



NPTTEL ONLINE CERTIFICATION COURSES

Basics of Mental Health & Clinical Psychiatry

Dr. Arijita Banerjee

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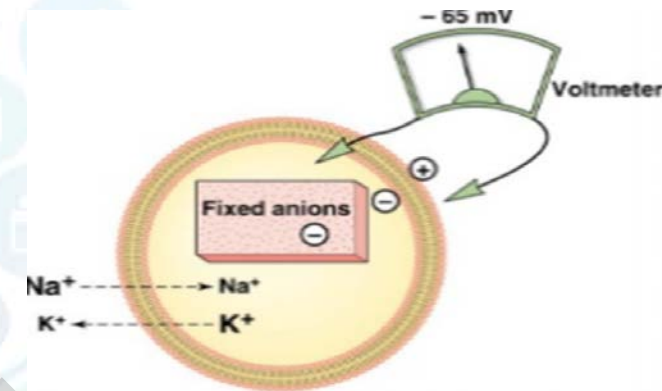
Lecture 6 : Synapse & Neurotransmitters-1

CONCEPTS COVERED

- Resting membrane potential & Action potential
- Types of synapses
- Structure of synapse
- Events at presynaptic terminal
- Neurotransmitters
- Events at Post synaptic terminal

BASIC CONCEPTS OF PHYSICS OF MEMBRANE POTENTIAL

- An electrical potential difference exists across the membrane of all living cells.
- At resting state of the cell, the membrane potential is called **resting membrane potential** (RMP)
- Membrane potential is mainly due to **selective permeability** of the cell membrane to various ions at rest & **Equilibrium potential**.



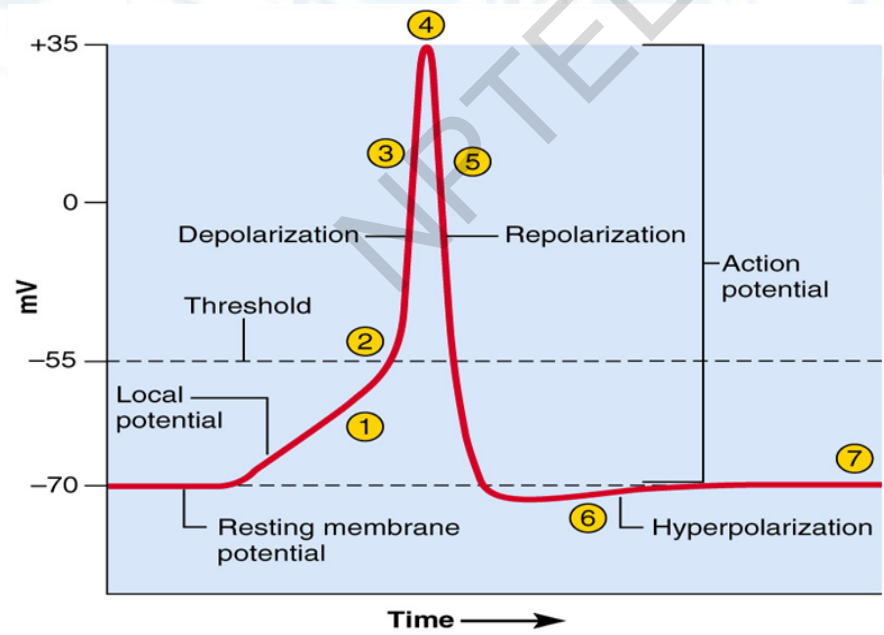
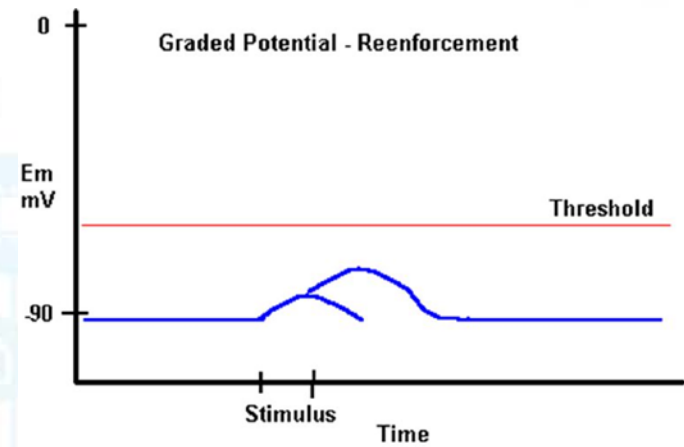
- Two types of physicochemical disturbances are produced:

Synaptic, Generator, Graded or Electrotonic Potentials

- Local, Non-propagated Potentials.

Action Potentials:

- Propagated Potentials.
- Depolarization to **Threshold level**.



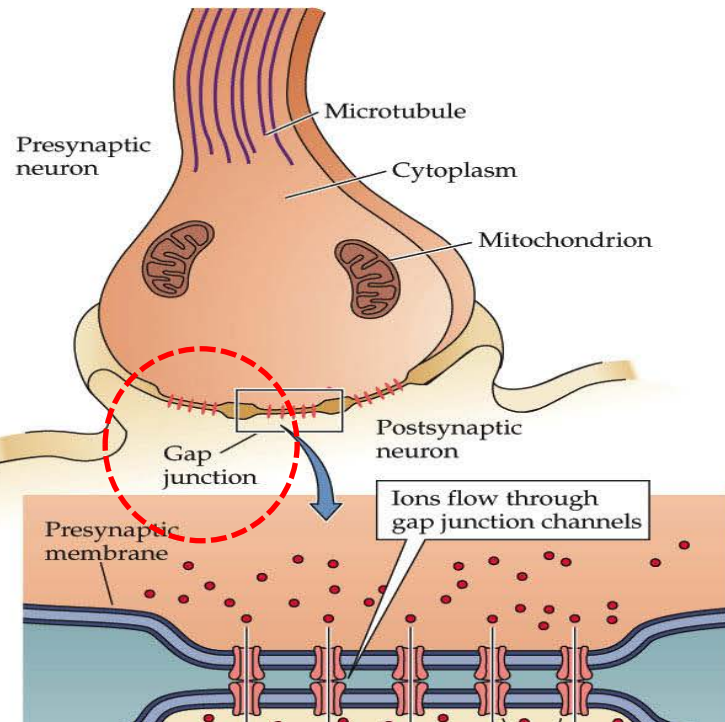
Synapse

- Charles Sherrington coined the term.

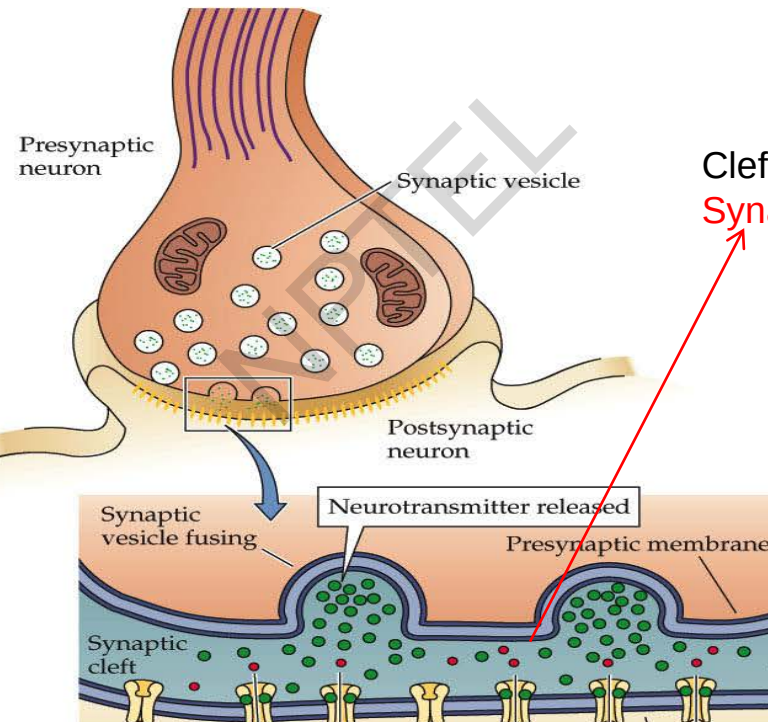
Synaptic delay-nil (electrical)

Eg. Inferior olivary nucleus,
olfactory bulb, thalamus,
hypothalamus

(A) ELECTRICAL SYNAPSE



(B) CHEMICAL SYNAPSE

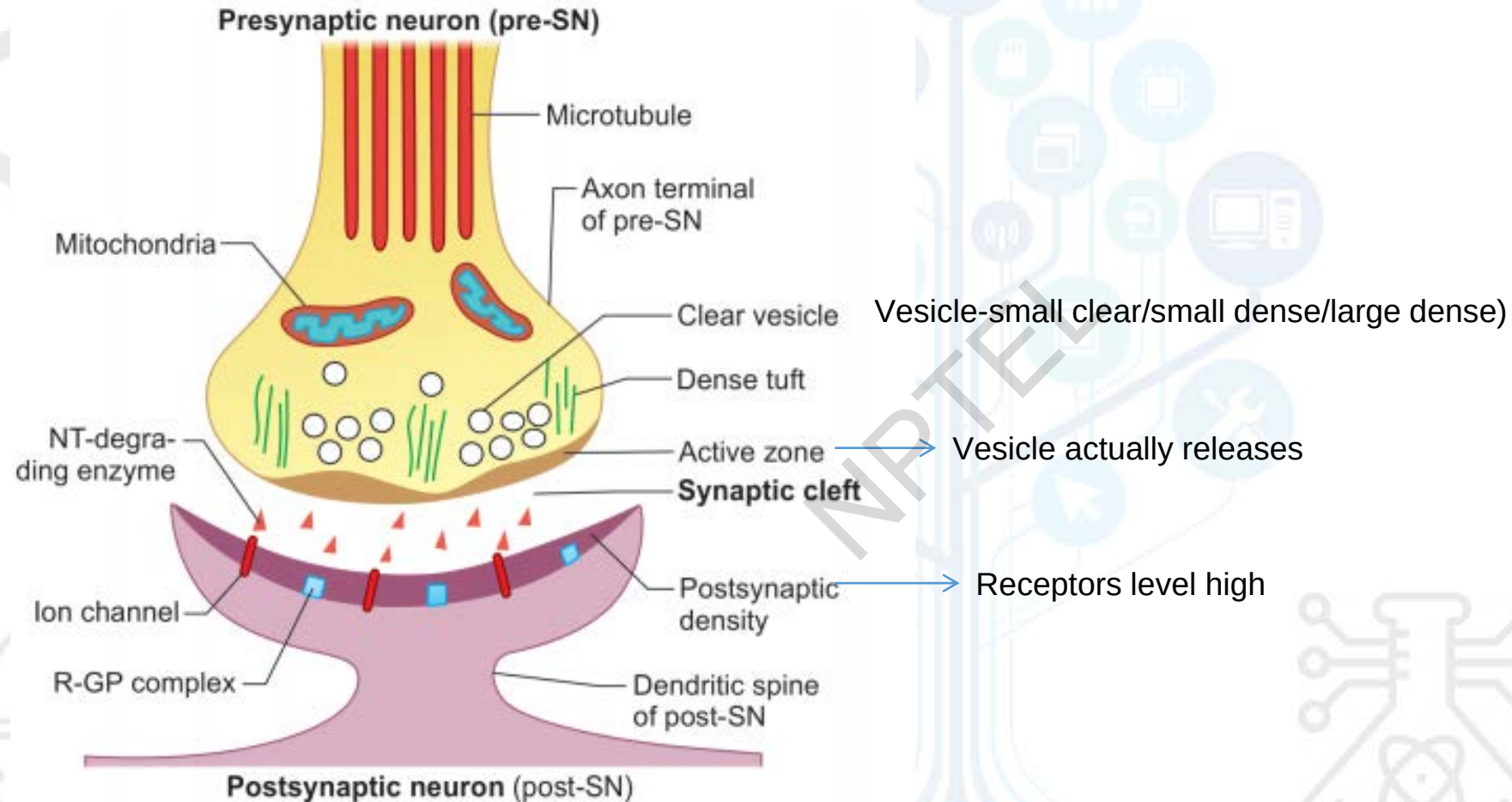


Cleft -20 -40nm

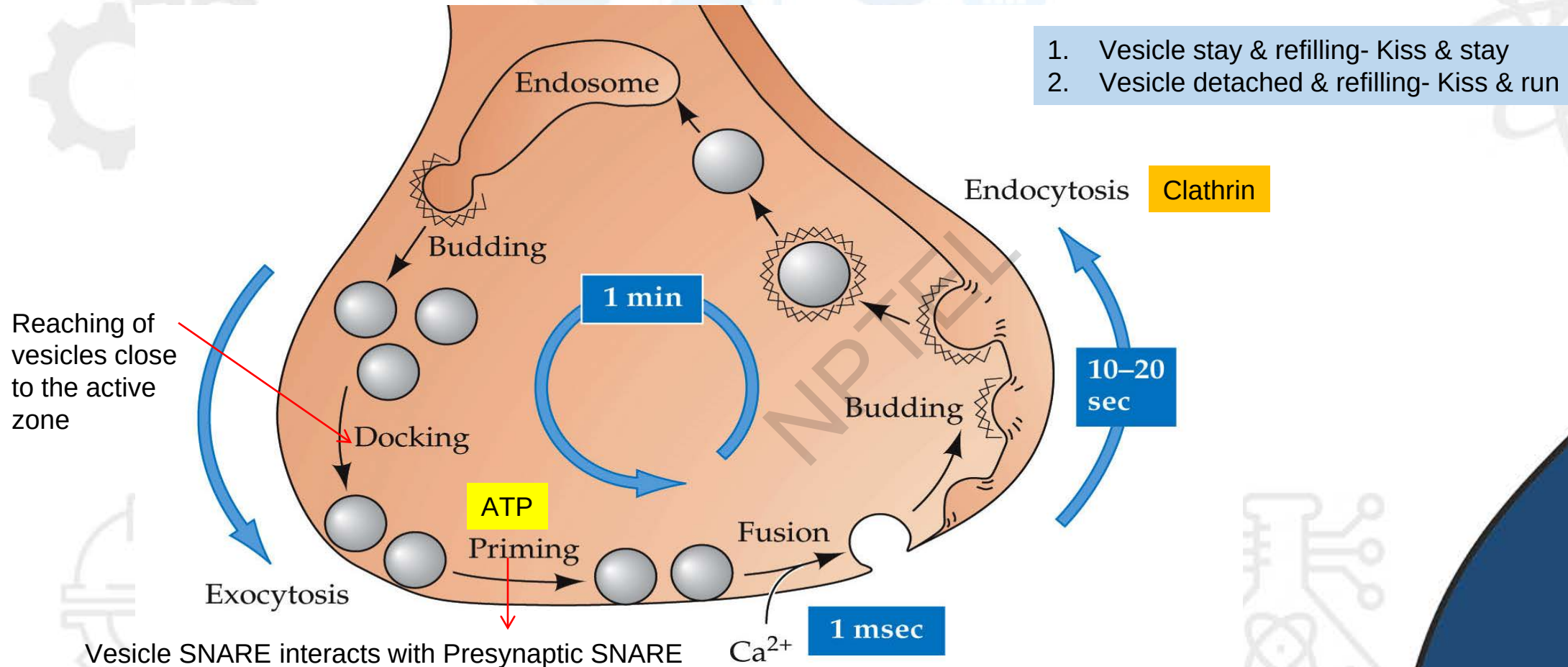
Synaptic delay- average 0.5ms

Structure of synapse

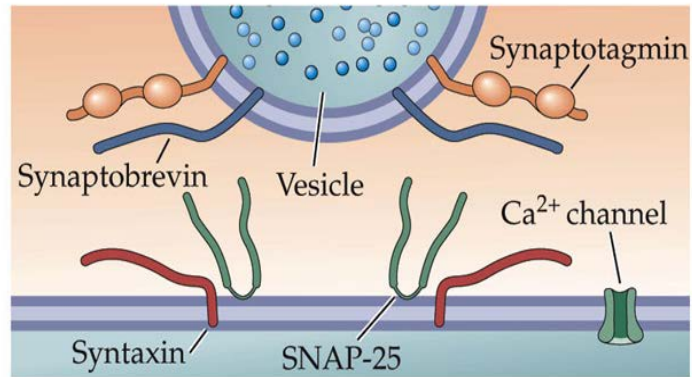
Synaptic specificity- neurexin & neuroligin



Events at presynaptic terminal

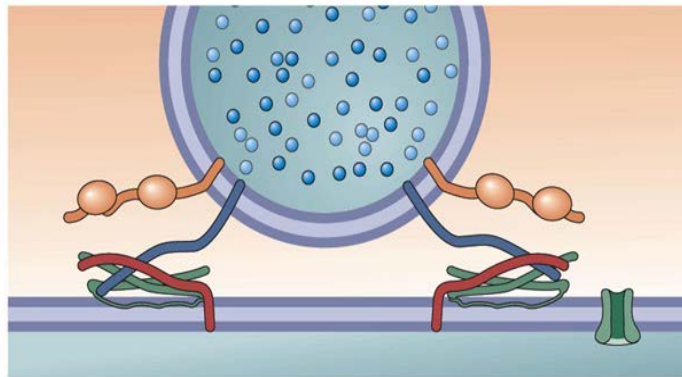


(1) Vesicle docks



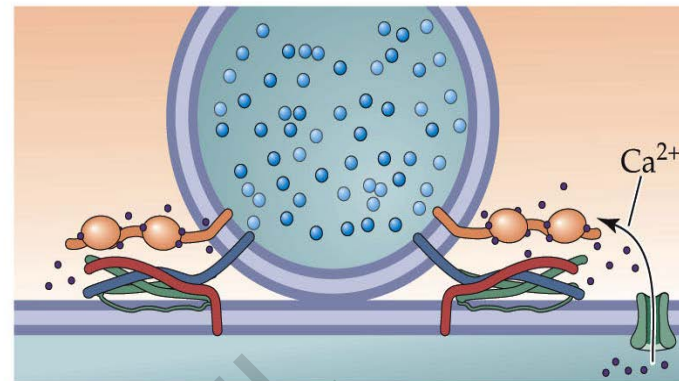
(2) SNARE complexes form to pull membranes together

