

Dystonia :- Muscle contract involuntarily & is painful.

Akathisia :- Restless, urge to tap finger or wiggle legs.

Parkinsonism - tremors, stiffness of facial muscle, difficulty with balance & co-ordination.

Atypical :-

- Second generation Antipsychotics
- They are also used to treat psychotic disorders.
- Powerful $5HT_2A$ Receptors antagonist & weak D_2 Receptor antagonist.
- The $5HT_2A$ use serotonin receptors and are responsible to inhibit dopamine pathway. Hence when $5HT_2$ inhibited dopamine level (\downarrow)

so serotonin (+) $5HT_2A \rightarrow$ dopamine pathway (\downarrow)

$\hookrightarrow 5HT_2A \rightarrow D_2$ pathway (\uparrow) \leftarrow done by atypical antipsychotics.

As they are involved in both \downarrow & \uparrow dopamine level can treat both + & - symptoms of schizophrenia such as

- Hallucination
- delusion
- social withdrawal
- Reduced emotions.

very few side effect (extrapyramidal) as compared to typical psychotics as they weakly antagonise D_2 receptors.

However they have high metabolic side effect compared to typical psychotics such as.

- weight gain
- diabetes
- (↑) cholesterol

- chlorpromazine can cause a serious side effect i.e., agranulocytosis \rightarrow Bone Marrow not able to produce WBCs.

- chemical nature similarities are not found among drug belonging to atypical antipsychotics

Pharmacology of Phenothiazines:

① CNS :- in Non-psychotic \rightarrow disturbs thoughts & emotions and causes extrac psychomotor side effects.

In psychotics \rightarrow controls psychosis Behaviour like Hallucinations, agitation, anxiety etc.

- drugs with low potency can cause sedative effect
- It Blocks the D₂ Receptors at ^{CTZ} centre of Brain and act as anti-emetic drug.
- (↓) Seizure threshold and so a person becomes more liable to seizures

② CNS \rightarrow Antipsychotics Have the ability to Block α-Receptors & M₁ Receptors, that can cause dry mouth & constipation.

③ CVS \rightarrow ↓ BP & at low dose cause ↑ HR
High dose " ↓ HR

④ Glands \rightarrow (T) Prolactin Release centre in Man \rightarrow erectile dysfunction & infertility
In women \rightarrow infertility.

Anti-depressants

- depression is a disorder of mood and at severe condition it can be fatal.

Mainly ② types ① unipolar
② Bipolar.

Unipolar :- constantly feeling sad & hopeless

Bipolar :- feeling over Happy for long period of time & feeling over sad for long period of time

Antidepressants :- are drugs that provides relief from depression and are classified on basis of MoA.

Unipolar :- depression is caused due to deficiency of serotonin, dopamine, noradrenaline
symptoms :- loss of interest, suicidal thoughts, loss of appetite, loss of conc. etc.

Classification

	Antidepressants		
Drug that Block NE & SHT Reuptake	selective serotonin Reuptake Inhibitors	atypical anti depressant	MAO inhibitors
Duloxetine	serotonin & norepinephrine Reuptake Inhibitors	Trazodone Nefazodone	Selegiline

Note on
SSRI :- (Selective serotonin Reuptake Inhibitors) MOA of
Anti-depressant

- These are serotonergic neurons in CNS that produce neurotransmitter serotonin.
- In its presynaptic neurons are vesicles containing serotonin. These vesicles fuse with membranes and release serotonin to synaptic cleft.
- These are serotonin receptors on post synaptic membrane and on binding with it serotonin gives its action.
- Serotonin Reuptake transporter is present at pre-synaptic membrane & it allows serotonin to enter back to neuron that can be used again.
- SSRIs inhibits this serotonin Reuptake transporter & so serotonin levels ↑ in synaptic cleft.

so - SSRIs are first line treatment for depression.

