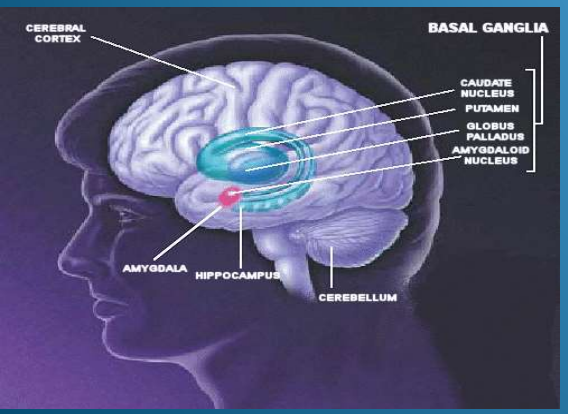
PHYSIOLOGY OF MEMORY

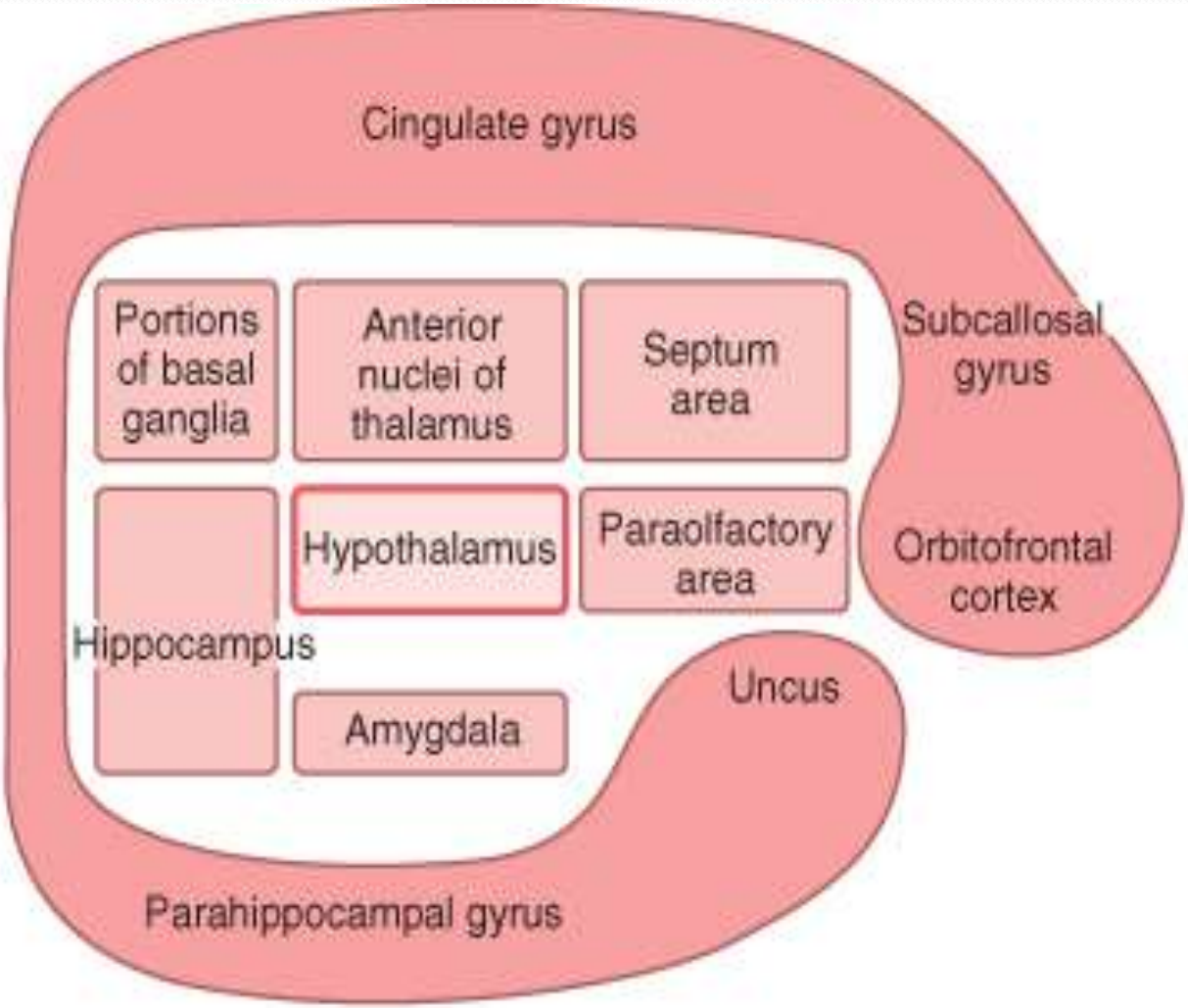
Dr. Pallavi Badhe

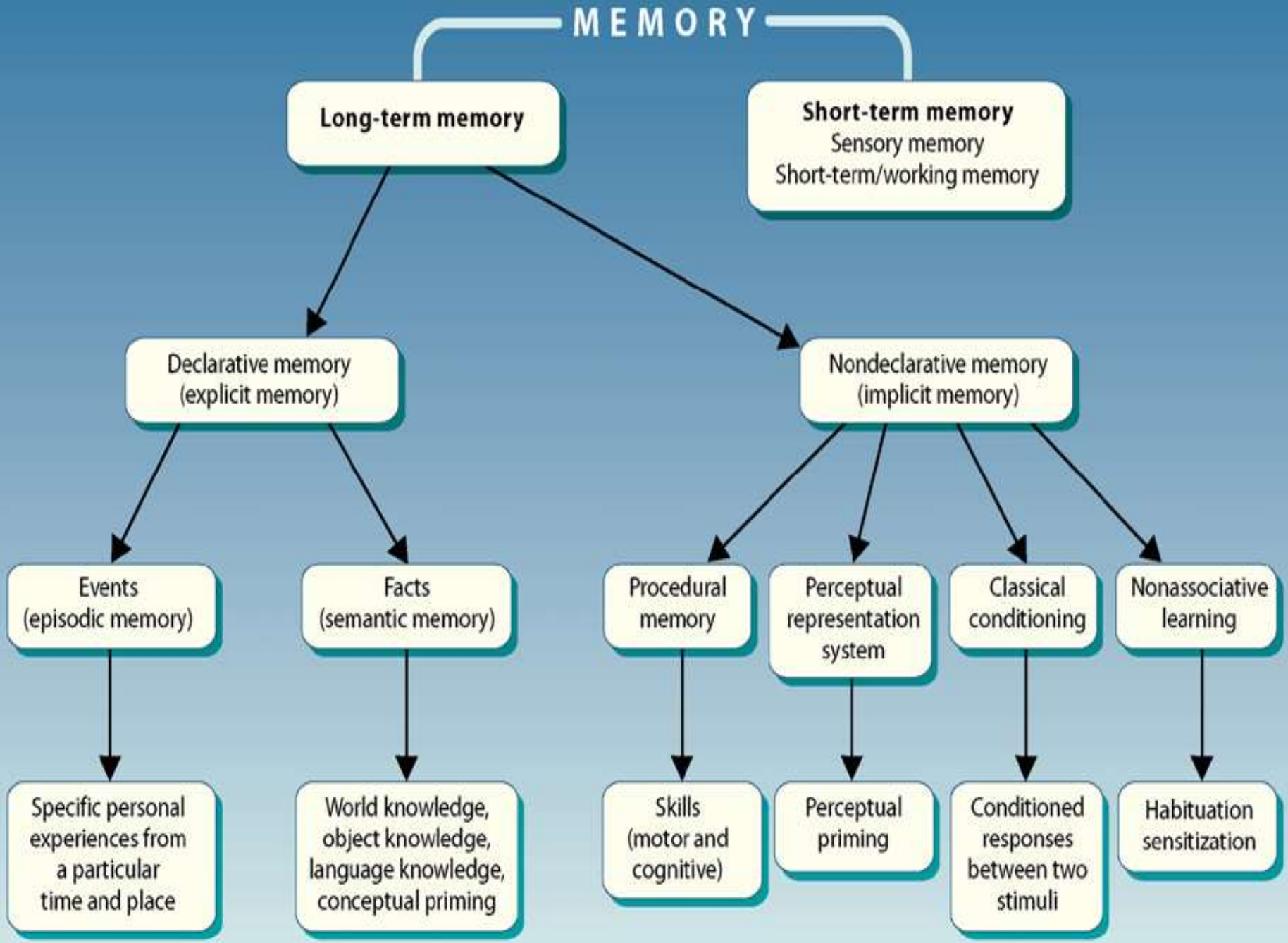


- Learning: It is a relatively permanent change in behavior as a result of training, practice or experience. The process of acquiring knowledge about the world.
- Memory: It is the ability to recall past events.
- It is the process by which the knowledge is encoded, stored and later retrieved.
- It is multifaceted, involves many processes, systems and brain regions.

History

- Wilder Penfield (1940): Memory processes localised to specific regions of brain.
- Brenda Milner : Studied case of H.M. (Henry Molaison)
- Endel Tulving : Explicit memory as Episodic & Semantic.
- Pavlov (1927): Conditioning phenomenon.
- Ivan Pavlov & Sherrington: Habituation.




