

Anti-depressants



Symptoms of depression:

emotional symptoms

- Anhedonia : loss of interest
- Apathy and loss of self esteem
 - Loss of motivation

biological symptoms

- Sleep disturbance and loss of appetite
 - Loss of libido
 - Chronic pain

Depression types

unipolar

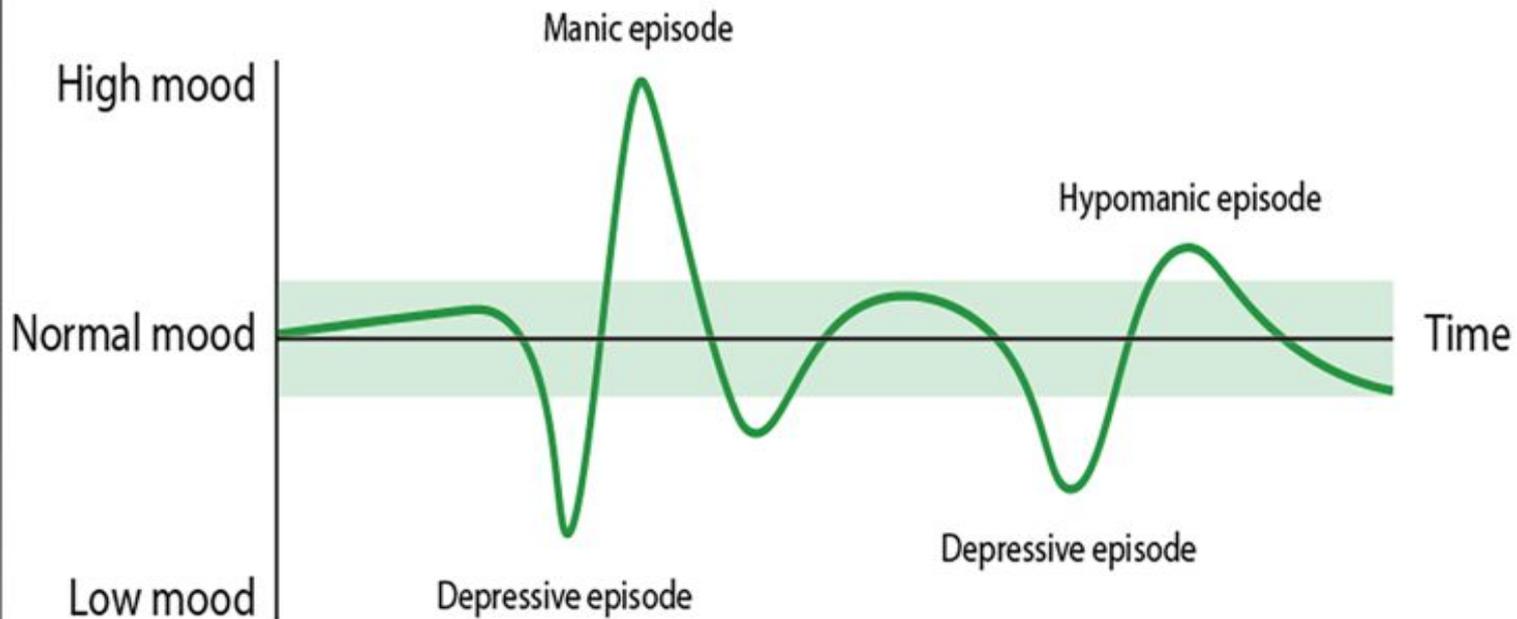
- major depression disorder
(95%)

bipolar

- manic depressive disorder
(5%)



