# Learning & Memory

- **Learning:**
  Learning is acquisition of new information

- **Memory:**
  Memory is the retention and storage of that information

- **Learning : neural mechanism by which there is change in behavior due to past experience**

# Learning

- “Synaptic plasticity”
- Changes in the synaptic function
- Modification of synaptic transmission is  the basis for learning

1. Incidental learning

2. Reflex learning

# Types of Reflex Learning

1. **Non-associative learning**

2. **Associative learning**

# 1. Non-associative Learning

- Repeated exposure to single type of stimulus
- 2 forms of associative learning:

  - Habituation

  - Sensitization

- Habituation

  - Orientation reflex or ‘what is it’

  **- Cellular basis of habituation:**

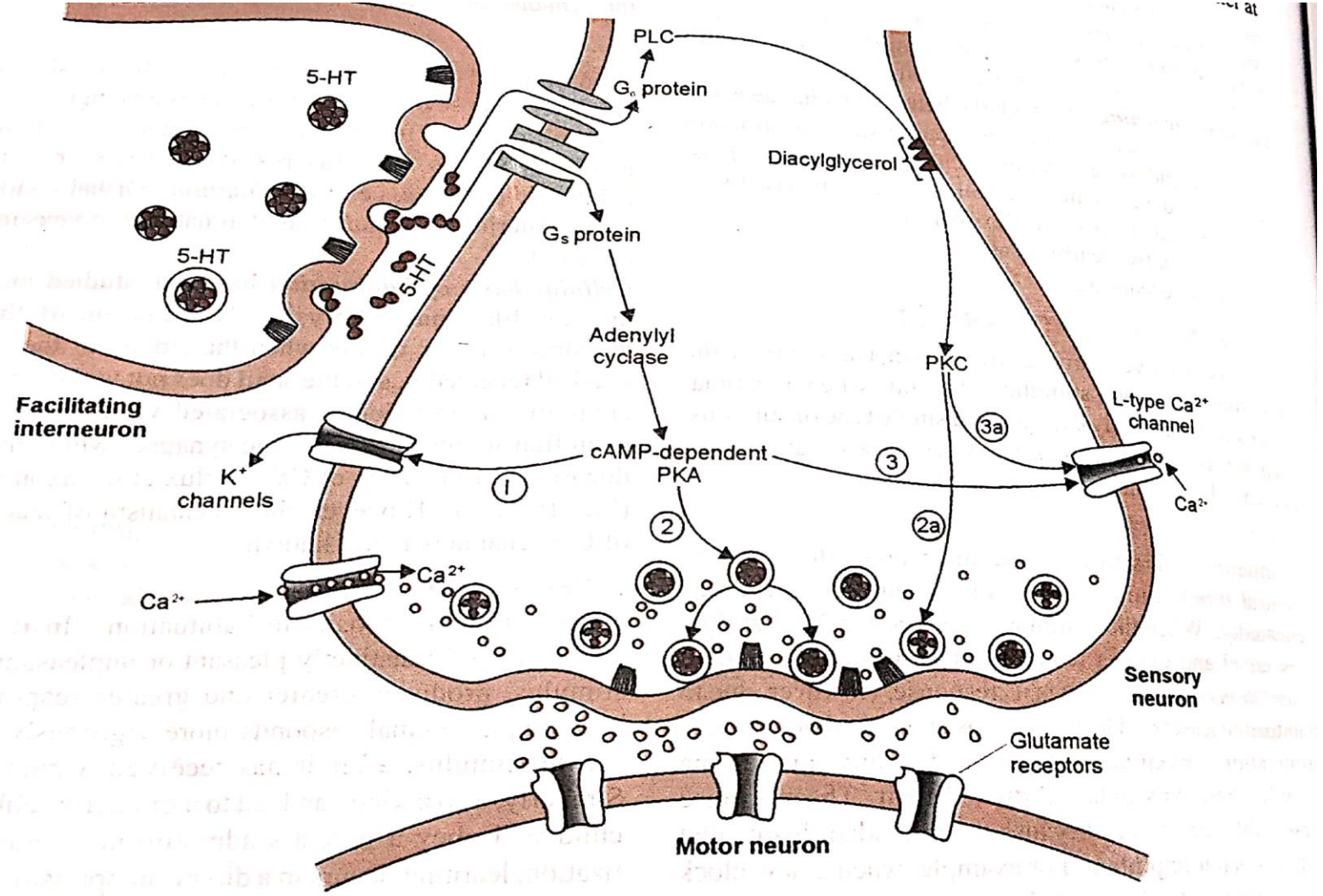
  ? inactivation of calcium channels → decrease release of neurotransmitters

- Sensitization:
  - opposite to habituation
  - Repeated application of distinctly pleasant or unpleasant strong stimulus produces greater and greater response

- **Cellular basis of Sensitization :**

  **increased release of neurotransmitters from axonal endings of sensory neurons due to presynaptic facilitation of synaptic transmission brought about by facilitatory neuron**

# Pathways involved in increase release of neurotransmitter (in sensitization)



# 2. Associative learning

- Learning based on observation
- Repeated observation
- Association or relationship  between 2 events or stimuli
- Cause- effect relationship → change in behavior
- **This type of learning occurs by the " conditioning"  of the animals by paired stimuli**

# Types of conditioning

1. **Classical conditioning/pavlovian conditioning**

2. **Operant conditioning/instrumental conditioning**

# 1. Classical conditioning

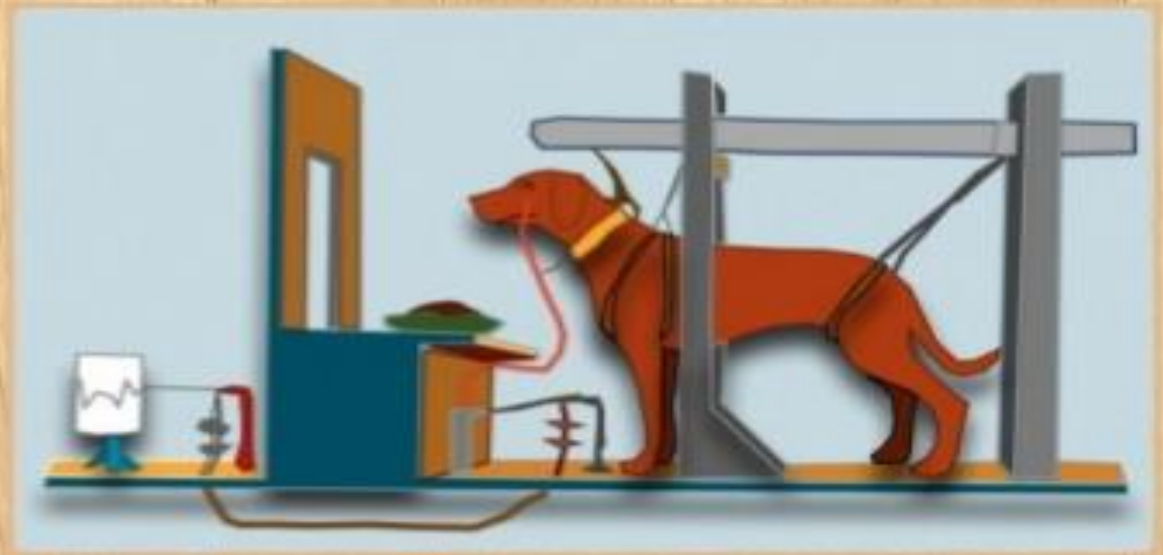
- Classical conditioning involves learning a relationship between two stimuli
- Also termed as
  - Pavlovian conditioning: as type of conditioning was studied by Pavlo in dogs , **Pavlov's conditioned reflex**
  - conditioned reflex type I
  - respondent conditioning
  - type-S conditioning
- Reflex process
- Passive process
- **The reflex response to the conditioned stimulus is called "conditioned reflex"**