MEMORY
Long-term memory
Short-term memory
Sensory memory
Short-term/working memory
Declarative memory (explicit memory)
Nondeclarative memory (implicit memory)
Events (episodic memory)
Facts (semantic memory)
Procedural memory
Perceptual representation system
Classical conditioning
Nonassociative learning
Specific personal experiences from a particular time and place
World knowledge, object knowledge, language knowledge, conceptual priming
Skills (motor and cognitive)
Perceptual priming
Conditioned responses between two stimuli
Habituation sensitization

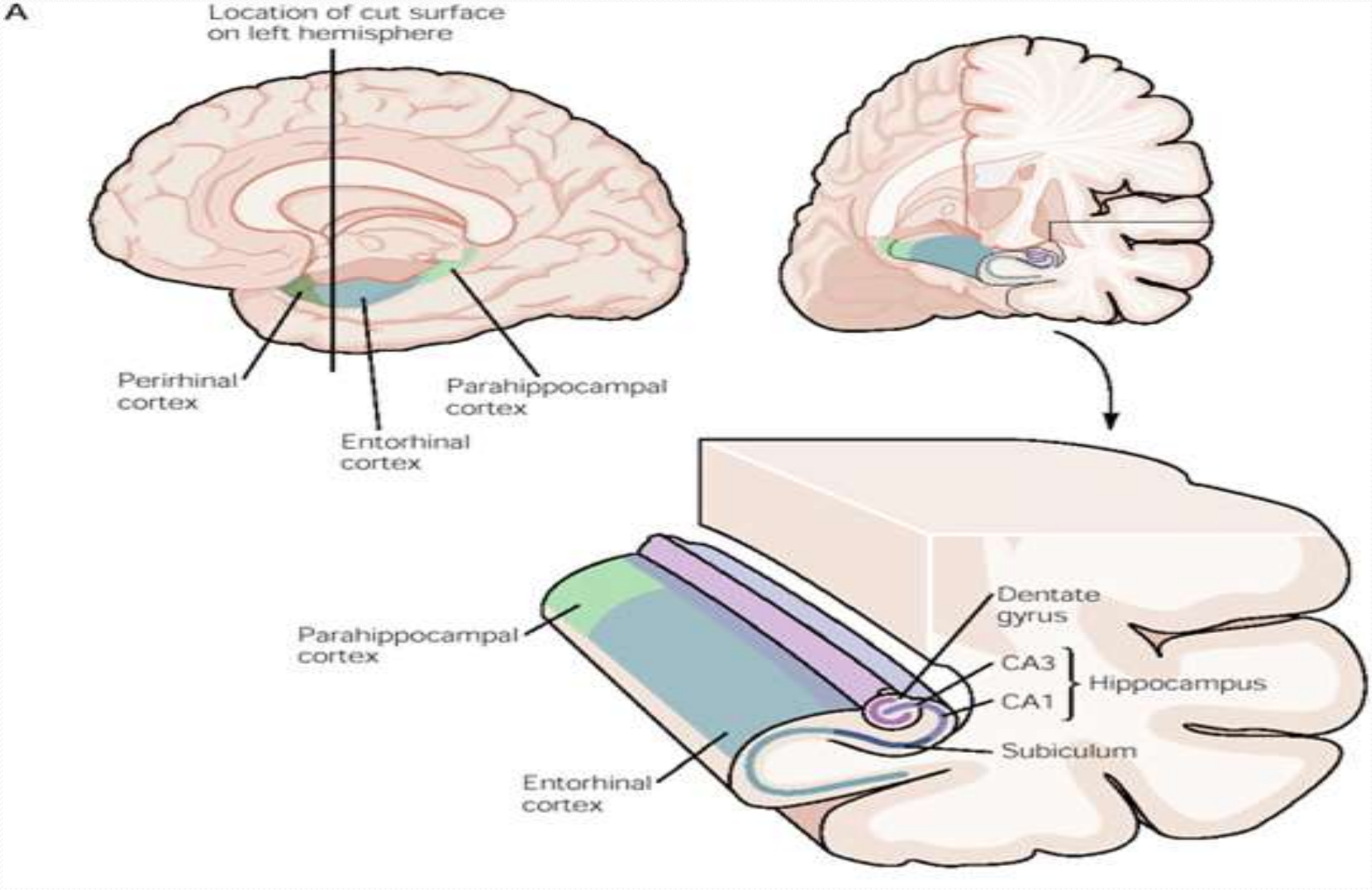
Explicit or declarative memory

- knowledge regarding people, places, and things.
- Highly flexible.
- Associated with consciousness or at least awareness.
- Recalled by deliberate conscious efforts.
- It is depends on the hippocampus and other parts of the medial temporal lobes of the brain for its retention.
- It is divided into
- 1) Episodic (memory for events and personal experiences)
- 2) Semantic (memory for facts)

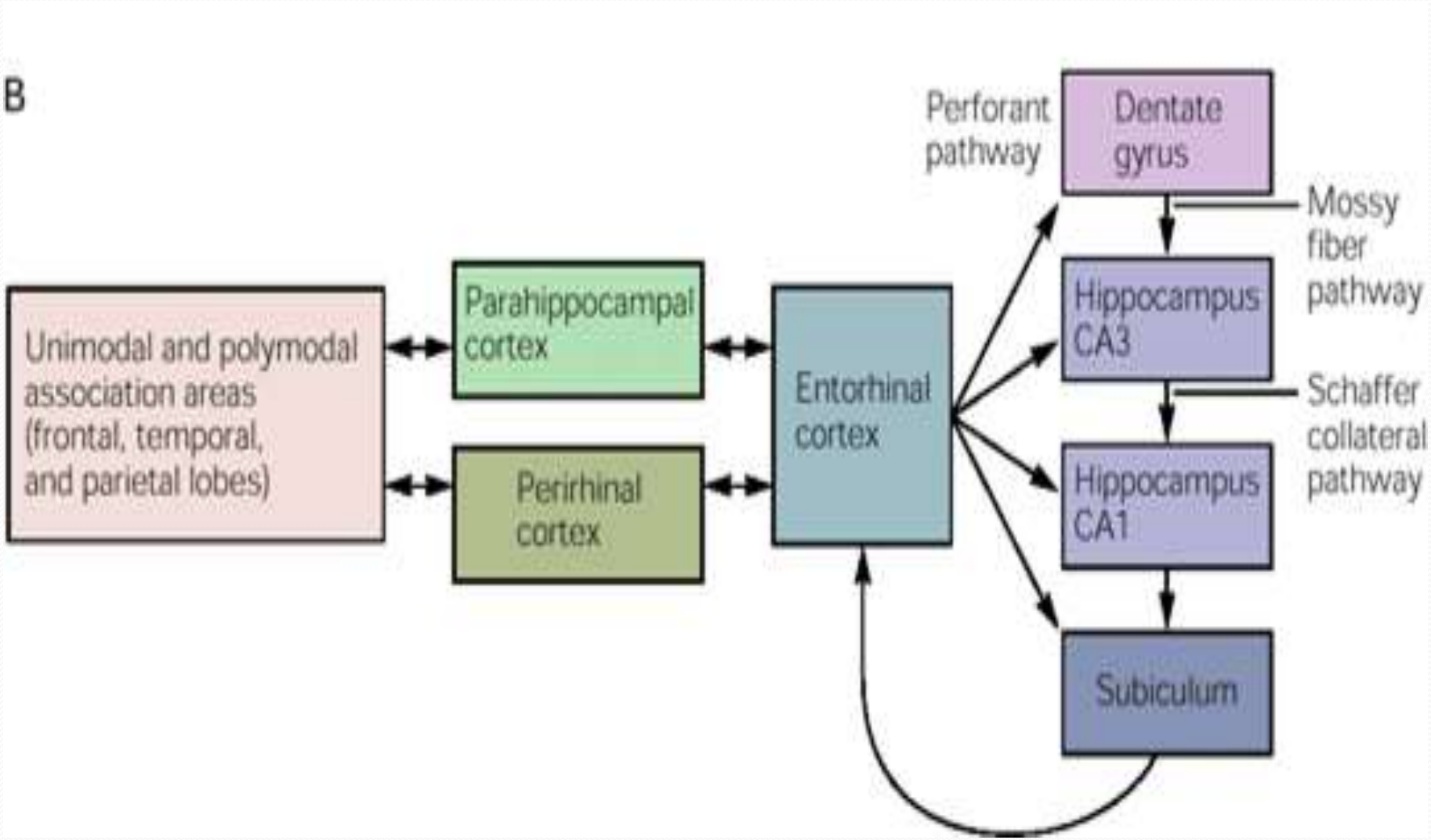
Implicit or Nondeclarative memory

- It is typically involved in training Reflexive motor or perceptual skills.
- Refer to information about how to perform something?
- More rigid.
- It does not involve awareness. Recalled unconsciously.
- Its retention does not usually involve processing in the hippocampus.

Explicit Memory storage



Explicit Memory storage



Entorhinal cortex

- It has dual functions
  - It is the main input to the hippocampus.
  - It is also the major output of the hippocampus.
- The information converges in the entorhinal cortex.
- Damage to it is associated with severe memory impairments.
- Alzheimer's disease, the major degenerative disease affects explicit memory storage, occurs in the entorhinal cortex.

Hippocampus

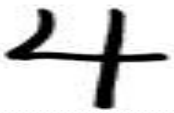
- Temporary way station for long-term memory.
- Imp. in processing storage of memory.
- It is not a place where all Long term memory is stored.
- Hippocampus : object recognition.
- Lesions of the right hippocampus : spatial orientation.
- Lesions of the left hippocampus : defects in verbal memory.
- Hippocampus, perirhinal and para-hippocampal cortices damage—produces clear impairment of explicit memory.
- Amygdala: damage doesn't affect explicit memory, mainly concerned with emotions.

Association area

- Association areas ultimate repositories for explicit memory.
- Damage to these areas result in:
- Inability recall events before damage
- Inability to store new information

- Semantic (factual) knowledge is stored in the **neocortex**. (distributed fashion)
- Episodic knowledge about time and place involves the prefrontal cortex.
- Damage to the posterior parietal cortex: Associative visual agnosia: Inability of patient to name objects but can identify objects. Can copy the drawing but can not name it.
- Damage to the occipital lobes and surrounding region: Apperceptive visual agnosia: Inability to draw objects but can name the objects.

- lesions in the inferotemporal cortex : (FFA of Temporal lobe) Prosopagnosia
- The inability to recognize familiar faces or learn new faces

	Model drawing	Patient's drawing	Verbal identification of object
A Associative agnosia			—
			—
			—
B Apperceptive agnosia			"Circle"
			"Square"
			"Diamond"
			"Three"
			"Four"

Explicit Knowledge Involves Four Distinct Processes

1. Encoding: It is the processes by which newly learned information is attended and processed. Activity in the left prefrontal cortex
2. Consolidation: Long-term storage becomes more stable involving the expression of genes and the synthesis of new proteins.
3. Storage: Mechanism and sites by which memory is retained over time.
4. Retrieval: Permit the recall and use of the stored information. Brings different kinds of information together, stored in different regions.Dependent on short term working memory.

Activity in the right frontal cortex is associated with retrieval

Working Memory: Short-Term Memory Required for Encoding and Recall of Explicit Knowledge.

- Keeps incoming information available for short time, may enter into long term memory.
- 3 components :

1. Central executives located in prefrontal cortex. Actively focuses perception on specific events in environment. (attentional control system)

- two rehersal system in posterior association cortices.