ATP/Munc13-1/18

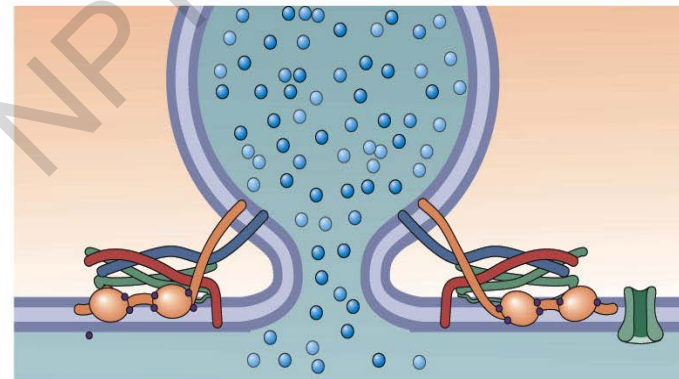


- More interaction- coiling
- Inhibitory domain, folds back on itself
syntaxin doesn't fold properly

(3) Entering Ca²⁺ binds to synaptotagmin



(4) Ca²⁺-bound synaptotagmin catalyzes membrane fusion



NT Release

- Tetanus toxin- synaptobrevin
- Botulinum toxin –SNARE proteins

Events at Post synaptic terminal

Neurotransmitters

Excitatory – Glutamate (75%)

Inhibitory- GABA, Glycine

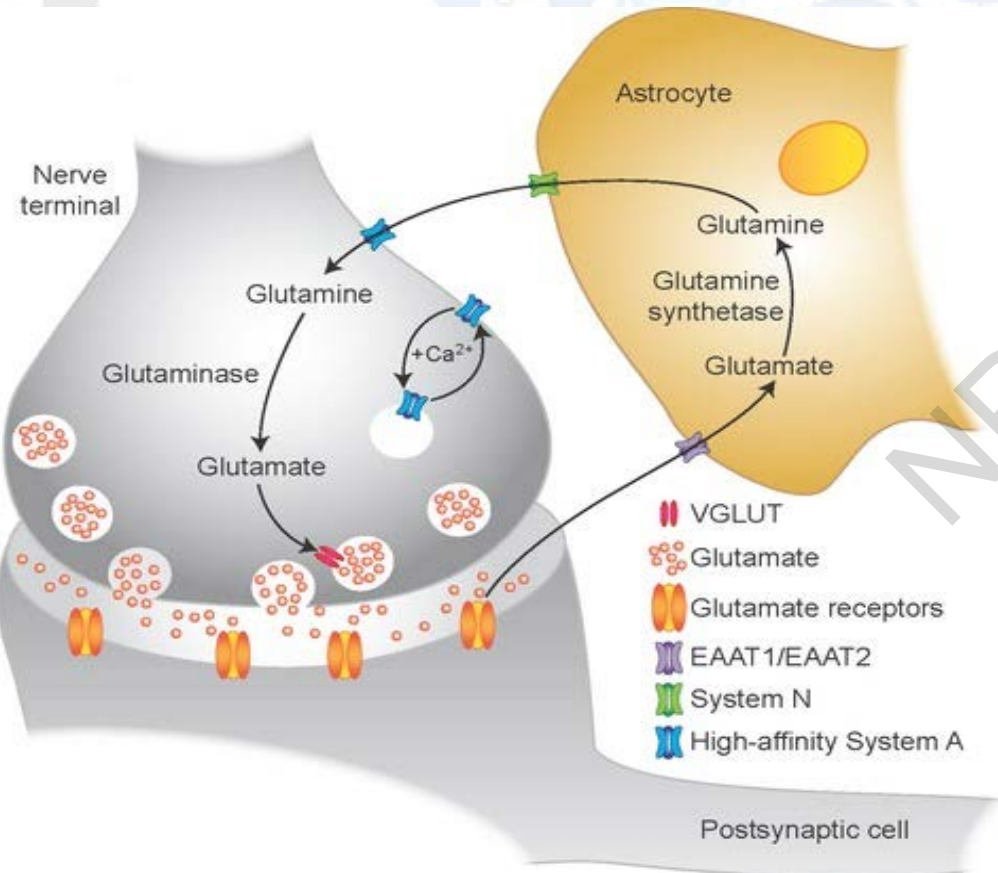
Other Neurotransmitters

1. Dopamine (Substantia nigra)
2. Serotonin (Raphe nucleus)
3. Norepinephrine (Locus ceruleus)
4. Acetylcholine (Pyramidal cells, Basal forebrain)
5. Histamine (Hypothalamus)

Glutamate

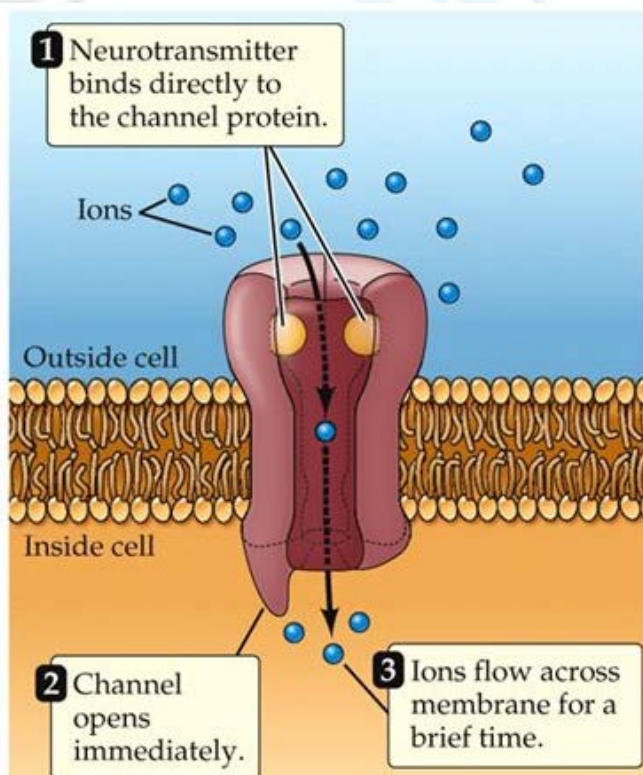
Glutamine $\longrightarrow$ glutamate

Reuptake of glutamate by astrocytes is necessary
To prevent glutamate induced neurotoxicity in brain

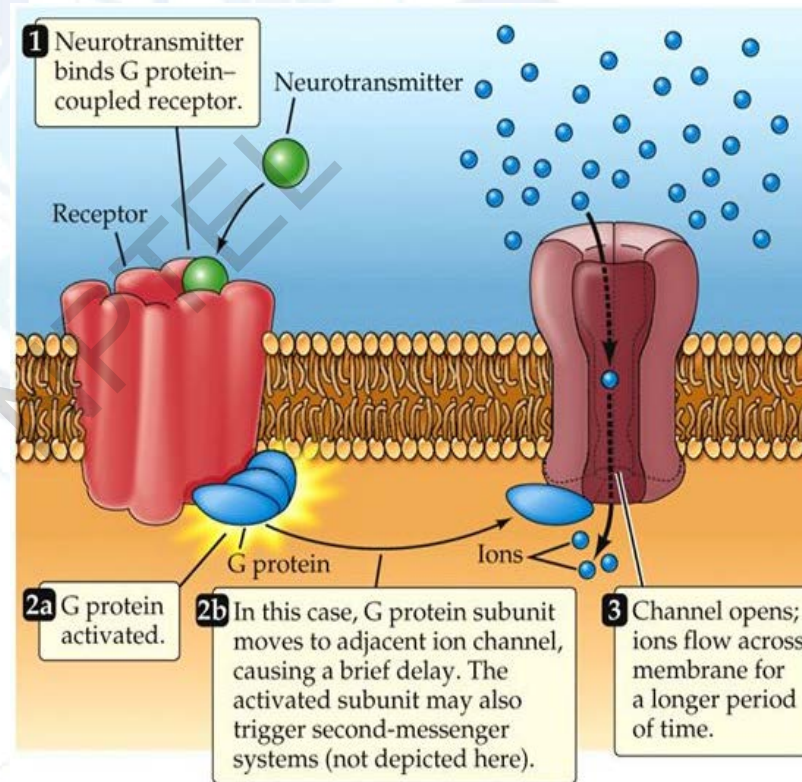


Glutamate receptors

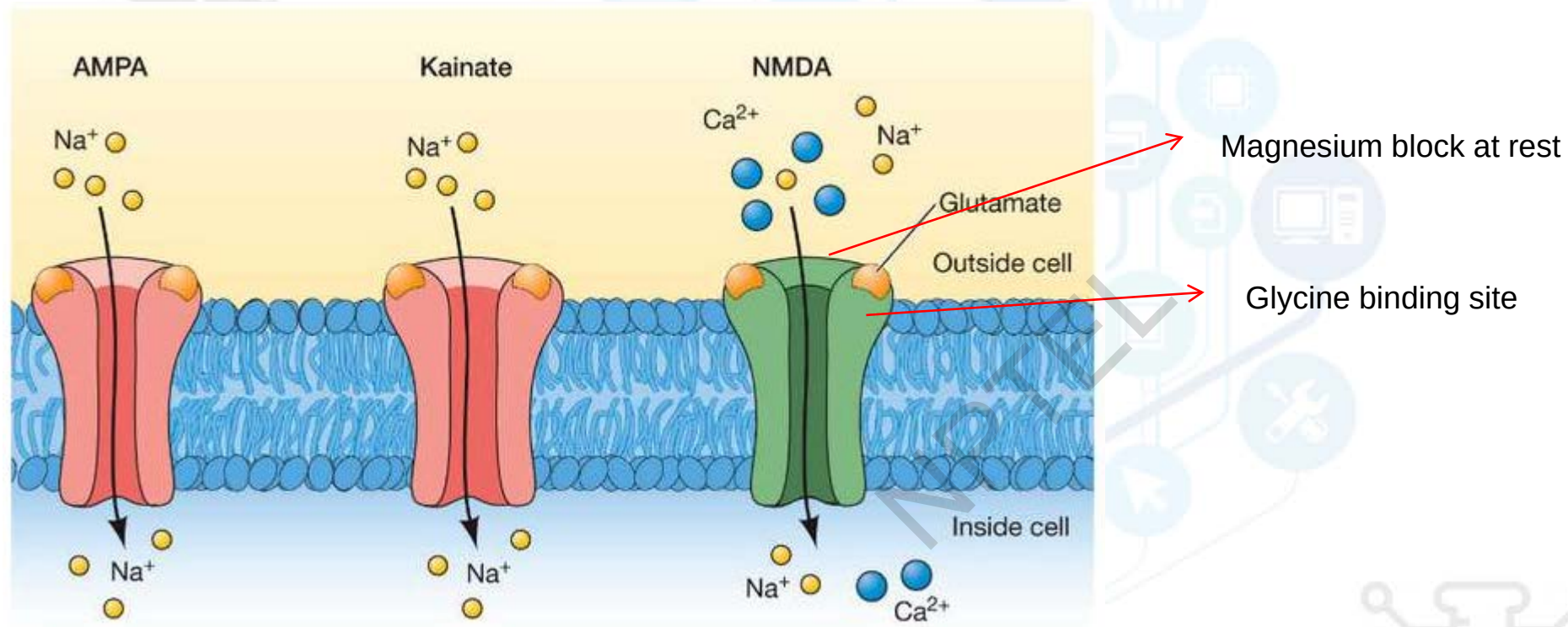
Ionotropic



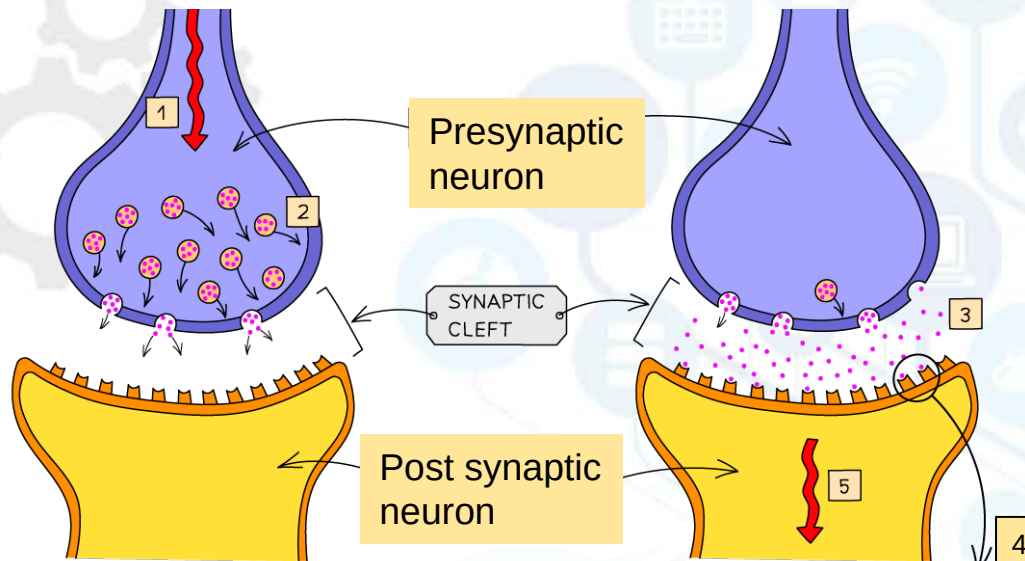
Metabotropic (mGluR)- Cerebellum/hippocampus



Ionotropic Receptors



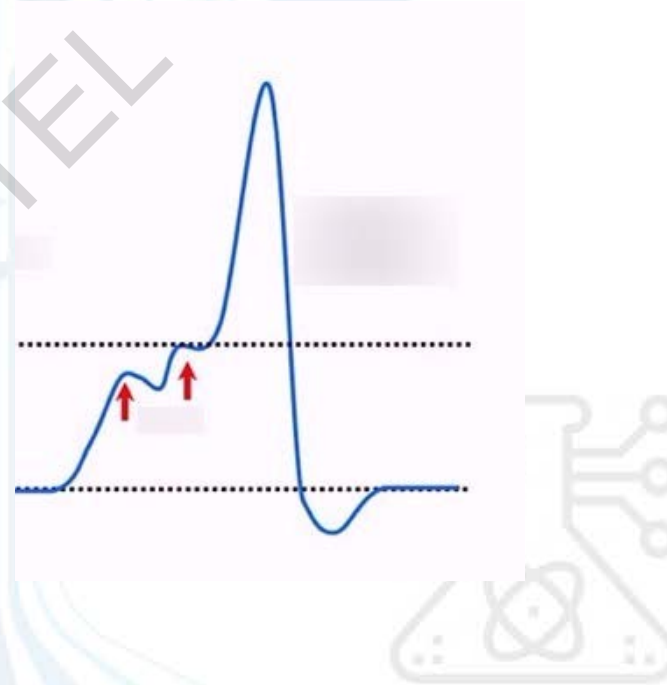
More cations – depolarization-
more sodium ions will enter



At Post-synaptic membrane- EPSP will be generated.

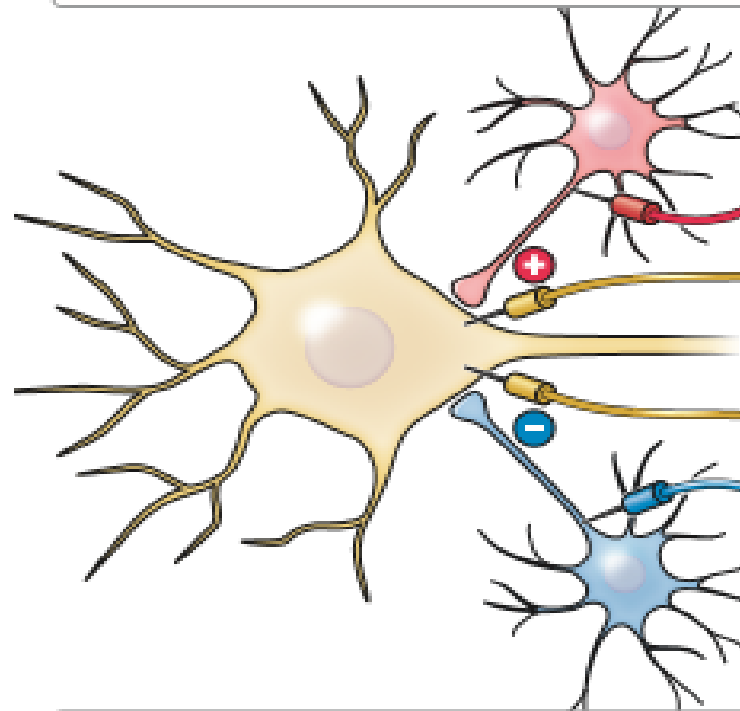
After reaching threshold, the potential will be transmitted As action potential across the neuron.