# Pavlo’s dog experiment……

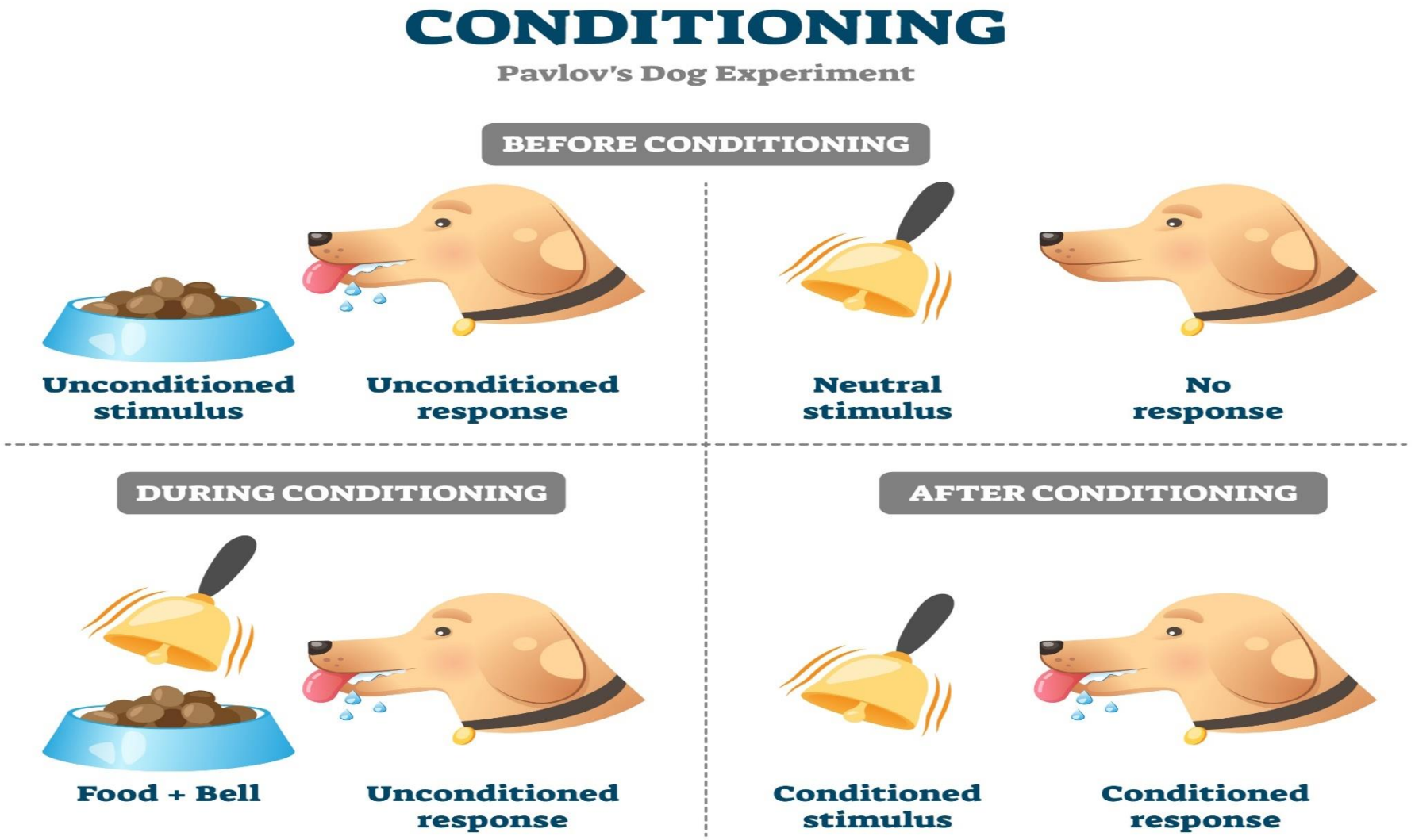
# The "Pavlov's Dog" Experiment

In the 1890s, Russian scientist Ivan Pavlov was studying aspects of the digestive process by observing salivation in dogs, when he made the observation that dogs began to salivate before the food arrived…for example, at the sight of the food tray or sound of the assistant's footsteps.

This work became the foundation for classical conditioning and the behavioral approach to psychology.



# Pavlov’s conditioned reflex



- Pairing of the two stimuli i.e unconditioned stimuli and conditioned stimuli cause animal to learn
- **Internal inhibition or extinction of conditioned reflex**
- **External inhibition of conditioned reflex**
- Reinforcement: process of following a conditioned stimuli with unconditioned stimuli is must for retaining  a conditioned reflex otherwise it will be extinct

# Prerequisites for development of conditioned reflex

1. Alertness and good health
2. Timing of unconditioned stimuli (US) and conditioned stimuli (CS)
3. Duration of conditioned stimulus
4. Reinforcement
5. No external inhibition
6. Type of unconditioned stimuli (US)
7. Pleasant and unpleasant stimulus  versus neutral US

# Physiological basis of conditioned reflex

- Formation of new functional connection in the nervous system
- For example, in Pavlov's classical experiments, salivation in response to ringing of a bell indicates that a functional connection has developed between the auditory pathways and the autonomic centers controlling salivation.

# Cellular mechanism of conditioned reflex

- presynaptic facilitation of synaptic transmission involving both presynaptic and postsynaptic neurons
- Activity dependence: pairing of two stimuli i.e CS & US at a critical interval leads to greater presynaptic facilitation
- Classical conditioning requires the activation of NMDA receptors for glutamate present in motor cell

# 2. Operant conditioning

- "Operate on the environment"
- Form of conditioning in which animal is taught to perform some task, in order to obtain a reward or avoid punishment
- "Active" form of learning
- Unconditioned stimulus is  pleasant or unpleasant event involves associating a specific behavior with a reinforcement event.
- In it the organism's behavior is instrumental in conditioning. Therefore, the organism learns which of its actions are responsible for the occurrence  of reinforcement event.
- Also termed as
  - instrumental conditioning
  - type II conditioning
  - trial and error conditioning
  - type-R conditioning

# Operant conditioning

- **2 types:**

**1. reward conditioning**

positive reinforcement → Reward

**2. aversive conditioning**

negative reinforcement → punishment

# Experiment to demonstrate operant conditioning

A hungry animal (e.g. rat) is placed in a cage with a lever (bars) protruding in the cage.

Because of naturally occurring(innate) response the rat will randomly press the lever.

- If pressing of lever is not associated with any event the pressing of the lever will be at a random rate.

- If pressing a lever is associated with a positive reinforce, i.e. reward (e.g. food) the rate of pressing the lever will be much more than the random rate (*reward conditioning*).

- If pressing of lever is associated with a negative reinforce, i.e. punishment (e.g. electric shock), the lever-pressing rate will be much less than the random rate (*aversive conditioning*).

# Neural mechanism of operant conditioning

- The laws of operant and classical conditioning are quite similar, suggesting that the two forms of learning may use the same neural mechanisms.

- Classical conditioning involves learning an association between two stimuli whereas operant conditioning involves learning the association between a behaviour and a reward

# Memory

- **Memory is learning of information , retention of learned information and then recall it later on conscious or unconscious level**
- Synaptic plasticity or modulation of the synaptic transmission
- Memory refers to the acquisition, storage and retrieval of sensory information; while learning is the change in behaviour based on the sensory information stored in the brain.

