
بسم الله الرحمن الرحيم

# CNS NEUROTRANSMITTERS

Dr Memuna Kanwal

**SOURCE :**
**BERTRAM G.KATZUNG BASIC & CLINICAL PHARMACOLOGY 15TH EDITION**
**GOOGLE FOR IMAGES & RESEARCH ARTICLE**

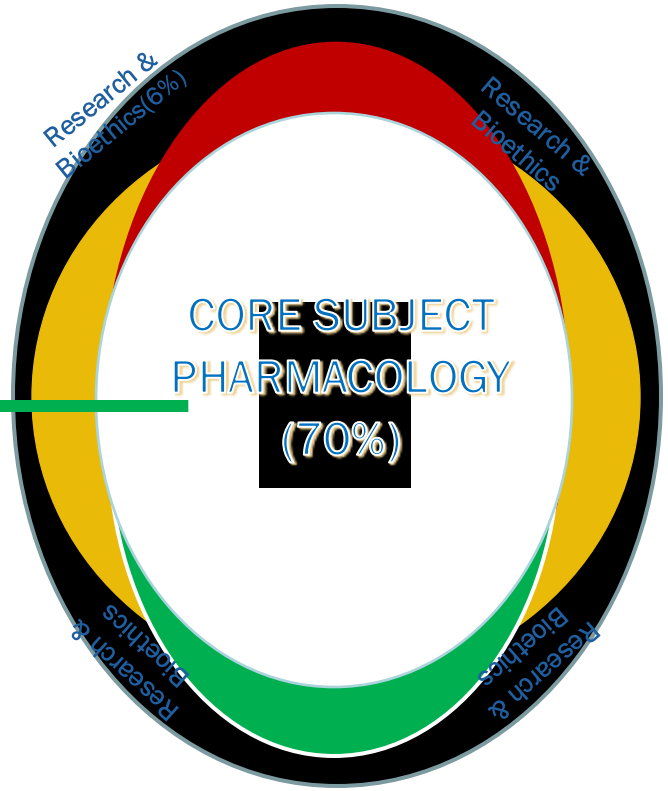
# MOTTO AND VISION


- To impart evidence based research oriented medical education
- To provide best possible patient care
- To inculcate the values of mutual respect and ethical practice of medicine

# PROFESSOR UMAR'S CLINICALLY ORIENTED INTEGRATION MODEL INTERACTIVE LECTURES

VERTICAL INTEGRATION
Clinical Subjects (18%)

SPIRAL INTEGRATION
ANATOMY / PHYSIOLOGY ( 6% )




| 4TH Year Pharmacology LGIS(19 slides) | |
|---|---|
| Core Subject – 9slides (48%) | |
| Vertical integration (Clinical Subjects) | • 4 slides (21%) |
| Spiral Integration (basic sciences subjects) | • 1 slide (5%) |
| Spiral integration | • 5 slides (26%) |

# LEARNING OBJECTIVES

- To know about different neurotransmitters in CNS
- Classify the CNS Neurotransmitters
- To understand the different neurotransmitters function
- Role of neurotransmitters in different diseases
- Drugs acting on different neurotransmitters

# NEUROTRANSMITTERS

- What are neurotransmitters?
- Properties of neurotransmitters:

| | |
|---|---|
| Present in higher concentration in synaptic area than in other areas | Localized to vesicles in presynaptic neuron |
| Released by electrical or chemical stimulation via Ca-dependant mechanisms | Rapidly removed from synaptic cleft by uptake or degradation |
| Presence of receptors on post-synaptic membrane | Binding to receptors elicit a biologic response |

CORE SUBJECT

# TYPES OF NEUROTRANSMITTERS

1. **Excitatory:**
   - Glutamate
   - Aspartate
   - Nitric Oxide
2. **Inhibitory:**
   - GABA
   - Glycine
   - Dopamine
   - Serotonin
3. **Both:**
   - Acetylcholine, Nor-epinephrine