Functions of glutamate receptors-synaptic plasticity

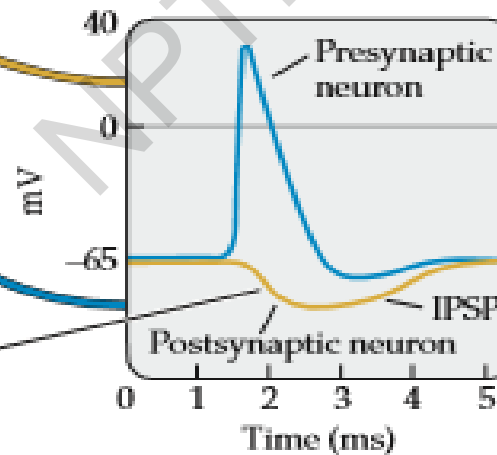
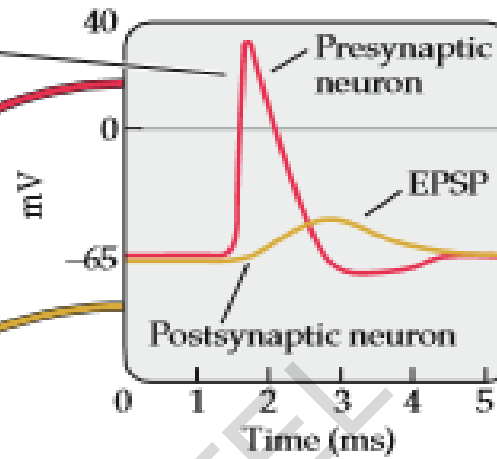


Post-synaptic potentials

In this schematic model, when an excitatory presynaptic neuron (red) fires, it shows a normal action potential and causes depolarization (EPSP) in the postsynaptic neuron (yellow).



When an inhibitory presynaptic neuron (blue) fires, it also shows a normal action potential, but it causes hyperpolarization (IPSP) in the postsynaptic neuron (yellow).



KEY POINTS

- Electrical synapse is fast while chemical synapse has a synaptic delay.
- SNARE proteins and Calcium play an important role in vesicle fusion at the presynaptic membrane.
- The postsynaptic events depends in neurotransmitter and receptors.
- Glutamate receptors are of two types-ionotropic and metabotropic, play an imortant role in synaptic plasticity.

REFERENCES

1. Review of Medical Physiology, William F Ganong, 23e
2. Kaplan & Sadock's Comprehensive Textbook of Psychiatry, 9e
3. Guyton and Hall Textbook of Medical Physiology, John E. Hall, 13e
4. Medical Physiology, Walter F. Boron, 3e
5. Fundamental identification of activity regulated, high affinity glutamate transport in hippocampus neurons inhibited by riluzole. Journal of Neurochemistry, Erickson, 2017.
6. Behavioural Neuroscience, Breedlove, 6e.



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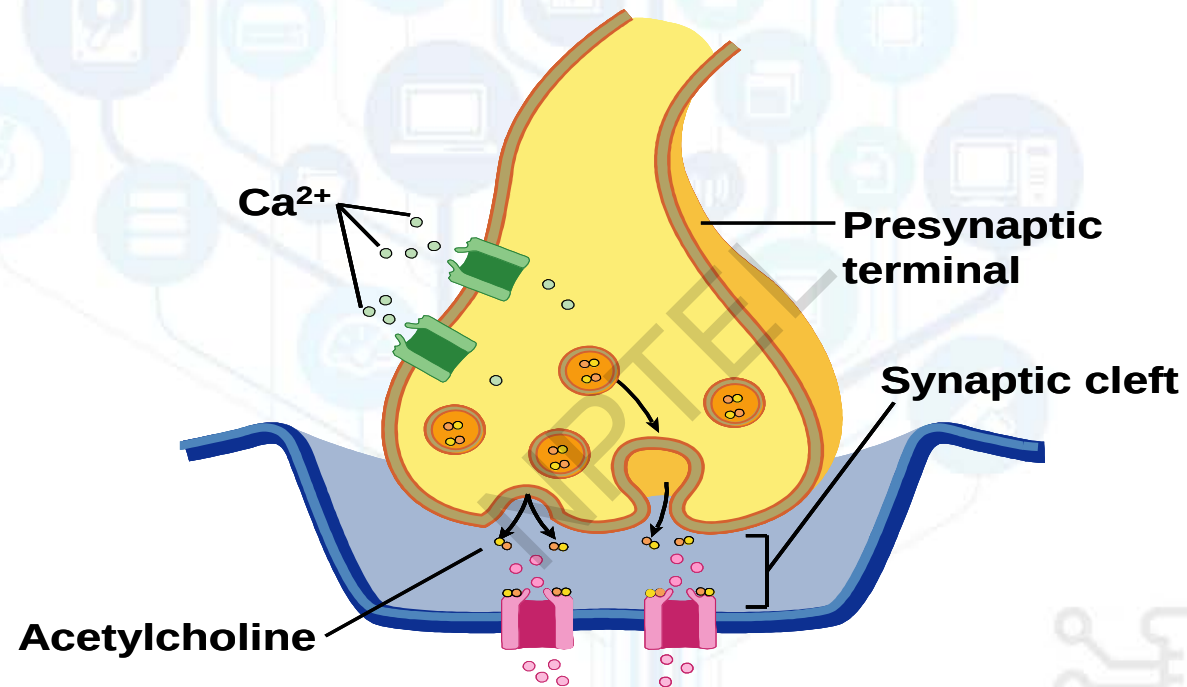
Lecture 7: Synapse & Neurotransmitters-2

CONCEPTS COVERED

- Resting membrane potential & Action potential
- Types of synapses
- Structure of synapse
- Events at presynaptic terminal
- Neurotransmitters
- Events at Post synaptic terminal

Sequence Of Events At Neuromuscular Junction

Ach- Otto Leowi



Ach travels across the synaptic cleft to postsynaptic membrane

- **Receptor:** Nicotinic Ach receptors

Blocked by curare

Ligand gated ion channels

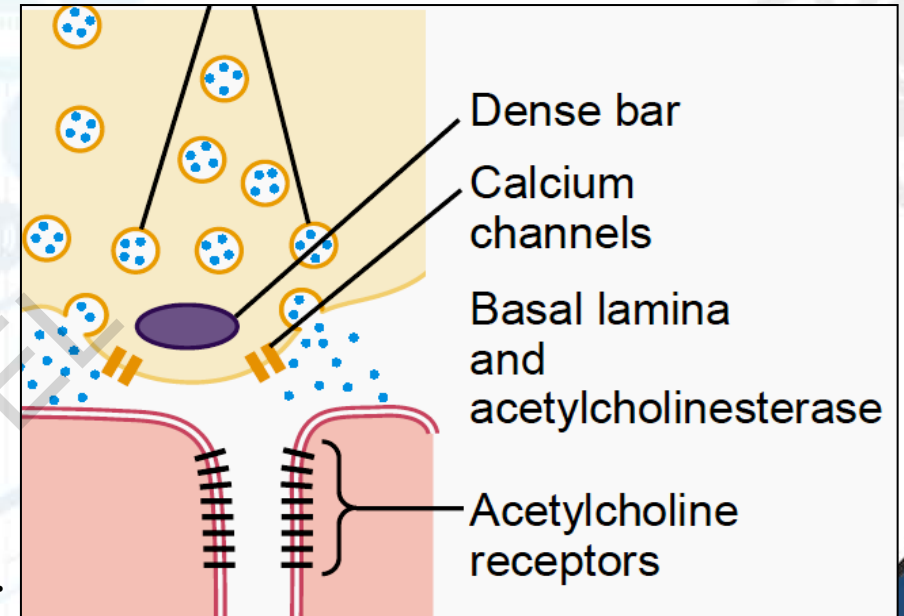
- Ach binds to Ach receptor & causes conformational change.
- Lead to ion channels opening & permeability of motor end plate to Na^+ & K^+ increases.

Acetylcholine Receptor

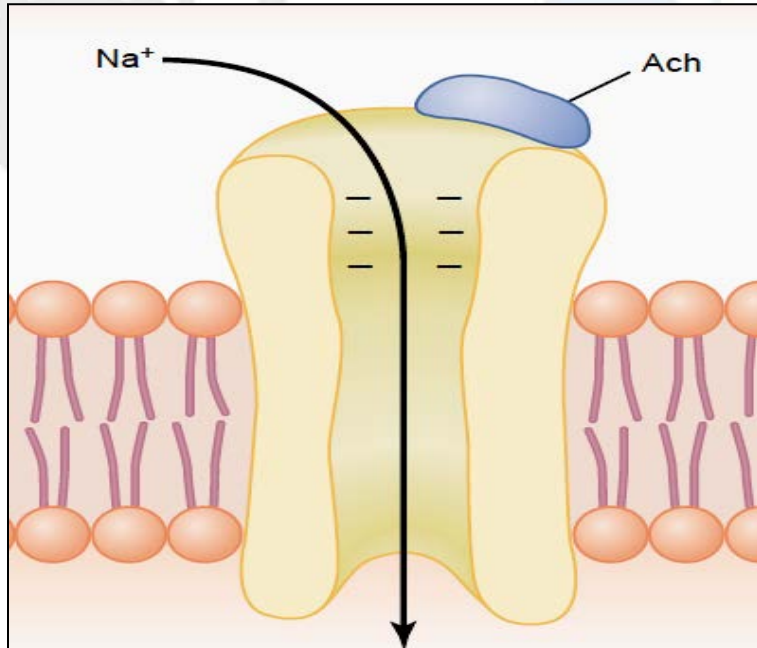
- **Location:** Near the mouths of the subneural clefts

Composed of five subunit proteins:

- *Two alpha proteins*
- *One each of beta, delta, and gamma proteins.*
- Two Ach molecules attach to the two *alpha subunit proteins*.



Acetylcholine Receptor



EPP:

When nerve impulse reaches the ending, it lead to fusion and release of about 60 Ach vesicle .

This result in generation of EPP.

EPP is not an action potential but a local, non-propagated Potentials.

Destruction of the Released Acetylcholine

Mode of destruction of Ach:

- Mostly by enzyme *Acetylcholinesterase*
- Small amount diffuses out of the synaptic space.
- About 50% of choline is returned to the presynaptic terminal to be reused for Ach synthesis.
- Prevents repetitive muscle excitation.

Myasthenia Gravis

- An Auto immune disease.

Cause:

- Due to antibodies against nicotinic acetylcholine receptors of NMJ.

Symptom:

- Extreme muscular weakness with repeated and sustained activity
- Weakness improves after a period of rest

Lambert-Eaton Syndrome

- An auto immune disorder.

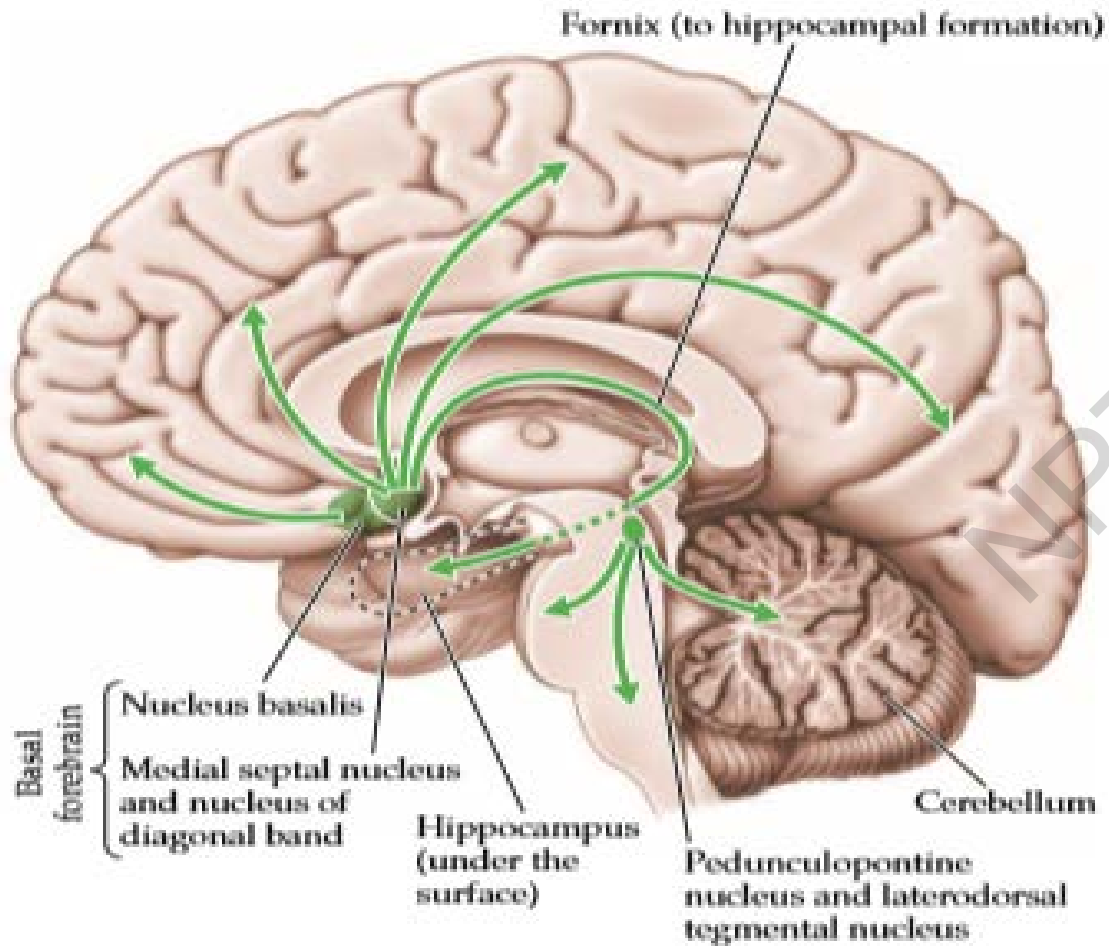
Cause:

- Due to antibodies against Ca^{2+} channels in the nerve end.

Symptom:

- Muscle weakness.
- Proximal muscles are primarily affected.
- Symptom improves with activity.

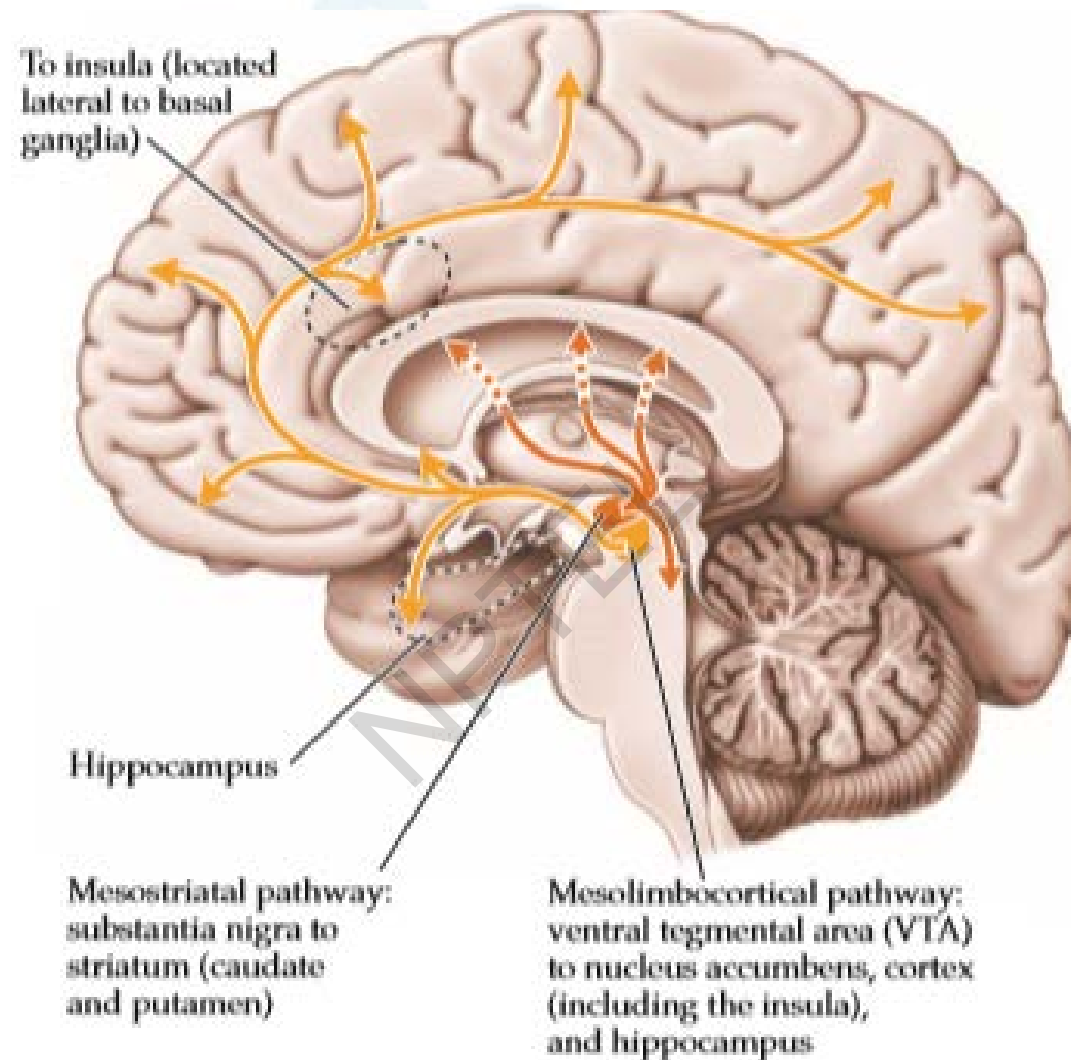
Cholinergic pathways in brain



- *Important clusters of cholinergic cells are found in the basal forebrain, including the medial septal nucleus, the nucleus of the diagonal band, and the nucleus basalis.*
- *These cholinergic cells project to the hippocampus and amygdala, as well as throughout the cerebral cortex.*