# TYPES OF MEMORY

Memory can be classified in two ways:

**I. Physiologically, on the basis of how information is stored and recalled**

- Implicit memory
- Explicit memory

**II. Depending upon permanency of storage memory is:**

**1. Short-term memory,** also termed as primary memory

- lasts for seconds to hours.

**2. Intermediate long-term memory** (or secondary memory)

- lasts for days to weeks but is eventually lost.

**3. Long-term memory** (or tertiary memory)

- which once stored, can be recalled years later or for a lifetime.

# Memory

- **Non-declarative or implicit memory**

  - It is generally unconscious
  - reflexive memory…does not involve awareness
  - does not involve processing in the hippocampus

- **Declarative or explicit memory**

  - Involves conscious recall of events
  - it is for factual knowledge about people , places and things
  - it can be semantic or episodic

# Non-declarative or implicit memory

- refers to the information about how to perform something.
- It does not depend directly on conscious processes nor does recall require a conscious search of memory.
- This type of memory builds up slowly through repetition over many trials and is expressed primarily in performance, not in words.

# Non-declarative or implicit memory

**Examples of implicit memory**

- include motor skills, habits, behavioral reflexes and the learning of certain types of procedures and rules which, once acquired, become unconscious and automatic.
- It also includes priming in which recall of words and objects is improved by prior exposure to them.

- Most forms of implicit memory are acquired through different forms of reflexive learning which comprise:

**1.** Non-associative learning that includes:

- Habituation and
- Sensitization.

**2.** Associative learning that includes:

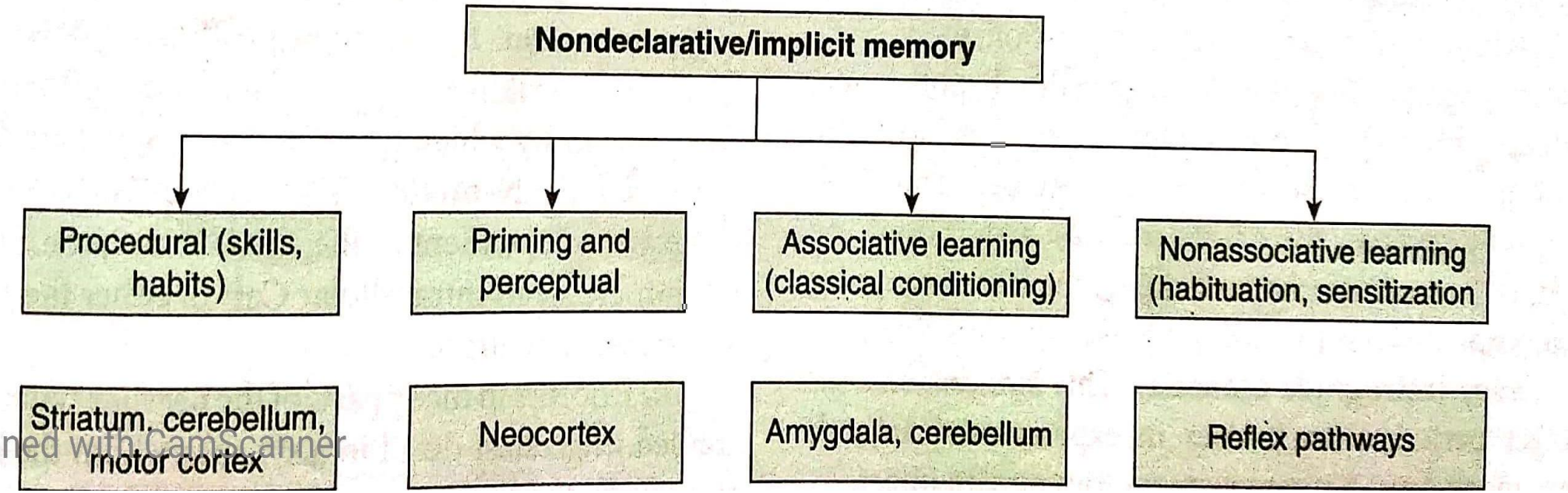
- Classical conditioning and
- Operant conditioning.

# Non-declarative or implicit memory

- Different forms of reflexive learning which comprise

  implicit memory  involve different brain regions:
- Memory acquired through *fear conditioning*, which has an emotional component is thought to involve *amygdala*.
- Memory acquired through *operant conditioning* requires *striatum* and *cerebellum*.
- Memory acquired through classical conditioning, sensitization and habituation involves changes in the sensory and motor systems involved in the learning.

# Forms of implicit memory



# Mechanism of implicit memory

- Most forms of implicit memory are acquired through different forms of reflexive learning (habituation and sensitization), and associative learning (classical and operant conditioning).
- Short-term storage of implicit memory for these simple forms of learning result from *changes in the effectiveness of synaptic transmission*:
- *Cellular basis of habituation*
- *Cellular mechanism of sensitization*
- *Physiological basis and cellular mechanism of classical conditioning*

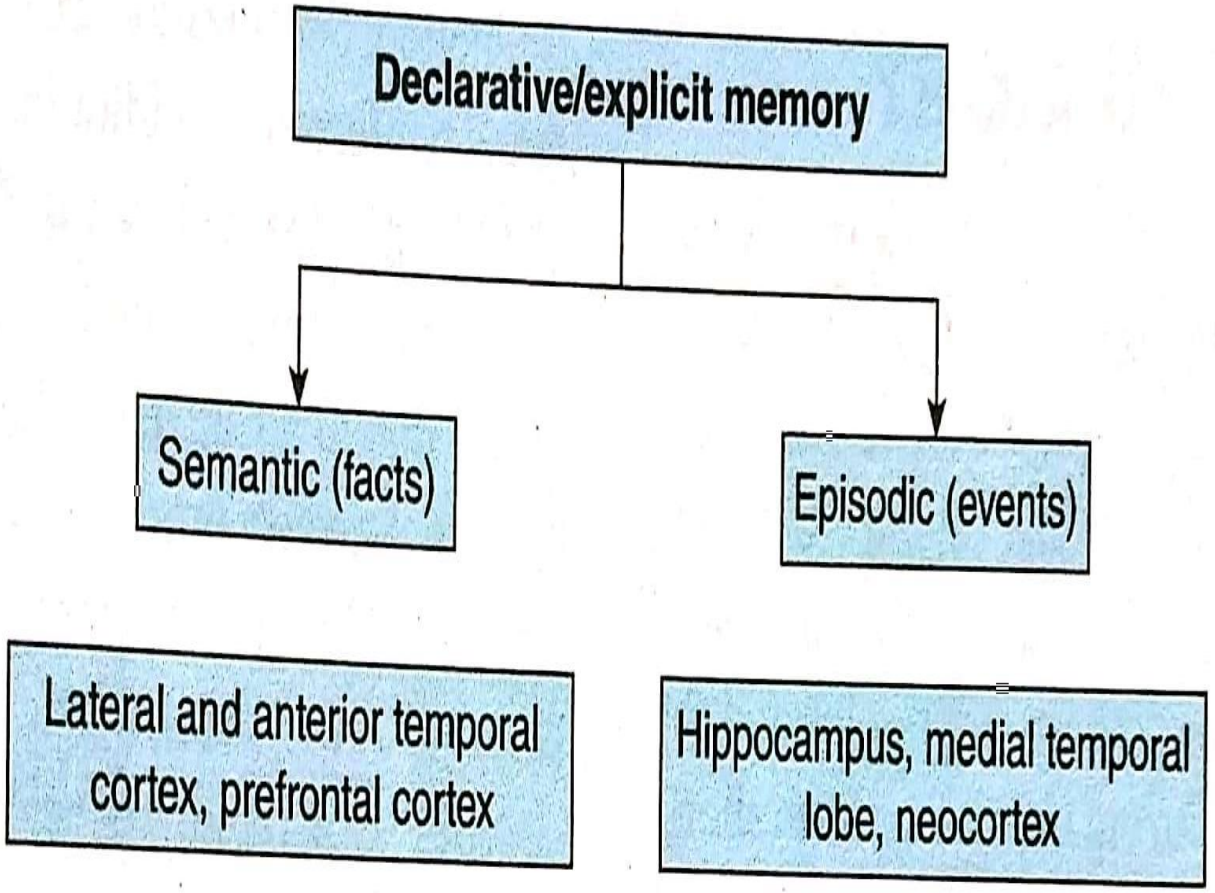
# Mechanism of long-term storage of implicit memory