# CLASSES OF NEUROTRANSMITTERS

## Amino Acids

- Aspartate
- Glutamate
- GABA
- Glycine

## Monoamines

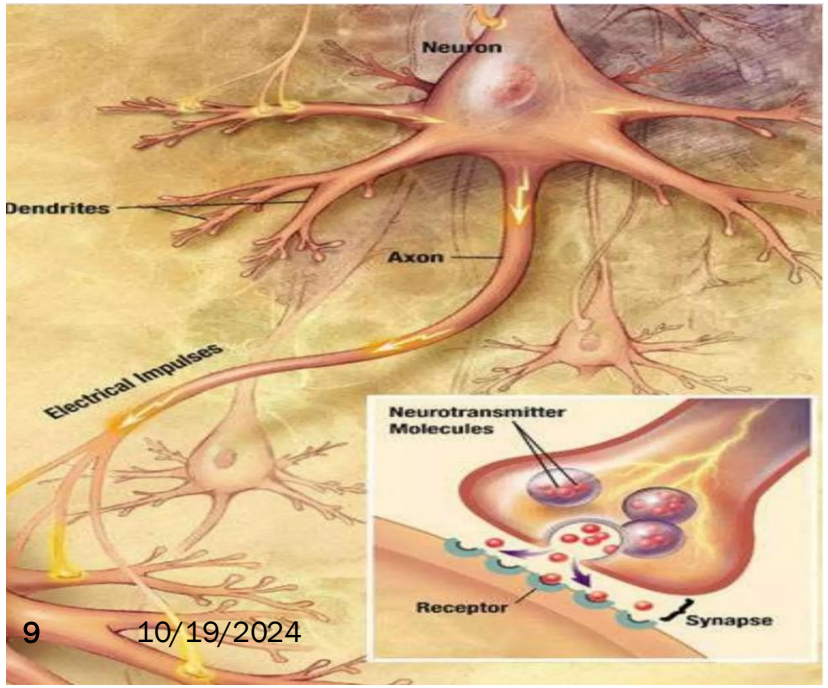
- Dopamine
- Epinephrine
- Norepinepherine
- Indolamines: Serotonin

