5×1 = 5 } must know
2×1 = 2 } Desirable to know
2×1 = 2 }

Unit - 5

Pharmacology of central nervous system

→ Anti-depressant Drug:-

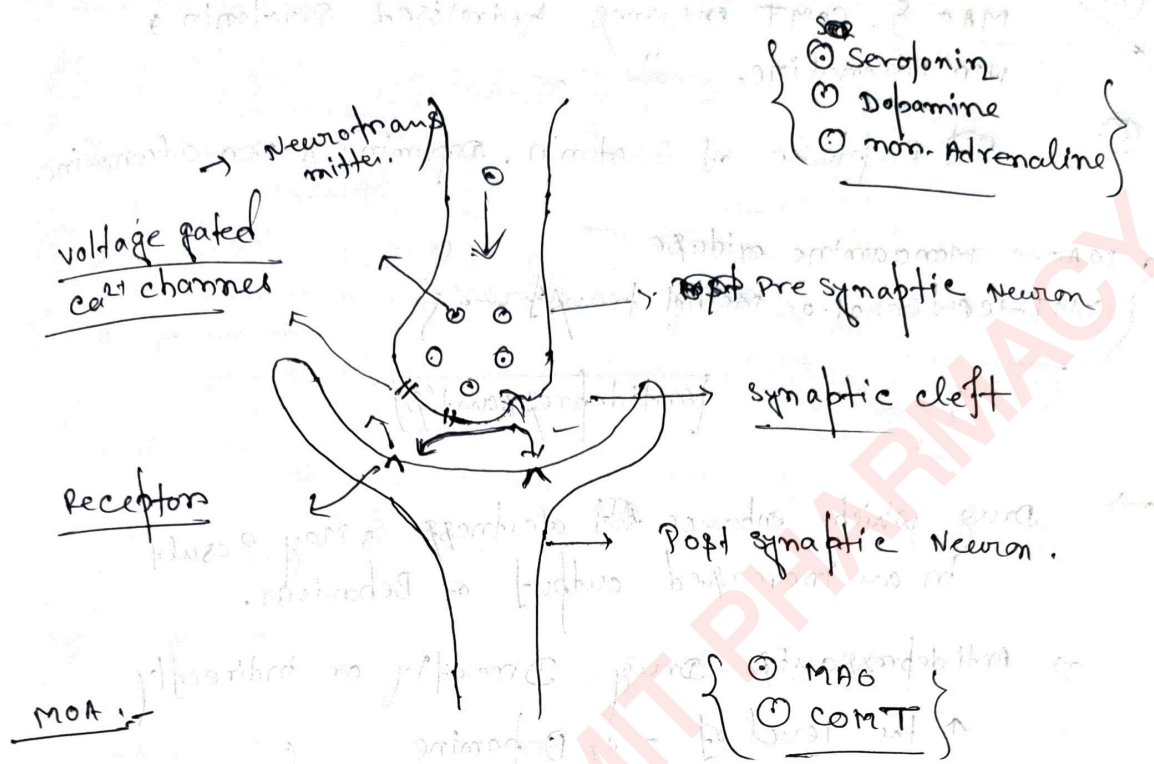
→ It is a mental illness characterized by Pathological changes in mood, loss of interest or Pleasure, felling of guilt or low self worth, Disturbed sleep or appetite, Poor concentration.

Symtomps :-

→ Depressed mood most of the day.
→ Markedly diminshed interest or pleasure
→ significant weight loss or gain
→ Insomnia or hypersomnia.
→ Agitation
→ Thought of Suicide or Death. ××

Types of Depressant

→ major depression
→ chronic Depression (Dysthymia)
→ Atypical depression.
→ Manic Depression / (Bipolar Disorder)
→ Seasonal Depression (SAD)



MOA :-

→ from Brain three most important neurotransmitters are release that is Serotonin, Dopamine & Noradrenaline which is responsible for the Mental Stage / mood.

→ when the neurotransmitter (Serotonin, Dopamine & non-adrenaline) Release form the Pre synaptic cleft & bind with the Receptor of Post-synaptic cleft then mood is normal. But that case this neurotransmitter can't bind with in over Receptor then it causes the Depression.

