

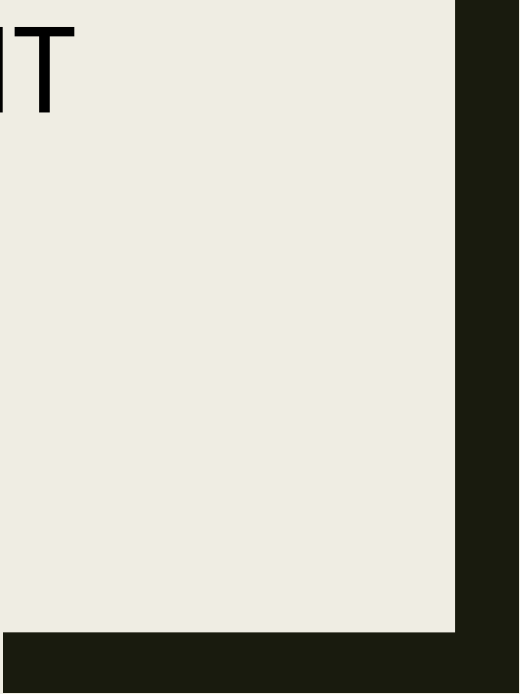


ANTIDEPRESSANT

Done by:

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Depression

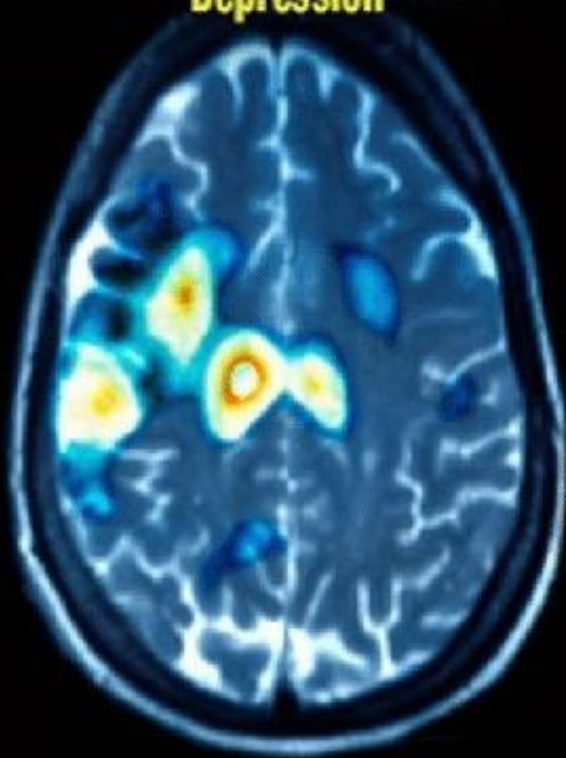
- It is a serious common disorder of mood.
- It affects 300 million adults worldwide.
- Women are more affected than men.