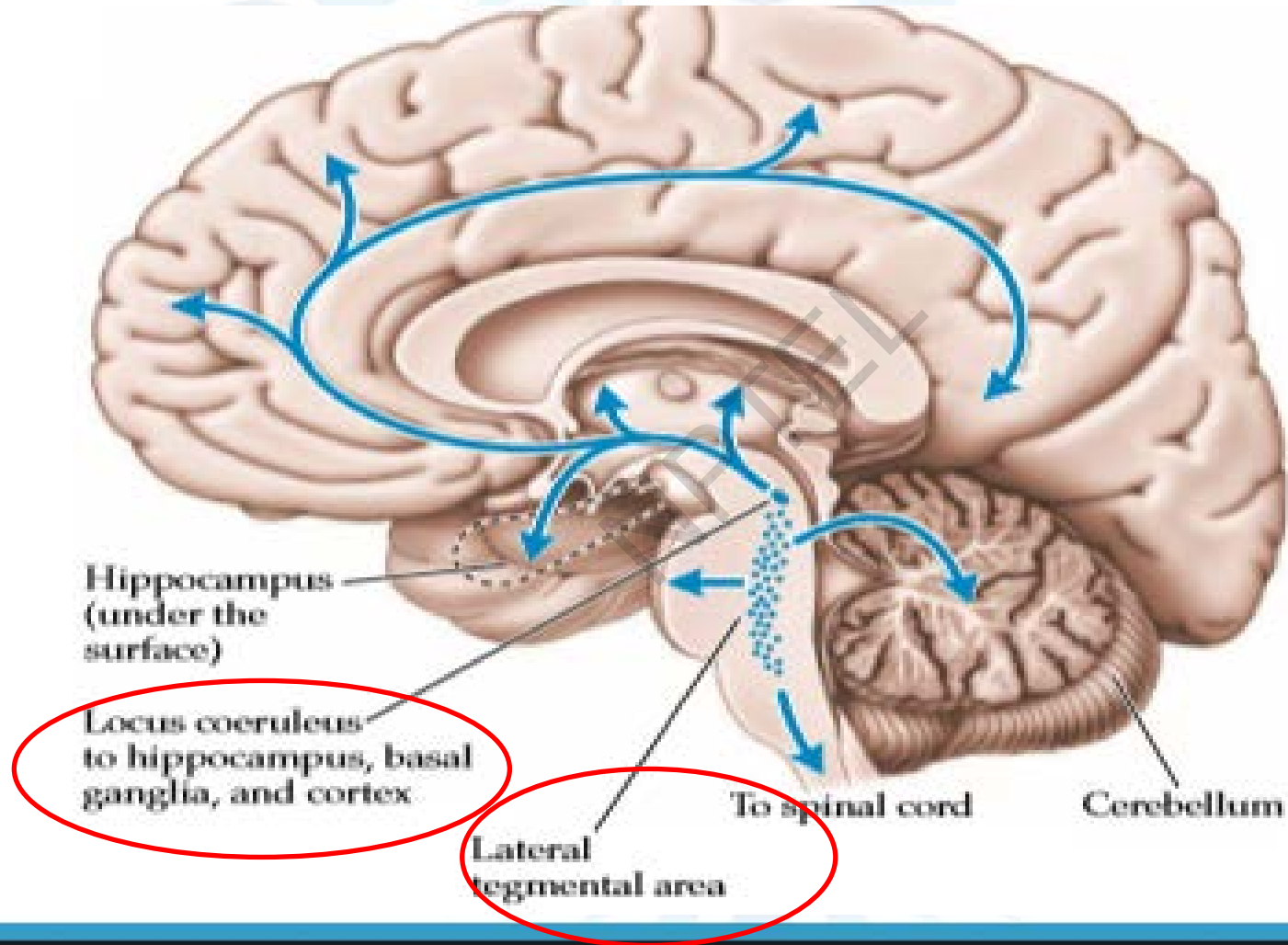
Dopamine

- D1, D2, D3, D4, and D5, in the order of their discovery
- Mesostriatal pathway- dopaminergic axons arising from the midbrain and innervating the basal ganglia, including those from the substantia nigra to the striatum.
- Mesolimbocortical pathway- axons arising in the midbrain and innervating the limbic system and cortex.



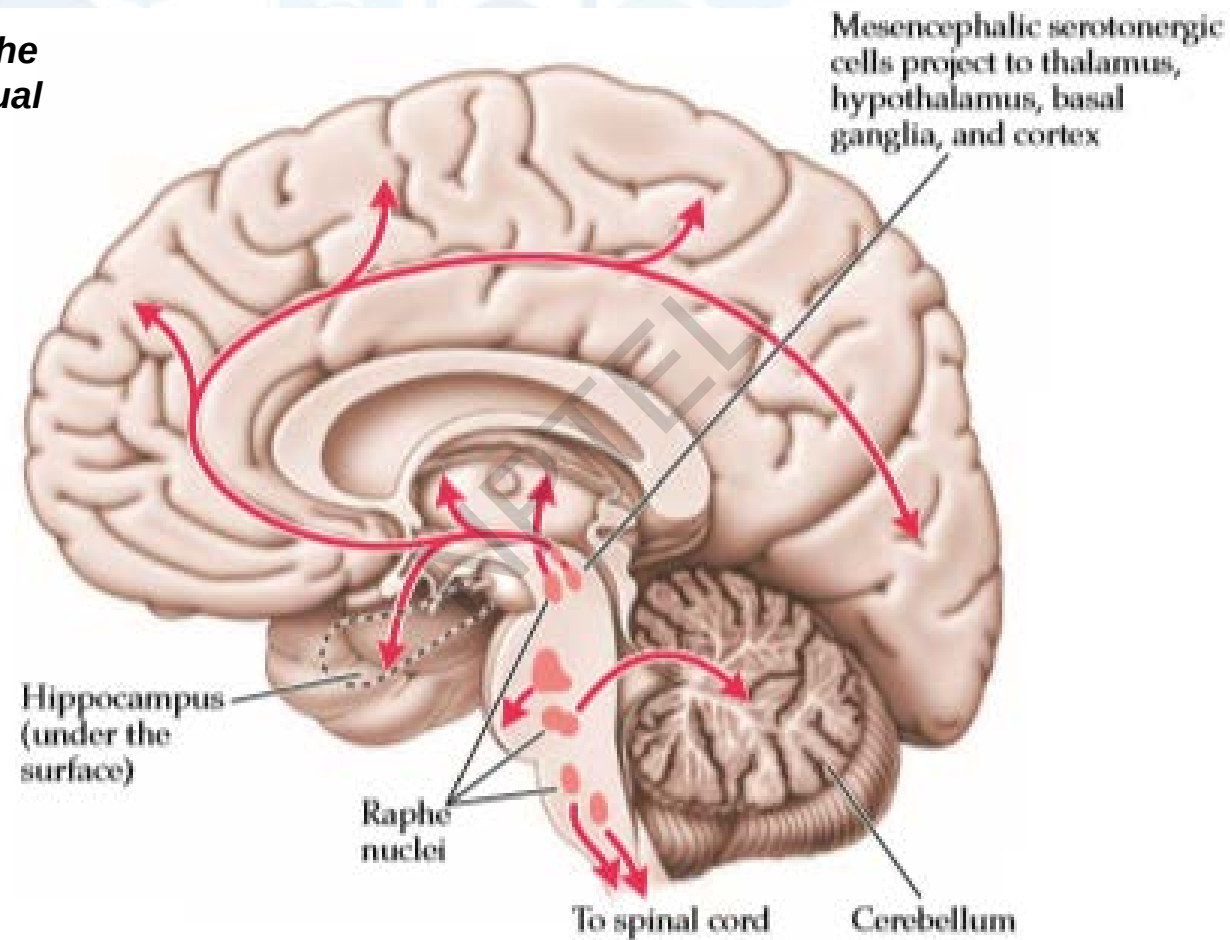
Noradrenergic pathways in the brain

Alpha 1,2
Beta 1,2



Serotonergic pathways in the brain

- *Serotonin has been implicated in the control of sleep states, mood, sexual behavior, anxiety.*
- *Several families of drugs that are used as antidepressants share an action on serotonin: they act to increase its synaptic availability.*
- *5-HT receptors.*

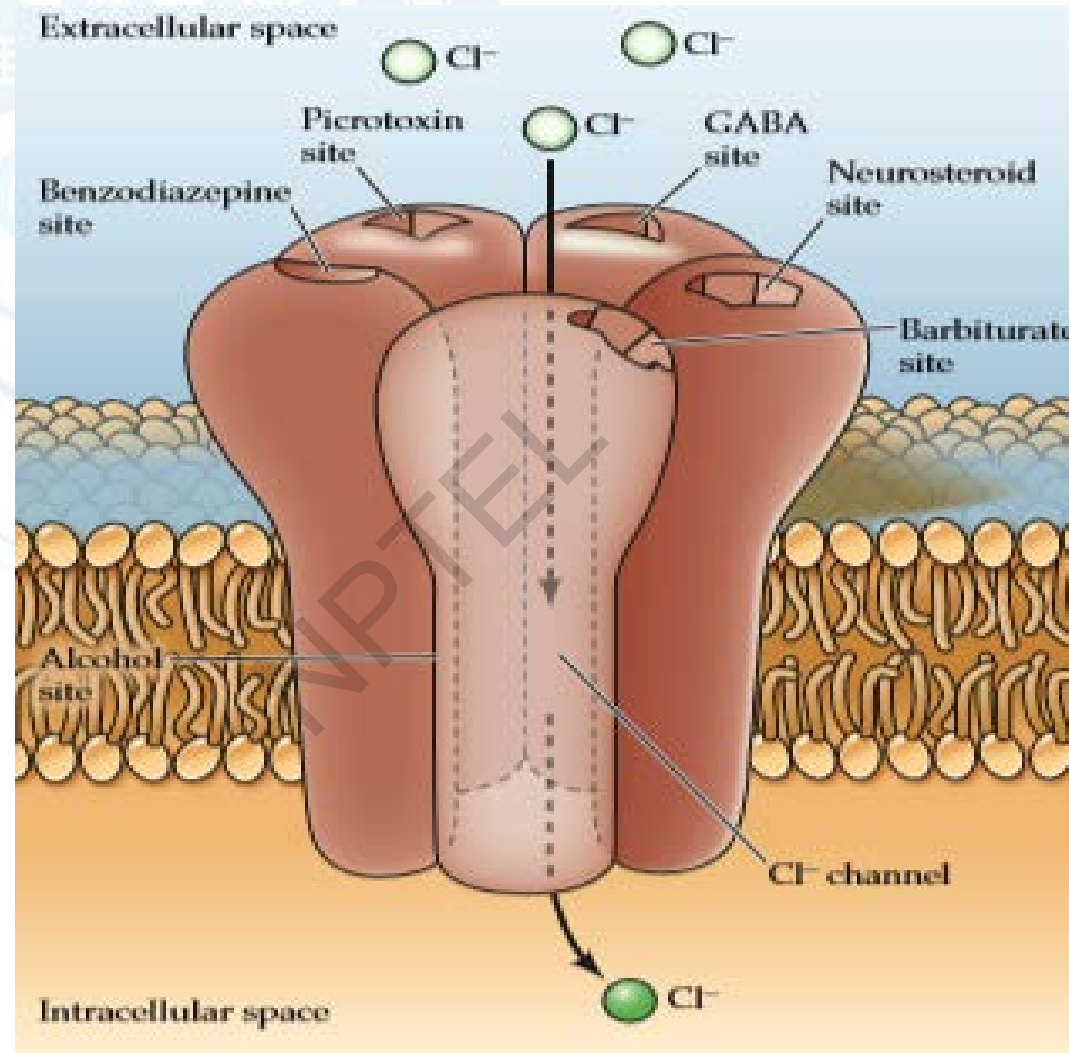


GABA

- Major inhibitory NT
- Robert & Frankel discovered
- Synthesized from L-glutamic a.
- Catabolized by GABA-transaminase
- 3 receptors-A,B,C

B receptor- more efflux of K^+ ,
GPCR, eg, purkinje cells

Alcohol role



The GABA-A complex is made up of five protein subunits surround a Cl^- ion channel at the core

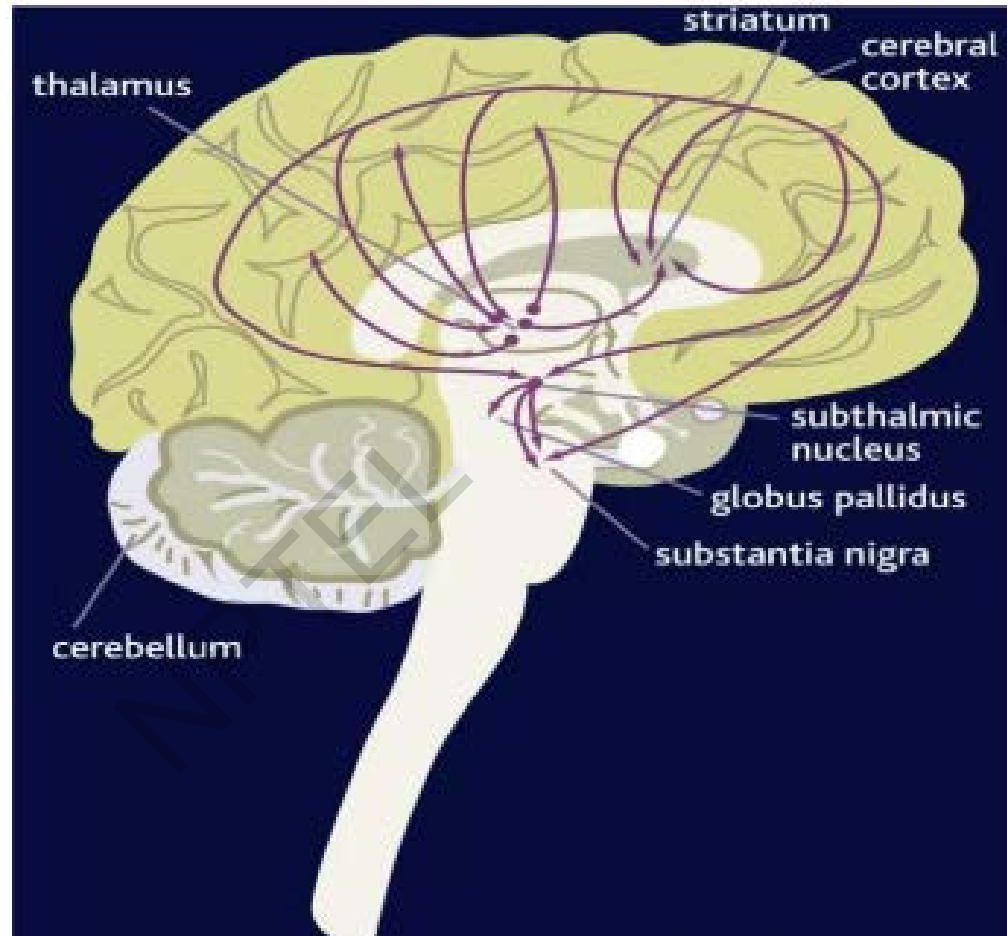
3 PATHWAYS-

- Cortico-limbic
- Striatum
- cerebellum

Role-

1. Antidepressants
2. Antianxiety
3. Promote sleep
4. anticonvulsants

Pyramidal cells inhibit



- The most studied endocannabinoid is anandamide (from the Sanskrit ananda, “bliss”) which has diverse functional effects, including alterations of memory formation, appetite stimulation, reduced sensitivity to pain, and protection from excitotoxic brain damage
- Local anesthetic A drug, such as procaine or lidocaine, that blocks sodium channels to stop neural transmission in pain fibers.

Keypoints

- The substance exists in presynaptic axon terminals.
- The presynaptic cell contains appropriate enzymes for synthesizing the substance.
- The substance is released in significant quantities when action potentials reach the terminals.
- Specific receptors that recognize the released substance exist on the postsynaptic membrane.
- Experimental application of the substance produces changes in postsynaptic cells.
- Blocking release of the substance prevents presynaptic activity from affecting the postsynaptic cell.

