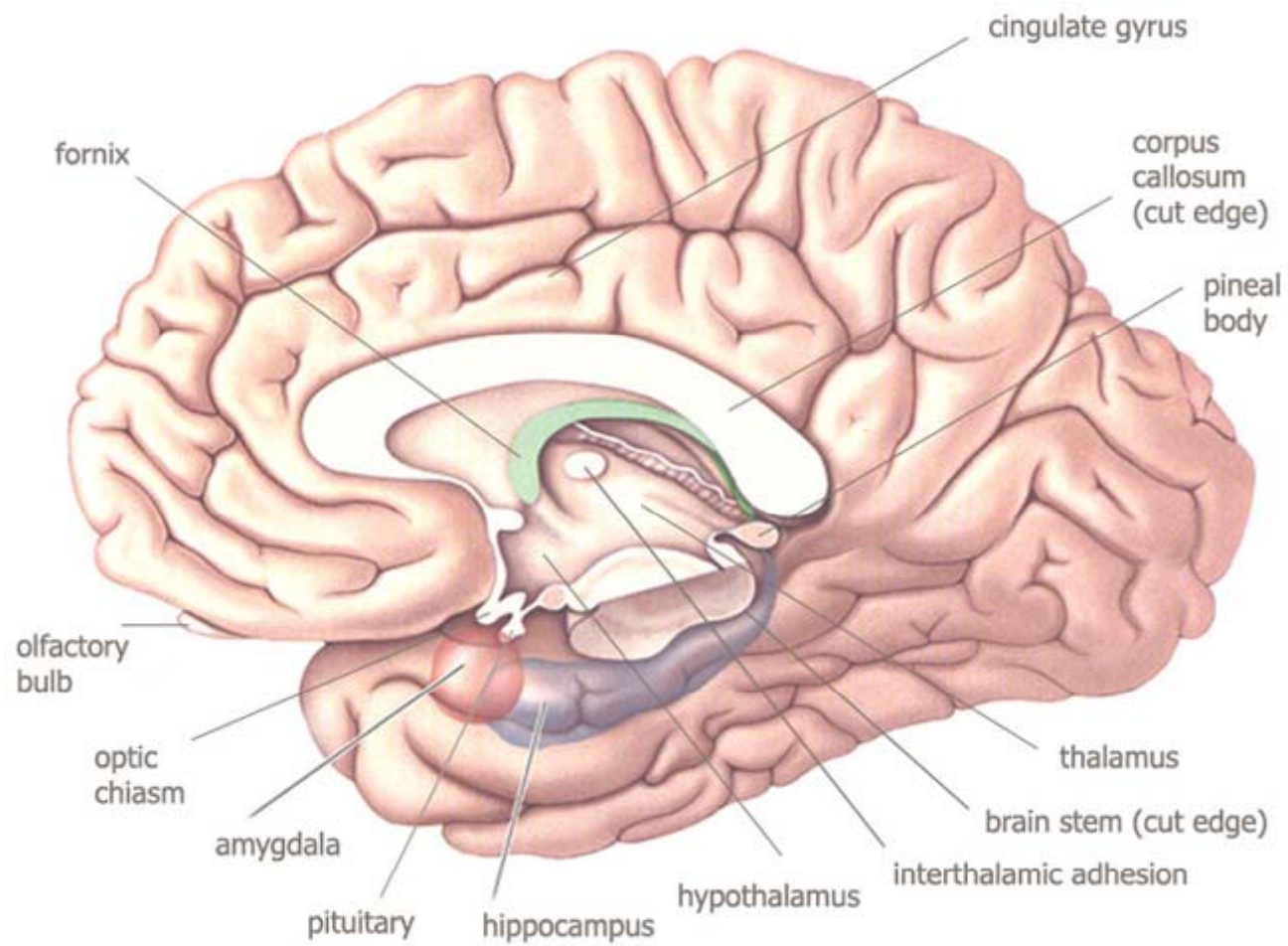
Sensory: just a second observation

Short-term (primary or active): cf. working memory

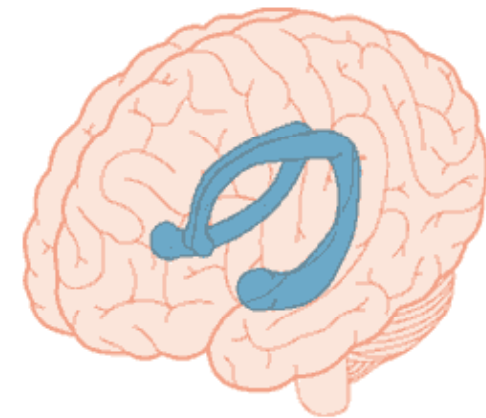
Long-term: implicit & explicit (semantic & episodic)





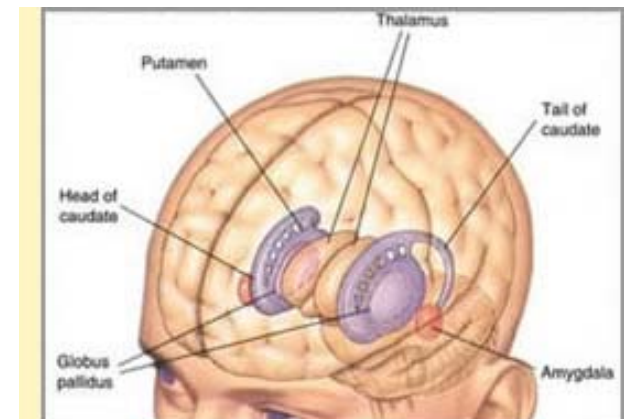


hippocampus



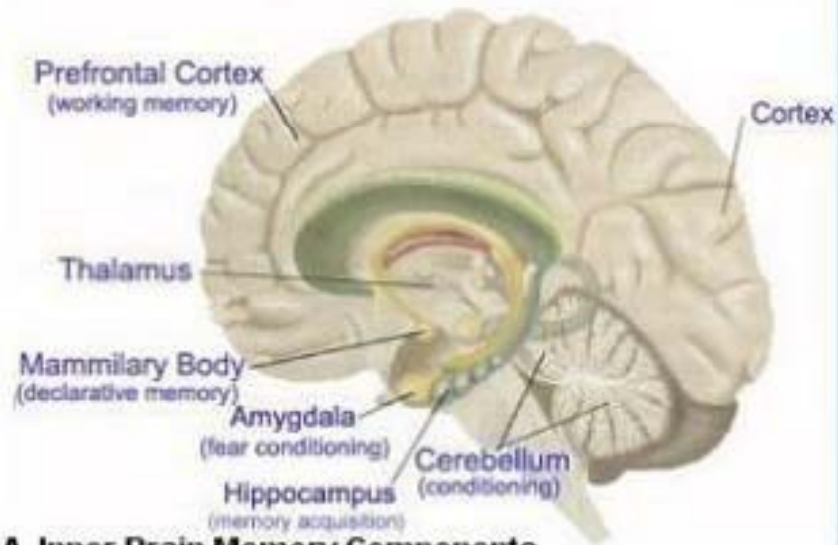
www.BrainConnection.com  
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thalamus