- **The process by which transient short-term memory is converted into a stable long-term memory is called consolidation.**
- *Consolidation of long-term implicit memory* for simple forms of learning involves three processes:
- Gene expression
- New protein synthesis
- Growth (or prunning) of synaptic connections

# Declarative or Explicit memory

- Explicit memory, also termed as declarative or recognition memory
- refers to the factual knowledge of people, places, things and what these facts mean. This is recalled by a deliberate conscious effort.
- Explicit memory is highly flexible and involves the association of multiple bits and pieces of information.
- In contrast, implicit memory is more rigid and tightly connected to the original stimulus conditions under which the learning occurred.

# Forms of explicit memory



# Semantic (factual) memory

- The semantic memory is that form of long-term explicit memory that embraces knowledge of objects, facts and concepts as well as words and their meaning.
- It includes the naming of objects, the definition of spoken words, and verbal fluency.

# Semantic (factual) memory

- **Semantic memory is stored** in a distributed fashion in different association cortices.
- For example, the word alarm clock, immediately brings its features in our mind from our past experience (stored memory) as follows:
- Visual memory reminds us about its shape, needles depicting hours, minutes and seconds, and markings for 1–12 O'clock hours, etc.
- Auditory memory reminds us about its sound (ringing of alarm);
- Somatosensory memory reminds us that it is made of a plastic or metallic box, having a smooth transparent glass.
- Thus, there is no general semantic memory store, i.e. semantic knowledge is not stored in a single region.

# Episodic (autobiographical) memory

- **Episodic memory refers to memory of events and personal experiences.**
- Episodic memory is stored in association areas of prefrontal cortex.
- These prefrontal areas work with other areas of the neocortex to allow recollection of when and where a past event occurred.
- Therefore, particularly striking symptom in patients with frontal lobe damage is *source amnesia*, i.e. tendency to forget how information was acquired.
- a deficit in source information interferes dramatically with the accuracy of recall of episodic knowledge.

# Declarative or explicit memory

- **Depending on how long a conscious memory last  it is of  3 types:**

1. Short-term memory
2. Intermediate term memory
3. Long-term memory

# Mechanism of Explicit memory

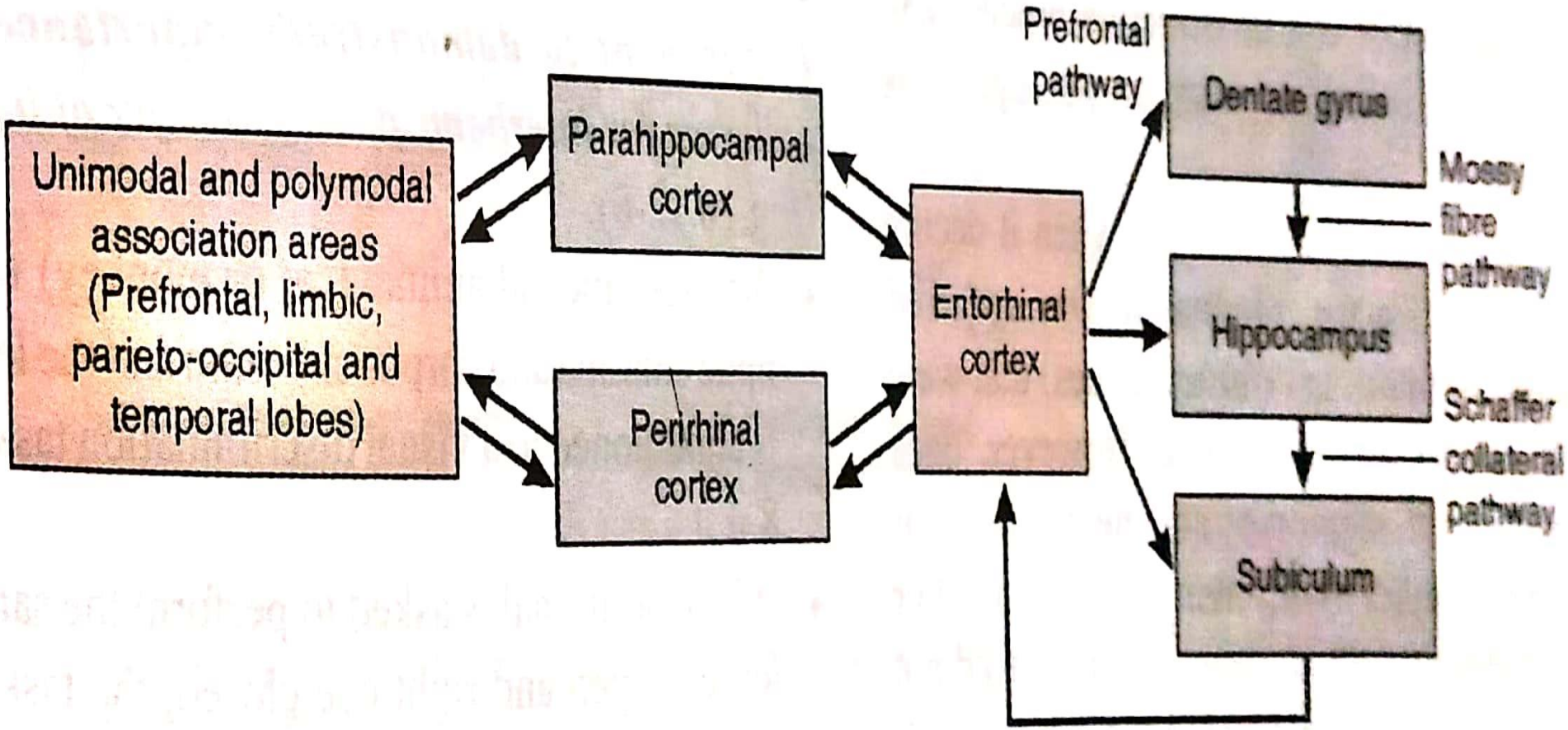
semantic and episodic types of explicit memory are the result of at least four related but distinct types of processing.

- encoding
- consolidation
- storage
- retrieval

# Mechanism of short-term explicit memory

- ***Encoding*** refers to the process by which newly learned information is attended to and processed when first encountered.
- The extent and nature of this encoding are critically important for determining how well the learned material will be remembered at later times.
- For a memory to persist and be well remembered, the incoming information must be encoded thoroughly and deeply.