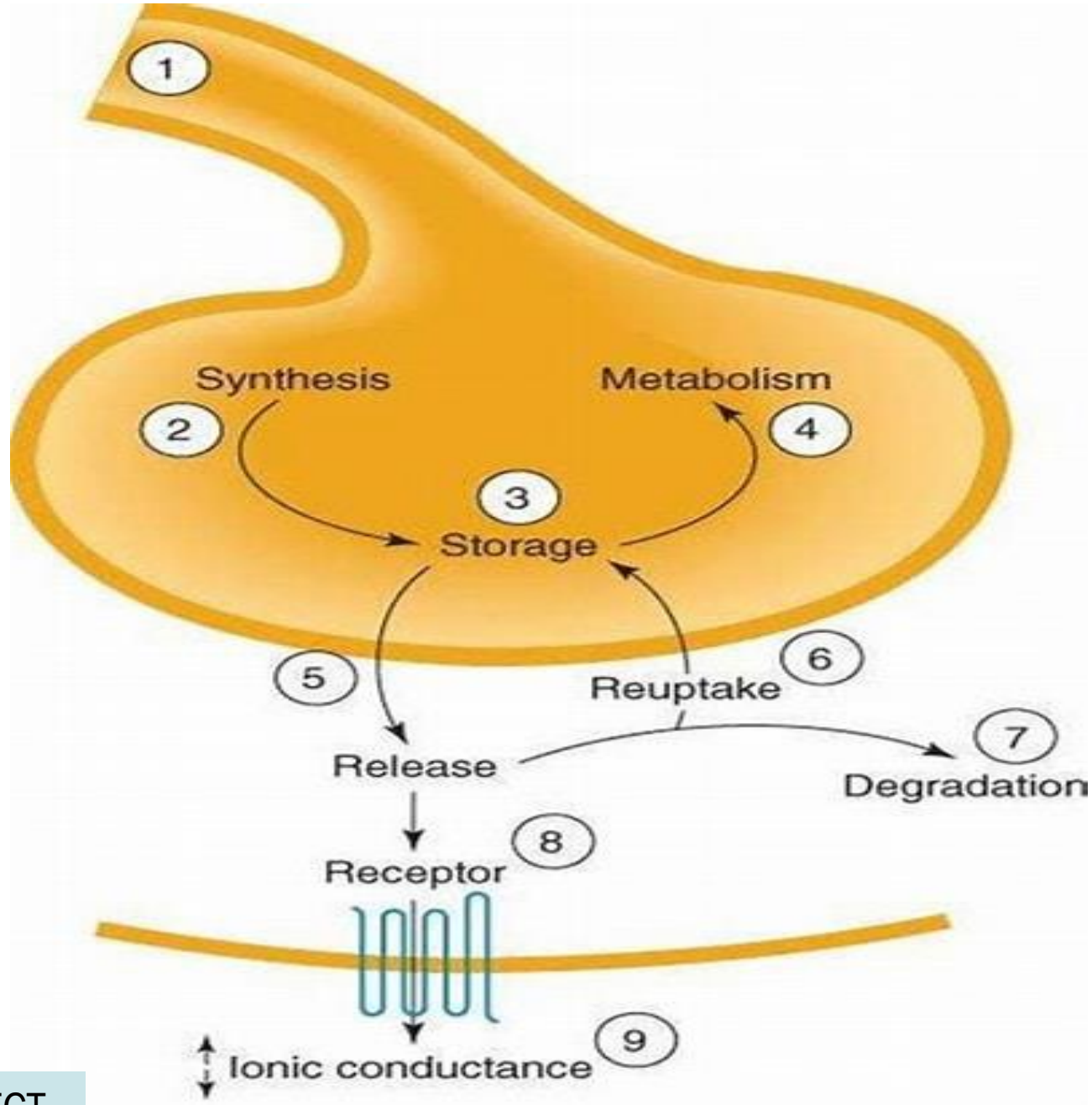
## Soluble Gases

- Nitric Oxide
- Carbon Monoxide
- Miscellaneous: Acetylcholine

CORE SUBJECT

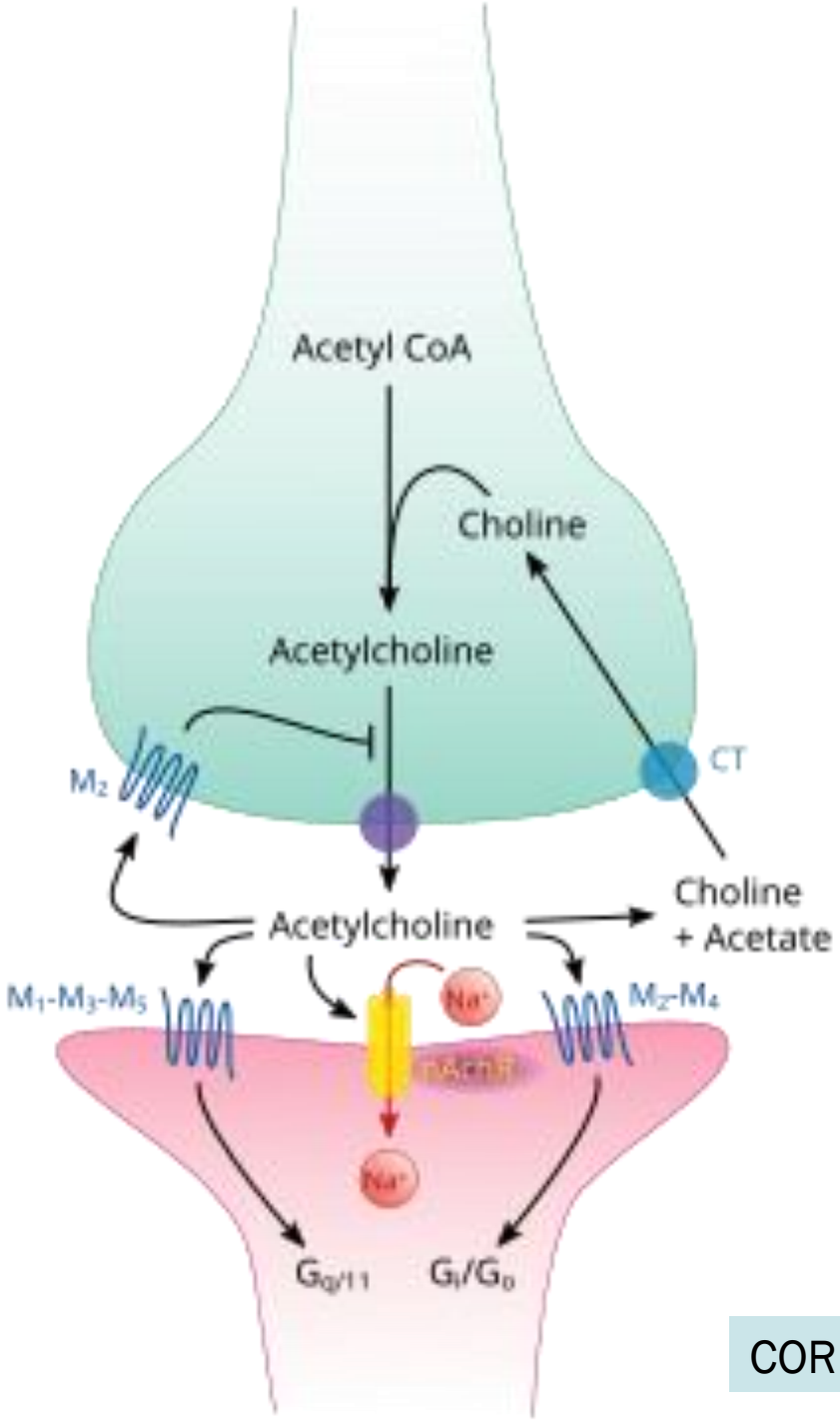
# How drugs can affect neurotransmitters action?