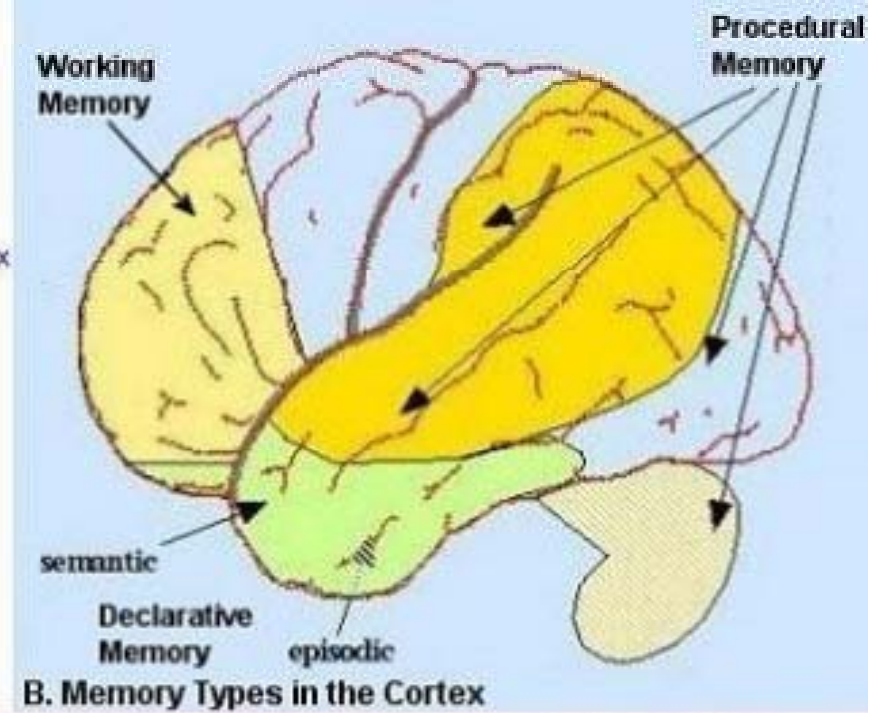




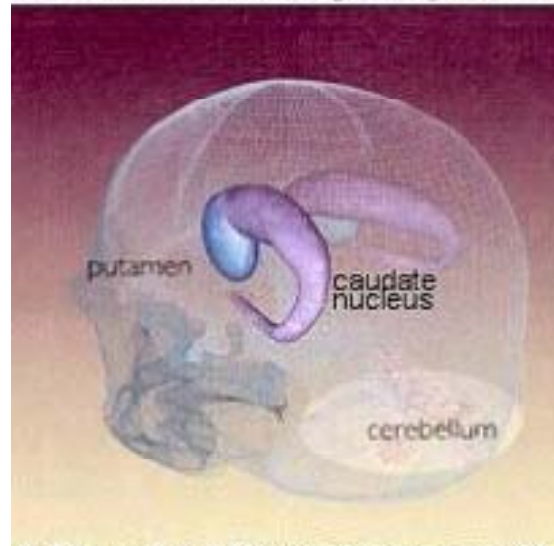
## The Brain and Memory



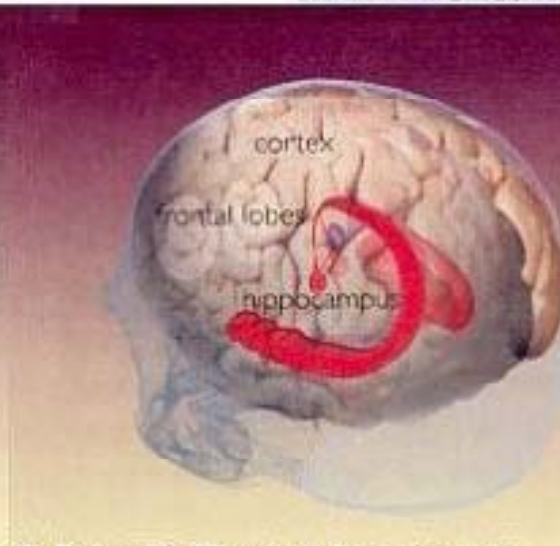
**A. Inner Brain Memory Components**



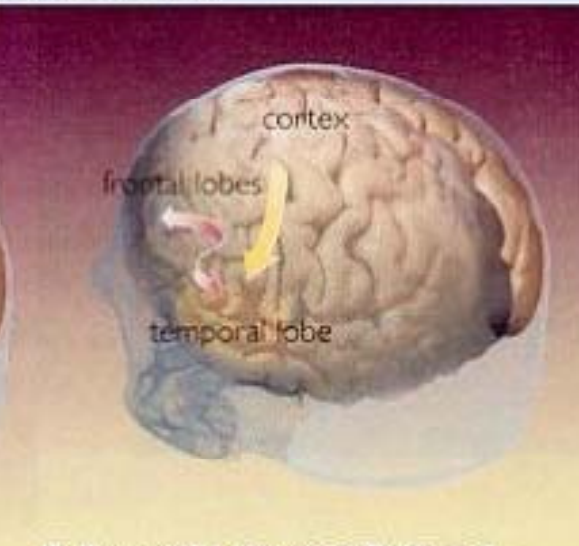
**B. Memory Types in the Cortex**



**C. Procedural Memory Components**

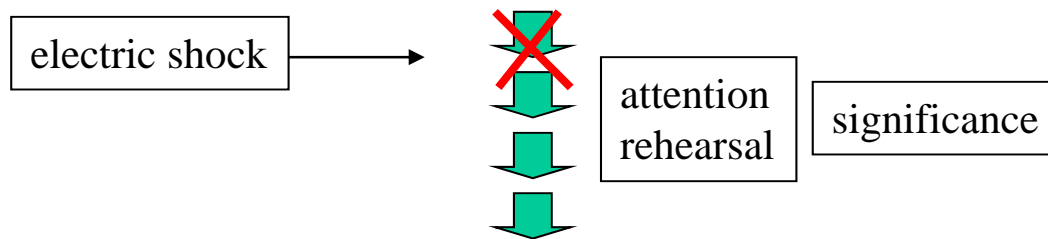


**D. Episodic Memory Components**



**E. Semantic Memory Pathway**

Short-term memory: transient, highly unstable, vulnerable process



Long-term memory: more permanent and dormant

## H.M.

Brain surgery to control epilepsy: medial temporal lobe

Trapped in the present: remember events before operation (up to two years beforehand)

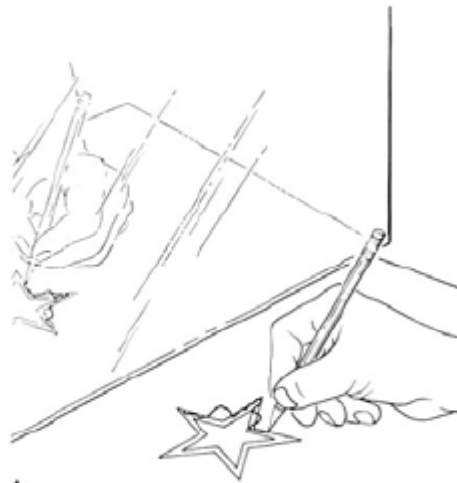
Amnesic: short-term memory is working but not lead to long-term memory

Implicit memory is working: mirror tracing task

Does not conscious of remembering the event of learning

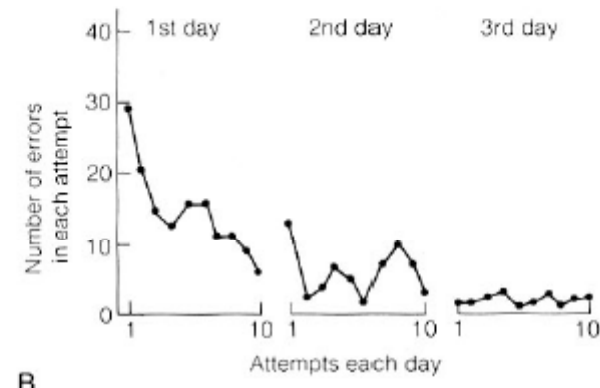
### HM: Amnesic

- Mirror tracing task, Milner, 1965

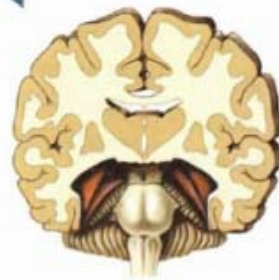
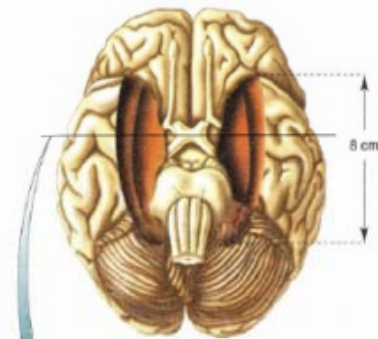


### HM: Amnesic

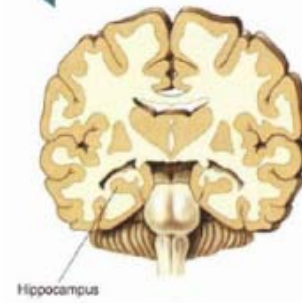
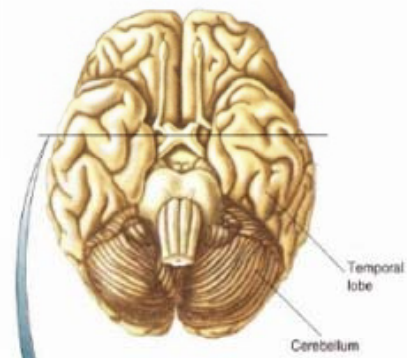
- improvement in H.M. for mirror tracing task
- no conscious recollection of previous training episodes