W - It usually takes around 4-6 weeks before improvements can be seen using SSRIs

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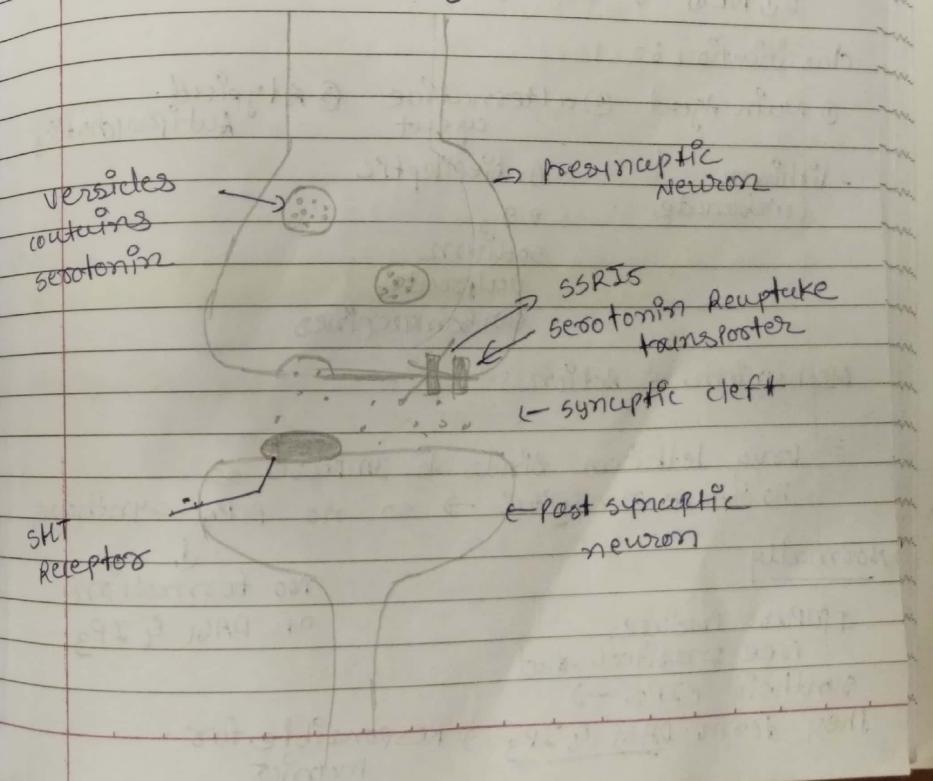
Effects → Have mild side effect, compare to other anti-depressants.

• Insomnia, GIT distress, sexual dysfunction

- Many SSRIs inhibit CYP450 & Heve metabolism of drug (↓) leading to toxicity.

e.g. citalopram & sertraline

- ↑ risk of serotonin syndrome when used with other drug that ↑ SHT levels.



④ Antimanic :- (Mood stabilizing drug)
drugs used for Bipolar disorder

⇒ Mania is characterized by Bipolar disorder
in which patient excessive desire &
too much of Euphoria (happiness).

⇒ Majority of patient experience Mania &
depression in cyclic order (and is called
MDD or manic depressive psychosis).

- Lithium carbonate is used to treat MDD

DT NET → Euphoric

D↓ NE ↓ → depression.

Classification :-

① Main Agent ② alternative agent ③ Atypical Antipsychotics

- Lithium - Antiepileptic e.g.,

sodium valproate,
carbamazepines

Mechanism of Action :-

⇒ Drug lithium binds to IP₃R so
no free inositol → so no PIP₂ synthesis

Normally

Impulse produce
free inositol that
synthesis PIP₂ →

they form DAG & IP₃ → responsible for
mania

No formation
of DAG & IP₃

③ Anti-anxiety drugs :-

Anxiety → an emotional state, unpleasant
in nature, fear about some defined
or undefined future threat

Symptoms :- sweating, trembling, shout,
↑ HR, ↑ BP, Red eyes

Classification

Anti-Anxiety drugs

Azipirones	Antihistamines	Benzodiazepines	β -Blockers
e.g.)	- Hydroxyzine	- Alprazolam	• propantheline
oxipipzone	isopipzone	• oxazepam	• loxapepam
		• diclofenac	• diazepam
			• alprazolam

④ Ant

⑤ Hallucinogens :- (Psychomimetics)

Hallucinogens → false perception of Having
Heard, Seen or touch that wasn't
there.

- drug that cause Hallucinogens are
called as Hallucinogens.

e.g., Cannabinoids

Anti-Parkinson drugs:-

- Parkinsonism is a Neuro-degenerative disorder.
- A person suffers from Rigidity & tremors symptoms - excessive salivation, ↓ BP, ↓ HR & abnormal posture.

Etiology :- due to imbalance between inhibitory dopamine and excitatory Acetylcholine
→ This occurs due to destruction of dopaminergic neurons at substantia nigra.

drugs used

- It can be treated by (↑) Brain dopamine levels and by (↓) Brain cholinergic levels

(1) drug that affect dopaminergic system

- (a) dopamine precursor → Levodopa
- (b) peripheral decarboxylase → carbidopa inhibitor

- (c) MAO-B inhibitors → Selegiline

- (d) COMT inhibitors → tolcapone

- (e) dopamine facilitator → Amantadine

① Levodopa & carbidopa

- Dopamine cannot cross BBB to give its action at CNS, levodopa is the precursor of DA & can cross BBB.