REFERENCES

1. Behavioural Neuroscience, Breedlove, 6e
2. Nestler, E., Hyman, S., and Malenka, R. (2014). Molecular Neuropharmacology (3rd ed.). New York: McGraw-Hill.
3. Guyton and Hall Textbook of Medical Physiology, John E. Hall, 13e
4. Medical Physiology, Walter F. Boron, 3e



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Lecture 8 : Limbic System

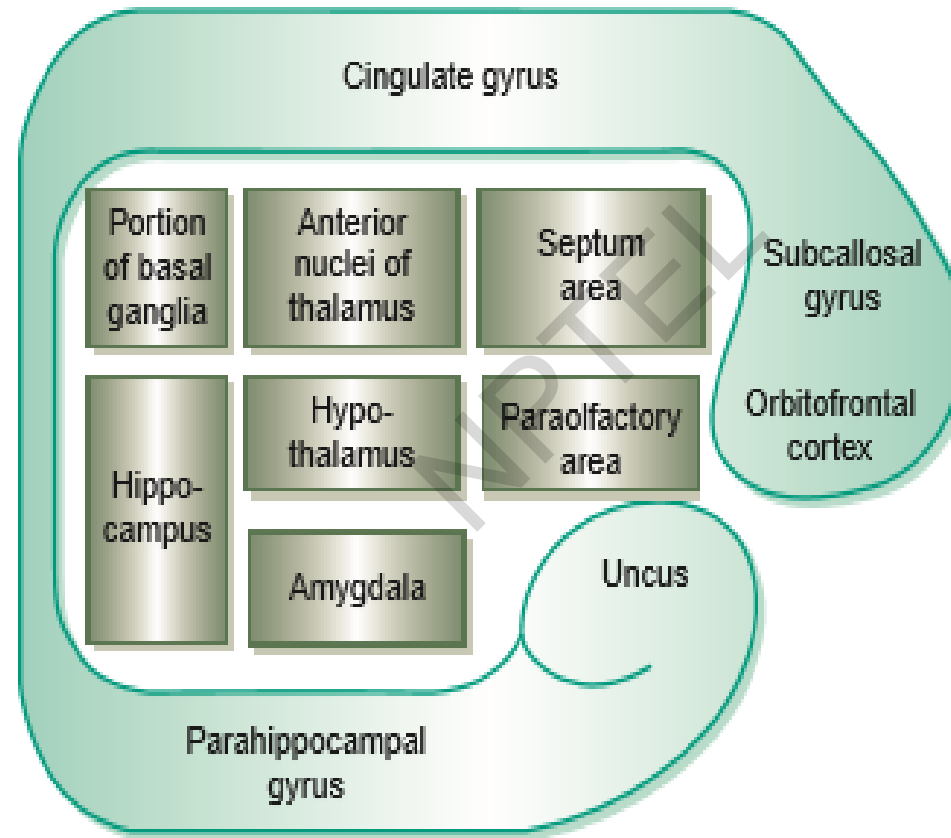
CONCEPTS COVERED

- **Components of Limbic System**
- **Neural circuits**
- **Functions**
- **Applied aspects**

Limbic System components

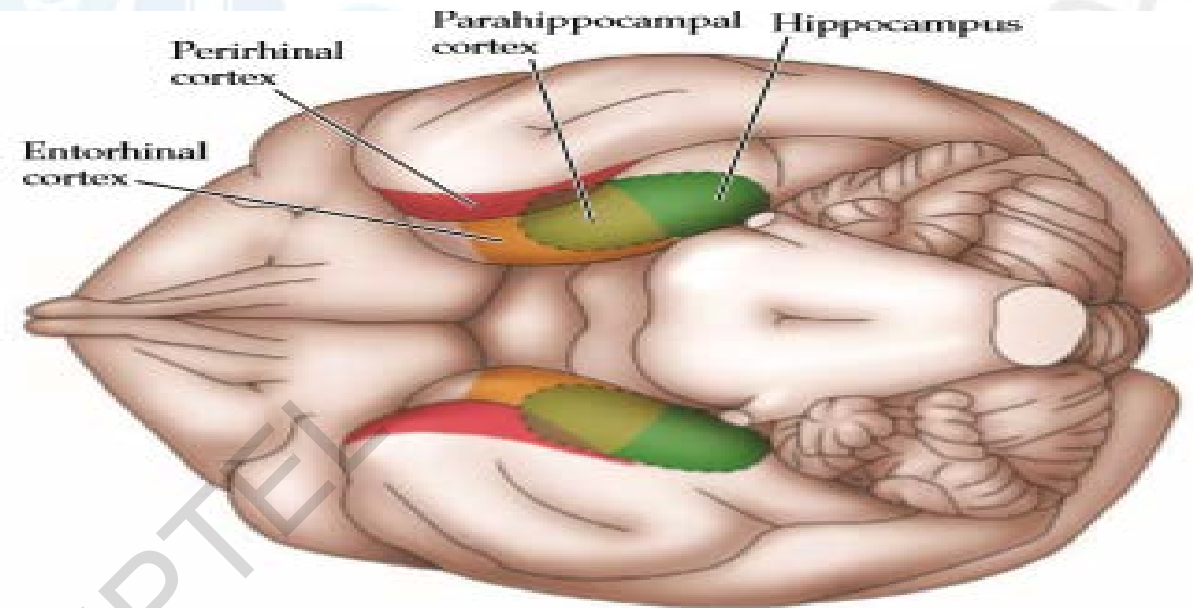
- Paul Broca coined the term
- Ancient functions

HOME



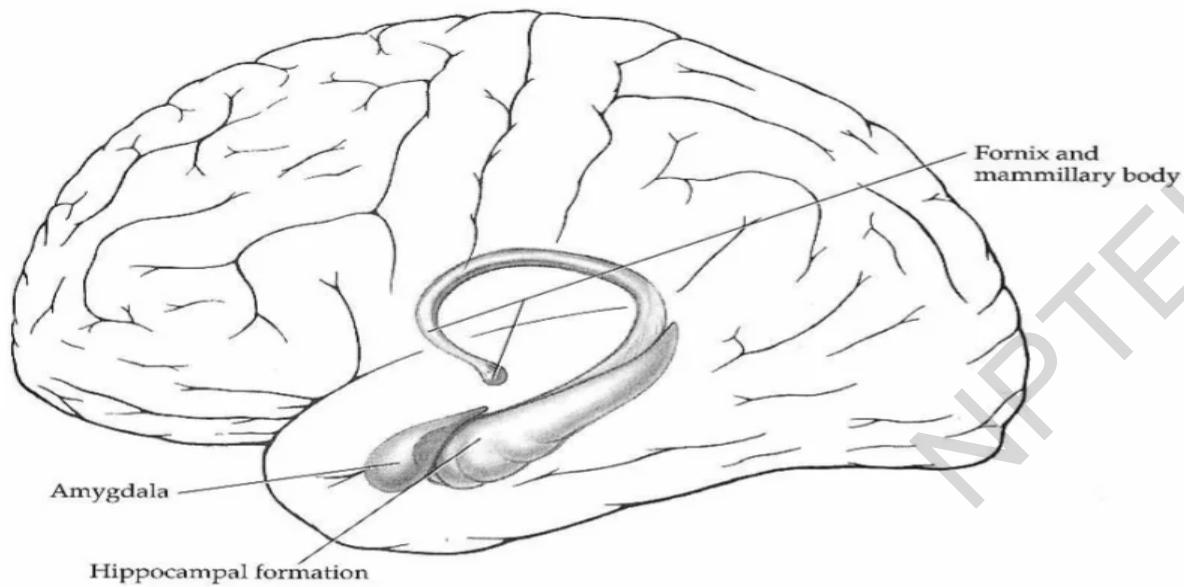
Limbic Cortex

- Cingulate gyrus & Para hippocampal gyrus
- Other cortices giving inputs to Entorhinal cortex

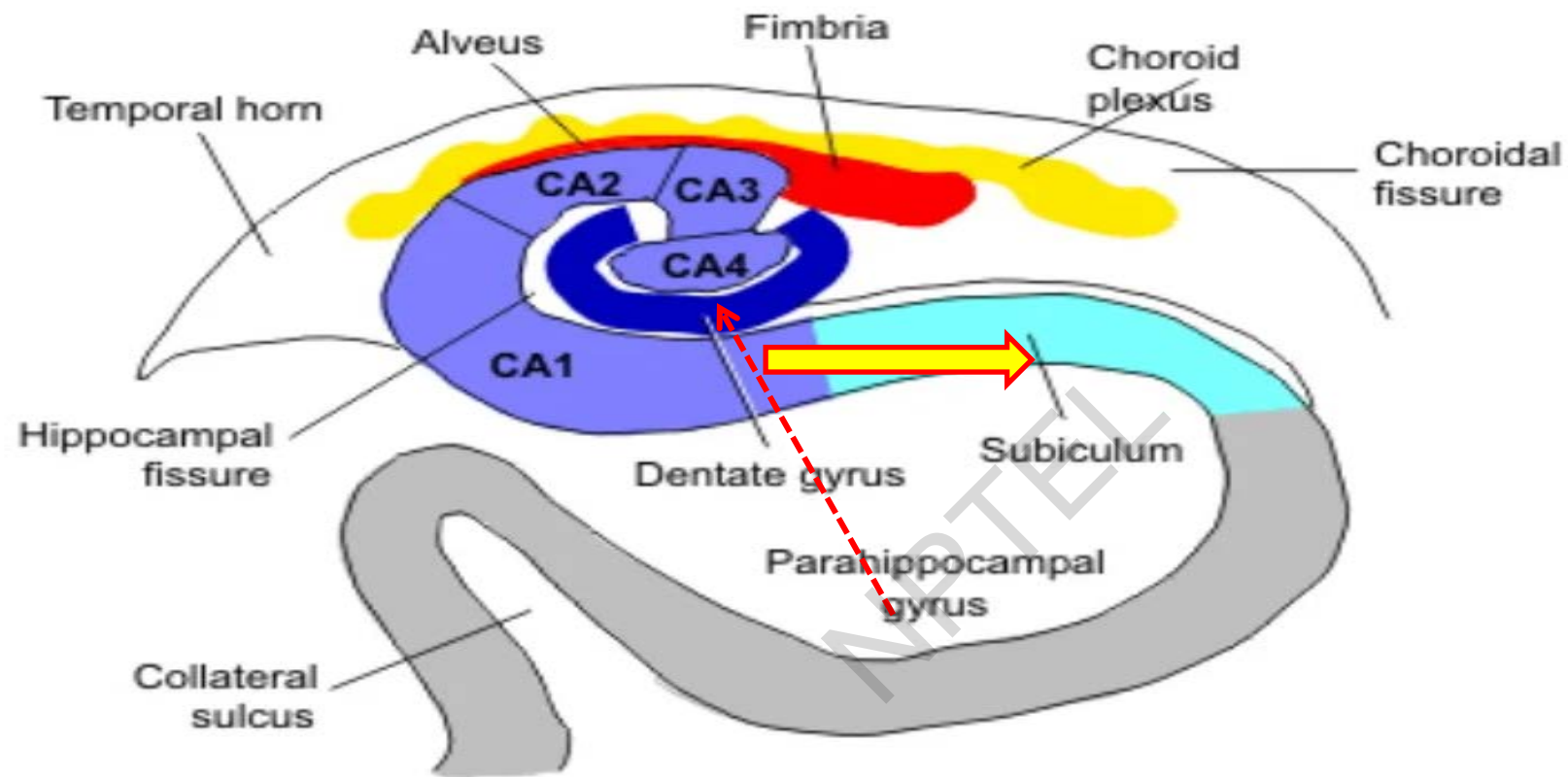


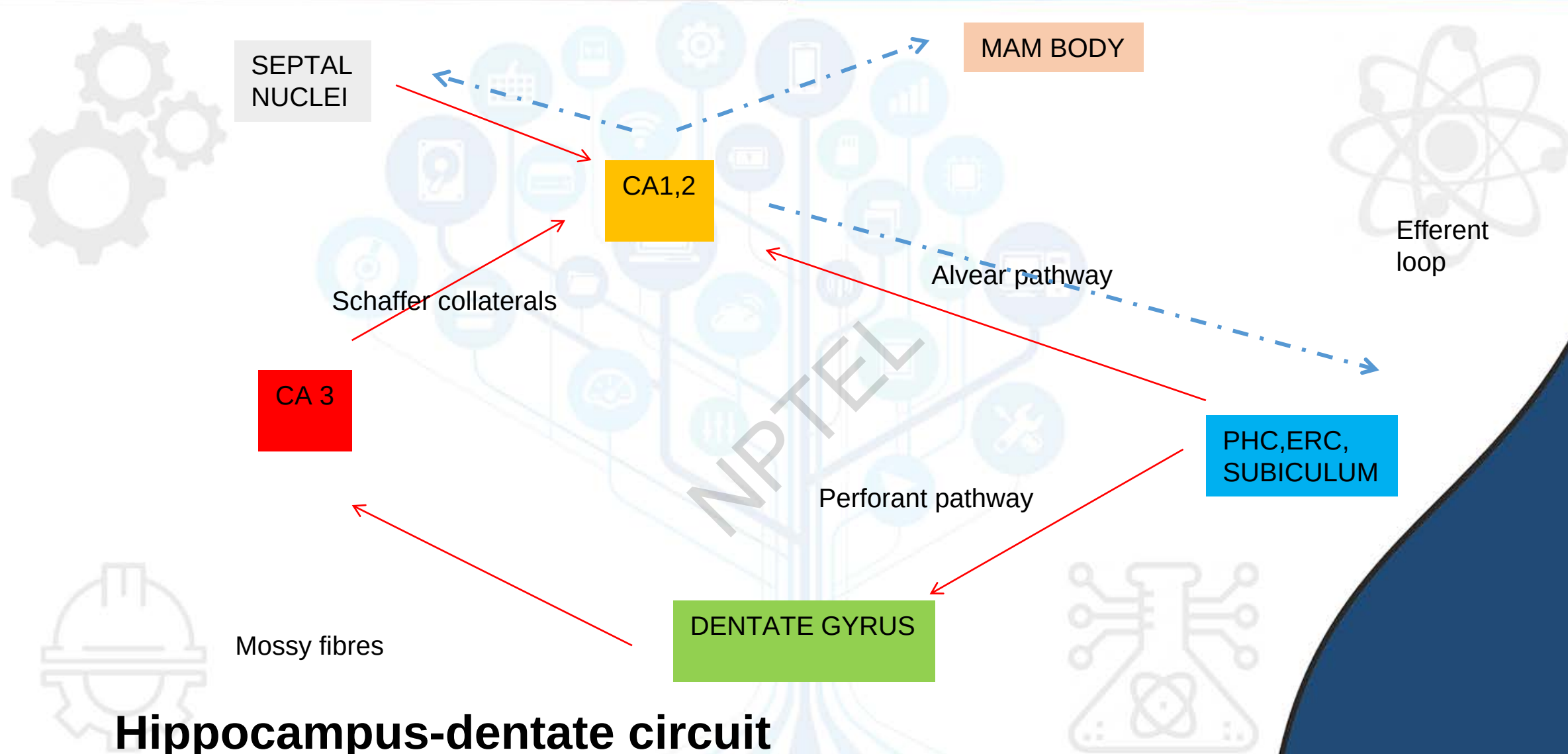
Hippocampal formation

Note the “C” shape, along with the major output paths for the hippocampus: the fornix.



Dentate Gyrus, Hippocampus,
Subicular complex





Hippocampus-dentate circuit

Amygdala

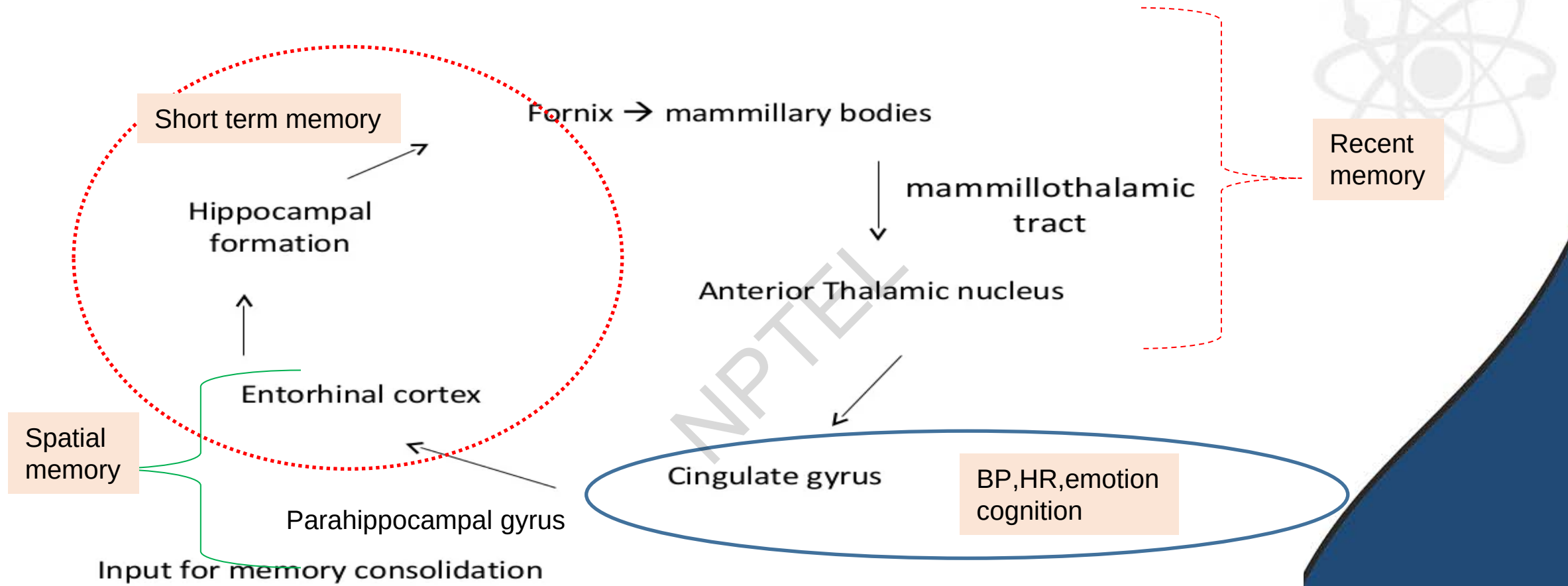
- Located in the medial temporal lobe, anterior to hippocampal formation.
- Group of nuclei
- Largest- Basolateral → connected to cortical regions → relay information to thalamus
- Centromedial nucleus- hypothalamus