# Neural substrate for encoding of explicit memory



# Physiological process in neural substrate involved in short-term memory

- Short term memory involves mechanisms that cause immediate recall of events that occurred sometime ago(seconds/minutes/hours)
- **Mechanism:**
  **- Post-tetanic potentiation**
  - repeated quick successive stimuli to particular synapse cause calcium ions to accumulate in the presynaptic neuron → neurotransmitter release by these neurons will be greater as long as calcium content in it is high → response gets potentiated

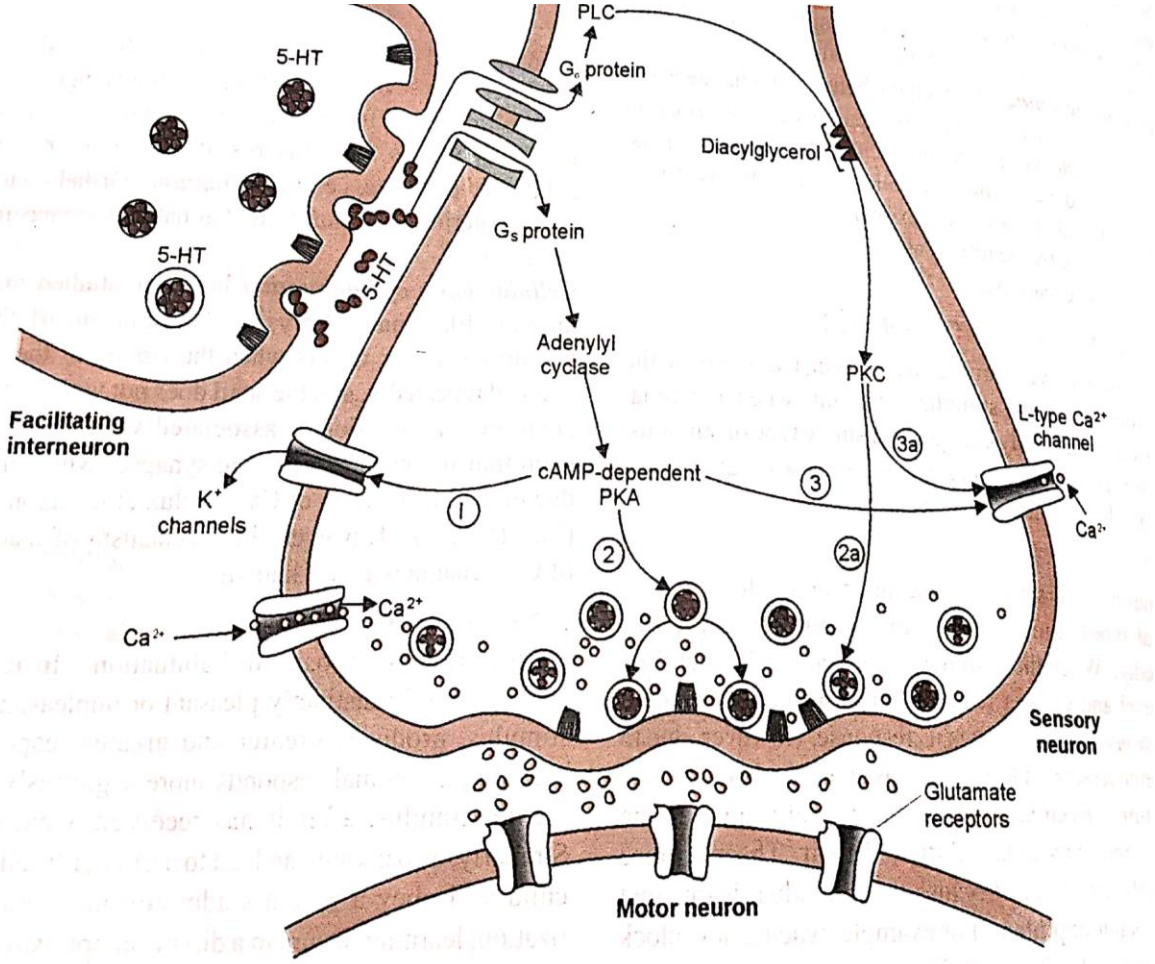
- Continuous neural activity in **reverberating circuits**

- Activation of synapses on pre-synaptic terminals that typically result in **prolonged facilitation, i.e. long-term potentiation or prolonged inhibition i.e. long-term depression**

# Mechanism of Intermediate-term memory

- Intermediate term memory last for several minutes or even weeks
- Eventually it is lost unless it is converted into long term memory(consolidation)
- Facilitation of synapses of the brain
- temporary chemical or physical changes in either the pre-synaptic or post-synaptic membrane that can persist for a few minutes to several weeks.

# Physiological process in neural substrate involved in Intermediate-term memory




**serotonin acts on the presynaptic terminal**

**activation of adenyl cyclase enzyme and formation of cAMP in the neuron**

**Adenyl cyclase activates cAMP dependent protein kinase**

**prolonged facilitation of synaptic transmission**

# Long-term memory

- The events and information can be recalled for years
- For memories to be converted to long-term memories, they must be consolidated.
- **Consolidation refers to those processes that alter the newly stored and still labile information so as to make it more stable for long-term storage.**
- **Minimum time for consolidation is 5-10 minutes and 1 hour for strong consolidation**
- Short-term memory is completely forgotten if consolidation does not happen

# Role of hippocampus in long-term memory

- LTP occurs at the synapses in the hippocampus
- Consolidation and storage of memory occurs here
- Neurons projecting from other parts of the brain to hippocampus release glutamate as neurotransmitter
- Glutamate acts on NDMA receptors → increased entry of calcium ions in the post-synaptic neurons

# Production of LTP in Hippocampus in Schaffer collateral

Glutamate released from presynaptic neuron

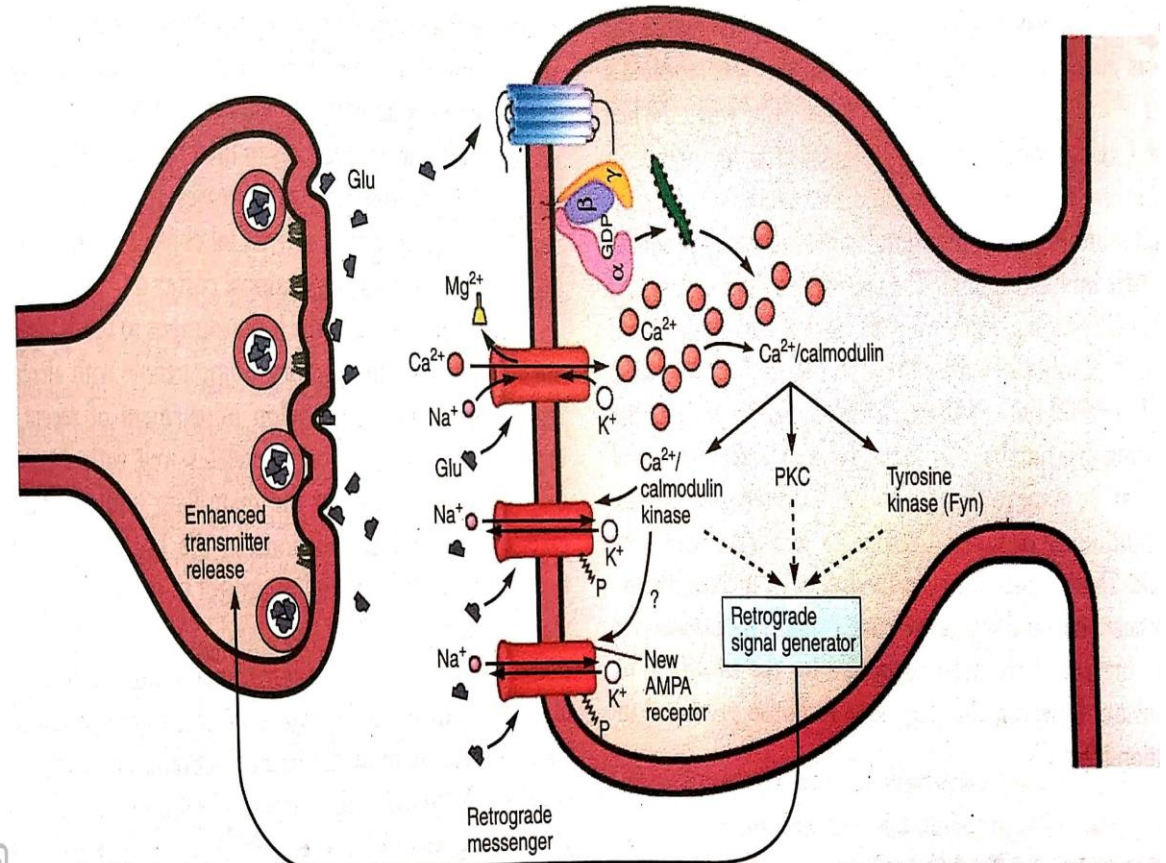
Glutamate binds to AMPA & NMDA receptors in membrane of post-synaptic neuron