HM



Normal Brain





## Memory: processing & consolidation

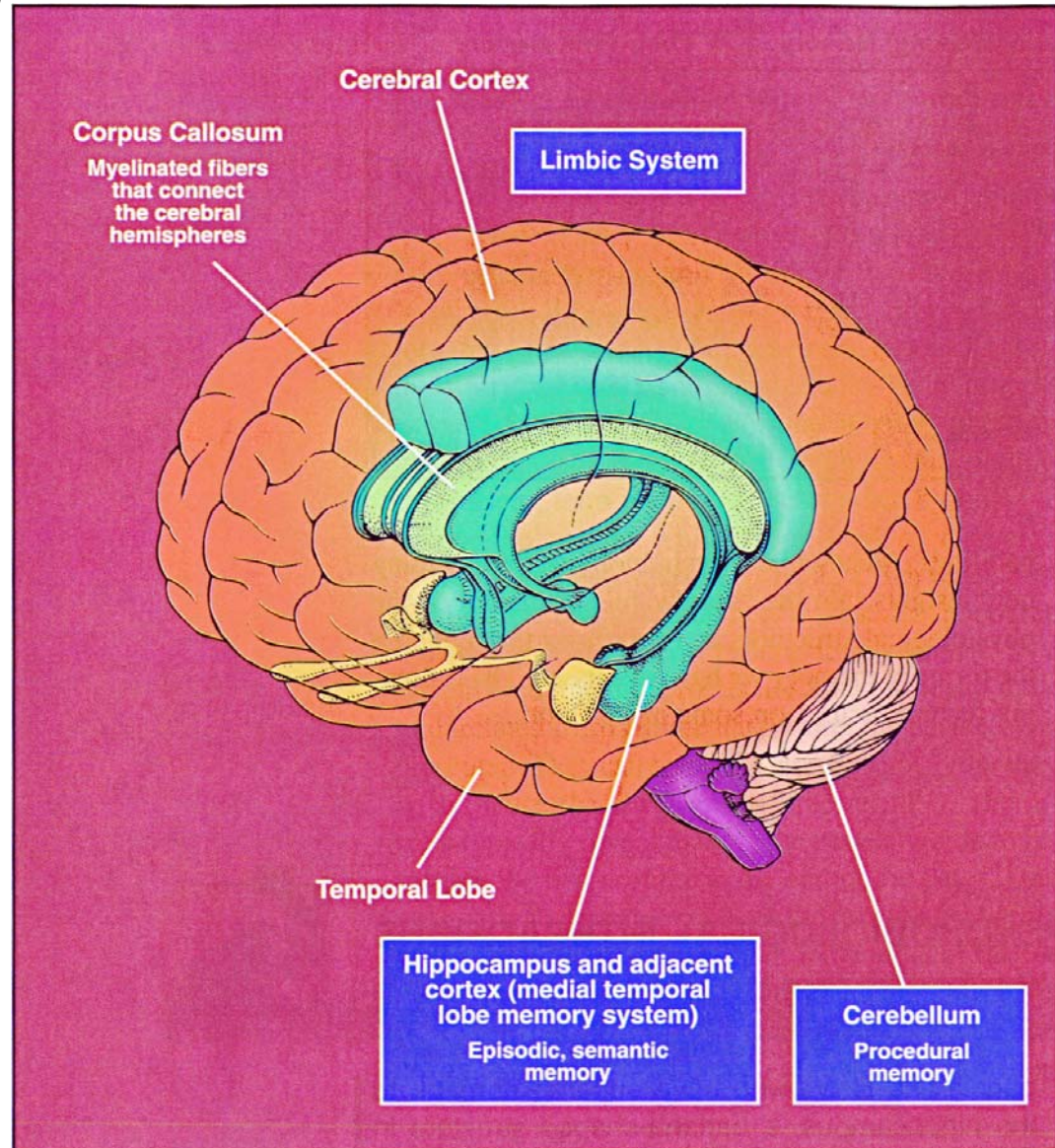
Medial temporal lobe (hippocampus)