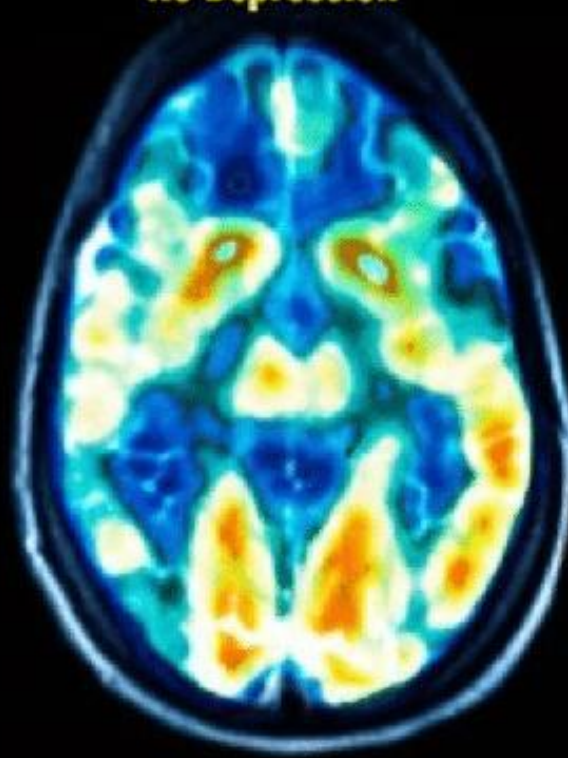
Pathophysiology of depression

- Genetics : to dates , 4 Genes were identified
- Biogenic amines and receptors theory:
 - low noradrenaline , serotonin and dopamine.
 - High 5HT2a and 5HT2 Receptor.
- Neurotrophic and cytokines theory:
 - Low brain derived neurotrophic factor (BDNF)
 - Proinflammatory cytokines

Depression



No Depression

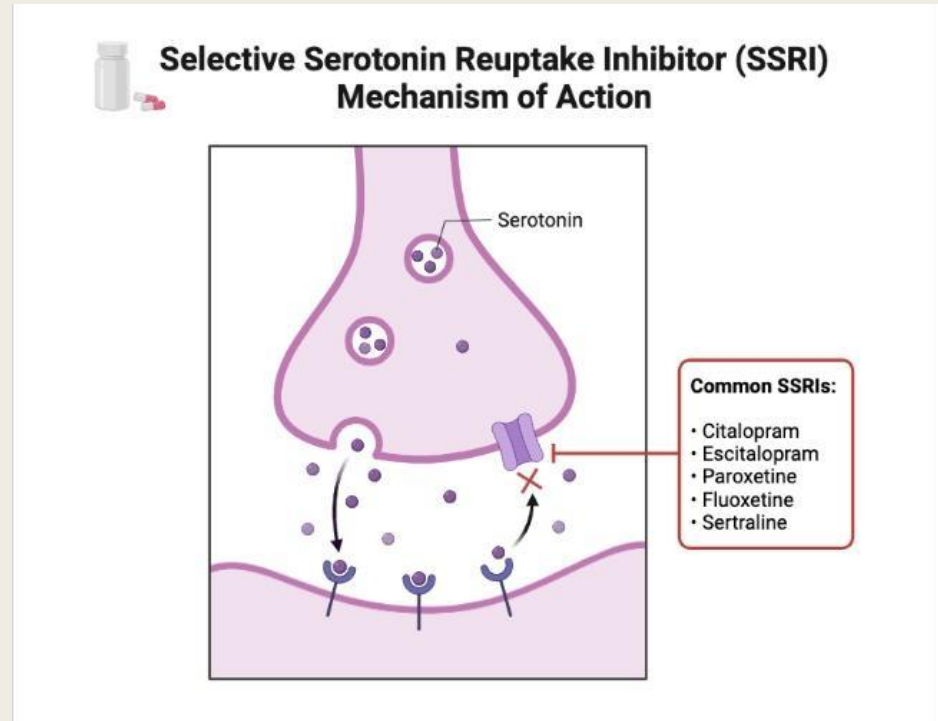


Antidepressant

- Selective serotonin re-uptake inhibitors (SSRIs)
- Tricyclic antidepressants (TCAs)
- Atypical antidepressants >> (SNRI)
- Monoamine oxidase inhibitors (MAOs)

Selective serotonin re-uptake inhibitors

- Inhibit 5-HT reuptake by neurons
- Lead to ↑ 5-HT levels in synaptic cleft
- Take 4-8 weeks to have effects
- Used in many psychiatric disorders
 - Depression
 - Generalized anxiety disorder
 - Panic disorder
 - Obsessive-compulsive disorder
 - PTSD
 - Bulimia
 - Social anxiety disorder



Example of SSRI

- **Fluoxetine (Prozac)**—longest half-life with active metabolites
- **Sertraline (Zoloft)**—evidence of for MI patient cause it is not cardiotoxic.
- **Paroxetine (Paxil)**—most serotonin specific, most activating (stimulant).
- **Citalopram (Celexa)**—used in Europe for 12 years prior to FDA approval in the United States.
- **Escitalopram (Lexapro)**—iso of citalopram; similar efficacy, fewer side effects .