2 Verbal system

3 Visiospatial System

Type of Memory	Region
Priming	Neocortex
Procedural memory	Striatum
Semantic	Neocortex
Episodic	Prefrontal cortex.
Associative visual agnosia	Posterior parietal cortex
Apperceptive visual agnosia	Occipital lobes
Prosopagnosia	Inferotemporal cortex

Implicit Memory

- Implicit memory does not depend on conscious process
- Its recall do not require a conscious search of memory
- Type-
- 1 Priming- Neocortex
- 2 Preocedural skills and habits-Striatum
- 3 Associative learning
  - A. emotional response- Amygdala
  - B Memory through Operent conditioning-Striatum and cerebellum

Applied

- Amnesia : Anterograde & Retrograde Amnesia **Ex** - Korsakoff's Syndrome
- Dementia: Alzheimer's Disease

  Lewy body dementia

  Parkinsonism

  Prion Diseases - Creutzfeldt-Jakob disease
- Dyslexia
- Drug facilitating memory
- Deja - vu - phenomenon

Korsakoff's Syndrome

- (Thiamine (B_6) deficiency)
- Observed in chronic alcoholics
- Prominent anterograde amnesia (declarative memories)
- Severe retrograde amnesia occurs later on in the course of the disorder.
- Damaged areas: Mammilary bodies, mediodorsal thalamus,

  neocortex, hippocampus, & cerebellum.

Alzheimer's Disease

- Memory deterioration greater than normal ageing population
- Eventually loose abilities to perform simple activities.
- Anterograde & Retrograde amnesia for explicit memory
- Progressive loss of short-term memory f/b general loss of cognitive & other brain functions.
- Early changes include atrophy of Hippocampus & Enterorhinal cortex.

Amyloid precursor protein

↓

Abnormally hydrolysed by secretase

↓

Polypeptide 40-42 amino acids

↓

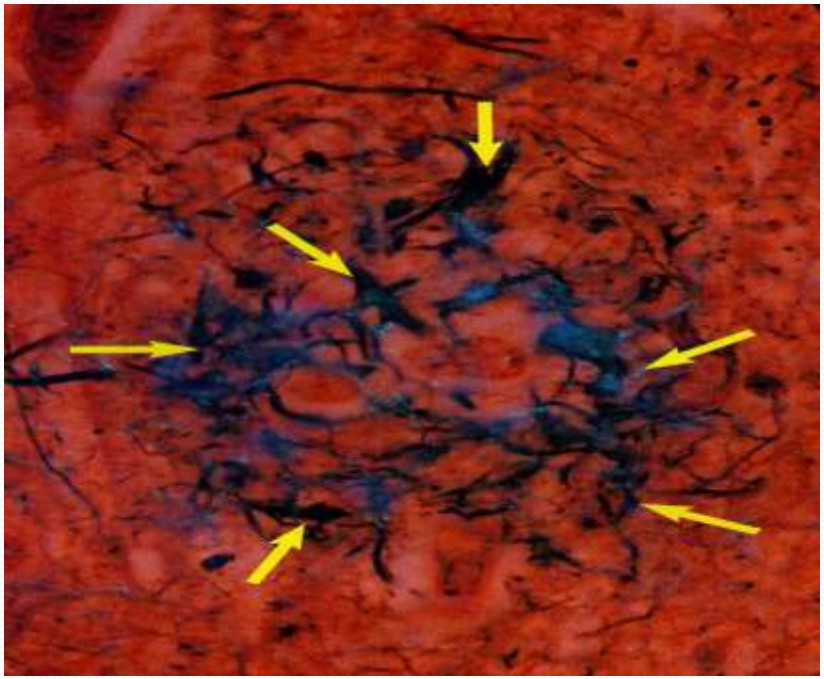
Formation of plaques

↓

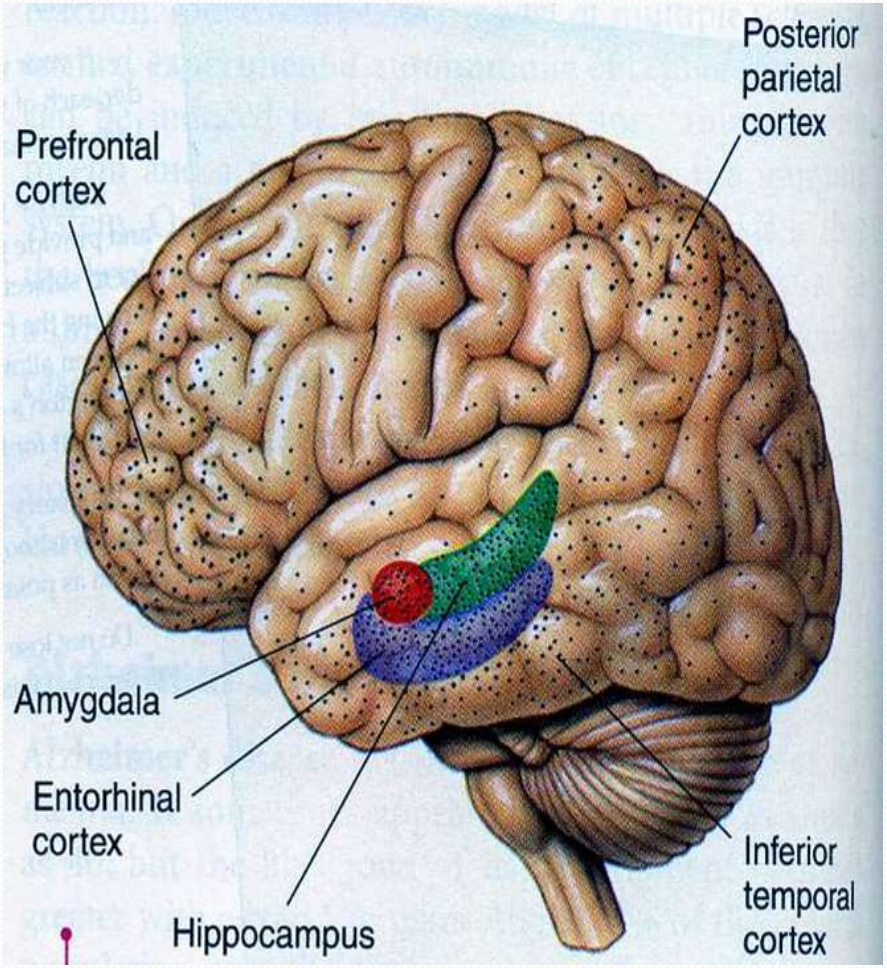
Inflammatory reaction

↓

Formation of neurofibrillary tangels



- Degeneration of acetylcholine-producing cells in basal forebrain
- Senile Amyloid plaques
- Neurofibrillary tangles
  - Twisted fibers within neurons
- Widespread cortical damage

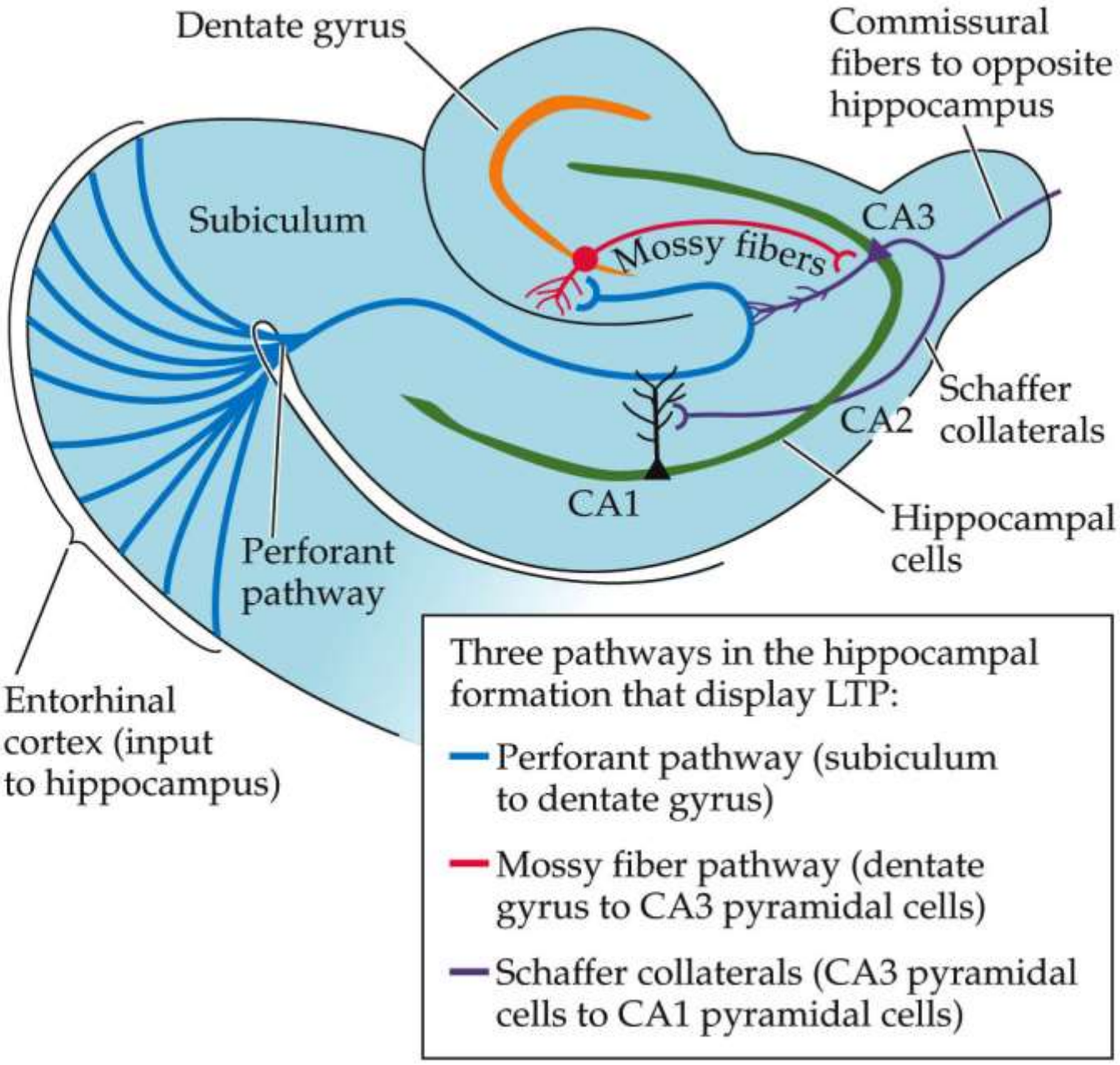


Synaptic plasticity

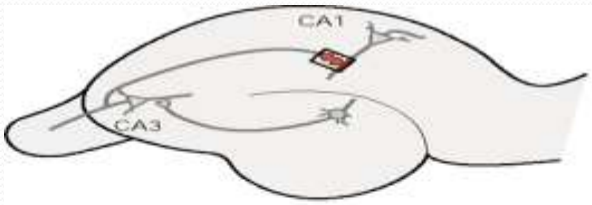
- Strengthening or weakening of synaptic conduction on the basis of past experience and represent forms of learning and memory.
- It can be presynaptic or postsynaptic in location.
- It includes post-tetanic potentiation, LTP, LTD, Habituation & Sensitisation.
- **Posttetanic potentiation:** Enhanced postsynaptic potentials in response to brief (tetanizing) train of stimuli in the presynaptic neuron. This enhancement lasts up to 6o seconds.
- Ca^{2+} accumulates in the presynaptic neuron, intracellular binding sites that keep cytoplasmic Ca^{2+} low are overwhelmed.