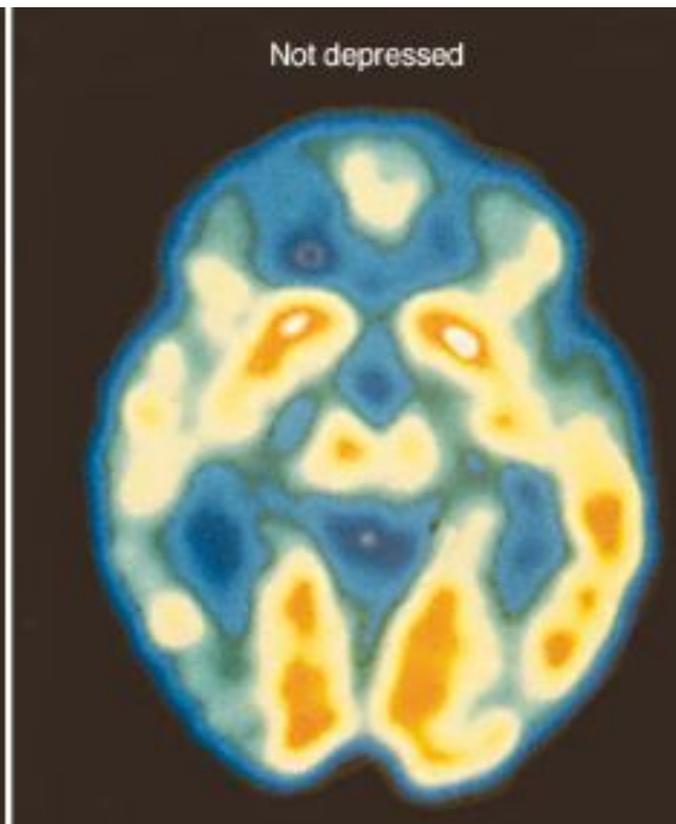
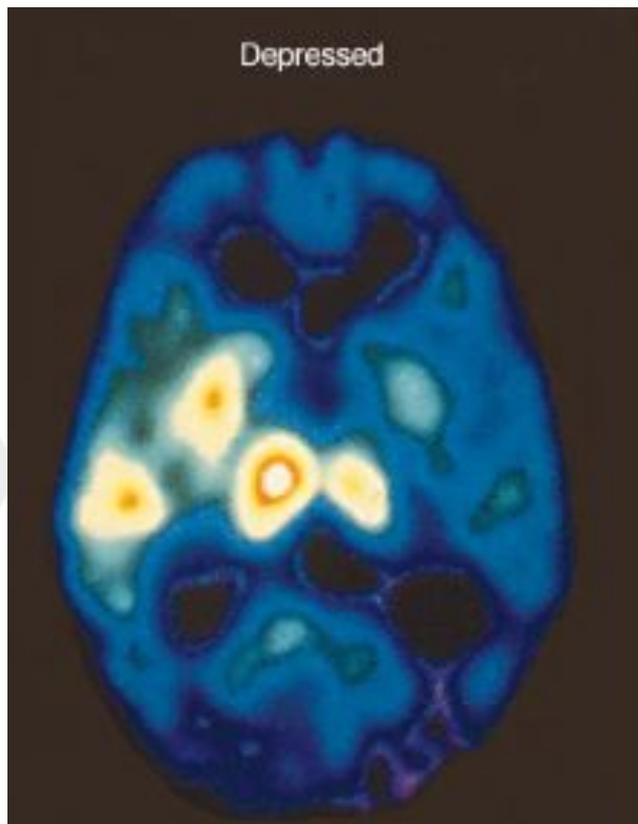
Bipolar disorder





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





Antidepressants

- 1. Selective serotonin re-uptake inhibitors (**SSRIs**)
- 2. Tricyclic antidepressants (**TCAs**)
- 3. Atypical antidepressants >> (**SNRI**)
- 4. Monoamine oxidase inhibitors (**MAOs**)