- levodopa gets decarboxylated in Brain & forms dopamine that further gives action.

- if levodopa is administered orally only 1% enters Brain & other is metabolised in GIT & peripheral tissue by peripheral decarboxylase to form DA. But now this can't cross BBB and is useless.

- To prevent peripheral degradation levodopa is administered with carbidopa i.e., a peripheral decarboxylase inhibitor.

- levodopa is widely used for treatment of all types of Parkinsonism except one associated with antipsychotic therapy.

ADR :- Delusions, Hallucinations, confusion, and sleep disturbances.

→ Prolonged therapy of carbidopa + levodopa can cause schizophrenia like symptoms.



- ② COMT - inhibitors :- COMT metabolises DA and its precursor levodopa. It converts DA into inactive metabolites. Inhibiting COMT will ↑ DA levels.

- ③ MAO-B inhibitors - This enzyme metabolizes DA in dopaminergic neurons. Hence inhibiting it, will ↑ DA levels.

(d) Dopamine facilitators

→ Amantadine, is a anti-viral drug. It acts as:

- prevent DA uptake
 - facilitates pre-synaptic DA release
 - weak anticholinergic action
- } treat PD

⇒ pharmacology of levodopa :-

- It is effective only when given with carbidopa. Hence pharmacological effects of levodopa + carbidopa.

- If pharmacological effects of carbidopa is asked, carbidopa acts on dopamine decarboxylase, inhibits it, to return levodopa. Hence ans will be same.

- ④ L-dopa :- eliminates most of symptoms of PD
(i) tremors & improvement in facial expressions.

it is less effective to eliminates parkinson instability.

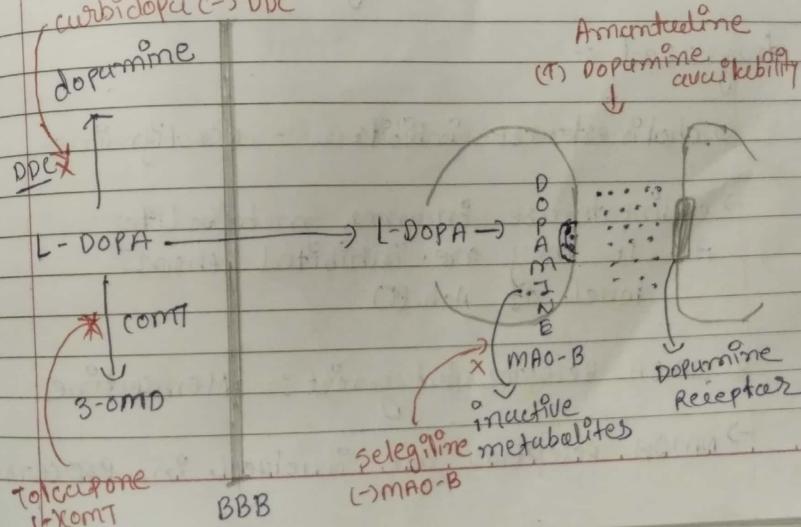
- ⑤ CHS :- ↑ HR, Postural Hypotension i.e., blood pressure ↓ when you stand up after sitting or lying.

- ⑥ CTZ :- DA Receptors cause stimulation to nausea & vomiting.

(e) Endocrine :- (i) Prolactin (ii) GTH

→ carbidopa has no personal effects, it just inhibits decarboxylase & ↑ level of L-DOPA. Hence effects observed on taking carbidopa are of L-dopa so same Ans.

carbidopa → DDC



ED Alzheimer's disease

- it is a neurodegenerative disease. That involves progressive impairment of memory and cognitive functions.
- caused due to destruction of cholinergic neurons as a result Acetylcholine level decrease. Ach (↓)
- It can be treated by (i) Ach levels by inhibiting AChE enzyme that is responsible for its degradation.

Symptoms → loss of memory
→ difficulty in performing simple test
→ change in mood & behaviour
→ Poor judgement

drugs used :-

- ① Cholinesterase inhibitors - Neostigmine
- cholinesterase enzymes metabolites Ach. If they are inhibited their level of Ach (↑)

② NMDA Receptor Antagonist:- Memantine

- NMDA receptors are involved in processes

excite toxicity (over excitement of neurons) that can degenerate neurons.