Long-term potentiation (LTP)

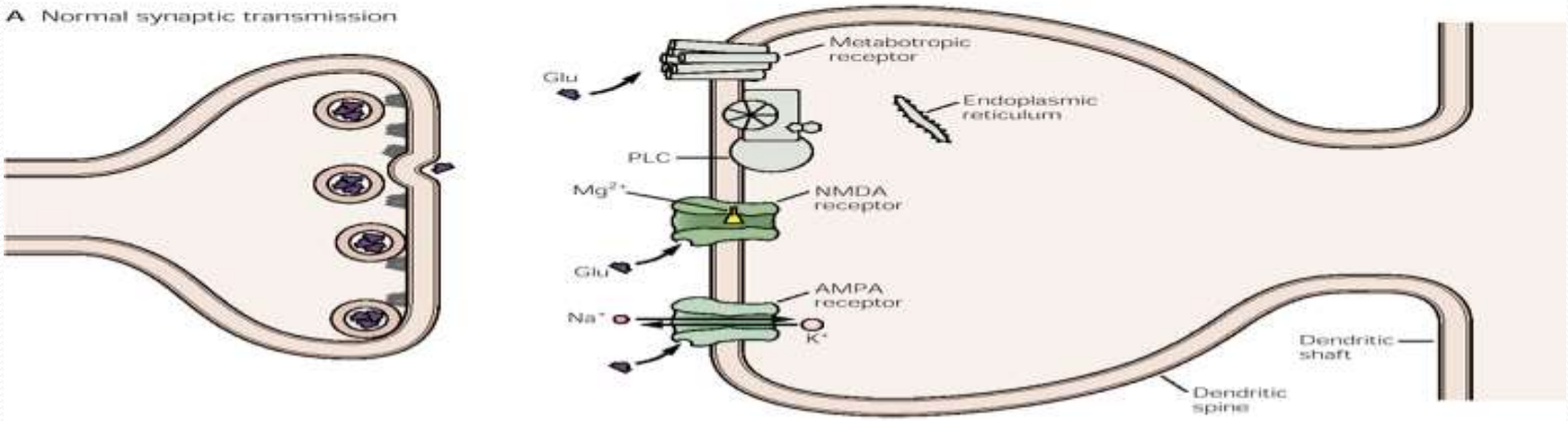
- Rapidly developing persistent enhancement of the postsynaptic potential.
- Growth of the presynaptic and postsynaptic neurons and connections.
- It is much more prolonged and can last for days.
- Initiated by an increase in intracellular Ca^{2+} in the presynaptic or postsynaptic neuron.
- Some mechanism dependent on changes in NMDA receptors.



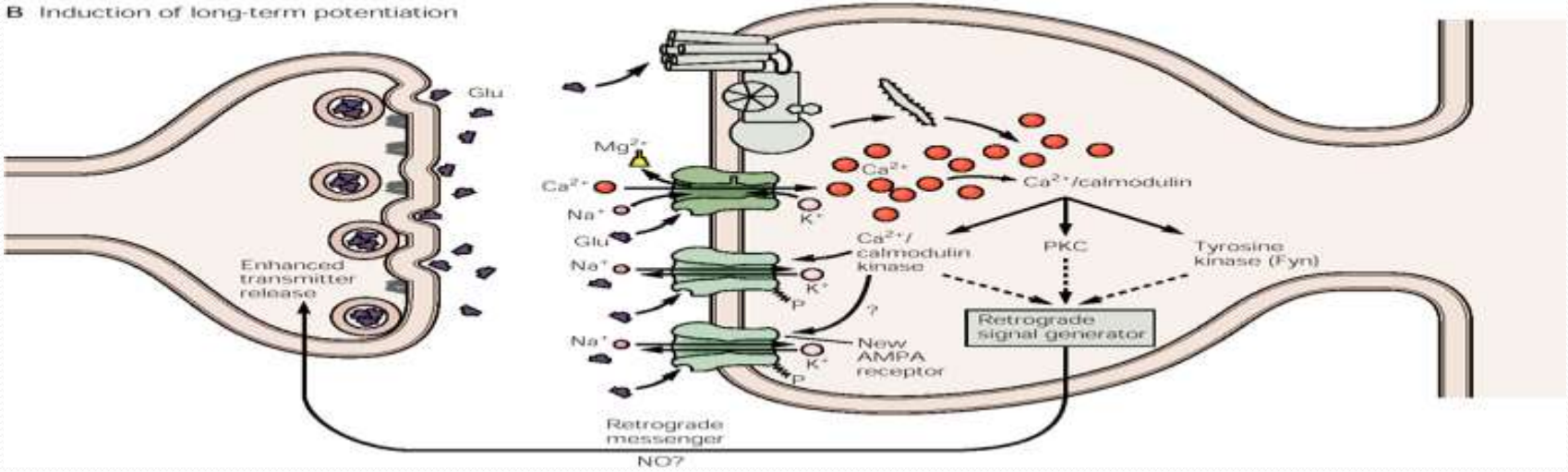
***Biological Psychology 6e*, Figure 17.21 (Part 3)**



A Normal synaptic transmission



B Induction of long-term potentiation



Ca^{2+} influx in presynaptic neuron after tetanus

↓

Activation of Ca^{2+} Calmodulin dependent adenyl cyclase

↓

- Increase cAMP

↓

- Activation of PKA in presynaptic neuron

↓

- Glutamate is released

↓

Acts on NMDA & Non NMDA

Long-term depression

- Decrease in the strength of synaptic connections.