CORE SUBJECT




# ACETYLCHOLINE

- 5% brain neurons have receptors for ACh.
- Receptors
  - Metabotropic: M1
  - Ionic: decrease in K permeability
- Involved in learning and memory

CORE SUBJECT

# ACETYLCHOLINE

Diseases affecting cholinergic systems in CNS include

- **Alzheimr's disease**
- **Parkinsonism** (disturbed balance between dopamine & acetylcholine)

Drugs affecting the cholinergic pathways are

- **Acetylcholinesterase inhibitors in Alzheimr's disease**
- **Muscarinic blockers in Parkinsonism**

VERTICAL INTEGRATION

# DOPAMINE

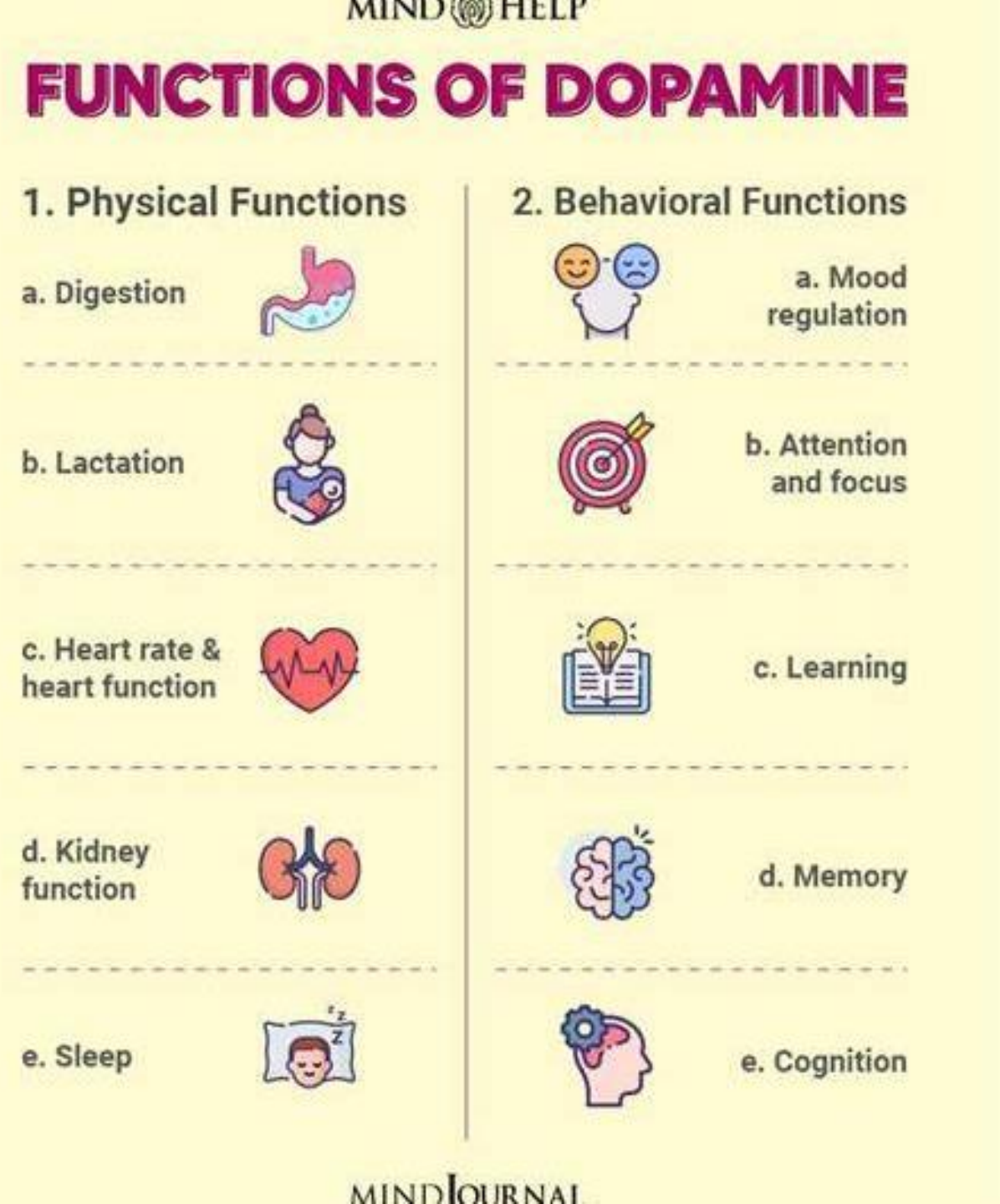
- Slow inhibitory action at synapses
- Postsynaptic: G-protein coupled activation of K-channels
- Presynaptic: inhibition of Ca-channels
- D1, D2, D3, D4 &D5 receptors
- D2: found in basal ganglia
- In parkinsonism: dopamine deficiency