Side effects

- Non-specific side effects that often subside with use
 - Headache
 - Insomnia
 - GI upset (nausea, diarrhea)
 - Drowsiness
- Rare, dangerous effects
 - SIADH and hyponatremia
 - QT prolongation
 - Serotonin syndrome
- Sexual dysfunction

Discontinuation Syndrome

- Abrupt discontinuation of antidepressant
- Can occur with any antidepressant
- Most common with **SSRIs**
- Exception: fluoxetine (long half life)
 - Dizziness
 - Fatigue
 - Headache
 - Nausea
- Avoid by **slowly tapering off drug**

Serotonin-norepinephrine reuptake inhibitors

- Inhibit 5-HT and NE reuptake by neurons
- Take 4-8 weeks to have effects
- Used in many psychiatric disorders
 - Depression
 - Generalized anxiety disorder
 - Panic disorder
 - Obsessive-compulsive disorder
 - PTSD
 - Bulimia
 - Social anxiety disorder

Example of SNRI

- Venlafaxine :

- Often used for depressive disorders, anxiety disorders like generalized anxiety disorder (GAD), and neuropathic pain.

- Side-effect profile similar to SSRIs, with the exception of increased blood pressure (BP) in higher doses; do not use in patients with untreated or labile BP.

- Duloxetine:

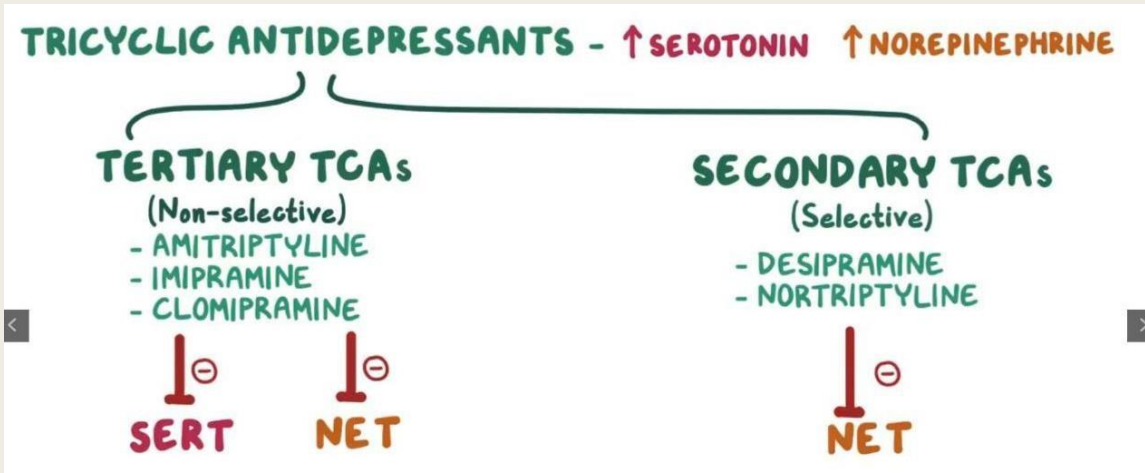
- Often used for people with depression, neuropathic pain, and in fibromyalgia.

- Side effects are similar to SSRIs, but more dry mouth and constipation relating to its norepinephrine effects.

- Hepatotoxicity may be more likely in patients with liver disease or heavy alcohol use.