weak impulse

↓

Partial depolarization

↓

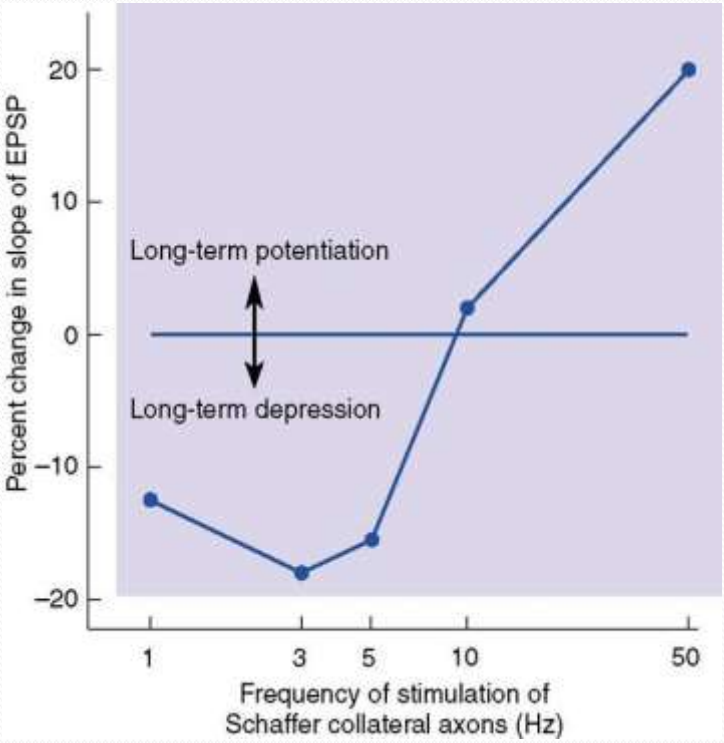
No removal of Mg^{2+} block

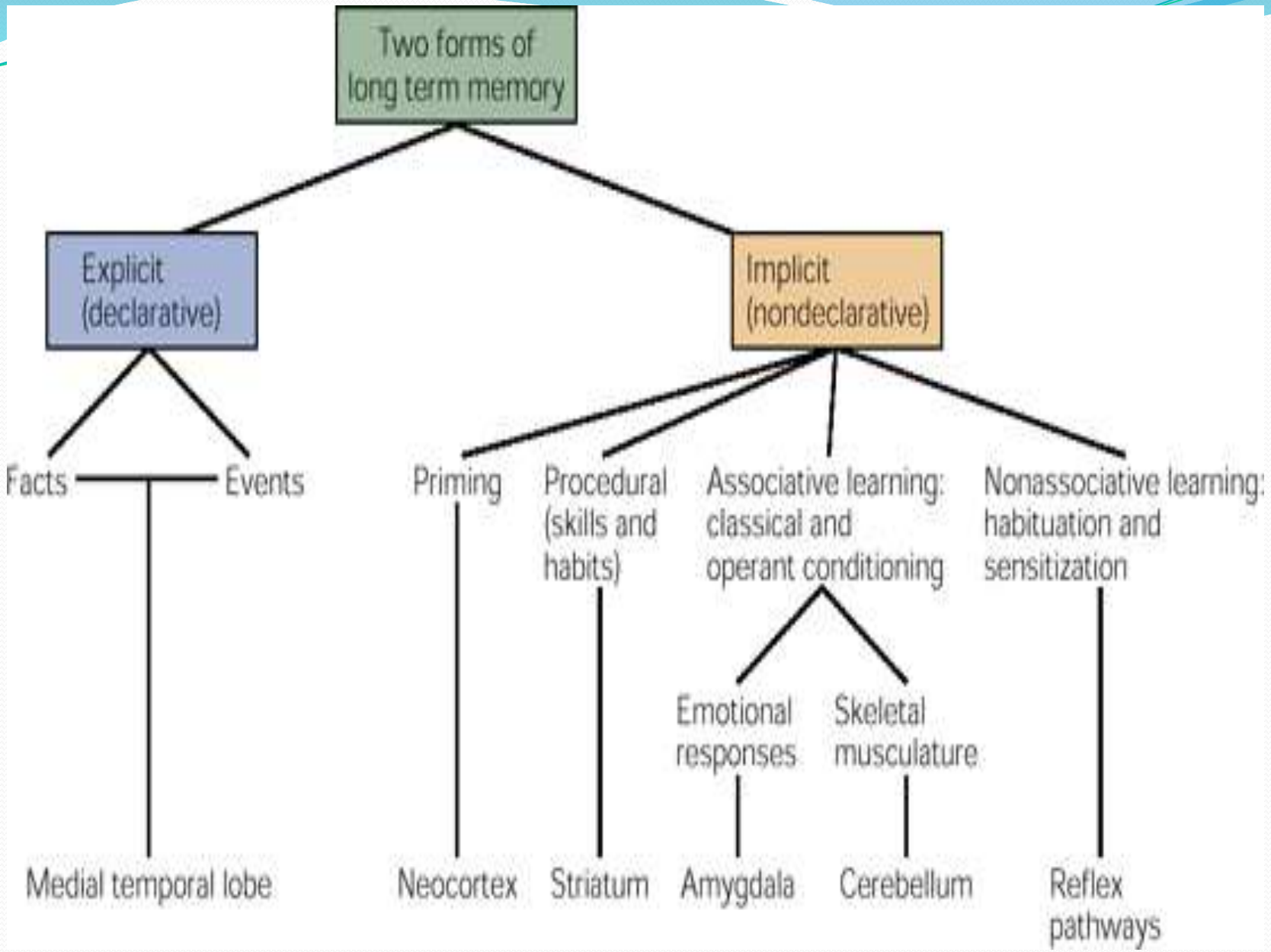
↓

Less entry of Na^{+} & Ca^{2+}

↓

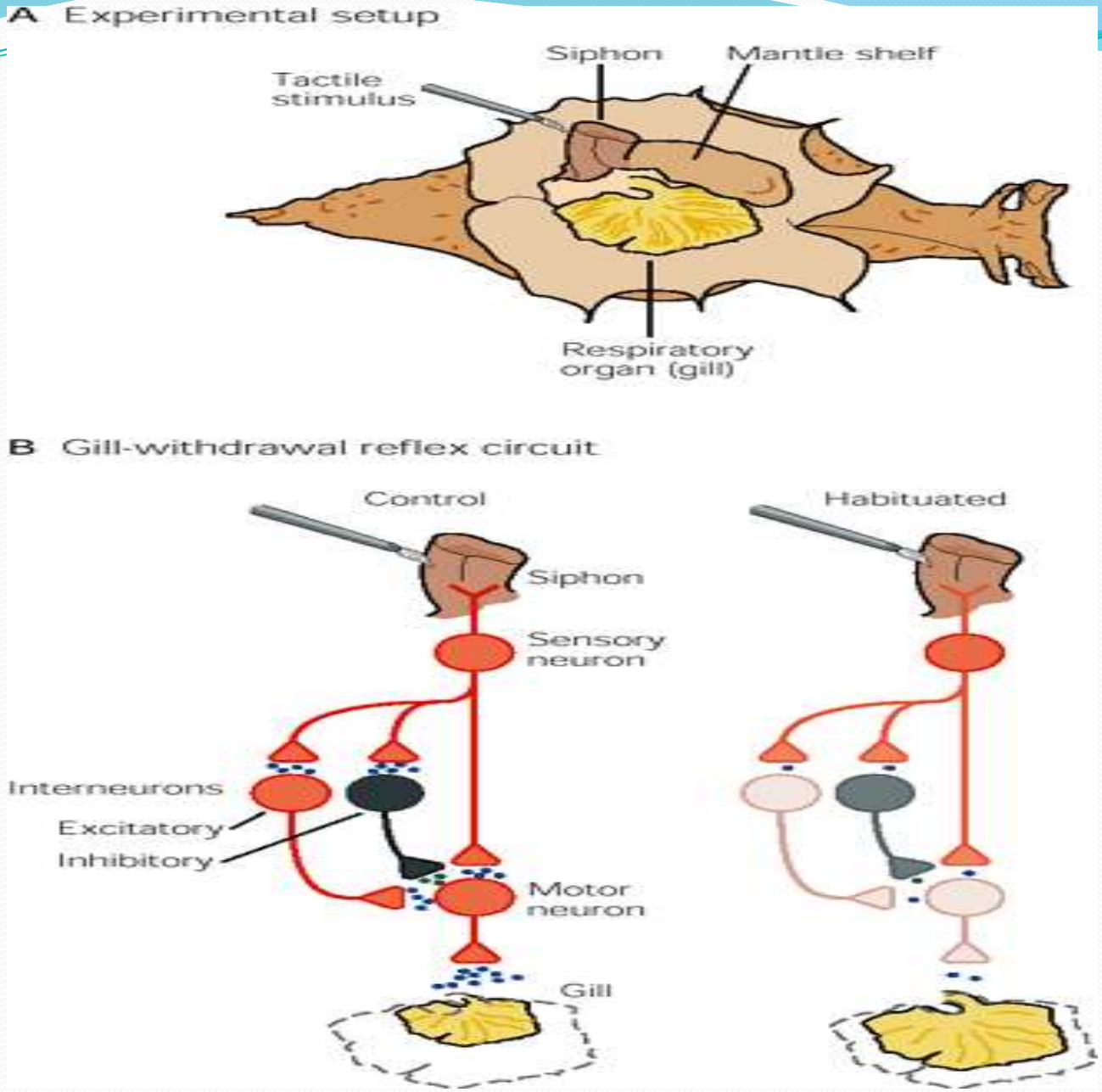
Decrease in EPSP




Two forms of long term memory
Explicit (declarative)
Implicit (nondeclarative)
Facts
Events
Priming
Procedural (skills and habits)
Associative learning: classical and operant conditioning
Nonassociative learning: habituation and sensitization
Emotional responses
Skeletal musculature
Medial temporal lobe
Neocortex
Striatum
Amygdala
Cerebellum
Reflex pathways

Habituation

- It is a simple form of learning
- Decrease in response to a repeated stimulus.
- It involves an activity-dependent presynaptic depression of synaptic transmission.

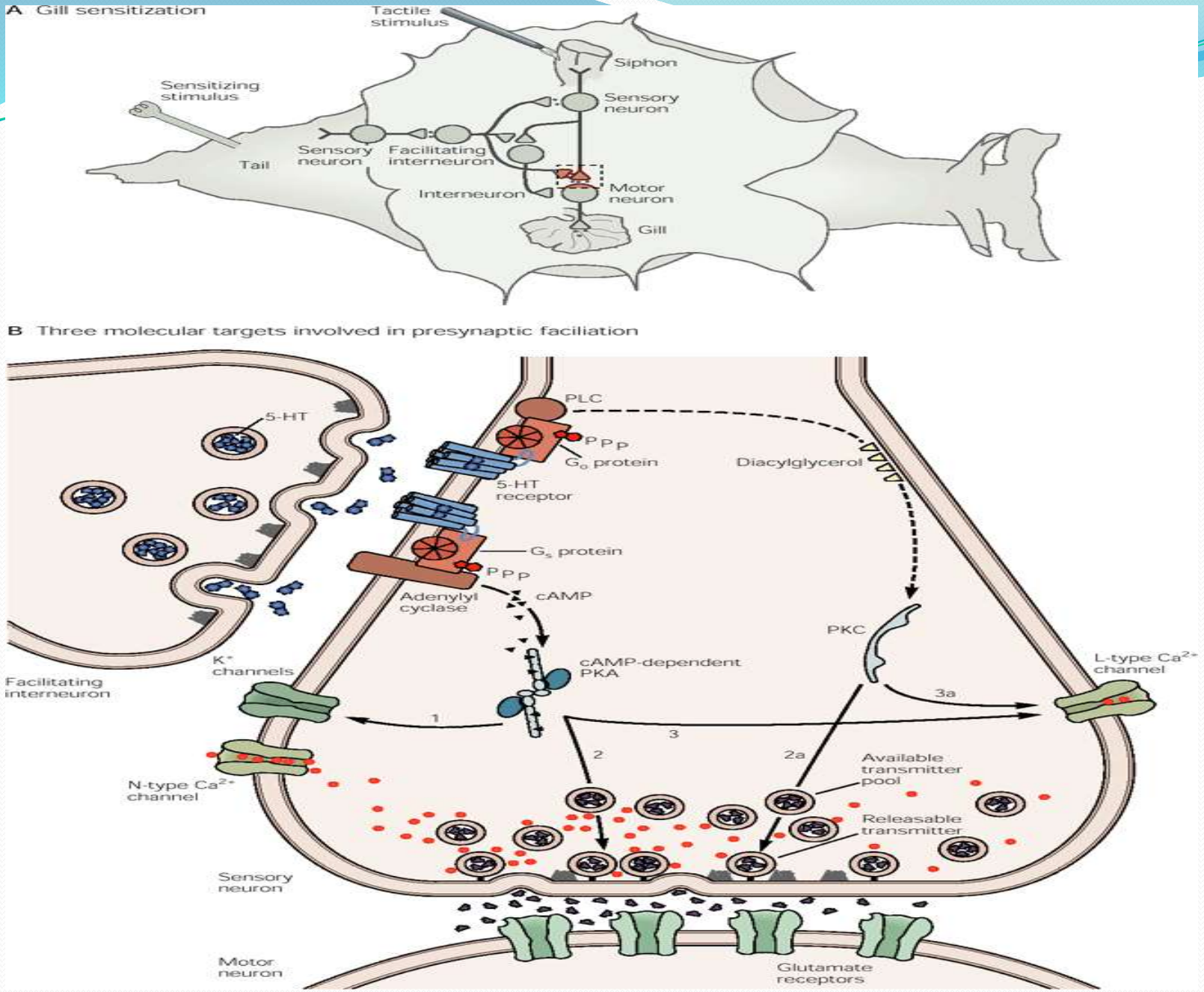

A Experimental setup
Siphon
Mantle shelf
Tactile stimulus
Respiratory organ (gill)
B Gill-withdrawal reflex circuit
Control
Habituated
Siphon
Sensory neuron
Interneurons
Excitatory
Inhibitory
Motor neuron
Gill