# DRUGS ACTING ON DOPAMINERGIC PATHWAYS

- Drugs that block the pathway
  - Chlorpromazine
  - Haloperidol
- Drugs that increase dopaminergic activity
  - CNS stimulants (amphetamine)
  - Levodopa

VERTICAL INTEGRATION





# NOREPINEPHERINE

- Mainly located in the brain stem
- Fan out broadly to provide CNS with diffuse noradrenergic input.
- Excitatory: alpha 1, beta 1
- Inhibitory: alpha 2, beta 2
- Drugs enhancing noradrenergic patways: amphetamines, cocaine, TCA, MAO inhibitors

# SEROTONIN

- Found in pons & brainstem
- Multiple 5-HT receptors
- All are metabotropic except 5-HT3
- Excitatory and inhibitory function


CORE SUBJECT

1. Used in treatment of major depressive disorders
    - TCA, SSRIs, SNRIs
2. Newer antipsychotics: olanzapine

Reserpine:

- depletes vesicular stores of both serotonin & norepinepherine, thus causes severe depression

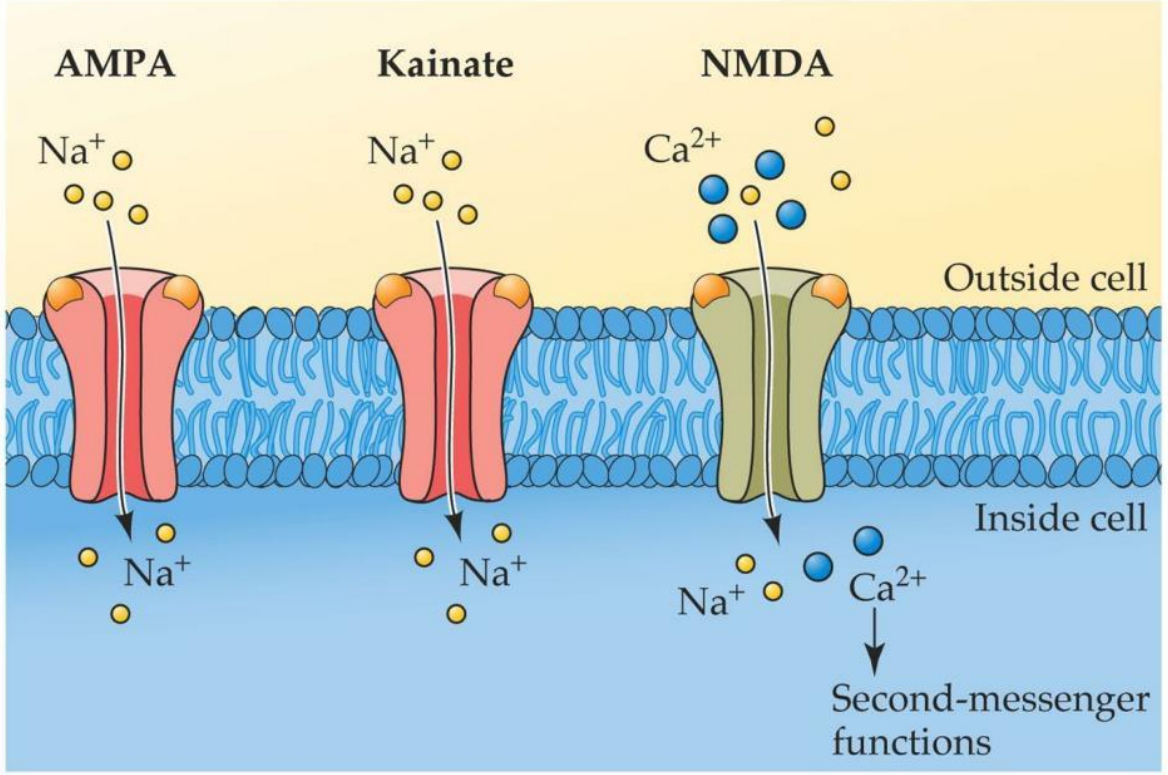
# DRUGS AFFECTING SEROTONERGIC PATHWAYS

CORE SUBJECT

# GLUTAMIC ACID

- Excitatory neurotransmitter
- Glutamate deficiency leads to congnitive impairment and inability to learn new things
- NMDA receptor: synaptic plasticity related to learning and memory

7.4 All ionotropic glutamate receptor channels conduct $Na^+$ ions into the cell




PSYCHOPHARMACOLOGY, Figure 7.4 © 2005 Sinauer Associates, Inc.