Depolarization is triggered by activation of AMPA receptors relieves the Mg block on NMDA receptor

Entry of calcium along with sodium in the neuron

Increase cytoplasmic calcium activates calcium/calmodulin kinase ,PKC,Tyrosine kinase which leads to long term potentiation

- **Connection of a pyramidal cell in CA3 region & pyramidal cell in CA1 region via Schaffer collaterals**



# Long-term memory

- Process of consolidation involves the expression of genes and synthesis of new proteins, giving rise to structural changes

- Structural and functional changes at the synapses lead to facilitation of synaptic transmission on a long term basis

- **Structural changes:**

1. An increase in the number of synaptic vesicle release sites,
2. An increase in the number of available synaptic vesicles,
3. An increase in the number of synaptic terminals and
4. Changes in the shape or number of postsynaptic spines.

- ***Rehearsal mechanism*** is thought to represent the consolidation
- *Rehearsal mechanism* is thought to represent the consolidation process.
- Rehearsal of the same information again and again in the mind potentiates the transfer from short-term to long-term memory.

# APPLIED ASPECTS

- In patients with concussion injury and after electro-convulsive therapy (ECT), who are unable to recall the events immediately preceding the concussion or convulsion. This phenomenon is called ***retrograde amnesia*.**
- A similar retrograde amnesia occurs before the onset of sleep. This is the reason one is unable to remember the precise time of one's own sleep onset.

# HM the most important patient in the history of brain science

- Henry Gustao Molaison….defining link between Brain Function and Memory
- http://www.npr.org/templates/story/story.php?storyId=7584970

- ***Storage of memory*** refers to the mechanism and sites by which memory is retained over time.
- One of the remarkable feature about long-term storage is that it seems to have an almost unlimited capacity.
- In contrast short-term working memory is very limited.

- **Retrieval of memory**
- Retrieval refers to those processes that permit the recall and use of stored information.
- Retrieval involves bringing different kinds of information together that are stored separately in different storage sites.

# Working memory

- special short-term memory store called *working memory*.

Working memory has three component systems:

- Attention control system,
- Rehearsal systems that include:

– Articulatory loop

– Visuospatial sketch pad.

- ***Attentional control system*** or (central executive) actively focuses perception on specific events in the environment.
- It is located in the prefrontal cortex and has a very limited capacity (less than a dozen items).
- It regulates the information flow to two rehearsal systems that are thought to maintain memory for temporary use

# **Rehearsal systems** include the articulatory loop and the visuospatial sketch pad.

- **Articulatory loop** is a storage system where memory for words and numbers can be maintained by subvocal speech.

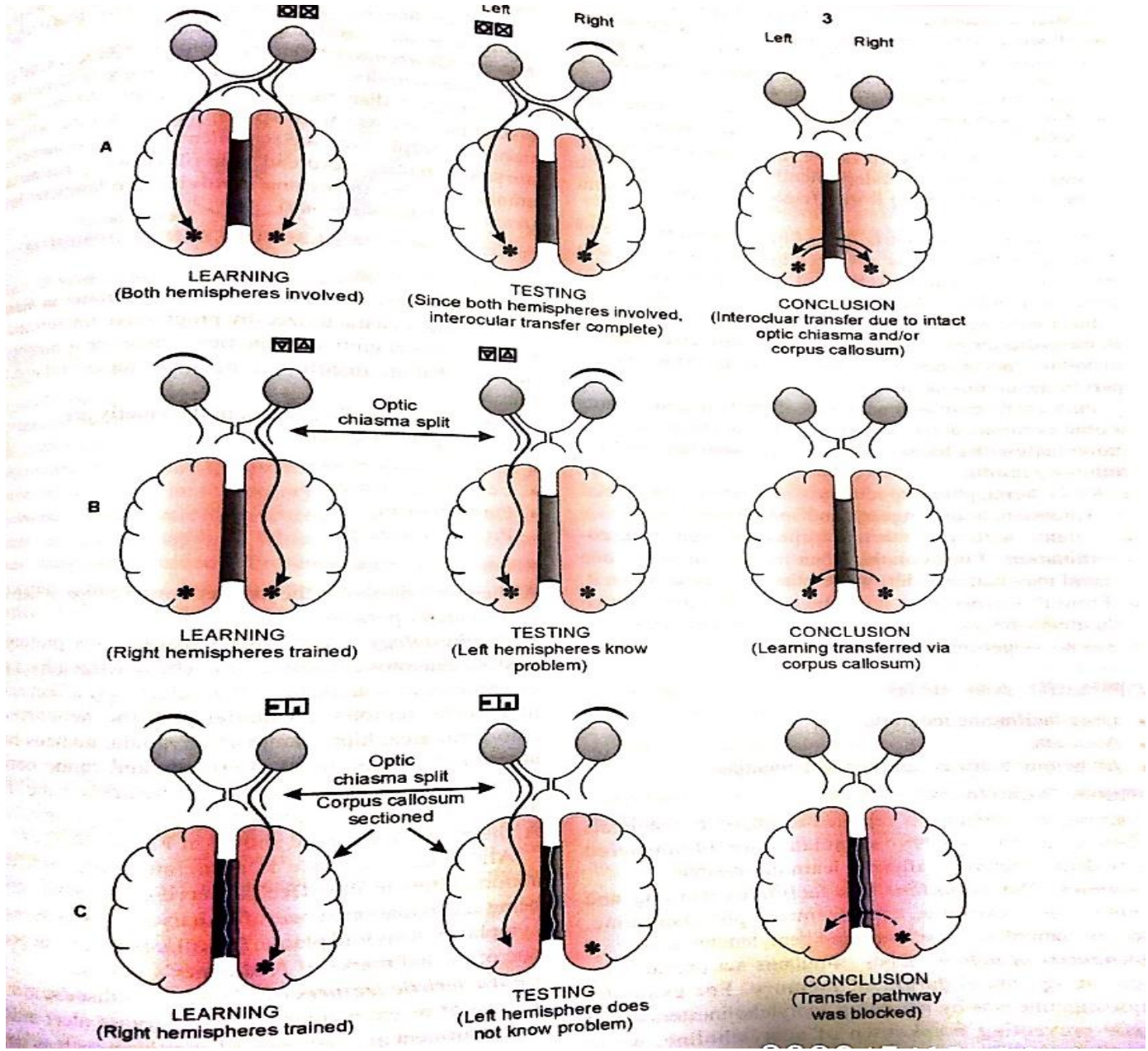
  - It is this system that allows one to hold in mind, through repetition, i.e. a new telephone number as one prepares to dial it.

- **Visuospatial sketch pad** represents both the visual properties and the spatial location of object to be remembered.