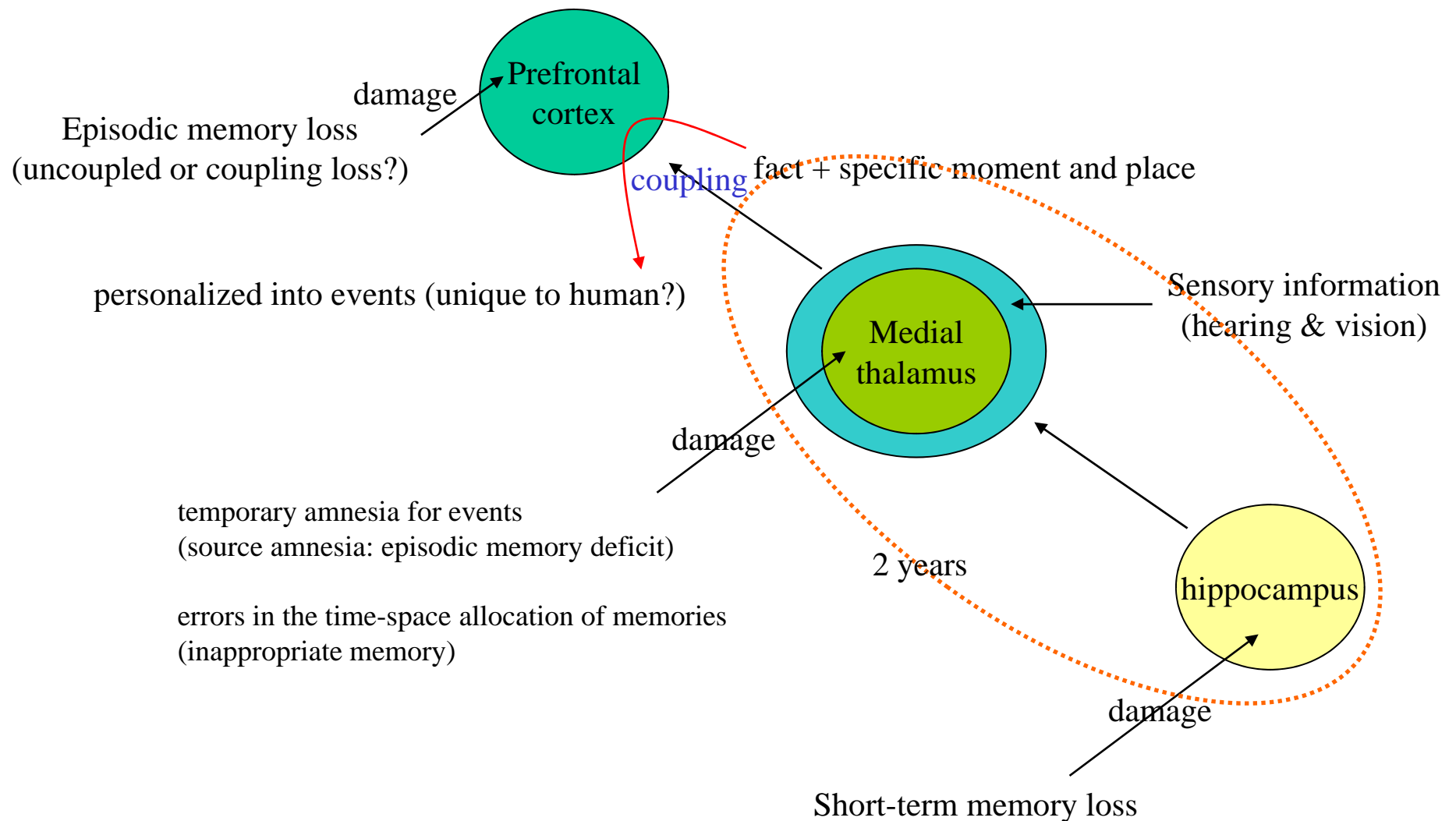


Medial thalamus



Cortex

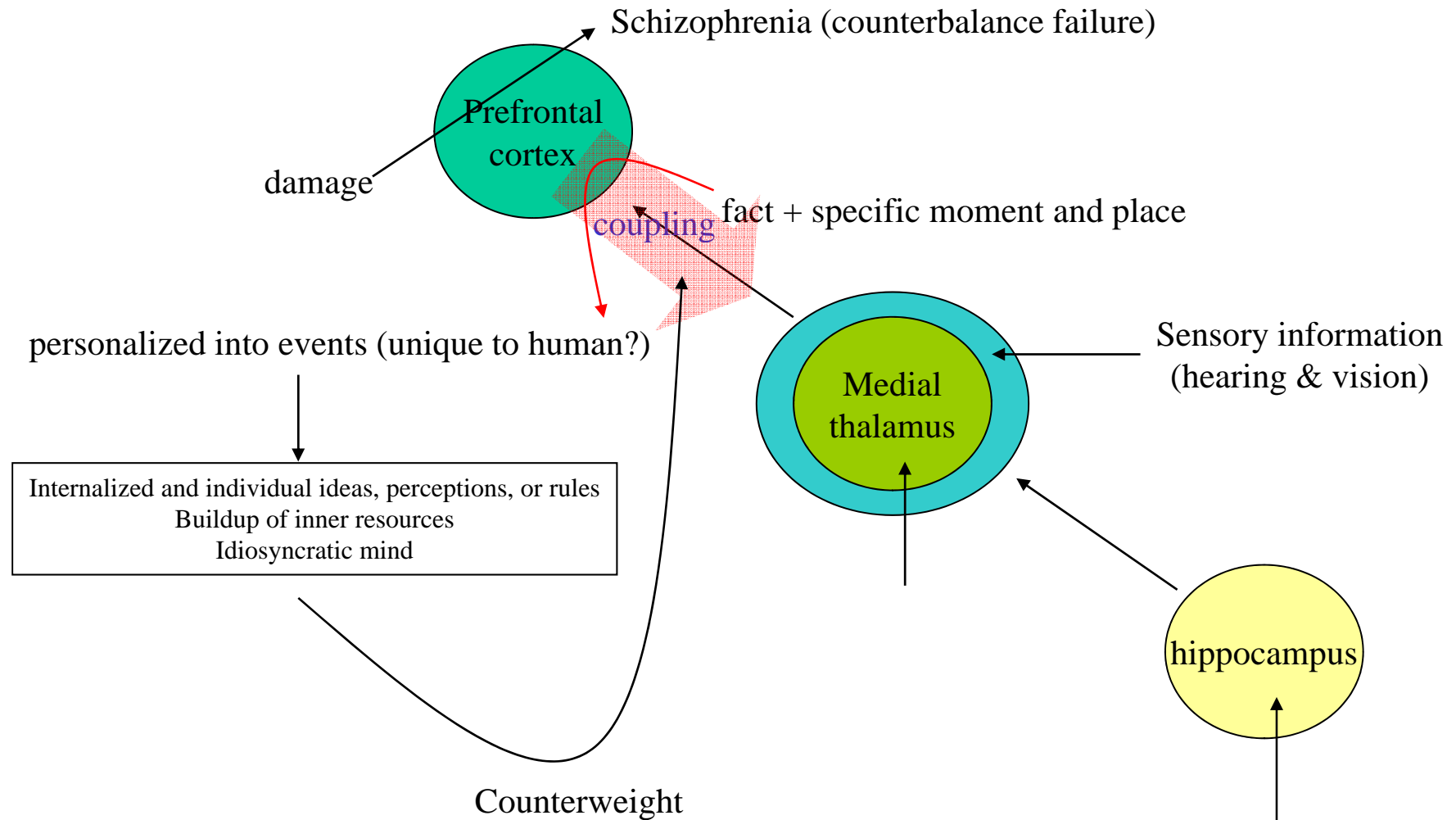




Events: unique & personal

Facts: generic & free of time and space frames of reference

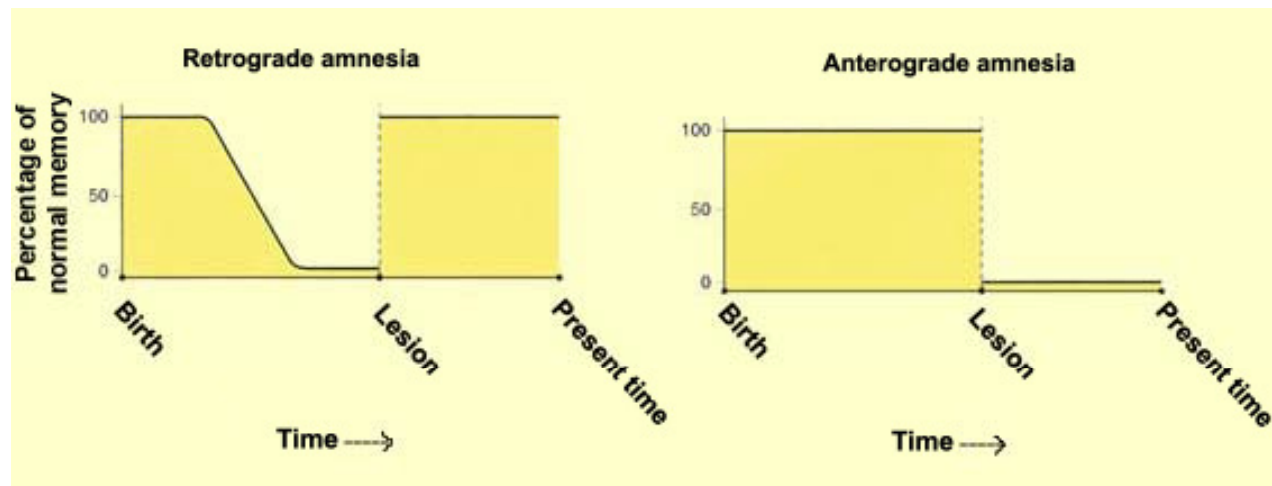
# Schizophrenia: counterbalance failure?



# Amnesia

Anterograde amnesia (진행성 기억상실): everything that happened since his surgery

Retrograde amnesia (역행성 기억상실): damage in large brain area  
loss of memory for everything that happened before being taken into the hospital,  
and even before the onset of the illness



## Amnesia

- Types:
  - **Retrograde**: cannot remember old memories
  - **Anterograde**: cannot form new episodic memories
- Retrograde amnesia is more rare
- Sources
  - Blow to head, Concussion
  - Korsakoff syndrome (severe vit. B1 deficiency)
  - Alzheimer's
  - Damage to hippocampus, thalamic structures
  - ECT (electroconvulsive shock therapy)
  - Midazolam: artificially induced amnesia

## Anterograde Amnesia

- Inability to acquire new information (think of "memento")
- Does not affect short-term memory
- Does not affect general knowledge from the past
- But, it is difficult to learn new facts
- Affects memory regardless of modality (visual, auditory, tactile, etc). Spares skilled performance
- Hyper-specific memory for those skills that are learned after onset – learning is expressed only in context in which it was encoded

## Retrograde amnesia

- Temporal extent can vary:
  - ECT: months or weeks
  - Korsakoff's, Alzheimer's: years
- **Temporal gradient**:
  - early memories are better remembered than memories before trauma
  - New memories continue to undergo neurological change: **memory consolidation**
- Retrograde amnesia often becomes less severe over time
  - Most remote memories are likely to return first
- Does not affect overlearned information (e.g. skills)

# How memory is stored in brain?

## Karl Lashley

Removal of rat cortex area: the more the worse

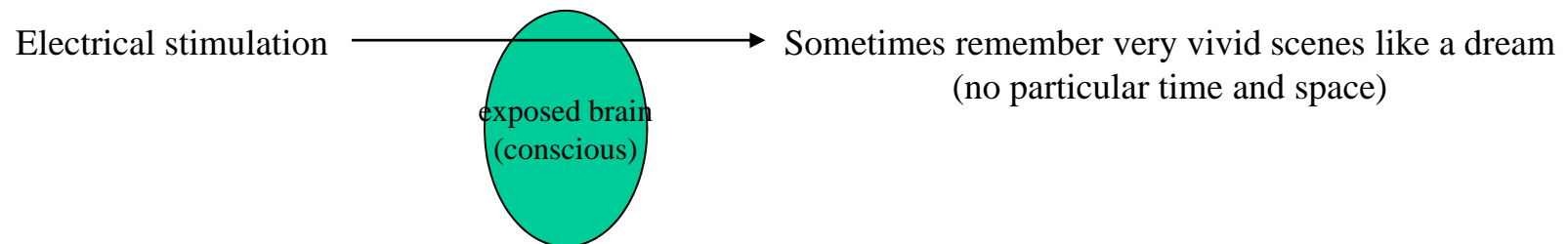
The entire cortex plays an important role in the storage of memory

## Penfield experiment (1881-1976)

No fixed area for a particular memory

Stimulation of different places led to same memory and the vice versa

Probably activated the same circuit



## Stephen Rose

The memory would be distributed by different levels of circuitry

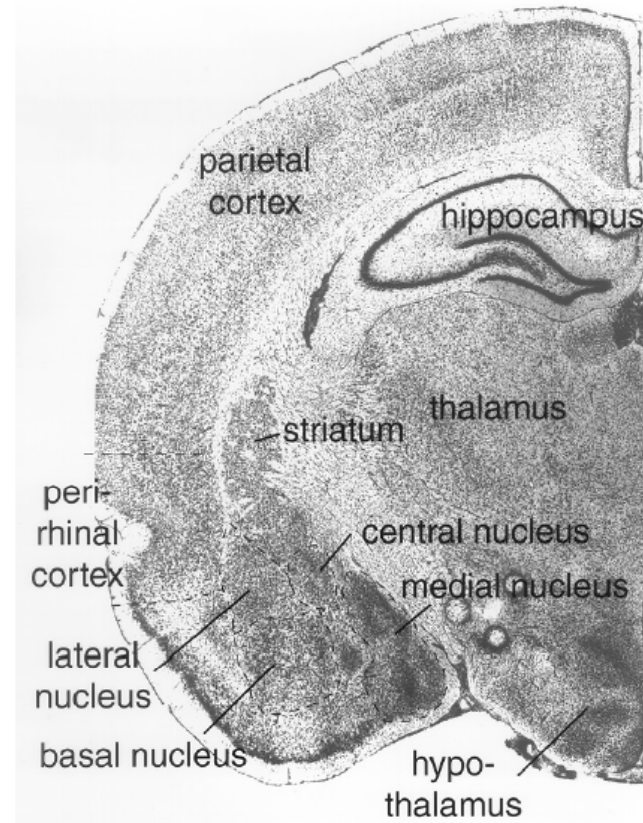
No single cell or exclusively committed group of cells