→ There are 3 Basically Reasons for the depression —

✓ a) Reduce the synthesis of Serotonin, Dopamine & non. Adrenaline due to any Physical changes.

(B) MAO & COMT enzymes hydrolysed Serotonin & Nor-Adrenaline.

(C) Reuptake of Serotonin, Dopamine & Nor-adrenalin

MAO → Monoamine oxidase
COMT → catechol-o-Methyl transferase

Antidepressant's

→ Drug which enhance alertness & may Result in an increased output of Behaviour.

→ Antidepressants Drug Directly or indirectly
↑ the level of - a) Dopamine
b) Nor-Adrenaline
c) Serotonin

(*) on that case take medicine 4-6 months.

Types of Antidepressants

(a) Tricyclic - Antidepressants (TCAs)
(b) Monoamine oxidase inhibitors (MAOIs)
(c) Selective Serotonin Reuptake inhibitors (SSIRs)
(d) Atypical Anti-depressants (others)

* classification :—

(a) Reversible inhibitors of MAO-A

→ Clorgyline

(b) Tricyclic Antidepressants (TCAs) —

* Imipramine, Trimipramine (NA+5HT-Reuptake inhibitors)

* Predominatly NA Reuptake inhibitors —

→ Amoxapine

(c) Selective Serotonin Re-uptake inhibitors —

→ Paroxetine, Dapoxetine

(d) Serotonin & NA Reuptake inhibitors —

→ Duloxetine.

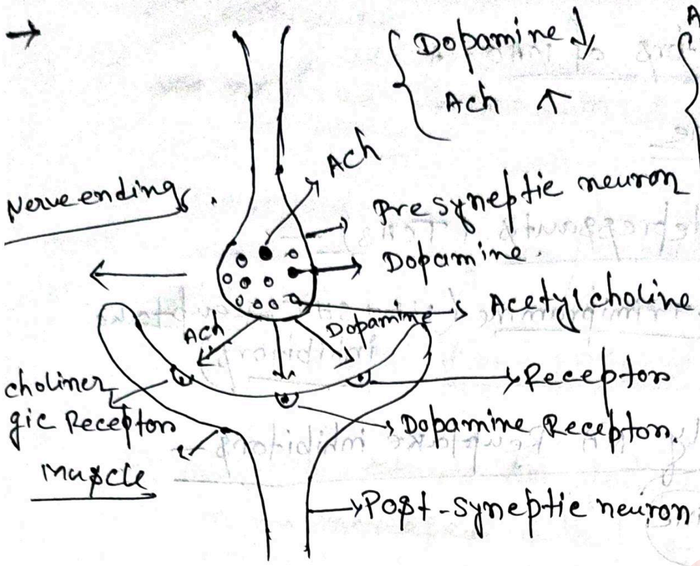
(e) Atypical Antidepressants :—

→ Bupropion, Trazodone (Main drug)

—o—

Dianeptine
Amineptine

Anti-Parkinsonism Drugs



{ Dopamine ↓
Ach ↑ }

Ach o – Dopamine → Muscle Relax

→ when Dopamine Binds with Receptor they Produce effect & Finally muscle Relax

→ when Ach Binds with the Receptor Muscle contraction.

- Parkinson's disease is an autonomic neurogenic disorder in which muscle are Permanently contract.

⊙ In this disease the Release of Acetylcholine ↑es & the Release of Dopamine is ↓es.

⊙ when high amount of Acetylcholine is bind with cholinergic Receptor then it causes contineous & Permanent contract.

⊙ Dopamine is responsible for muscle Relaxation But in Parkinsonism's disease their secretion is ↓es.

(Rigidity, Hypocinesia) (tremors) (Less movement)

MOA

→ MAO, Decarboxylase Both enzyme are Present in synaptic cleft. ~~Both are hydrolysis~~ on that case Dopamine are Hydrolised by this enzyme & the Level of Ach ↑ & Level of Dopamine ↓