CORE SUBJECT

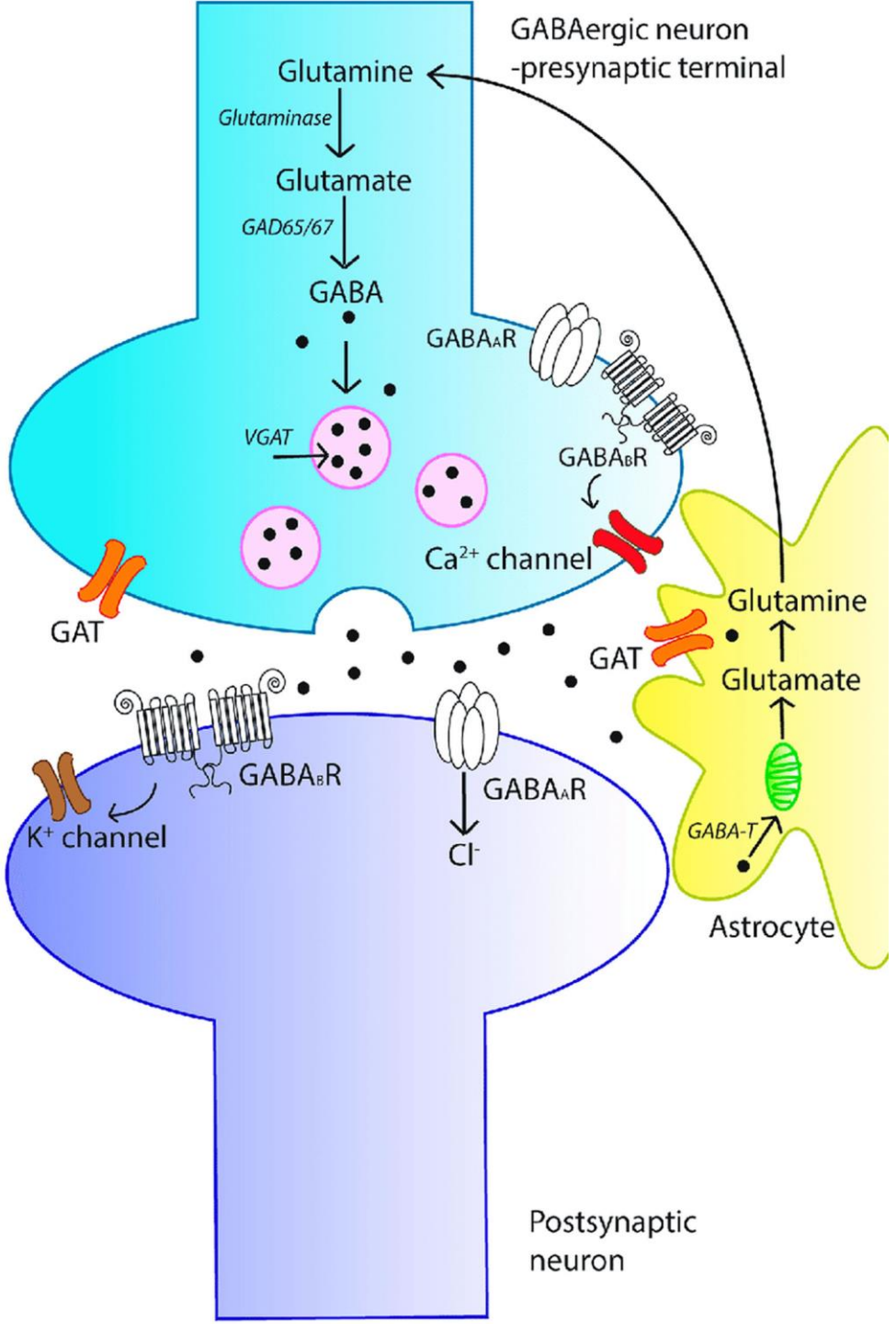
# DRUGS ACTING ON GLUTAMATE RECEPTORS

- Phencyclidine and ketamine block NMDA receptors
- Memantine is NMDA antagonist approved for Alzheimr's disease.
- Domoic acid: a toxin that activates kainate receptors and cause excitatory toxicity