**Memory function is distributed**



# Molecules and Genes for Memory

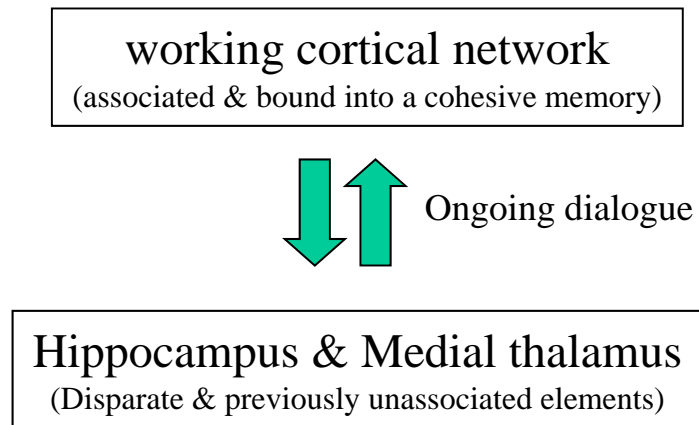
- Memory function is distributed
- Memories are stored in the connections between neurons: synapse
- Synaptic physiology: rules for plasticity, special channels, molecules and genes.



## Consolidation of memory in the cortex: association

Highly transient and dissociable phase of short-term memory

Short-term memory lasts at most for half an hour



# Implicit memory (암묵적 기억)

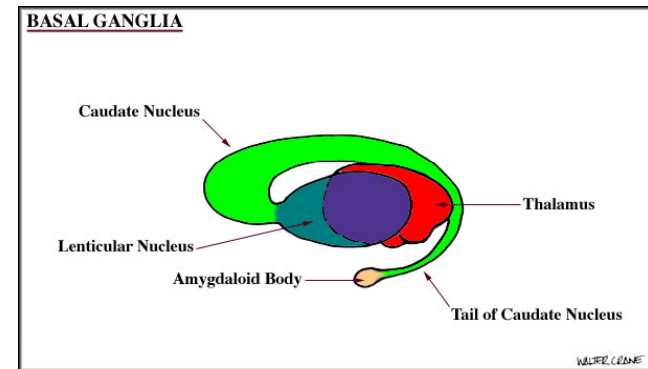
Habit & Skill

Basal ganglia: a sequence of movement

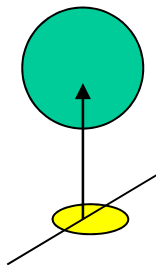
Cerebellum: conditioning involving movement

No direct reciprocal connection to cortex

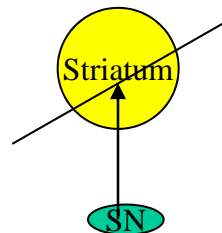
Without attention & conscious effect: probably an autonomous circuit



Parkinson's

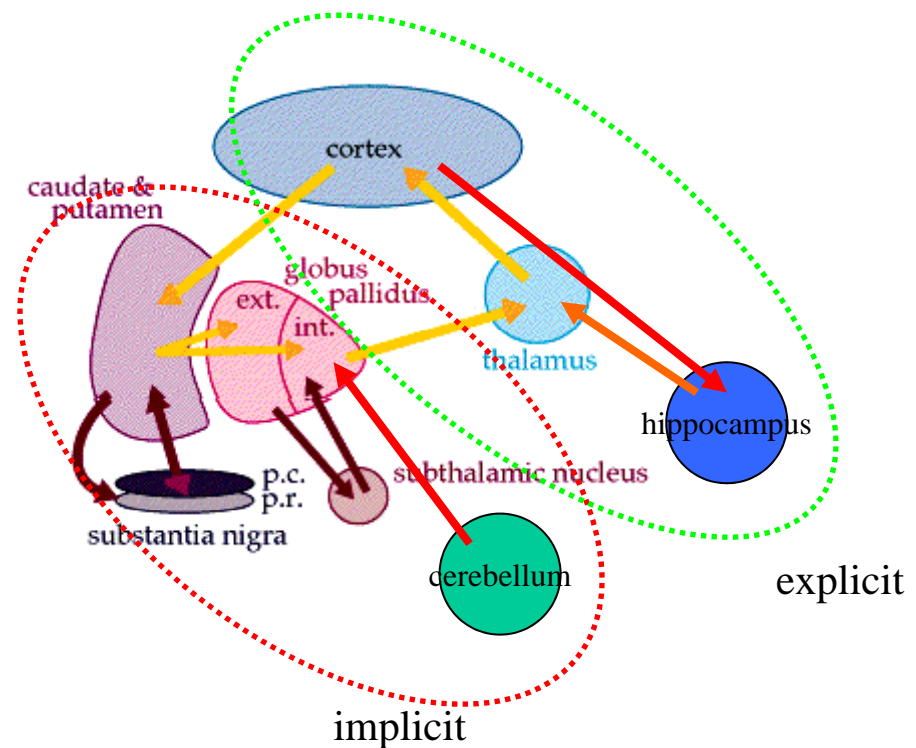


Huntington's



No dialogue  
One side reaction

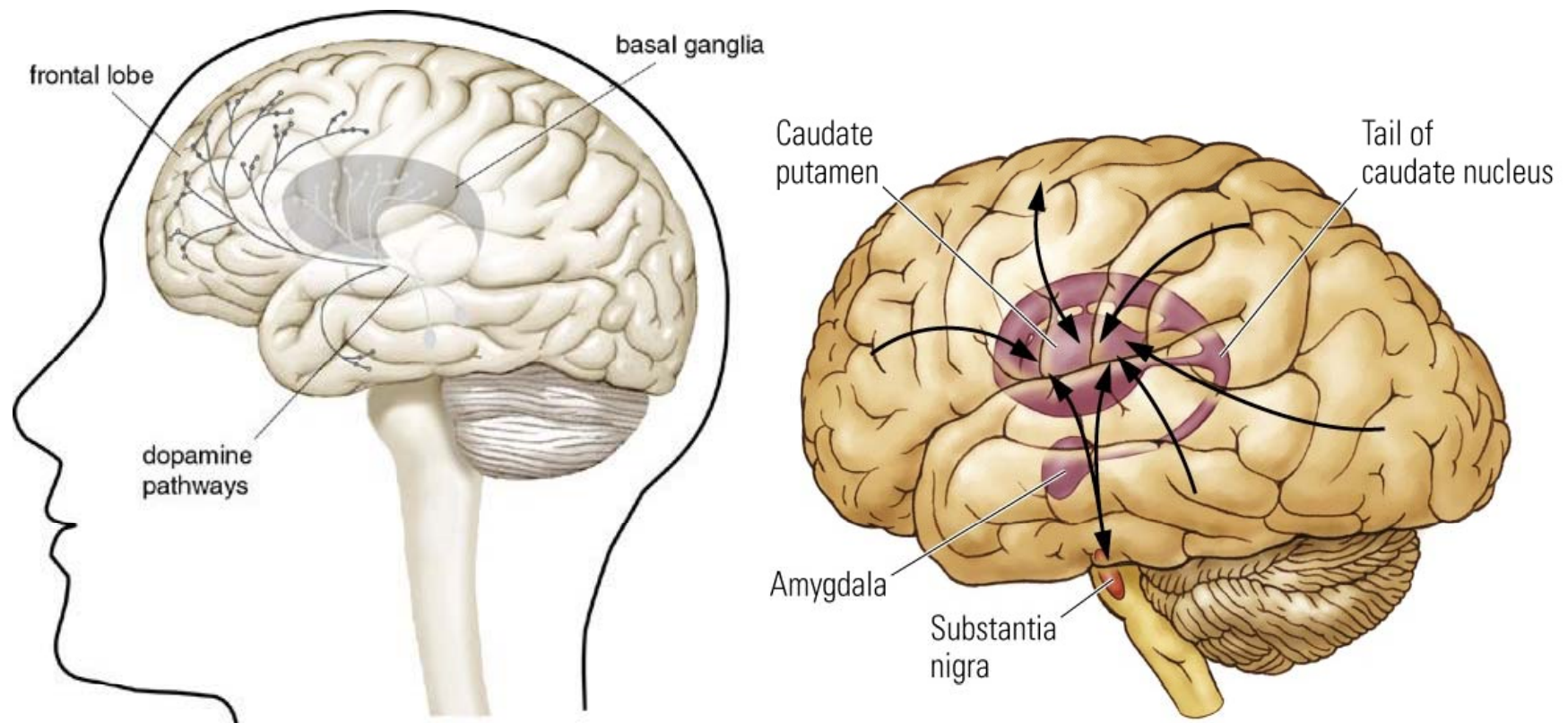
No problem in explicit memory  
But implicit memory is impaired