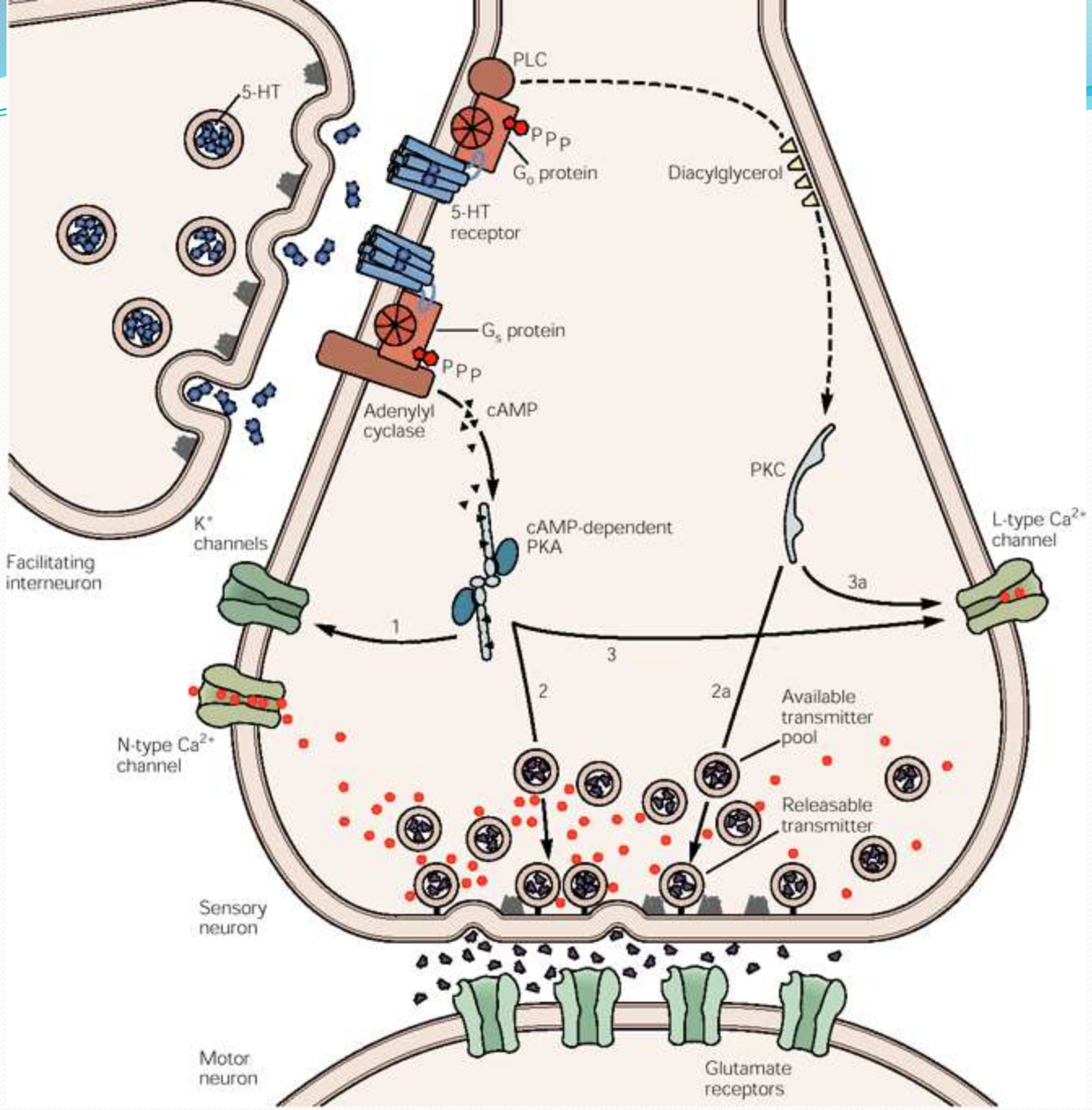
Habituation

- Associated with decreased no. of transmitter vesicles & decrease release of neurotransmitter from the presynaptic terminal.
- Reduced mobilization of transmitter vesicle to active zone.
- Short-term habituation is a homosynaptic process.
- Sensory neuron use glutamate as neurotransmitter.
- But no change in the sensitivity of receptor with habituation.

Sensitization

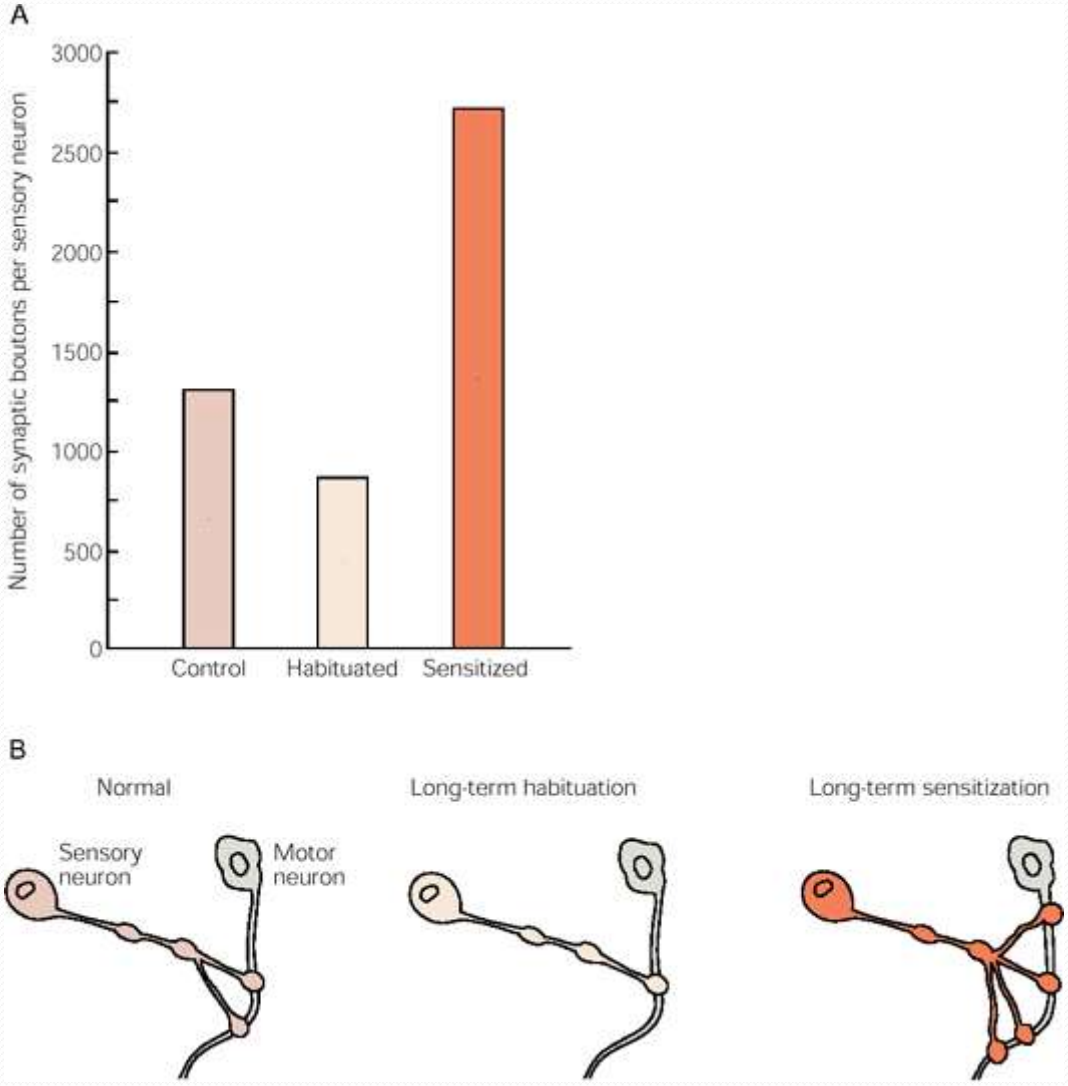
- Short-term sensitization involves presynaptic facilitation.
- Facilitating interneurons causes enhanced release of transmitters from the sensory neurons terminals.
- It is a heterosynaptic process.

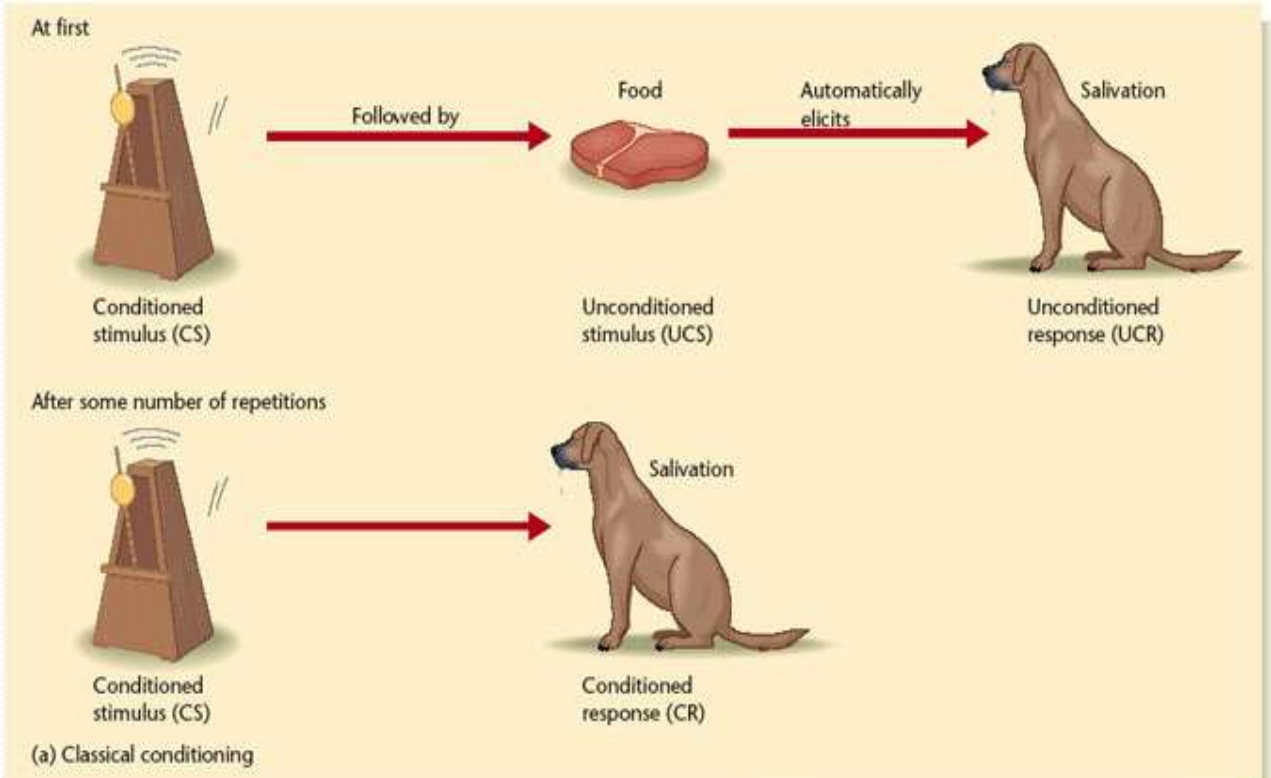

A Gill sensitization
Tactile stimulus
Siphon
Sensitizing stimulus
Sensory neuron
Tail
Sensory neuron
Facilitating interneuron
Interneuron
Motor neuron
Gill
B Three molecular targets involved in presynaptic faciliation
PLC
5-HT
P P P
G_o protein
Diacylglycerol
5-HT receptor
G_s protein
P P P
Adenylyl cyclase
cAMP
PKC
K+ channels
cAMP-dependent PKA
L-type Ca^{2+} channel
Facilitating interneuron
1
2
2a
3
3a
Available transmitter pool
N-type Ca^{2+} channel
Releasable transmitter
Sensory neuron
Motor neuron
Glutamate receptors