③ MAO Inhibitors - e.g., selegiline

- monoamines (dopamines, serotonin etc) are responsible for good mood & anti-anxiety
- ↑ levels of monoamines is a symptomatic treatment of Alzheimer's disease
- They are used to manage the behaviours of Alzheimer's patients.

④ NSAIDs

- delays onset of Alzheimer's disease
- neurons are believed to degenerate because of senile plaque within neurons they are abnormal clusters of proteins that causes inflammation.

- Hence, Exact action of NSAIDs on Alzheimer is not known, but it is believed that they reduce this inflammation due to senile plaque.



CNS stimulants: These are the type of drugs that release certain chemicals in brain causing alertness (↑) attention & physical activity.

- They ↑ HR, ↑ BP & ↑ Breathing Rate

Classification:-

① psychomotor stimulants → e.g., Amphetamines, Methylxanthines

- cause excitement & euphoria
- decrease feeling of fatigue
- ↑ Motor Activity.

② Hallucinogens (Psychomimetic drugs) (LSD)
e.g., Lysergic acid diethylamide (LSD)
cannabinoids

Produces changes in thought patterns & moods.

Pharmacology of Amphetamines:-

→ They acts by releasing neurotransmitter in synaptic spaces.

① CNS:- stimulates entire cerebrospinal axis, Brainstem & Medulla

→ (↑) alertness, (↓) fatigue, insomnia

② sympathetic N.S (ANS) → indirectly stimulates release of Nor-epinephrine.

③ CVS - ↑ H.R, ↑ B.P, Higher dose causes Tachycardia & Anginal pain.

④ GIT :- Vomiting, Abdominal cramps & diarrhea.

ADR :-
→ Tachycardia
→ abdominal cramps
→ Panic states
→ Hyper active reflexes.

Nootropics :-

→ Numerous Natural, synthetic, semi-synthetic molecules that improve cognitive function of brain (attention, memory, learning, creativity) are called as nootropics.

e.g., L-dopa, Amphetamines, Taurine, caffeine.

→ Refer A.D.

⇒ **Opioid Analgesics** :- Analgesics are drugs that cause analgesia. Analgesia is a state where there is insensitivity to pain without loss of consciousness.

Two types → Narcotic → opioid analgesic
Non-narcotic → NSAIDs.

- They are used to get relief from severe pain due to fracture, Burns or cancer.
- They also induce sleep.

Classification :-

① Classified on basis of origin :-

1. Natural opioids → codeine
→ morphine

2. Semi-synthetic opioids → Hydroxy Morphine
→ oxymorphone

3. Synthetic opioids → fentanyl citrate
→ methadone HCl

② On basis of their action on Receptors :-

① Opioid agonist → They bind to opioid receptors & activates them
e.g., morphine

② Mixed - They bind to receptors & activate them but compete with other opioids to bind at receptor
[(-) others opioid & (+) Receptor]

③ Antagonist - They bind to opioid receptors & do not activate them.

e.g., Naloxone & Nalorphine

Pharmacology of Morphine :-

① CNS :- Analgesic - Reduces pain sensitivity
Euphoric - Minded sense of relief & well being
Sedation - where pain is accompanied by insomnia
Stimulates - Nausea.
CTZ

② Effect on GIT :- (1) matting in severe part of GIT & causes severe constipation

→ gustic sensation & (1) Biliary secretion

③ CVS - ↓ BP & Bradycardia.

④ Smooth muscle - bronchi constriction
urinary bladder contraction

⑤ Immuno-suppressant effect :- It is due to its action on CNS, Morphine could also have higher risk of acids.

Pharmacology of opioid receptors:

- Opioid Receptors are mainly ③ types

$$\mu (\text{mu}) - \mu_1, \mu_2$$

$$\text{K (Kappa)} - \text{K}_1, \text{K}_2, \text{K}_3$$

$$\delta (\deltaelta) - \delta_1, \delta_2$$

→ They are present in Brain, spinal cord and peripheral nervous system.

→ μ - analgesic, respiratory depression (↓), GIT motility.

K - depersonalization & desensitization

δ - analgesia, mood change

- Opioid Receptors close Ca^{2+} and K^+ channels & inhibit Ca^{2+} transport

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(a) K^+ channel → Resist depolarisation

(b) Ca^{2+} channel → Neuron excitability (↑)
↑ excitability (↑)

Hence, Neurotransmitter will meet release.