TRICYCLIC ANTIDEPRESSANTS

Imipramine, Clomipramine,
Amitriptyline, Nortriptyline



Mechanism of action

- Block re-uptake of 5-HT and norepinephrine increasing their concentrations in the synaptic cleft

Also have "Broad spectrum" :

- Anti-histamine
 - Anti-cholinergic
- Block alpha-1 receptors

Therapeutic uses

- 1 . Major depressive Disorder
2. Chronic pain condition e.g. fibromyalgia
3. Nocturnal enuresis in children: imipramine

Side effects

- TCAs are highly protein bound and lipid soluble, and therefore can interact with other medications that have high protein binding
- The side effects of TCAs are mostly due to their lack of specificity and interaction with other receptors

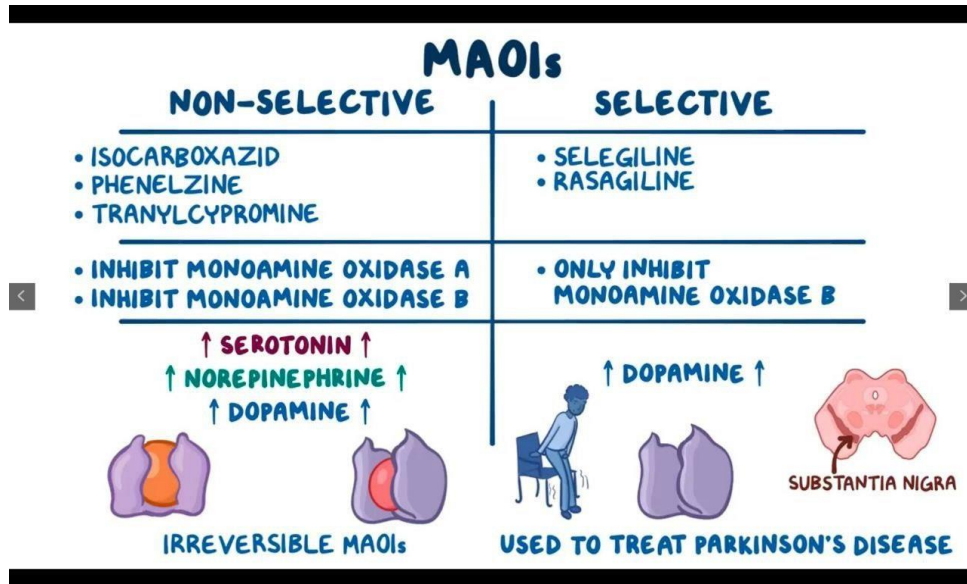
Side effects

- Antihistaminic properties: Sedation and weight gain.
- Antiadrenergic properties (cardiovascular side effects): Orthostatic hypotension, arrhythmias, and (ECG) changes (widening QRS, QT, and PR intervals).
- Antimuscarinic effects (also called anticholinergic): Dry mouth, constipation, urinary retention, blurred vision.
- Lethal in overdose—Symptoms of overdose include agitation, tremors, ataxia, arrhythmias, delirium, hypoventilation from central nervous system (CNS) depression, myoclonus, hyperreflexia, seizures, and coma.



MONOAMINE OXIDASE INHIBITORS

Phenelzine, Tranylcypromine, Isocarboxazid .



Mechanism of action

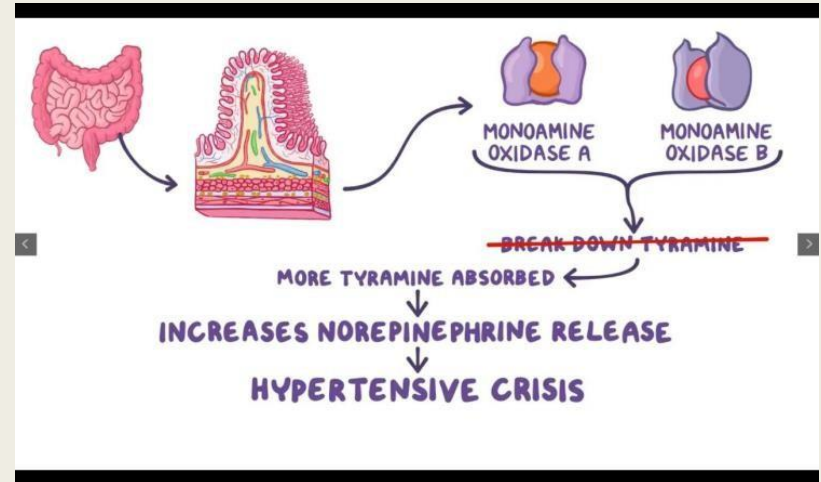
- **Prevent** the inactivation of biogenic amines such as norepinephrine, serotonin, dopamine, and tyramine .
- By **irreversibly** inhibiting the enzymes MAO-A and B, MAOIs increase the number of neurotransmitters available in synapses.
- MAO-A preferentially deactivates serotonin and norepinephrine, and MAO-B preferentially deactivates phenethylamine; both types also act on dopamine and tyramine.