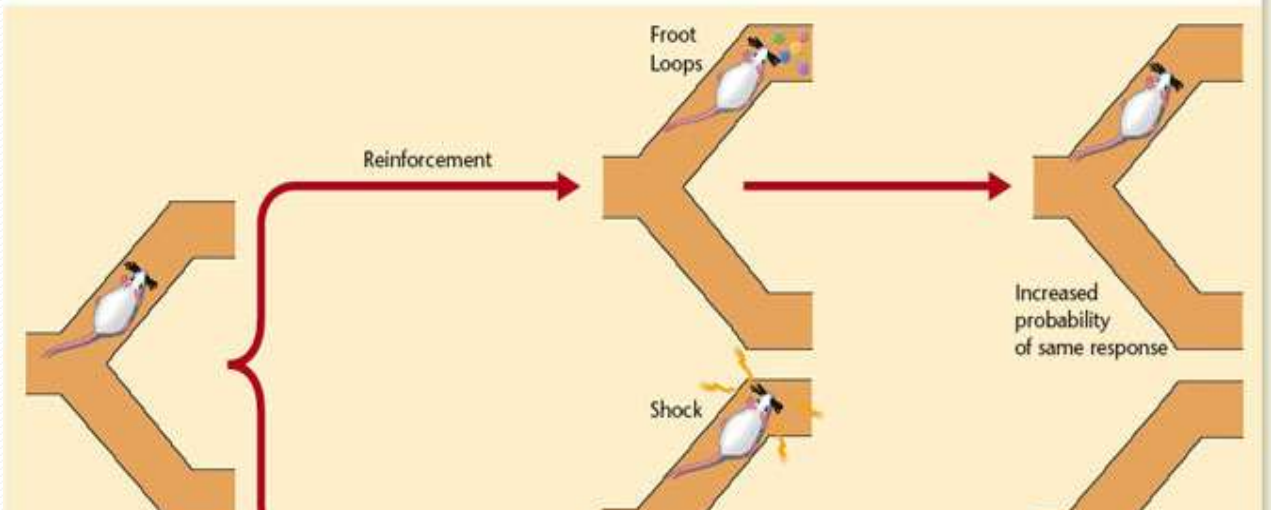

PLC
5-HT
P P P
G_o protein
Diacylglycerol
5-HT receptor
G_s protein
P P P
Adenylyl cyclase
cAMP
PKC
cAMP-dependent PKA
K^+ channels
Facilitating interneuron
L-type Ca^{2+} channel
3a
1
3
2
2a
Available transmitter pool
N-type Ca^{2+} channel
Releasable transmitter
Sensory neuron
Motor neuron
Glutamate receptors

Sensitization

- Associated with increased no. of transmitter vesicles & increase release of neurotransmitter from the presynaptic sensory neuron.
- Increased mobilization of transmitter vesicle to active zone.
- Enhanced efficiency exocytotic release machinery.

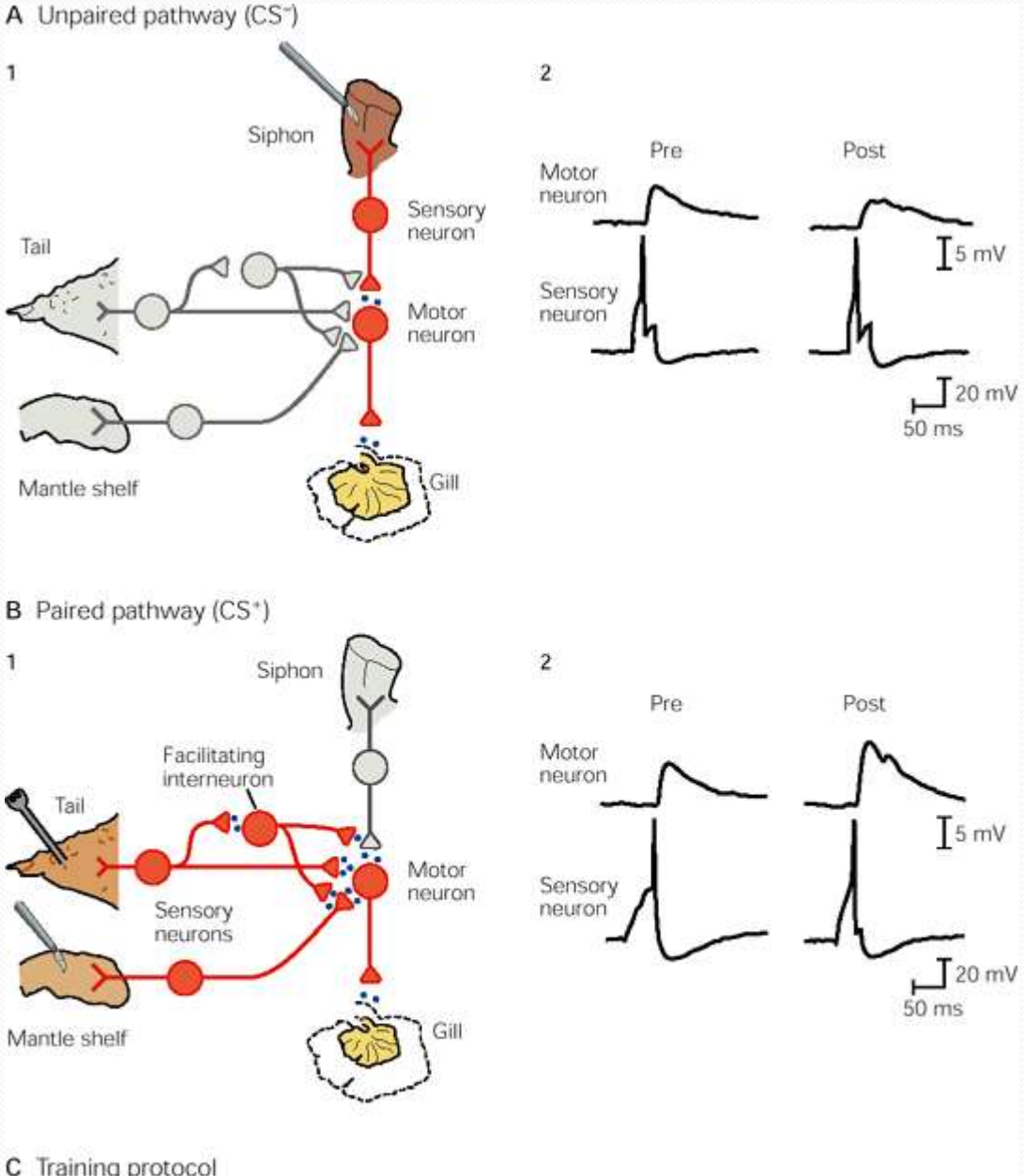

A
Number of synaptic boutons per sensory neuron
3000
2500
2000
1500
1000
500
0
Control
Habituated
Sensitized
B
Normal
Long-term habituation
Long-term sensitization
Sensory neuron
Motor neuron


At first
Followed by
Food
Automatically elicits
Salivation
Conditioned stimulus (CS)
Unconditioned stimulus (UCS)
Unconditioned response (UCR)
After some number of repetitions
Salivation
Conditioned stimulus (CS)
Conditioned response (CR)
(a) Classical conditioning


Froot Loops
Reinforcement
Increased probability of same response
Shock
Decreased probability of same response

- Classical conditioning or Pavlovian conditioning

- Organism learns to associate one type of stimulus with another.
- An initially weak conditioned stimulus can become highly effective in producing a response when paired with a strong unconditioned stimulus.
- Depends on the basis of formation of new functional connections in CNS.
- Conditioned stimulus must precede the unconditioned stimulus
- It involves presynaptic facilitation of synaptic transmission
- Dependent on activity in both the presynaptic and the postsynaptic cell


A Unpaired pathway (CS⁻)
1
Siphon
Sensory neuron
Tail
Motor neuron
Mantle shelf
Gill
2
Pre
Post
Motor neuron
Sensory neuron
5 mV
20 mV
50 ms
B Paired pathway (CS⁺)
1
Siphon
Facilitating interneuron
Tail
Motor neuron
Sensory neurons
Mantle shelf
Gill
2
Pre
Post
Motor neuron
Sensory neuron
5 mV
20 mV
50 ms
C Training protocol

Activity in conditional stimulus

↓

Ca^{2+} influx in presynaptic neuron

↓

Activation of Ca^{2+} binding protein calmodulin.

↓

Ca^{2+} calmodulin binds to Adenylyl Cyclase

↓

Adenylyl cyclase (coincidence detector)