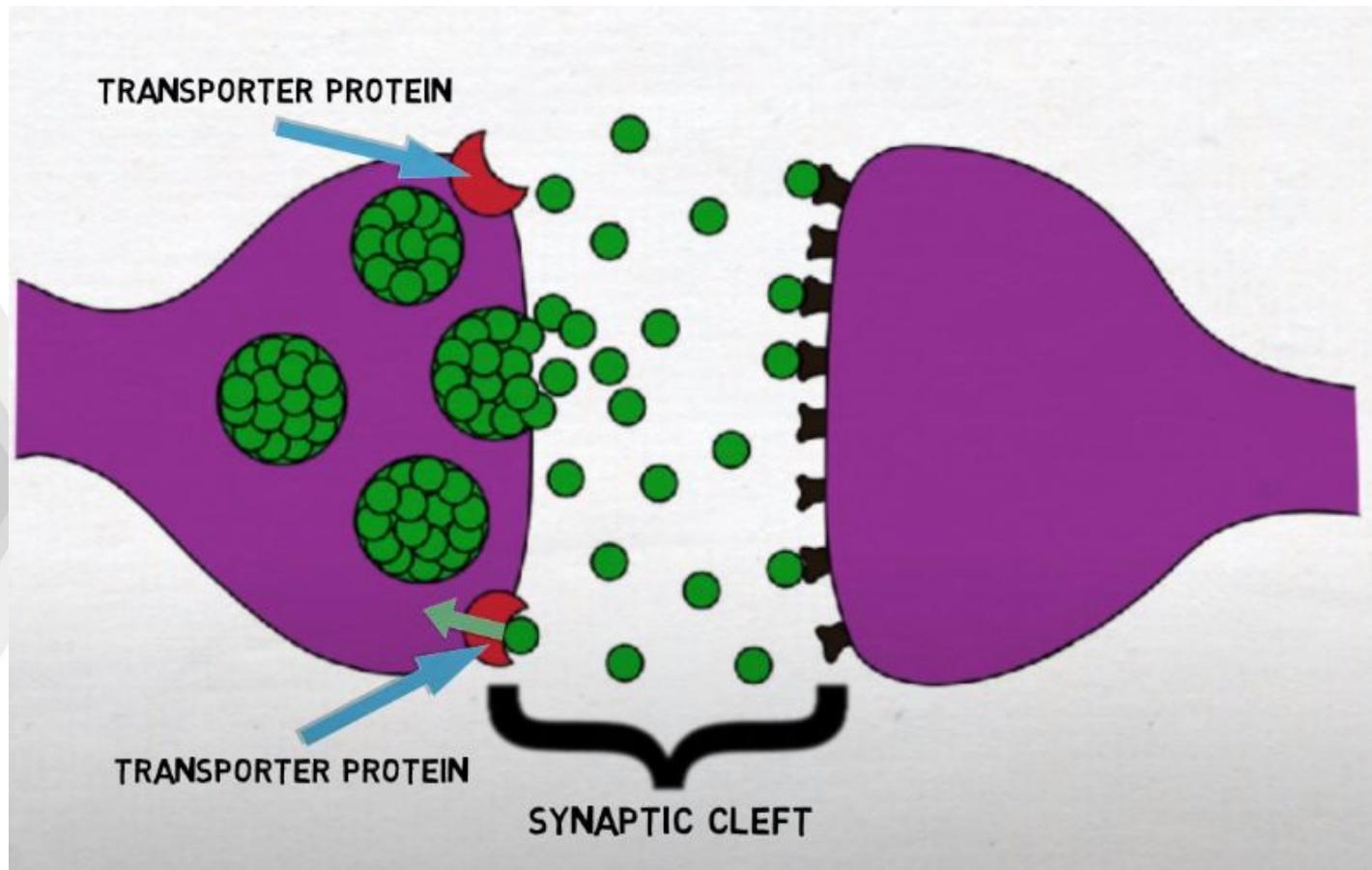


SELECTIVE SEROTONIN REUPTAKE INHIBITORS

I. SELECTIVE SEROTONIN REUPTAKE INHIBITORS

- **SSRIs block reuptake of serotonin**, leading to increased concentrations of neurotransmitter in synaptic cleft and, ultimately, to greater postsynaptic neuronal activity , thus increasing the amount of serotonin in the brain.
- Safer and better tolerated than other classes of antidepressants .
- Because they have **fewer adverse effects** and are relatively **safe even in overdose** .





Examples of SSRIs include:

- **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 .