# Basal ganglia

Responsible for ballistic movements (subconscious)

A group of various interconnected brain regions



**basal ganglia:** a collection of nuclei deep to the white matter of cerebral cortex

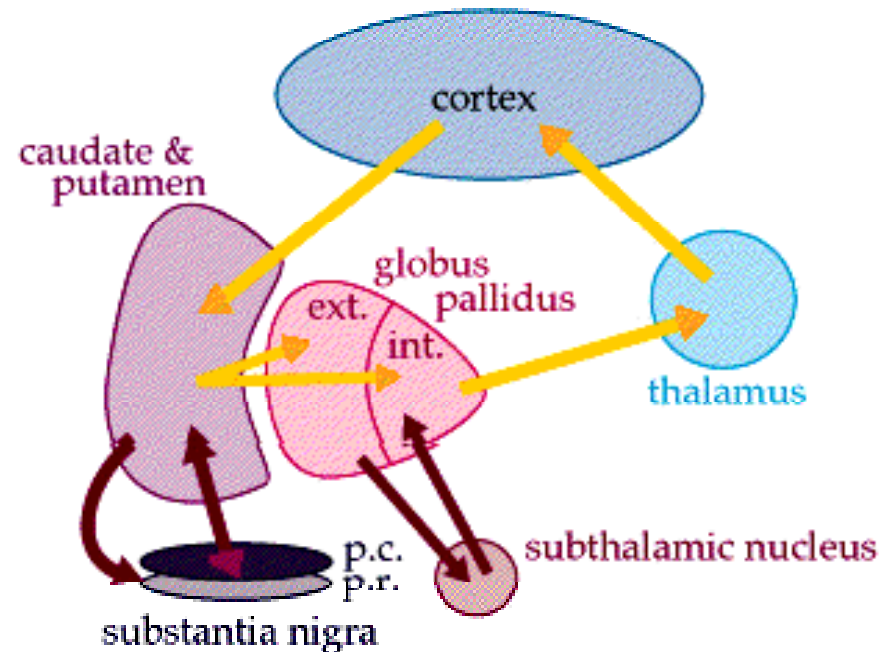
caudate + putamen + nucleus accumbens + globus pallidus + substantia nigra + subthalamic nucleus + (claustrum + amygdala)

the claustrum and the amygdala, however, do not really deal with movement, nor are they interconnected with the rest of the basal ganglia

**Striatum:** caudate + putamen + nucleus accumbens

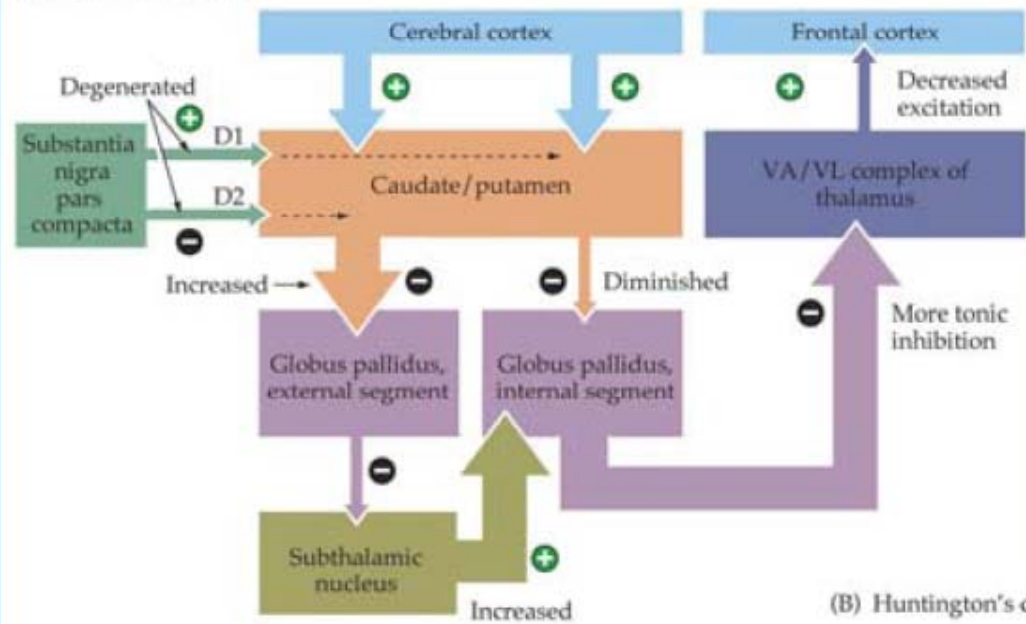
**corpus striatum:** striatum + globus pallidus

**lenticular nucleus:** putamen + globus pallidus

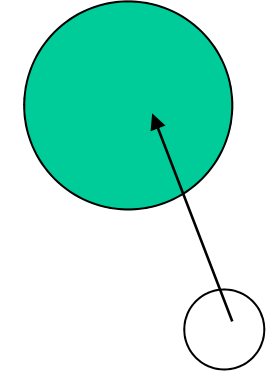




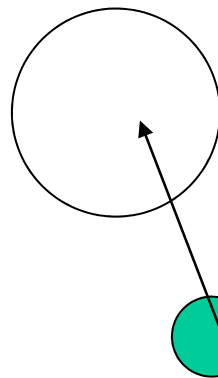
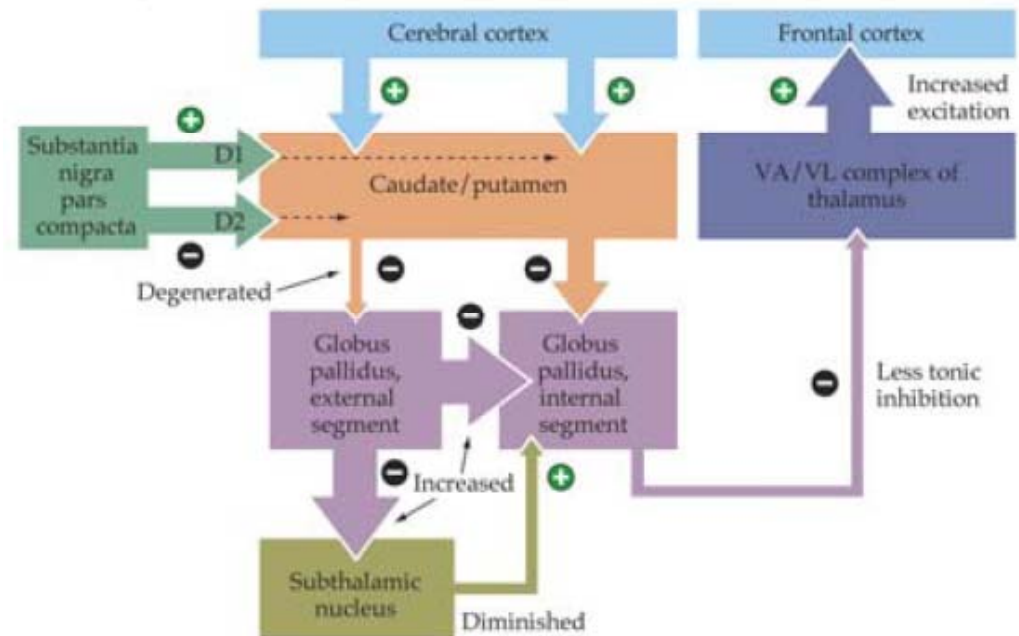
(A) Parkinson's disease