CORE SUBJECT

# GABA

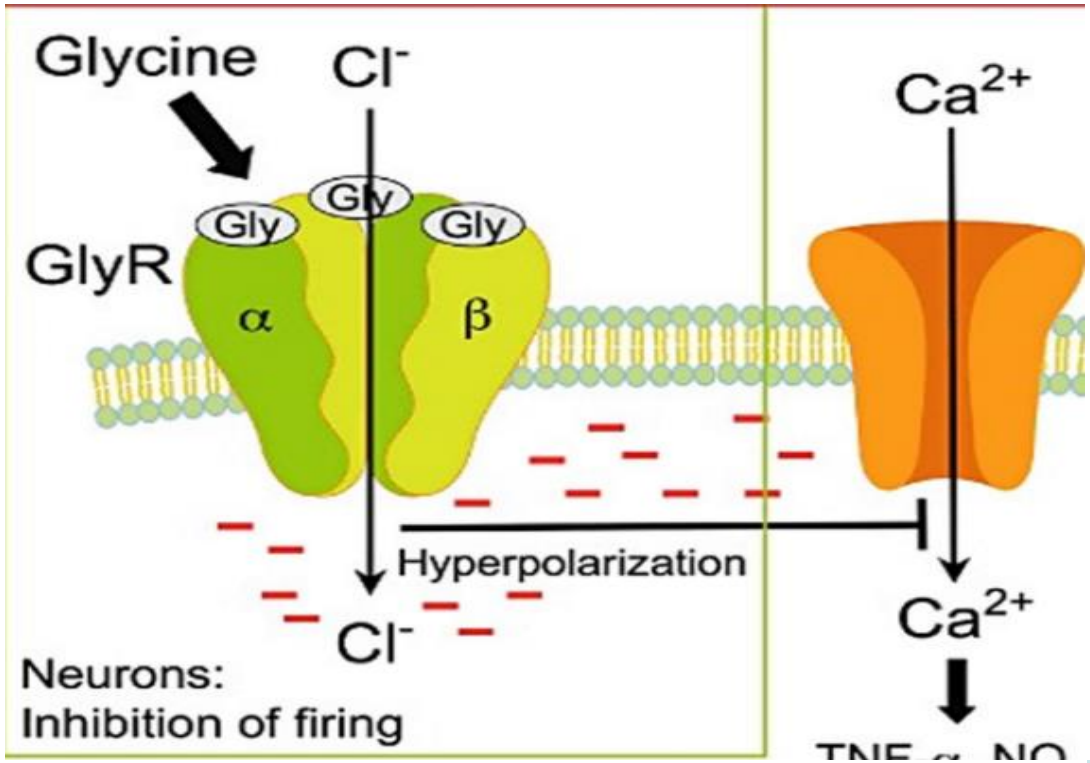
- Inhibitory neurotransmitter
- GABA-a receptors: chloride channel opening, Benzodiazeoines, barbiturates, anticonvulsants block GABA-a receptors. (Fast IPSP)
- GABA-b receptors: Either open K-channels, or close Ca-channels (Slow IPSP)






CORE SUBJECT

# GLYCINE




- Inhibitory neurotransmitter
- sedative effect
- Stimulate the production of serotonin
- Improves mood and cognition
- Strychnine: spinal convulsant