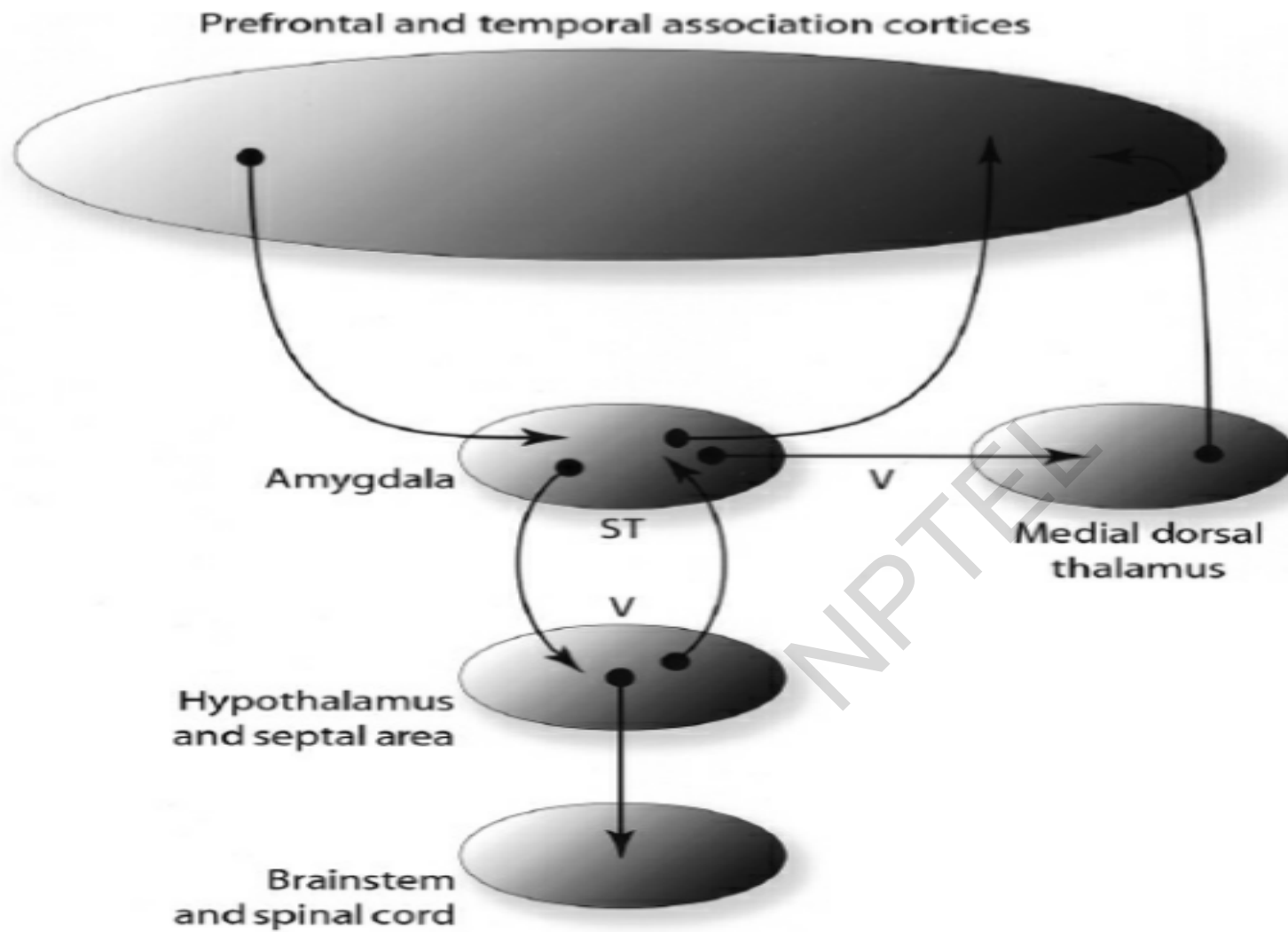
Septal area

Gray matter, connected to hippocampus, amygdala , hypothalamus.

Hypothalamus

Papez' Circuit:

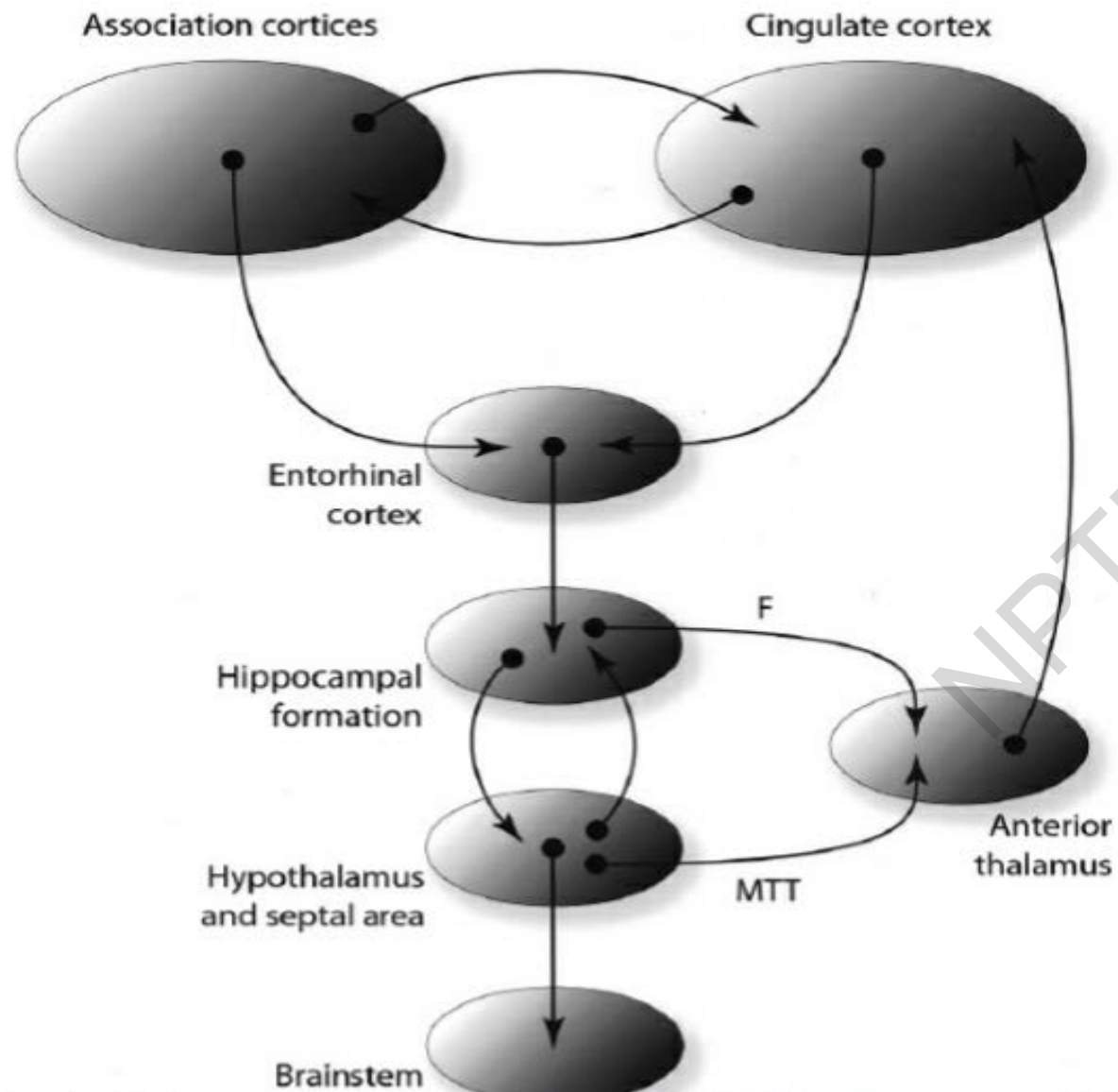




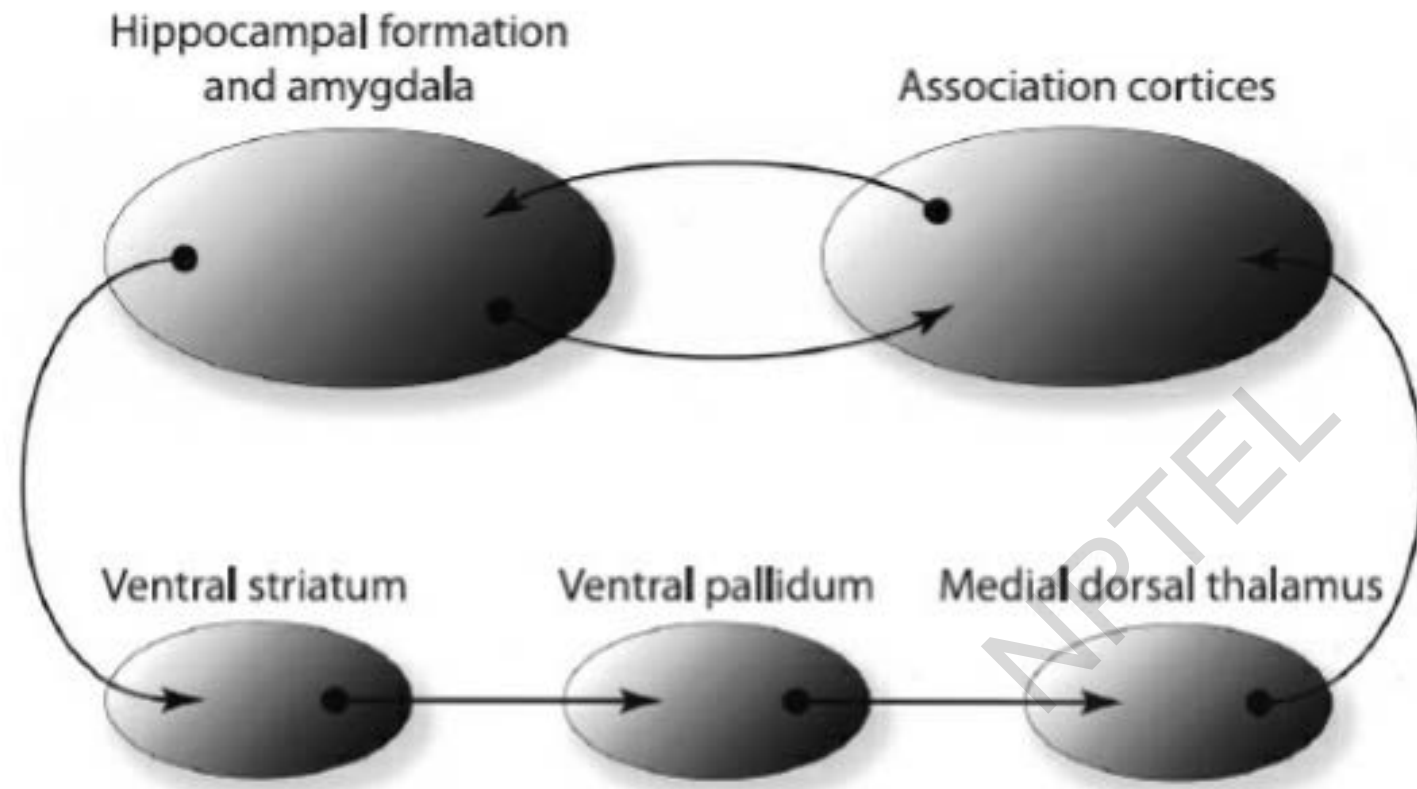
cognition



Amygdala, Hypothalamus & Cortex circuit



Hippocampal formation and anterior thalamus provide a mechanism for the integration of information between the cerebral cortex and the hypothalamus.



Interaction between the limbic system and certain components of the basal ganglia

Functions

➤ *Olfaction*

Olfactory receptors

axons

Olfactory bulb

Piriform cortex

Entorhinal cortex

Amygdala

➤ *Eating*

➤ *Sleep & dreams*

Limbic system ties emotions and memory during REM sleep- content of dreams.
Sleep promoting and wake promoting area-hypothalamus.

➤ *Autonomic & endocrine responses to emotions*

CRH release from Paraventricular nuclei of hypothalamus.

➤ **Sexual Behaviour**

MnPO and Medial Amygdala

➤ **Addiction & motivation**

Reward circuitry underlying addictive behaviour includes amygdala & Nucleus accumbens.

➤ **Memory**

➤ **Social cognition**

Cingulate gyrus & amygdala

Kluver- Bucz Syndrome

- b/l destruction of amygdaloid body & medial temporal lobe.
- Visual agnosia
- Hyperorality
- Hypersexuality
- Placidity
- Hypermetamorphosis
- Changes in dietary habits

Keypoints

- PD MacLean called the limbic system as “**the visceral brain**” for its close association with hypothalamus and visceral autonomic functions.
- Limbic system is primarily involved in
 - Motivation
 - Addiction
 - Emotions of Fear, Anxiety, Rage, and Aggression
 - Sexual Activity
 - Autonomic Responses

REFERENCES

1. Review of Medical Physiology, William F Ganong, 23e
2. Kaplan & Saddock's Comprehensive Textbook of Psychiatry, 9e
3. Guyton and Hall Textbook of Medical Physiology, John E. Hall, 13e
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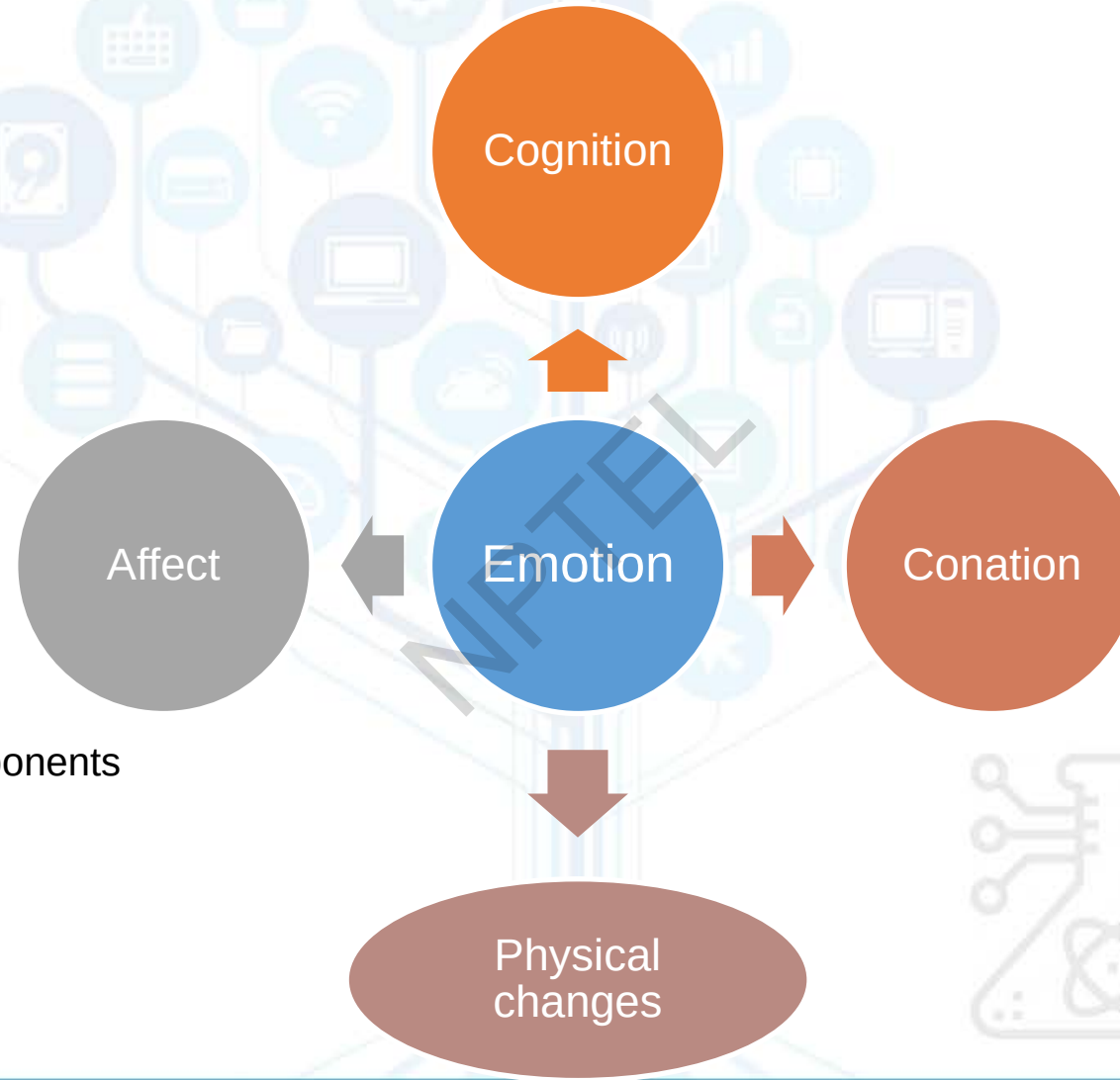
Lecture 9: Physiology of emotions

CONCEPTS COVERED

- **Components of Emotion**
- **Basic emotions**
- **Theories of emotions**
- **Biological basis of emotion**

Components of Emotion

- Derived from latin '**emovere**'



- Both mental & Physical components



Basic emotions

(Ekman's findings)