Therapeutic uses

- MAOIs are not used as first-line agents because of the increased safety and tolerability of newer agents, notably SSRIs/SNRIs. However, MAOIs are used for certain types of **refractory depression** and in refractory anxiety disorders
- MAO-B selective: selegiline • Used in Parkinson's

Side Effects

- Serotonin syndrome occurs when SSRIs and MAOIs are taken together.
- Hypertensive crisis “Cheese effect”: Risk when MAOIs are taken with tyramine-rich foods or sympathomimetics.
 - Foods with tyramine (cheese, chicken liver, fava beans, meats) cause a buildup of stored catecholamines.
- Orthostatic hypotension (most common).
- Drowsiness.



ATYPICAL ANTIDEPRESSANTS

Receptor blockers

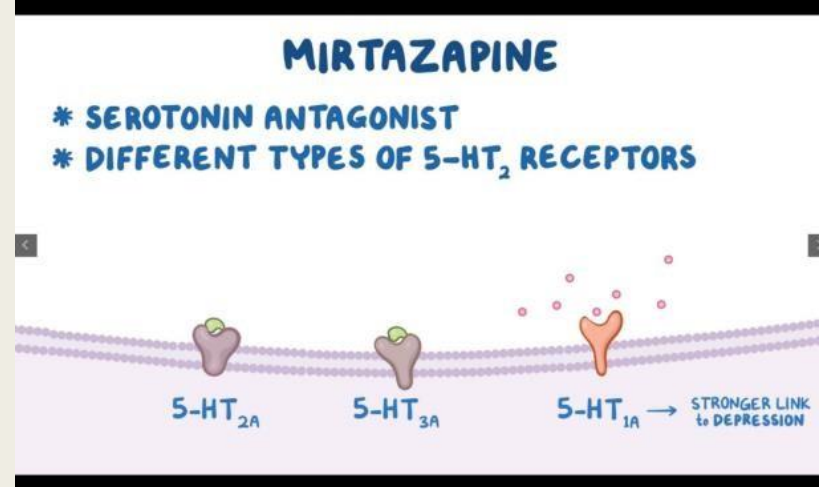
-Serotonin Receptor Antagonists (Trazodone):

-Blocks 5-HT_{2A} and 5-HT_{2C} receptors.

-Useful in the treatment of major depression, major depression with anxiety, and insomnia (secondary to its sedative effects)

-Side effects include nausea, dizziness, orthostatic hypotension, cardiac arrhythmias, sedation, and priapism.

- Because of orthostatic hypotension in higher doses, trazodone is not frequently used solely as an antidepressant.



- α 2-Adrenergic Receptor Antagonists (Mirtazapine) :
- Blocks α 2 adrenoceptors and 5-HT_{2C} receptors
- Useful in the treatment of major depression, especially in patients who have significant weight loss and/or insomnia.
 - Side effects include sedation, weight gain, dizziness, tremor, dry mouth, constipation (less GIT upset and dysfunction than SSRIs).

Bupropion :

- Norepinephrine-dopamine reuptake inhibitor.
- *Relative lack of sexual side effects as compared to the SSRIs.*
 - *Some efficacy in treatment of (ADHD)*
 - *Effective for smoking cessation.*
- Weight neutral
- Side effects include increased anxiety, as well as increased risk of seizures and psychosis at high doses.
 - *Contraindicated in patients with epilepsy or active eating disorders*



Thank you