(A) Drug effecting Dopaminergic system :-

→ 1. Dopamine Precursor → LevoDopa, Carbidopa

2. Decarboxylase inhibitor → Benserazid

3. Dopaminergic Agonist → Bromocryptine

4. MAO Inhibitor ⟷ Selegelin, Silegelin

5. Dopamine facilator → Amantadine.

(B) Drug Acting on cholinergic system :-

→ Anticholinergic → Atropine, Hyoscine

—o—

(*) Levodopa (L-Dopa) :-

- Metabolic precursor of Dopamine
- InActive by itself.
- 95% of an oral dose is decarboxylated in the peripheral tissue (mainly gut & liver) & convert into DA.
- Only about 1-2% Administered Levodopa crosses to the brain.
- L-Dopa —DOPA Decarboxylase→ Dopamine → Interact with D_2 Receptors → Relives symptoms of Parkinsonism

CTZ → chemoreceptor trigger zone

Kinetics

→ Absorption
- Absorved orally by Active transport
  - ↓ by the Presence of food
- Administered on empty stomach.

A ~
D ~
M ~
E —

→ Distribution
- Cross the BBB

→ Levodopa metabolised by $COMT_A$ & $COMT_B$ & Metabolised.

→ excretion
- Urine

Pharmacological Action

- On CNS —
  - effect on Behavior → General Alerting Response
- On CVS —
  - It Produce + inotropic Action it means the force of contraction ↑ & BP ↑.
- On CT2 —
  - Dopaminergic Receptors are present in this area & DA Act as an excitatory transmitter
- Endrocrine Action —
  - Release of Prolactin decrease

—

CT2 → chemoreceptor Trigger zone.

Adverse effect

CNS
- → Euphoria
- → Anxiety
- → Agitation
- → Insomnia.
- ⊙ ~~Disturbness~~ → Delusions, → hallucinations.

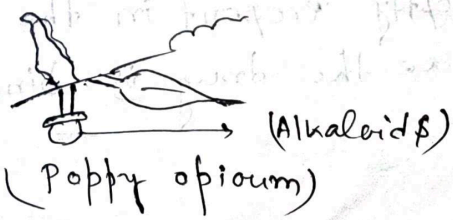
GIT
- → Nausea → Anorexia
- → Vomiting

CVS
- → Hypotension

opioid Analgesics

→ opioids :- Those pain reliveal drugs or Analgesic drugs which is obtained from the opium plant or Papaver plant or alkaloid of the opium plant they are called opioid Analgesic..

→ All those synthetic, semisynthetic or natural drugs which is directly or indirectly obtained form the opium plants they are called opioids



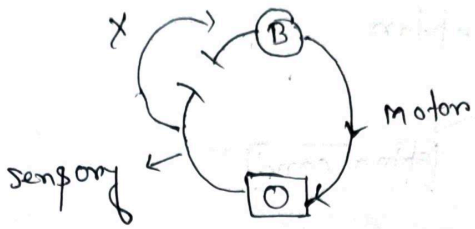
* **Analgesic:-** Analgesic are those drugs which are basically Pain Relieving by acting on CNS, but they don't have addiction, mood / behavior change, dependence and tolerance Property.

* **Narcotics:-**

Narcotics are basically analgesic. They act on CNS and peripheral & helps in Relieving the pain but they have addiction, mood / behaviour change, tolerance & Dependence property.

MOA (Mode of Action)

1. Basically the opoids analgesics blocks the sensory neurons so the formation of Pain from organ don't reach into the brain. or CNS the feeling of Pain is reduce.
2. Basically they blocks the calcium channel & open the potassium (K^+) channel & by hyperpolarisation they block the neurotransmission.
3. Basically these drugs are bind with specific Receptors - μ, δ, κ (kappa) & these Receptors are mostly Prepent in the CNS & peripheral organs where the drug is bind.



⊙ There are some part of brain where maximum no of opioids Receptors are present like—

(a) Nuclei of tracts
(b) Pre aqueductal greay area.
(c) cerebral cortex
(d) Thalamus

⊙ Basically the opioids Receptors are GPCR types of Receptor, they block the Ca^{++} channel & Hyperpolarize the cell.

Receptors

→ In our CNS & Spinal cord those Receptor in which opioid drugs are bind, called opioid Receptors. they are

(1) opioid Receptors are three types—

(A) μ or MOP (mu opioid Peptide Receptors)
(B) κ or KOP (kappa opioid Peptide Receptors)
(C) δ or DOP (Delta opioid peptide Receptors)

⊙ They are Basically GPCR in nature

They are linked with Peptide heli's.