  - This system, allows one to store the image of the face of a person one meets

# INTER-HEMISPHERIC TRANSFER OF LEARNING AND MEMORY

- Most information is transferred between the two hemispheres through the corpus callosum
- some is transmitted through other commissures (e.g. the anterior commissure or hippocampal commissure)
- Studies in subject indicate that the transfer of visual memory occurs in the posterior part of the corpus callosum, while transfer of auditory and somaesthetic memory occurs in the anterior part of the corpus callosum.


A
LEARNING
(Both hemispheres involved)
Left
Right
TESTING
(Since both hemispheres involved, interocular transfer complete)
3
Left
Right
CONCLUSION
(Interocluar transfer due to intact optic chiasma and/or corpus callosum)
B
Optic chiasma split
LEARNING
(Right hemispheres trained)
TESTING
(Left hemispheres know problem)
CONCLUSION
(Learning transferred via corpus callosum)
C
Optic chiasma split
Corpus callosum sectioned
LEARNING
(Right hemispheres trained)
TESTING
(Left hemisphere does not know problem)
CONCLUSION
(Transfer pathway was blocked)

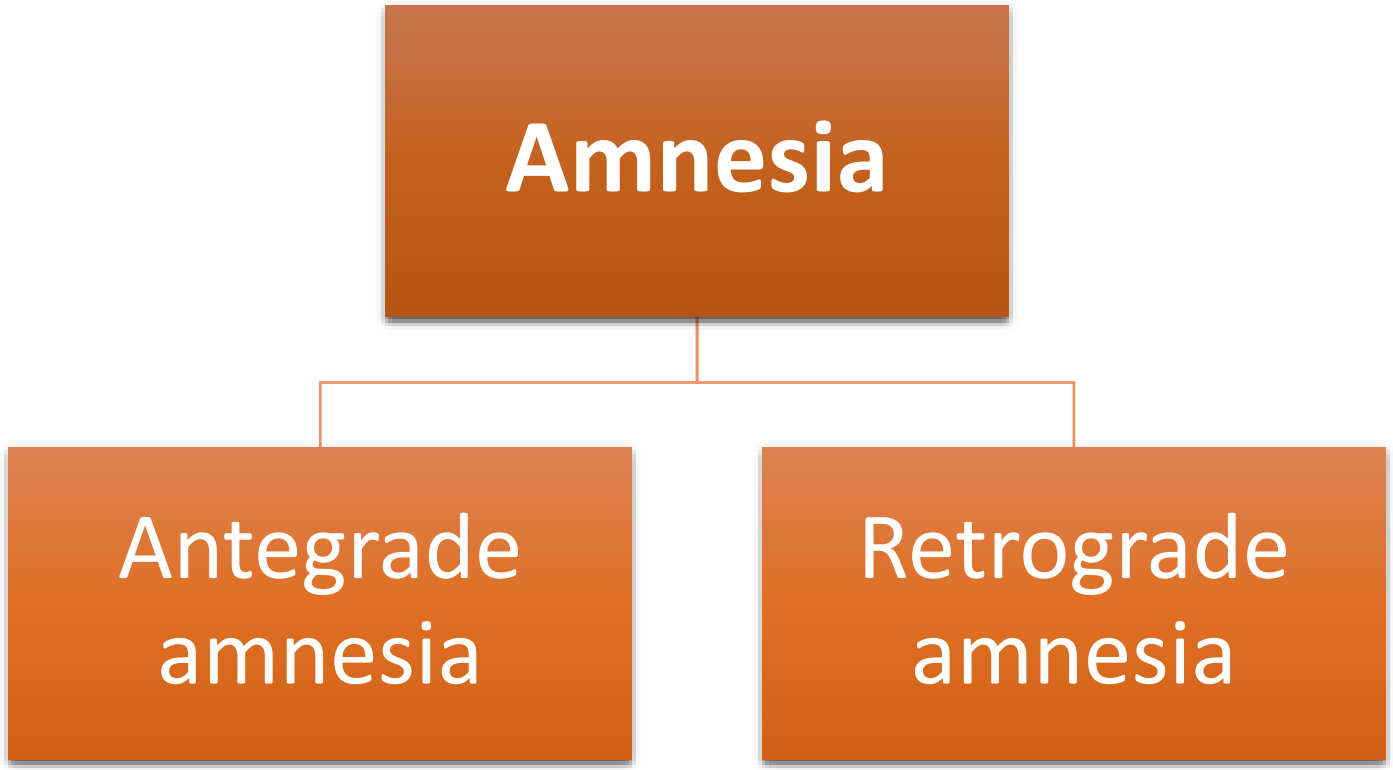
- Right hemisphere specializes in spatial task, facial expression, body language and speech into notion.
- Patients with a transected corpus callosum lack coordination.

  For example,
  when they are dressing, one hand may button a shirt while other tries to unbutton it.

# APPLIED ASPECTS

- **Amnesia**
- **Alzheimer’s disease and senile dementia.**
- **Drug facilitating memory**

# Amnesia refers to the loss of memory.



## Antegrade amnesia

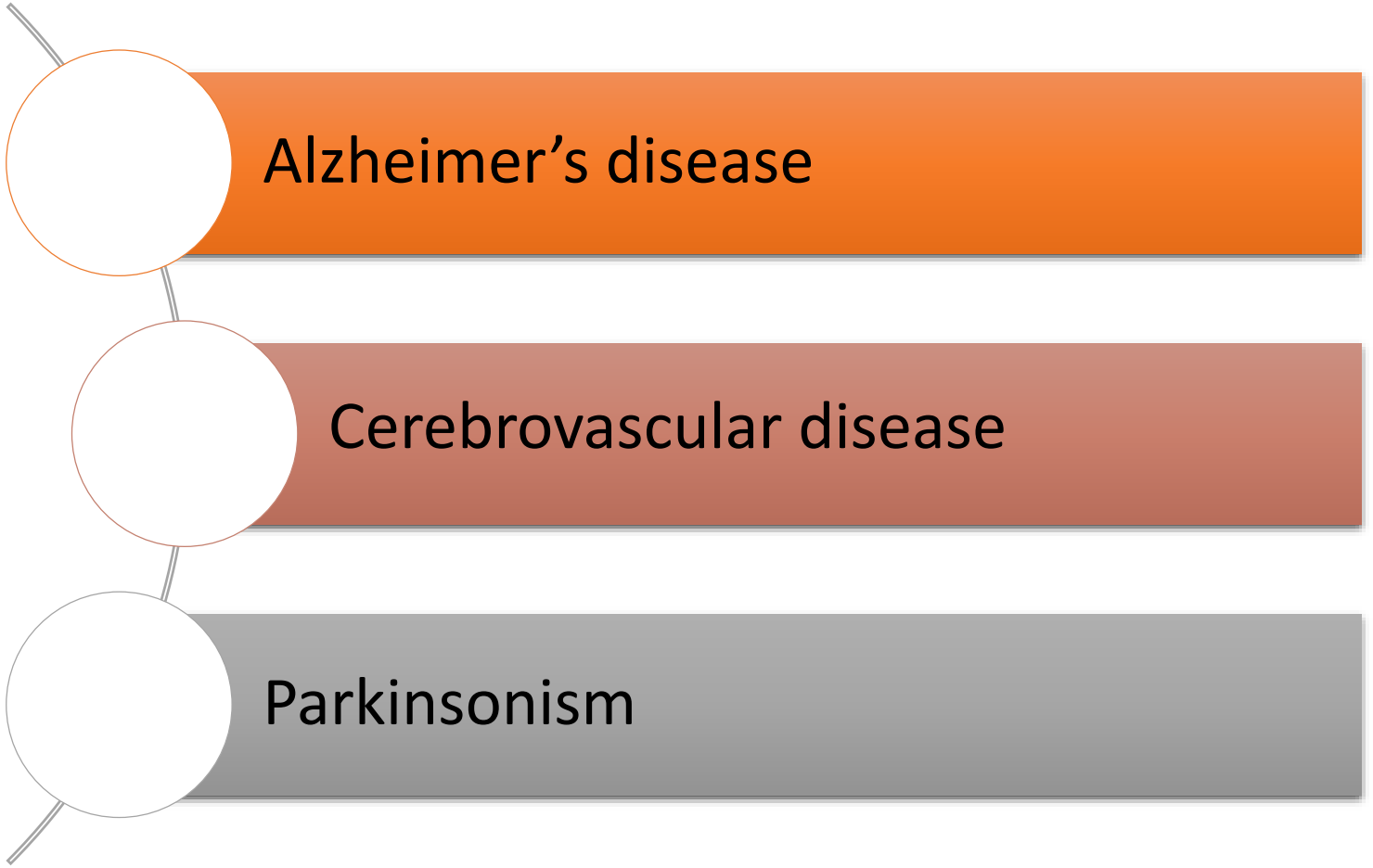
- refers to the inability of an individual to establish new long-term memories of those types of information that form the basis of intelligence.
- usually occurs in lesions involving hippocampus.