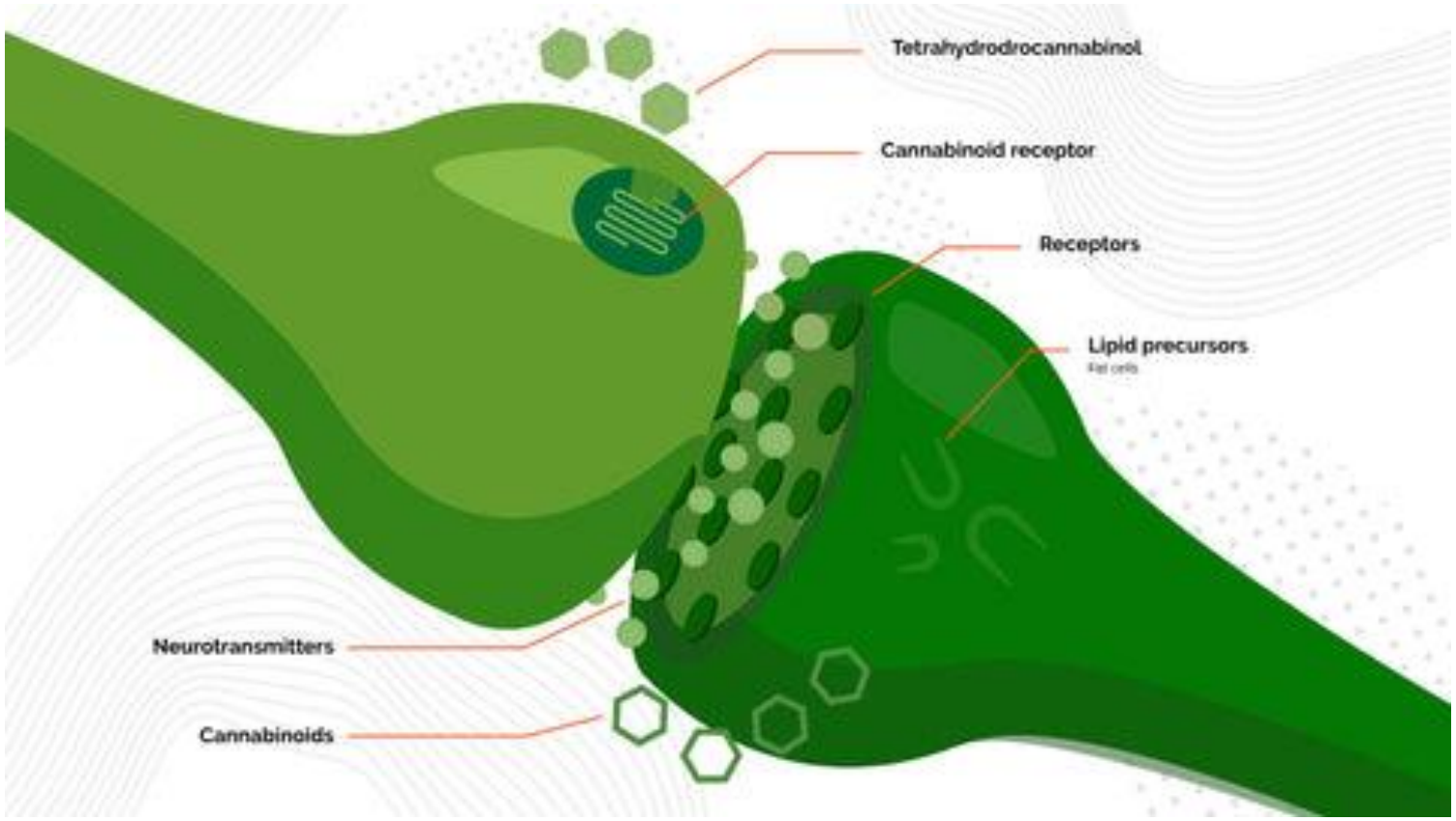
# PEPTIDE NEUROTRANSMITTERS

- **Synthesized in cell body & transported via axonal transport, no reuptake**
- **Opiod peptides**: endorphins, enkaphlins, dynorphin
- Opiod analgesics act through receptor activation for these endogenous peptides
- **Substance P**: mediator of slow EPSP involved in nociceptive pathways in brain stem & spinal cord.
- **Orexins**: promote wakefulness, associated with sleep-wake cycle



CORE SUBJECT

- Widely distributed brain lipids derivatives
- Phytocannabinoids: found in marijuna
- Involved in mood regulation, nociception, inflammation, appetite




# ENDOCANNABINOIDS

CORE SUBJECT

# OTHER NEUROTRANSMITTERS

- **Histamine:** sedative and anti motion sickness effect
- **NO:** synthesized on demand
- **Purines:** Cotransmitter
  - Receptors for ATP, UTP, adenosine and UDP are found on CNS
  - ATP inhibit calcium channels and reduce release of other neurotransmitters

CORE SUBJECT

# HOW TO ACCESS DIGITAL LIBRARY

- Go to the website of HEC National Digital Library.
- On Home Page, click on the INSTITUTES.
- A page will appear showing the universities from Public and Private Sector and other Institutes which have access to HEC National Digital Library HNDL.
- Select your desired Institute.
- A page will appear showing the resources of the institution
- Journals and Researches will appear
- You can find a Journal by clicking on JOURNALS AND DATABASE and enter a keyword to search for your desired journal.

SPIRAL INTEGRATION

# FURTHER READING


- Akyuz E, Polat AK, Eroglu E, Kullu I, Angelopoulou E, Paudel YN. Revisiting the role of neurotransmitters in epilepsy: An updated review. Life sciences. 2021 Jan 15;265:118826.

- Jiang SH, Hu LP, Wang X, Li J, Zhang ZG. Neurotransmitters: emerging targets in cancer. Oncogene. 2020 Jan 16;39(3):503-15.


SPIRAL INTEGRATION

# Thank you