Anger



Sadness



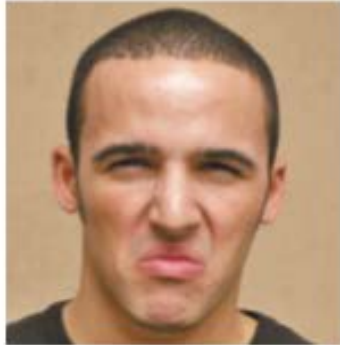
Happiness



Fear



Disgust



Surprise



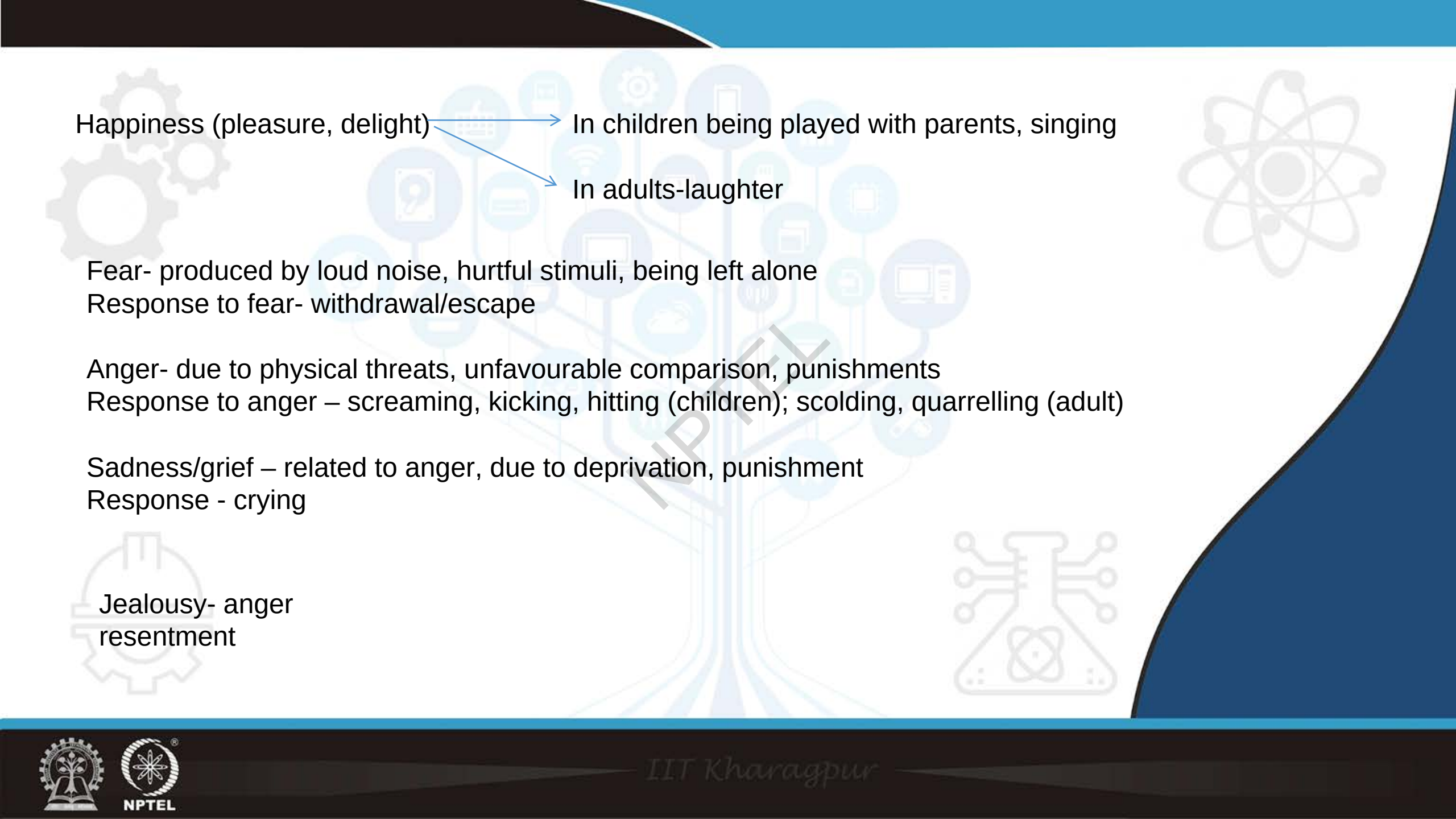
Contempt



Embarrassment



- Happiness
- Sadness
- Fear
- Anger
- Surprise
- Disgust
- Complex emotions- anger + disgust=contempt
- Sadness + surprise = disappointment



Happiness (pleasure, delight)

→ In children being played with parents, singing

→ In adults-laughter

Fear- produced by loud noise, hurtful stimuli, being left alone

Response to fear- withdrawal/escape

Anger- due to physical threats, unfavourable comparison, punishments

Response to anger – screaming, kicking, hitting (children); scolding, quarrelling (adult)

Sadness/grief – related to anger, due to deprivation, punishment

Response - crying

Jealousy- anger
resentment

Theories of emotion

Cannon-Bard

James Lange

Schachter-Singer

Opponent process

Cannon- Bard theory- Emotional exp

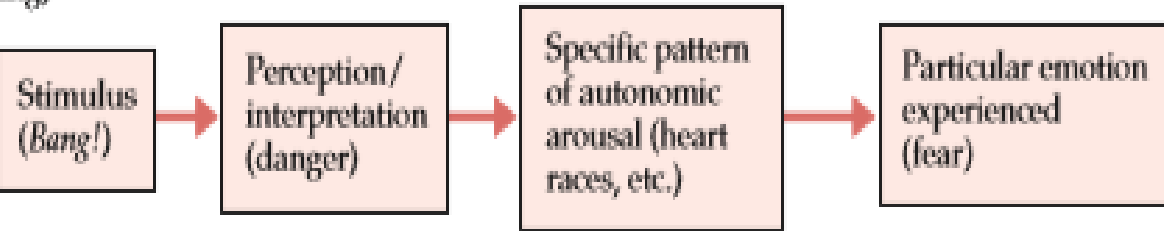
ANS

Brain

Eg. Influence of cerebral cortex in controlling emotion
Response unrelated to provocation, short lived

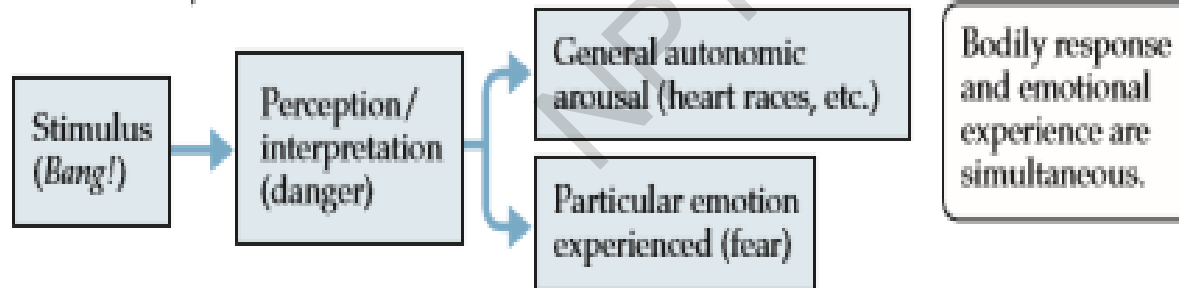
1 James-Lange theory
(autonomic reaction triggers feeling)

James and Lange argued that the bodily response evokes the emotional experience.



2 Cannon-Bard theory
(simultaneous feeling and autonomic reaction)

Cannon and Bard insisted that the brain must interpret the situation to decide which emotion is appropriate.



James Lange theory

emotional event → response in ANS → CNS detects → produce an emotional exp

Eg, Positive emotions accompanied with increased blood flow to limbs & constriction of pupil

Contradictions-

- spinal cord lesions-experience feeling of quite intense emotions
- Inj epinephrine-arousal, but no emotional experience

Schachter & Singers theory

- 2 factor theory

Perception of an environmental situation



Generalized state of bodily arousal which is perceived



Interpretation of the reasons for the generalized arousal state



Felt emotion depends upon the reasons given for the arousal state



Autonomic arousal is noticed by the person- come up with an explanation for the arousal -emotion



(A)

Some participants were injected with epinephrine but not warned of its effects.



Happy confederate

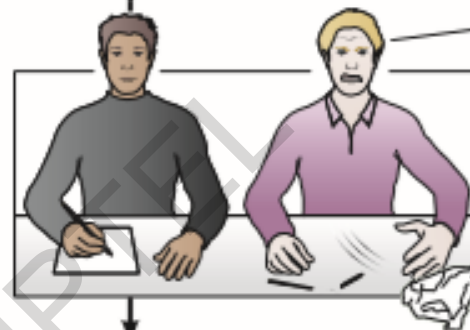
Some participants are exposed to a happy confederate while filling out the form.



These participants were more likely to report feeling elated.

Angry confederate

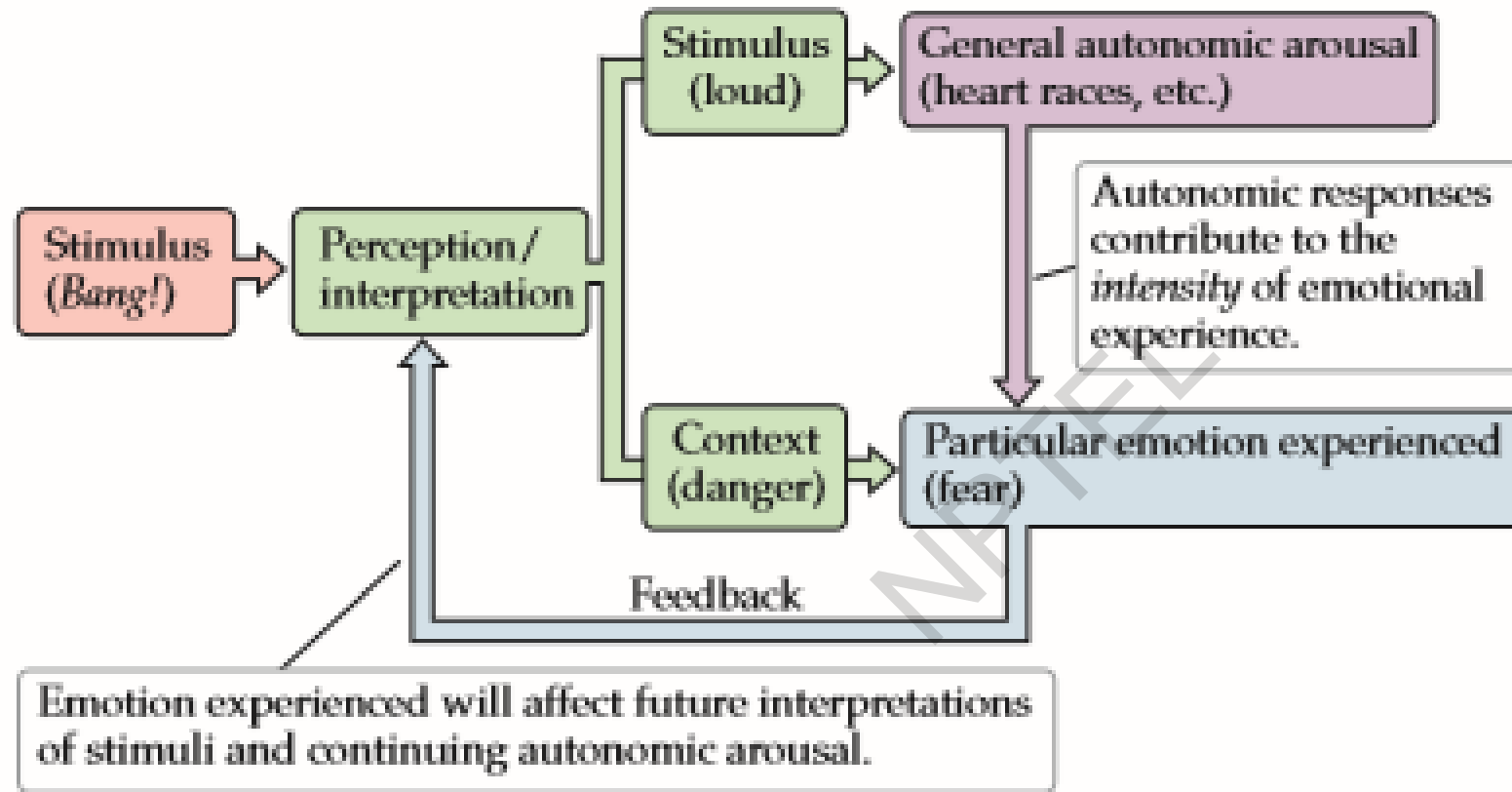
Other participants are exposed to an angry confederate while filling out the form.



These participants were more likely to report feeling angry and frustrated.



(B) Schachter's cognitive attribution model



Biological basis of emotion

- Rt cerebral hemisphere- emotional functions
- Lt cerebral hemisphere- positive affect
- Rt cerebral hemisphere-negative affect

Emotional processing

Prefrontal cortex

Cingulate gyrus /cortex

Hippocampus

Amygdala

Effects of emotions on different systems

ANS-
Stress

→ SNS

→ adrenaline

↓
Palms sweating, increased HR, increased conductance,
Focussed attention

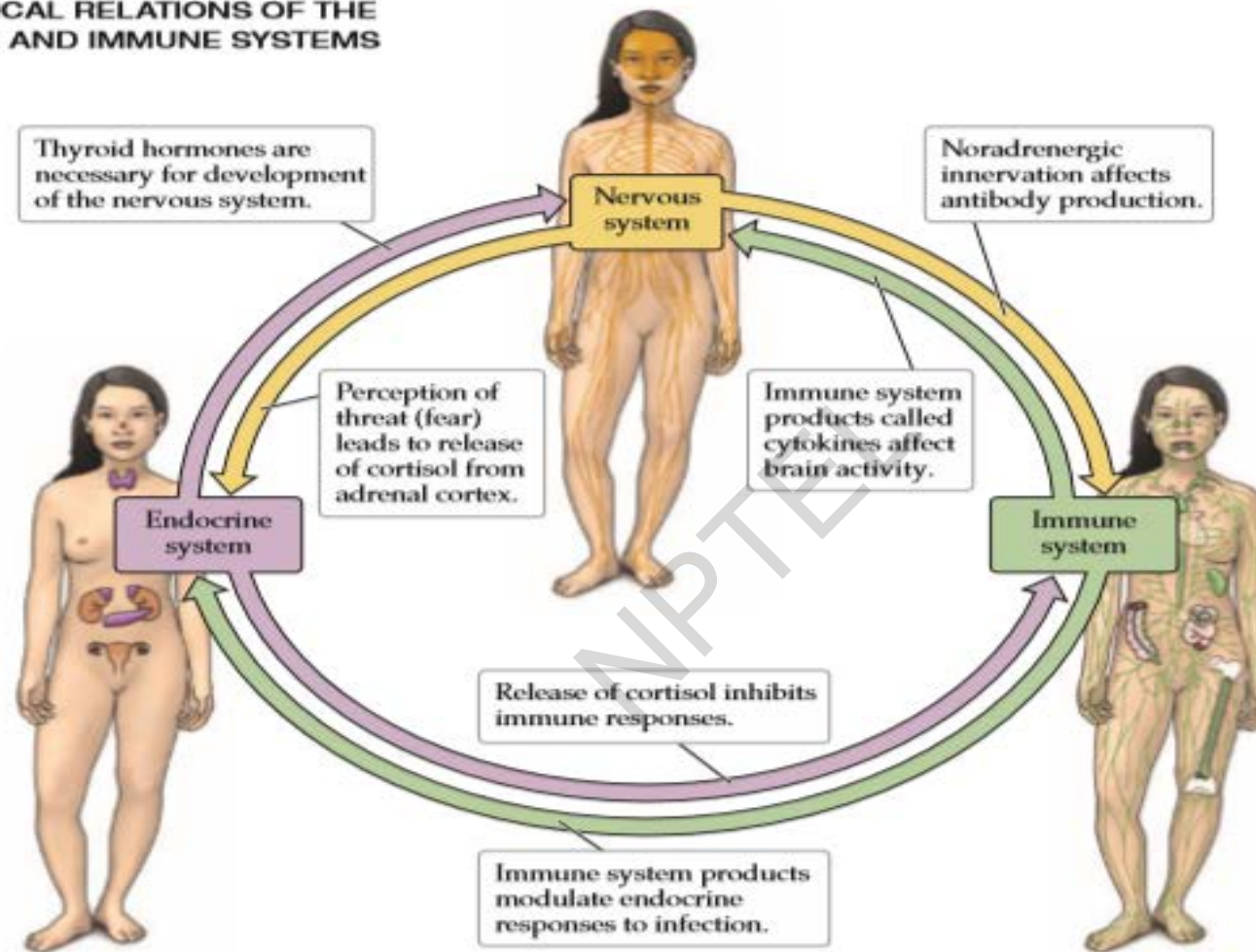
Immunological disturbance
Depression

→ decreased lymphocyte production

Endocrine system
HPA activity

→ elevated in stress, increased in depression, increased cortisol in depression

EXAMPLES OF RECIPROCAL RELATIONS OF THE NERVOUS, ENDOCRINE, AND IMMUNE SYSTEMS



Keypoints

1. Components of emotions, emotions influence our behaviour.
2. Theories of emotions
3. Stress elevates levels of hormones from the adrenal cortex (cortisol) and the adrenal medulla (epinephrine and norepinephrine), while suppressing other hormones (testosterone).