## Retrograde amnesia

- refers to the inability of an individual to recall past memories.
- Retrograde amnesia occurs in lesions involving the temporal lobe (temporal lobe syndrome).

# ALZHEIMER'S DISEASE AND SENILE DEMENTIA

- Senile dementia refers to a clinical syndrome in elderly people that is characterized by progressive impairment of memory and cognitive capacities.



# Alzheimer’s disease

- Alzheimer’s disease is the most common cause of dementia in the elderly persons.

- It is a neurodegenerative disease.

# It is characterized by a series of abnormalities in the brain that selectively affect neurons in specific regions

neocortex

the entorhinal area

hippocampus

amygdala

nucleus basalis

anterior thalamus

raphe complex

locus coeruleus

severe loss of cholinergic neurosis in the affected areas

# Alzheimer’s disease is associated with cytoskeletal abnormalities in the affected nerve cells

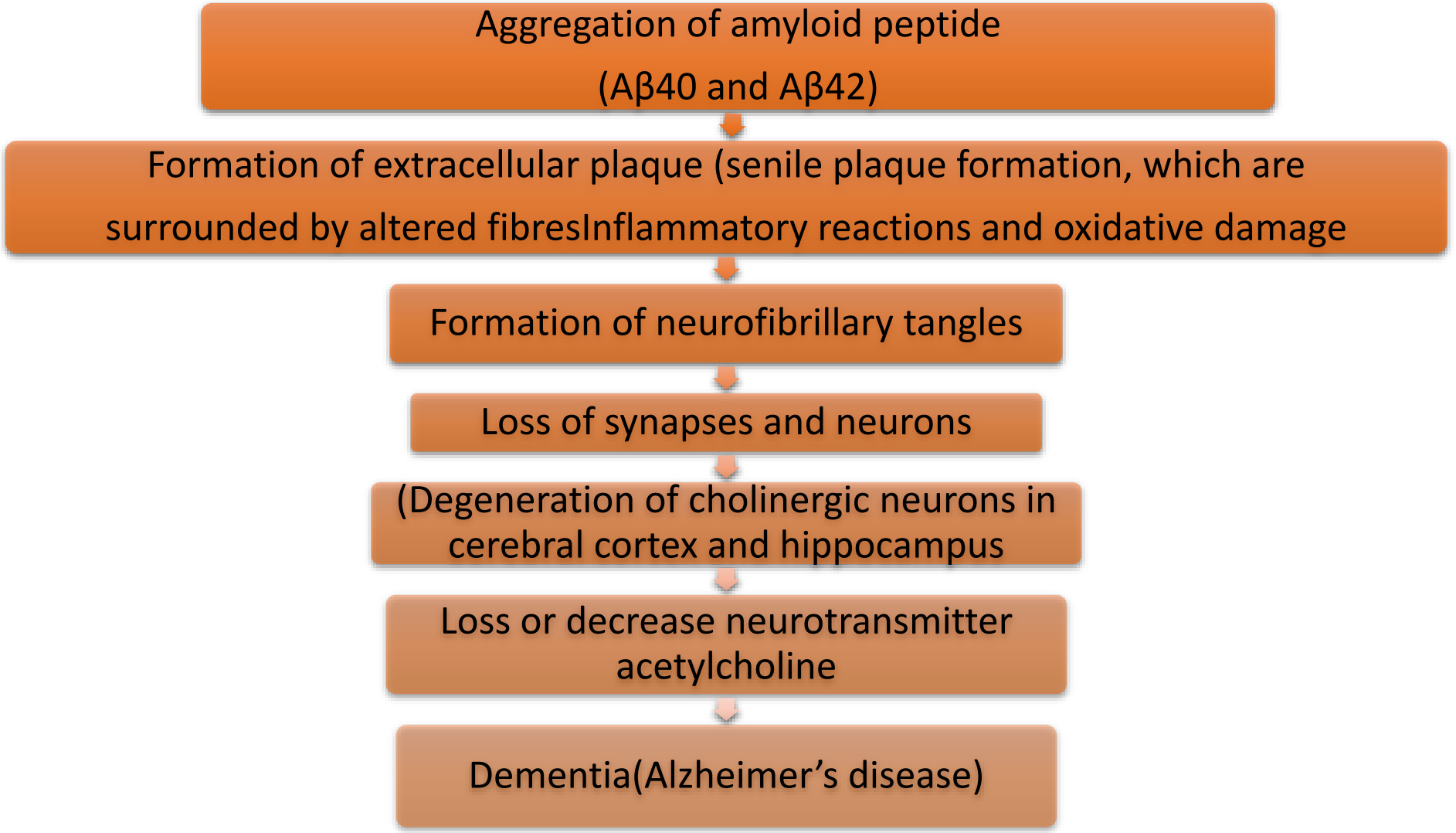
accumulation of neurofibrillary tangles in the neuronal cytoplasm

Amyloid plaque

(fibrillar peptides) deposits

hallmarks of Alzheimer’s disease.

# The sequence of events in the pathogenesis of Alzheimer's disease.



# **Characteristic features** of Alzheimer's disease

Loss of recent memory

Impairment in other areas of cognition, such as language,problem solving, judgement, calculation, attention, perception

Psychiatric symptoms begin to appear as the disease

progresses

Extrapyramidal and akinetic hypertonic symptoms also appear in later stages

loss of spatial orientation.

Finally, patient has to lead a vegetative life without memory, without thinking power, speechless, inability to understand anything,

apraxia (inability to performvoluntary movements),

agnosia (inability to recognize objects in spite of intact sensory modality)

# Treatment

- There is no effective treatment for Alzheimer’s disease, as yet
- physostigmine, which inhibits cholinesterase causes some improvement.
- Presently, focus is on treating associated symptoms, such as depression, agitation, sleep disorders, hallucinations and delusions

# DRUGS FACILITATING MEMORY

***Common CNS stimulant*** that facilitates learning and memory are:

caffeine, amphetamine, physostigmine, nicotine,pemoline, strychnine and pentylenetetrazol.

- ***Mechanism of action:***

  CNS stimulants act probably by facilitating consolidation of memory.
- **physostigmine** acts by inhibiting acetylcholinesterase and hence preventing breakdown of acetylcholine
- **nicotine** stimulates cholinergic receptors.