striatum



(B) Huntington's disease



substantia nigra



## Memories are stored in the connections between neurons: synapse

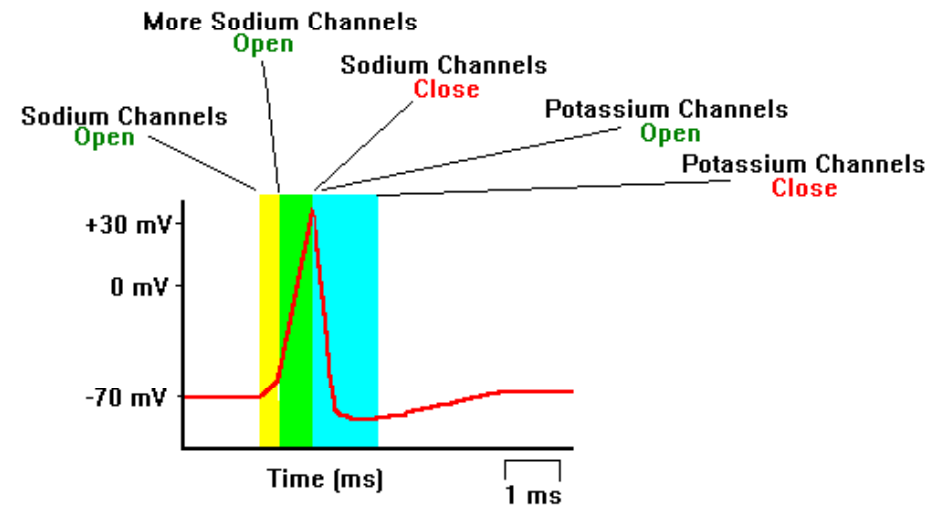
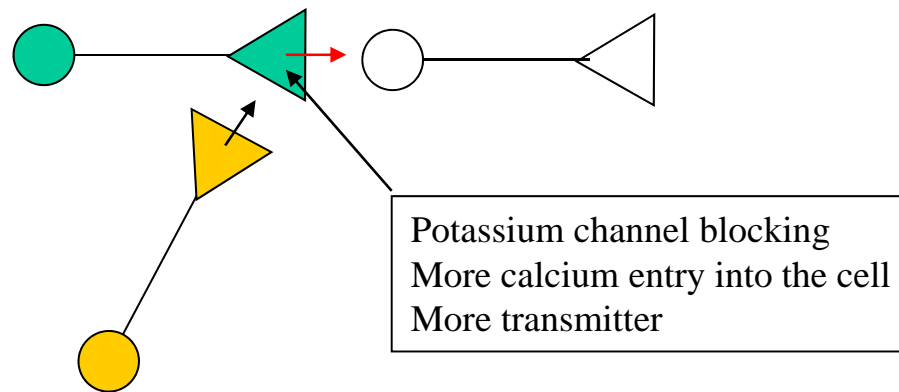
Ramon Y Cajal (1894)

Lord Sherrington (1897)

Donald Hebb (1949)

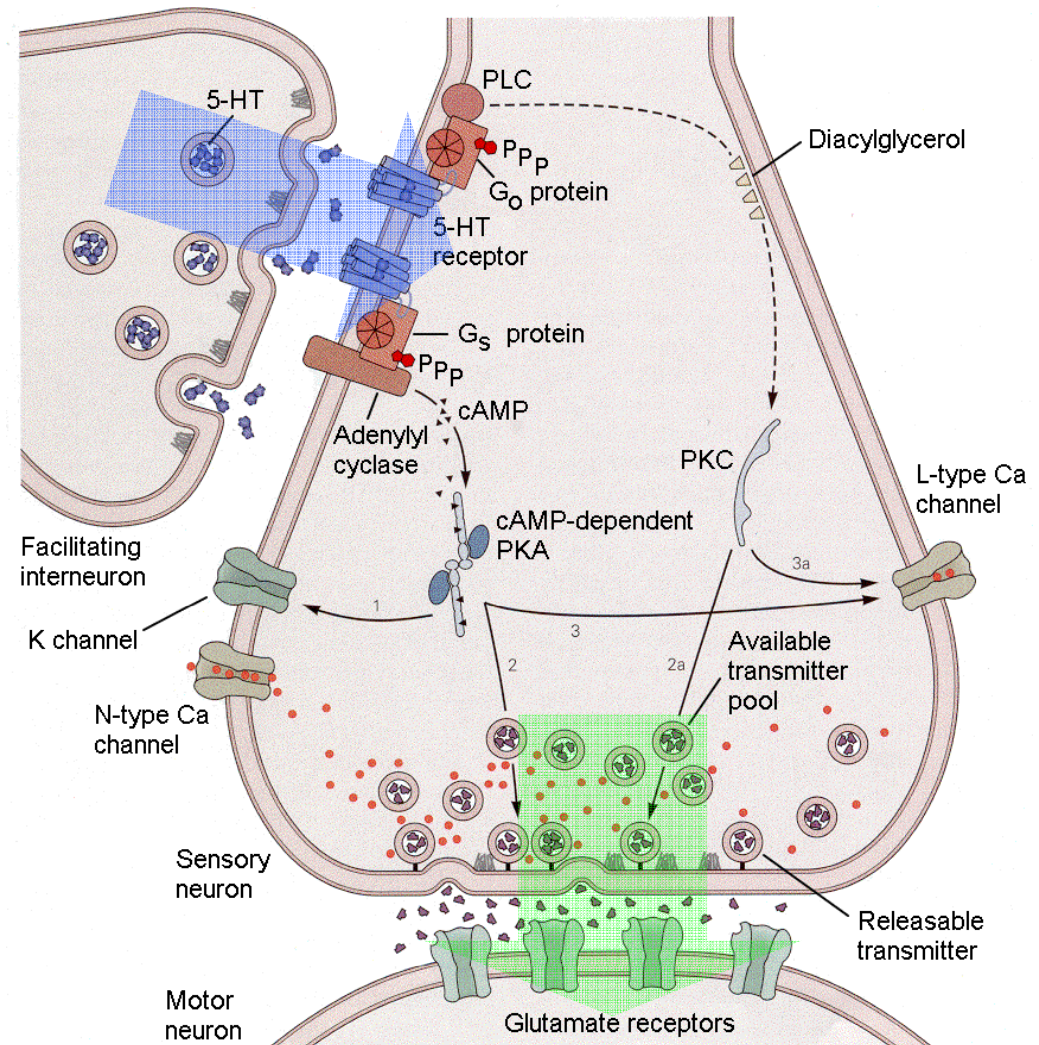
“When an axon of cell A is near enough to excite cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A's efficiency, as one of the cells firing B, is increased”

## Presynaptic & postsynaptic strengthening in Aplasia

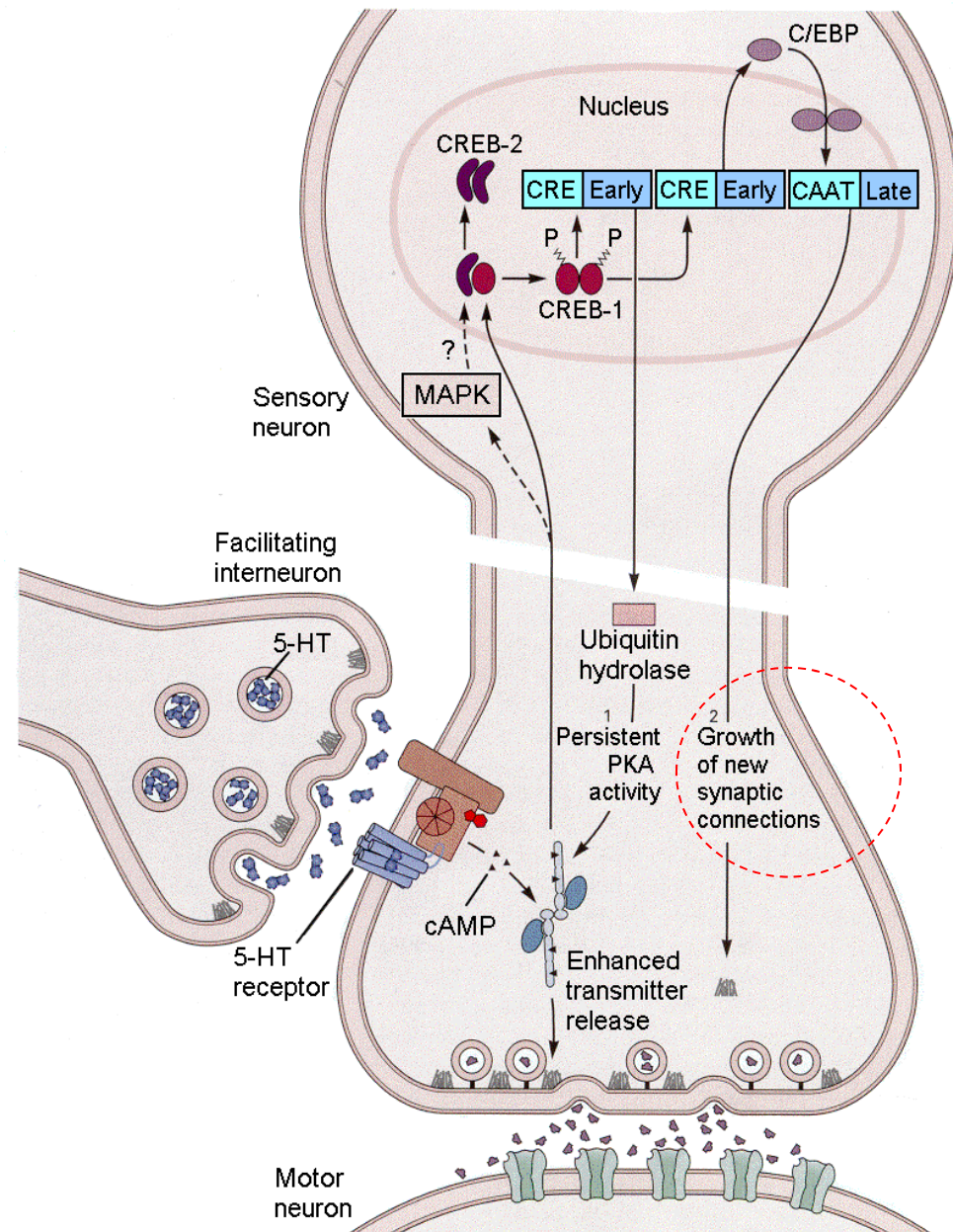


**The molecular mechanism of sensitization.** The synaptic and chemical events underlying presynaptic facilitation involved in producing sensitization. See text for details. (Kandel, ER, JH Schwartz and TM Jessell (2000) *Principles of Neural Science*. New York: McGraw-Hill.)