↙ ↘

Increased c AMP Activation of serotonergic receptors

pairing of CS &US

Action potential via Motor neurons

↓

Depolarization of postsynaptic cell

↓

Expulsion of Mg^{2+} from NMDA

↓

Ca^{2+} influx

↓

Retograde messenger

↓

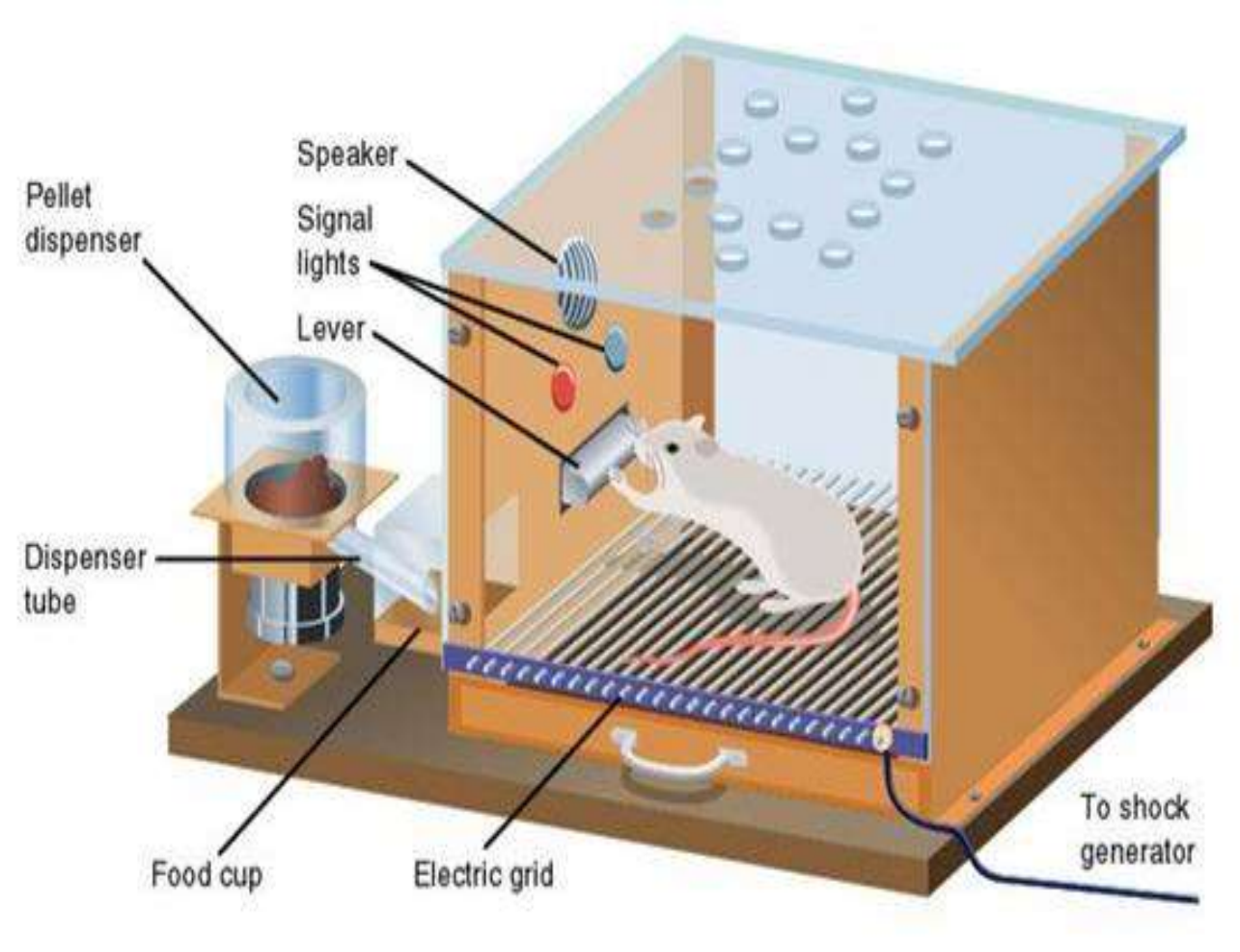
Enhanced release of neurotransmitter

Classical conditioning

- Three signals causes enhanced transmitter release from sensory neuron.
- Activation of Adenylyl cyclase by Ca^{2+} influx : Conditioned stimulus.
- Activation of serotonergic receptors coupled to Adenylyl cyclase : Unconditioned stimulus.
- Retrograde signal indicates activation of postsynaptic cell by Unconditioned stimulus.

Instrumental / Operant Conditioning

- Increa… button again

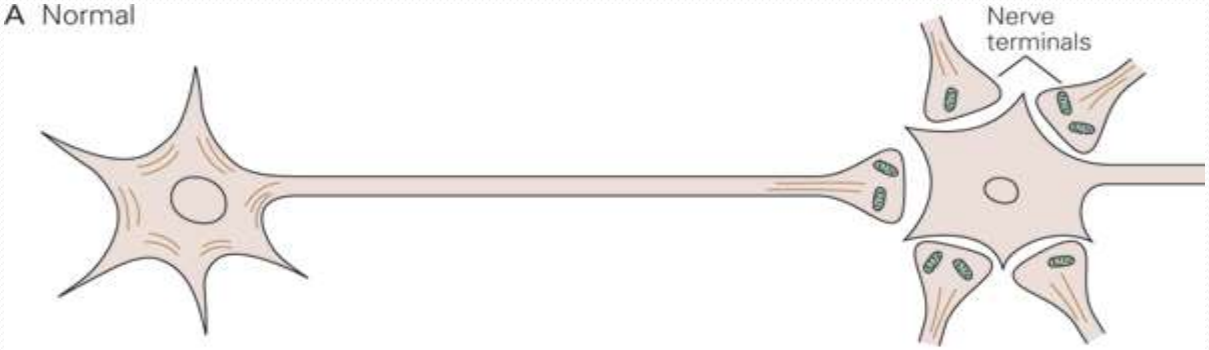


Operant conditioning or Instrumental learning or Trial & Error learning

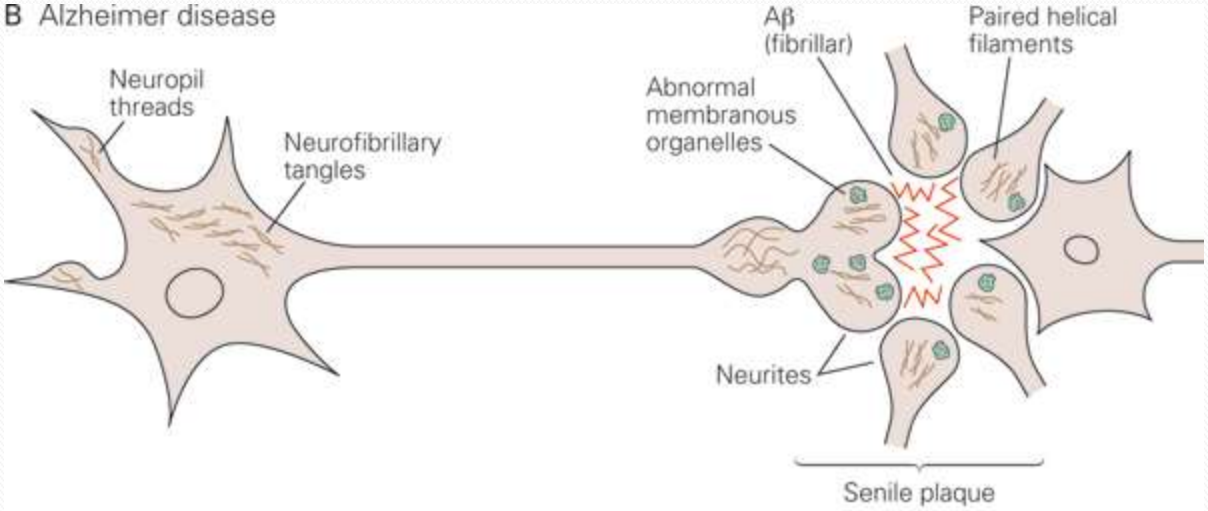
- Involves association of specific behaviour with reinforcement event.
- Reward conditioning: Naturally occurring response strengthened by positive reinforcement.
- Adversive conditioning: Naturally occurring response weakened by negative reinforcement.

Type of Memory	Region
Encoding	Left prefrontal cortex
Consolidation	Hippocampus
Retrieval	Right frontal cortex
Working Memory	Prefrontal cortex
visual image	Extrastriate cortex
spatial image	Parietal cortex
Intercortical transfer of memory	Anterior portion of corpus callosum.

Type of Memory	Region
Object recognition.	Hippocampus
Spatial orientation.	Right hippocampus
Verbal memory.	Left hippocampus
Emotions, fear conditioning	Amygdala
Explicit	Hippocampus, perirhinal and parahippocampal cortices
Operant conditioning	Stritum & cerebellum
Classical conditioning, Habituation, & Sensitisation	Sensory & motor system



Source: Barrett KE, Barman SM, Boitano S, Brooks H: *Ganong's Review of Medical Physiology, 23rd Edition*: http://www.accessmedicine.com



Source: Barrett KE, Barman SM, Boitano S, Brooks H: *Ganong's Review of Medical Physiology, 23rd Edition*: http://www.accessmedicine.com


THANK YOU

Memory can be subdivided into multiple categories

- involve distinct brain regions

Short-term memory

- Prefrontal cortex, sensory association areas

Declarative long-term memory

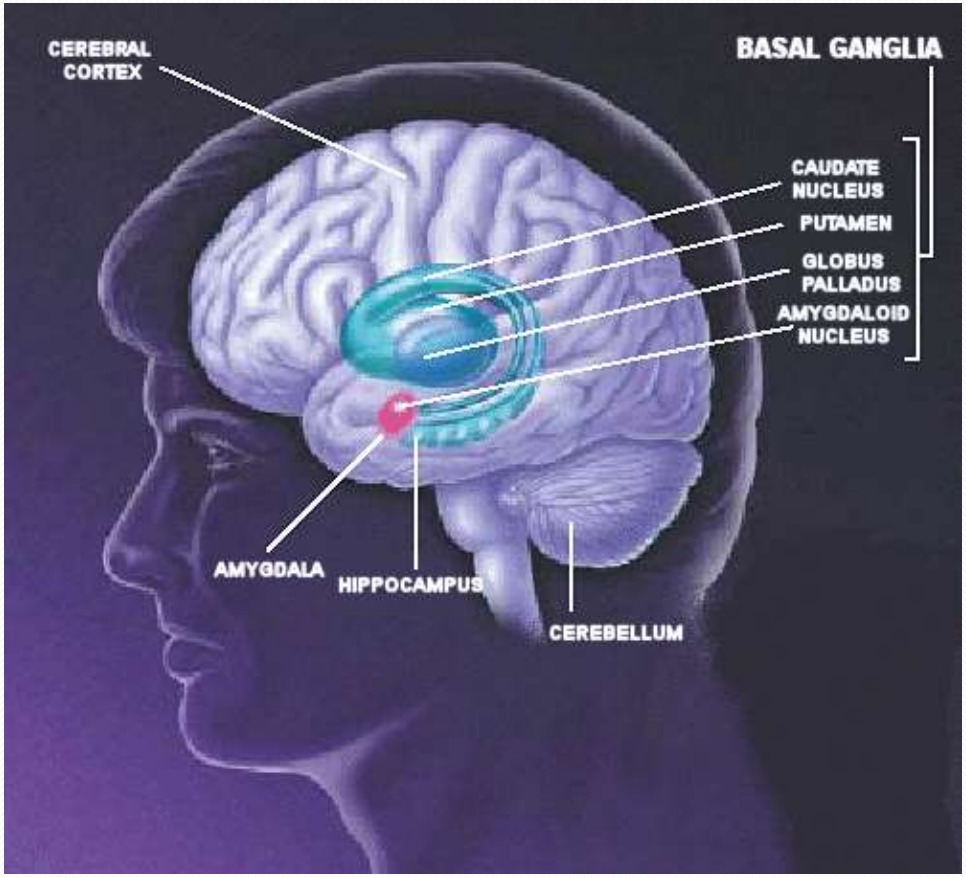
- Hippocampus

Procedural long-term memory

- Basal ganglia, motor association areas, cerebellum

Emotional long-term memory

- Amygdala



- **Priming :** It is recall of words or objects by prior exposure to them. dependent on neocortex. ex- Improved recall of a word when presented with the first few letters of it.
- **Procedural memory** : Includes skills and habits, once acquired, become unconscious and automatic. processed in striatum.
- **Associative learning,** relates to **classical** & **operant conditioning** in which one learns about the relation of one stimulus to another.
- **Nonassociative learning,** includes Habituation & Sensitization. Dependent on various reflex pathways.