REFERENCES

1. Behavioural Neuroscience, Breedlove, 6e
2. Guyton and Hall Textbook of Medical Physiology, John E. Hall, 13e
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Basics of Mental Health & Clinical Psychiatry

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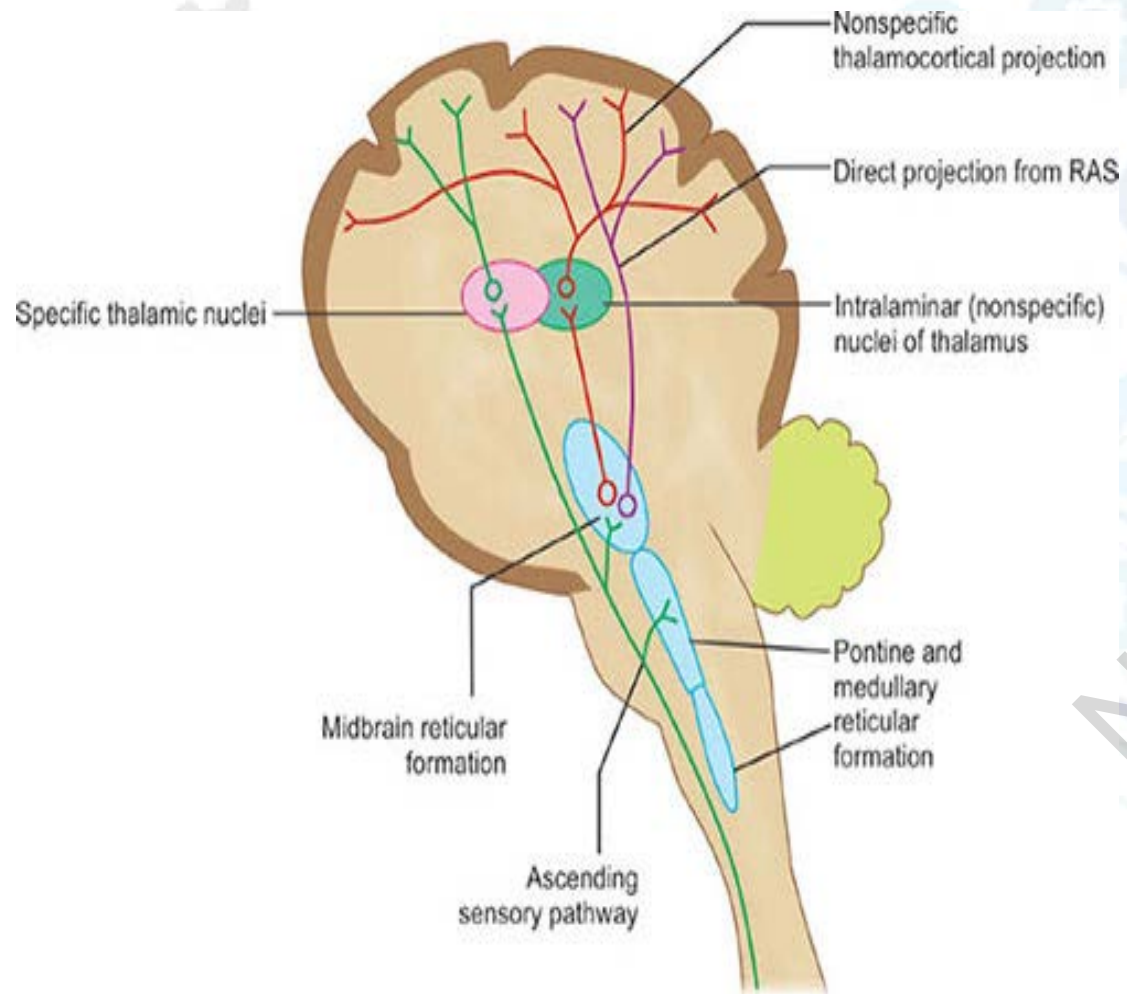
**Dr B.C. Roy Multi-speciality Medical Research Centre
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Lecture 10: Reticular formation

CONCEPTS COVERED

- Location
- Reticular nuclei
- Pathways
- Functions

NPTEL



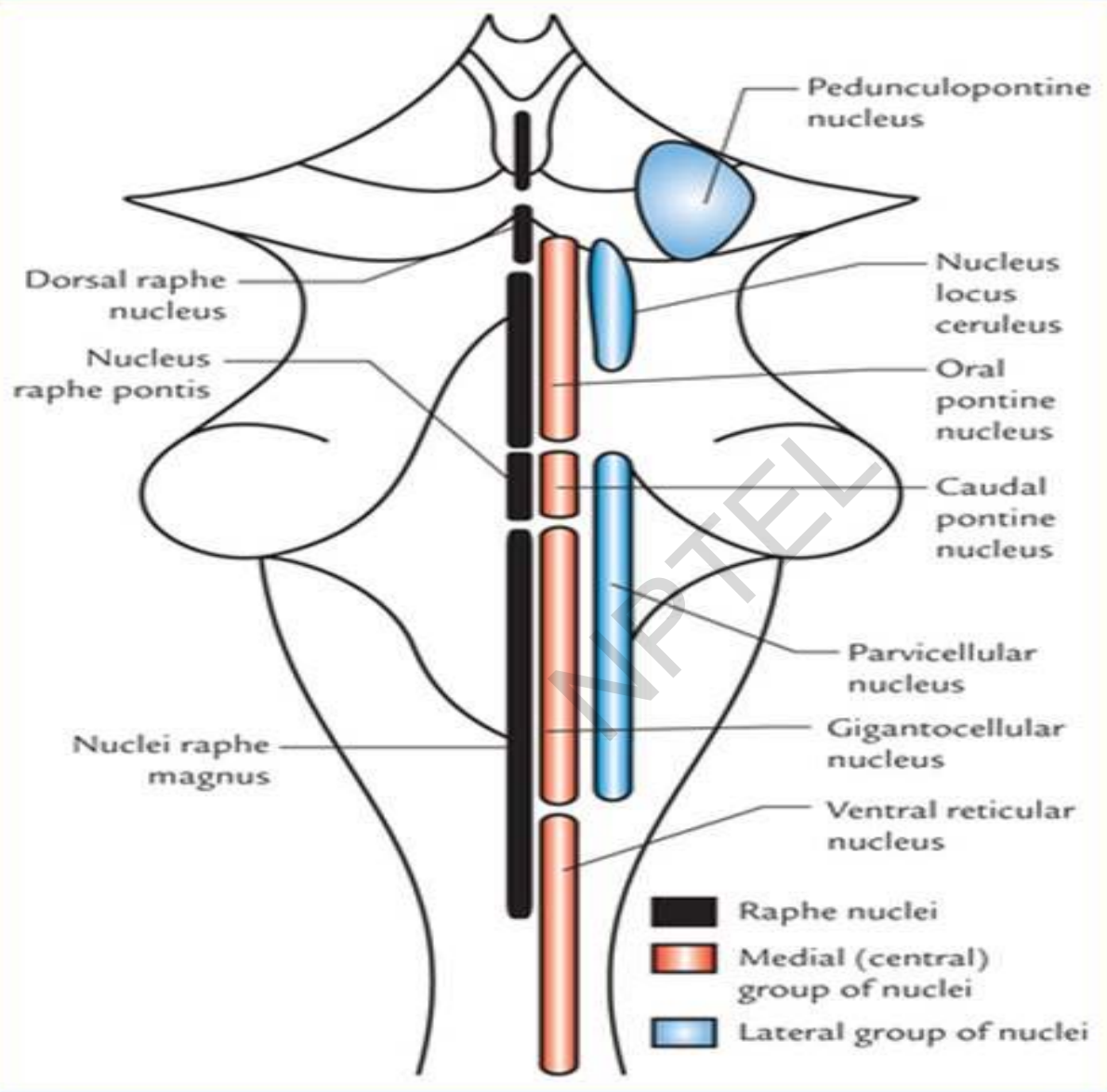
WHERE IS RETICULAR FORMATION

- LOCATED IN THE BRAINSTEM – TEGMENTUM
- RUNS ALONG THE LENGTH OF BRAINSTEM

- Comprises of Medullary, Pontine & Midbrain Reticular Formation.
- Poly synaptic.
- Has both ascending and descending components.

Reticular nuclei

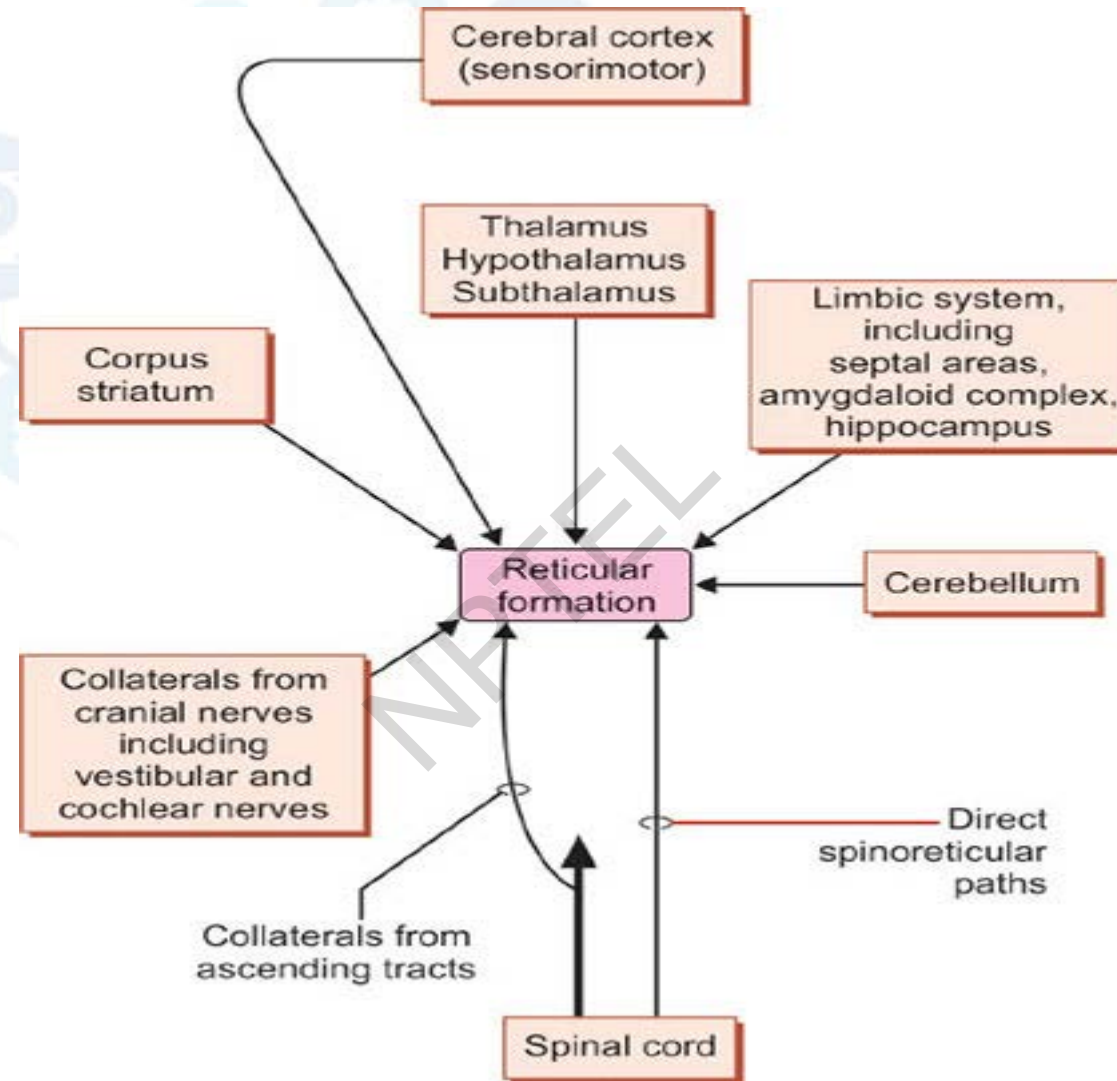
- Median column → Raphe nuclei, serotonin, arousal
- Medial column → Magnocellular cells, control of eye movements, swallowing & brainstem reflex
- Lateral column → Parvocellular cells, control of respiration, arterial pressure, visceral functions



RETICULAR PATHWAYS

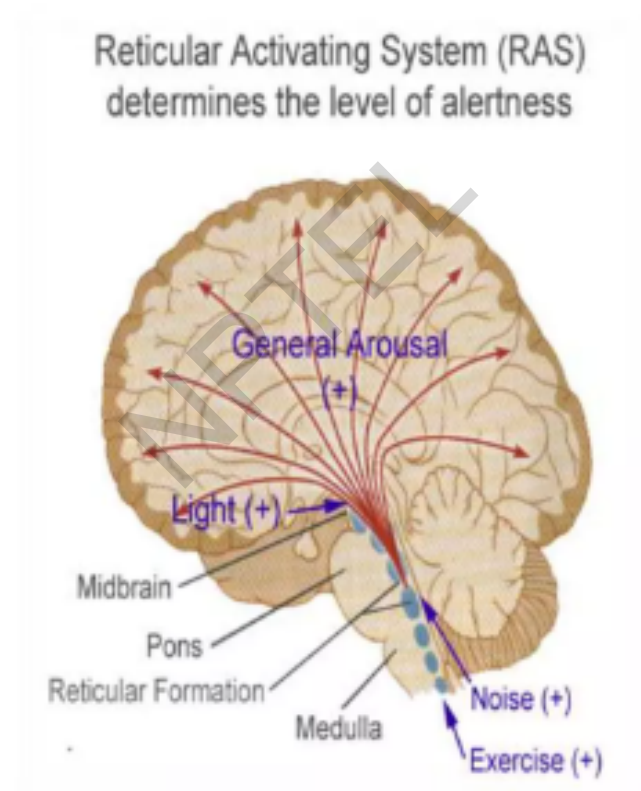
1. Ascending reticular activating system
2. Descending reticular activating system

Afferent pathways

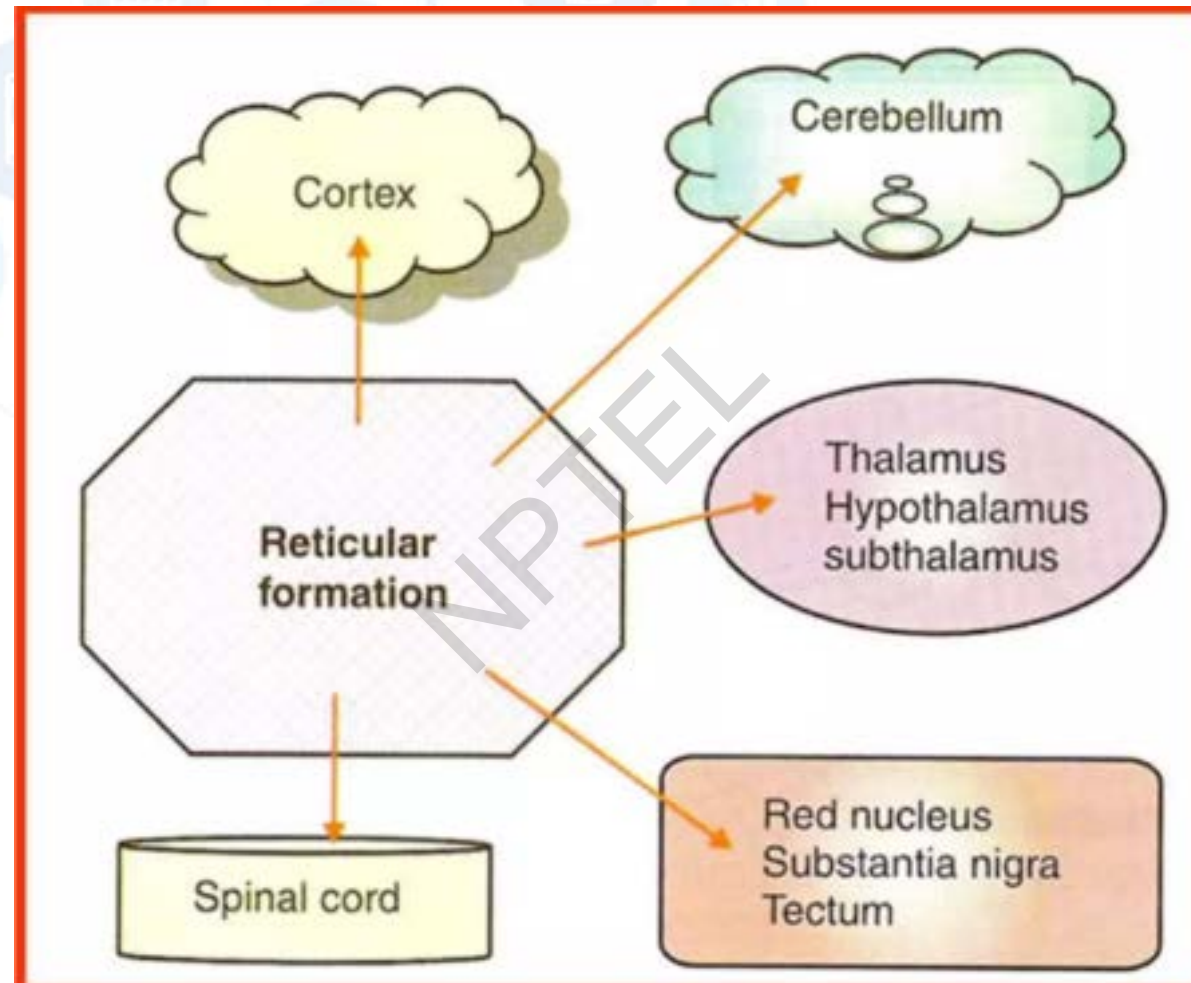


Ascending Reticular Activating System

- It projects into cerebral cortex in two ways
- 1. Through **Subthalamus** and
- 2. Through **Thalamus**
- Begins in lower part of brain stem, extends upwards through the Pons, midbrain, thalamus and finally projects throughout the cerebral cortex.



Efferent pathways



Functions of ARAS

- Wakefulness
- Selective attention & inattention
- Generation of alpha waves in EEG

Functions of DRAS

- Inhibitory
- Facilitatory

Reflex movements, regulation of tone, posture,
Smoothness & accuracy of voluntary movements

Muscle tone maintenance, autonomic functions
Activates ARAS

Regulation of posture by RAS

CORTEX
BASAL GANGLIA

CORTEX
CEREBELLUM
CAUDATE NUCLEUS

+
PONTINE RF

-
MEDULLARY RF

+
GAMMA MOTOR DISCHARGE

ALPHA MOTOR NEURON

Keypoints

- Reticular formation has long ascending branches projecting to the thalamus, hypothalamus, and cortex, and long descending branches projecting to the spinal cord.
- Reticular formation gives rise to reticulospinal tracts (RSTs). RSTs are important components of medial system pathways that are involved in regulation of posture.
- Increased activity in these projecting neurons causes excitation of cortical neurons and creates alertness and wakeful state.
- Major monoaminergic and cholinergic systems of the brain are located in the reticular activating system.
- These fibers are involved in integration of various sensory and behavioral activities.

REFERENCES

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2. Medical Physiology, Walter F. Boron, 3e
3. Comprehensive Textbook of Medical Physiology (Volume 2)
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**THANK
YOU !**