5-HT  
cAMP  
PKA activation  
Phosphorylation of K channel  
Closing K channel  
Increased Ca transport  
Increased neurotransmitter release



Long-term storage of implicit memory for sensitization involves changes in protein synthesis that result in formation of new synaptic connections. (Kandel, ER, JH Schwartz and TM Jessell (2000) *Principles of Neural Science*. New York: McGraw-Hill.)



Long-term memory

Permanent changes inside the targeting cell

Hebb rule:

The hypothesis proposed by Donald Hebb that the cellular basis of learning involves strengthening of a synapse that is repeatedly active when the postsynaptic neuron fires.

“Neurons that fire together get wired together.”



## What permanent changes?

Genes, proteins, cellular responses

(receptor gene, receptor, increased transport)

Connections (synaptic contacts)

The more experiences, the more connections

Two important proteins: cell adhesion molecules (CAM), growth-associated protein (GAP-43)

CAM: sugar incorporation is important

GAP-43: high expression during axon growth & activated during LTP

Memory improvement: by making more associations in any kinds

### Increase of Dendritic Spines in animals housing in a Complex Environment

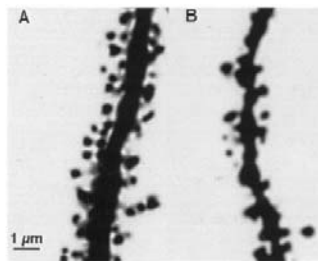
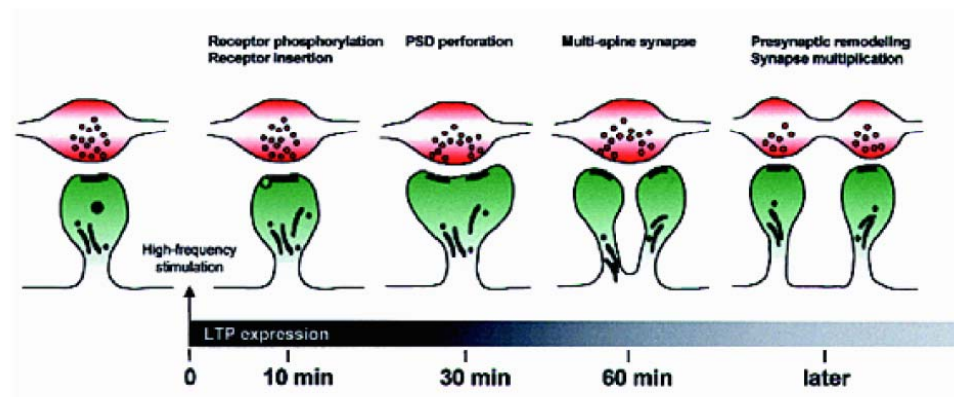


Figure 2. Examples of basal dendritic segments from CA1 pyramidal cells in a rat trained in the complex environment (A) and in an isolated rat (B). The spine densities for these two segments were 2.71 and 1.75 spines per micrometer, respectively. Spine densities in isolated rats were usually  $< 2.0$  spines per micrometer and never exceeded 2.4 spines per micrometer. Reprinted with permission from [56]; © (1994) National Academy of Sciences, USA.

*Moser et al. PNAS 1994*

## Strengthening of Synapse at different time-scales





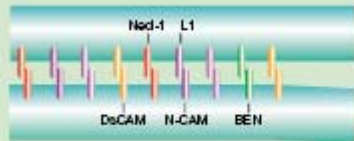
# Cell Adhesion Molecules in the CNS

Toshiaki Sakisaka and Yoshimi Takai

Journal of  
**Cell Science**  
jcs.biologists.org

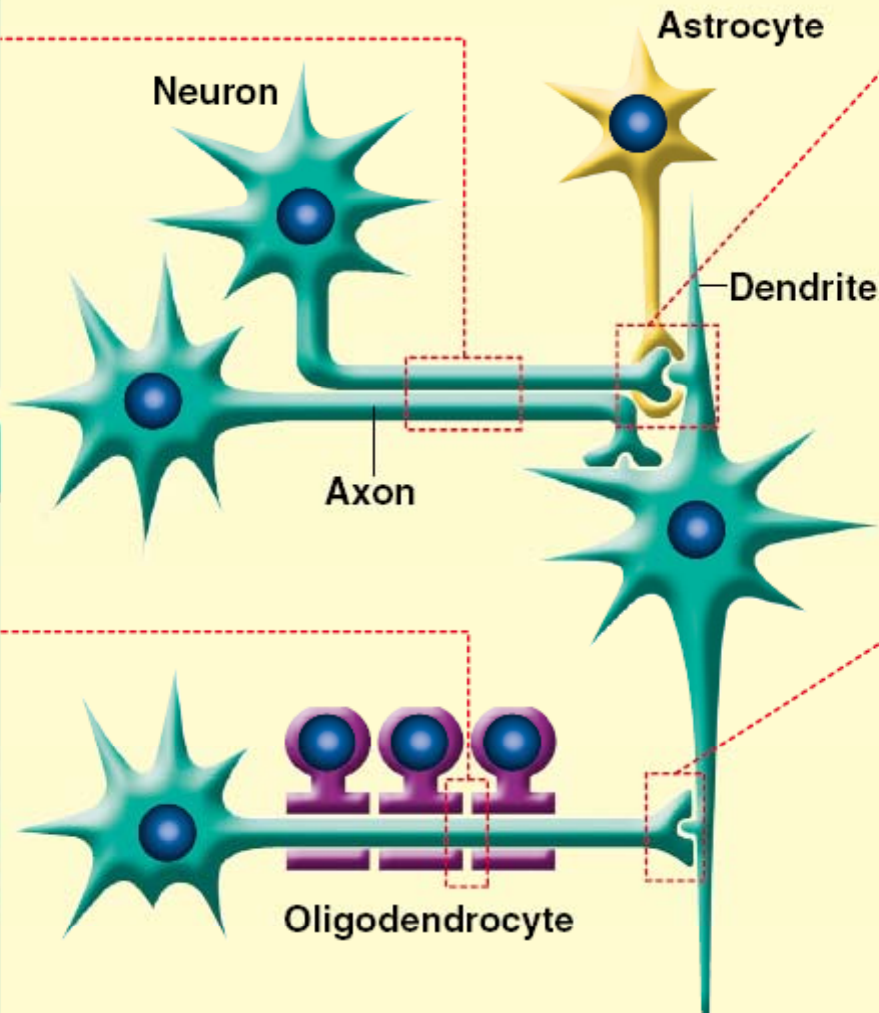
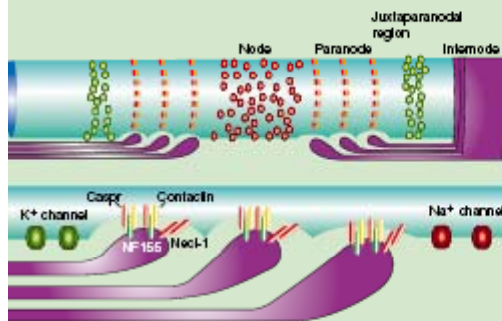
## Axon-axon contacts

L1  
N-CAM  
BEN/DM-GRASP  
DsCAM  
Necl-1



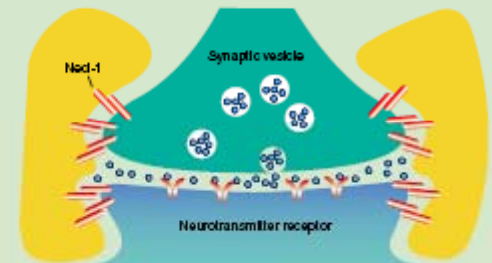
## Paranodal junctions

Contactin  
Caspr  
NF155  
Necl-1



## Axon-astrocyte contacts

Necl-1



## Synapses

Cadherins	N-CAM
Nectin-1/-3	Neurologin
Neurexin	SYG-1/SYG-2
Protocadherins	Sidekick
Eph/ephrin	L1