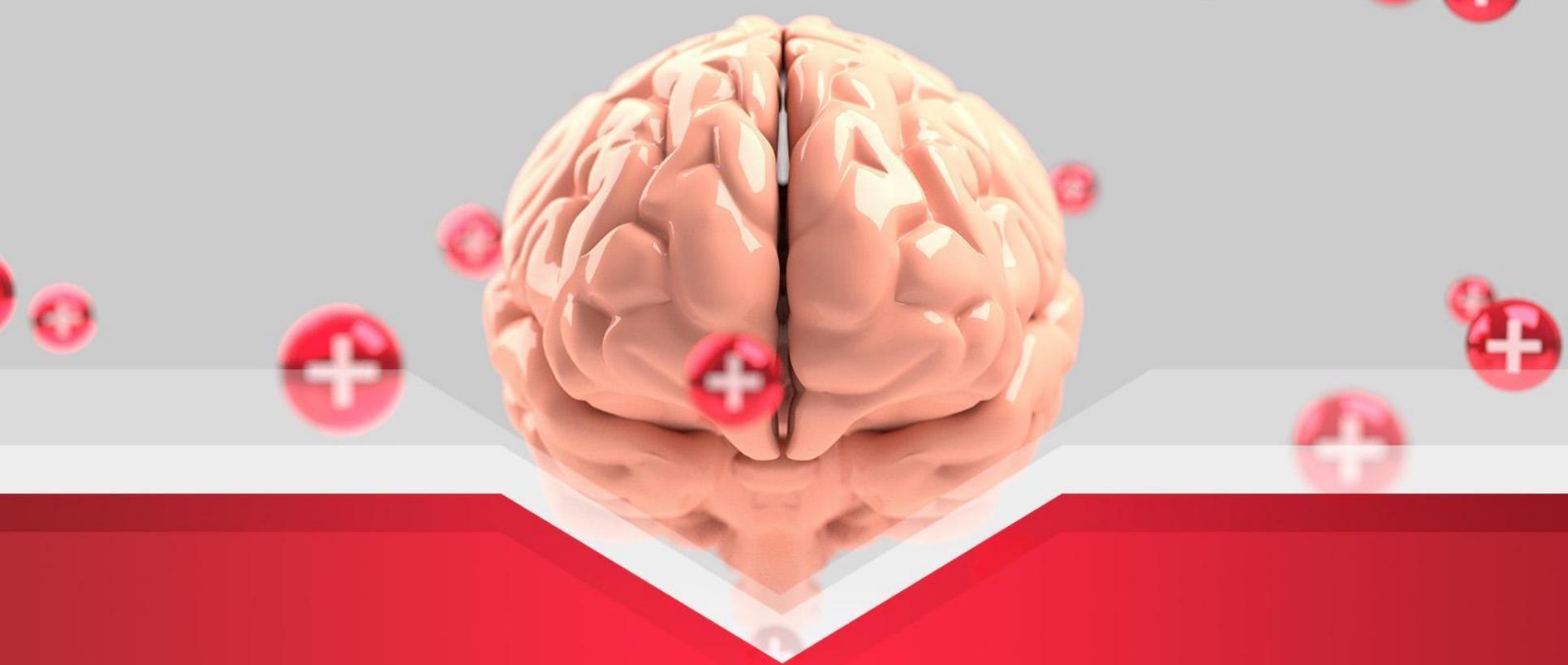
-SSRI can also be used in OCD and generalized anxiety disorder





SIDE EFFECTS SSRIs:

- orthostatic hypotension.
- serotonin syndrome.
- Sexual dysfunction.
- Headache
- gastrointestinal disturbance
- **Sleep disturbances:** sedation, insomnia
- **Overdoses:** seizures



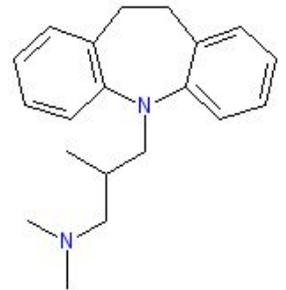
TRICYCLIC ANTIDEPRESSANTS

3. TRICYCLIC ANTIDEPRESSANTS

- Tricyclic antidepressants (TCAs) block norepinephrine and serotonin reuptake into the neuron
- They cause **increased concentrations of monoamines** in synaptic cleft, resulting in antidepressant effects

The TCAs include:

- Imipramine (the prototype drug)
- Amitriptyline
- Clomipramine



Pharmacokinetics

- well absorbed after **oral administration**
- Because of their **lipophilic nature**, they are widely distributed & **readily penetrate into CNS**
- **Have a narrow therapeutic index**



Therapeutic uses



1. Major depressive Disorder



2. Chronic pain condition e.g. fibromyalgia



**3. Nocturnal enuresis in children:
imipramine**



Adverse effects

- **Orthostatic (postural) hypotension.**
- **Atropine-like action:** very common - dry mouth, blurred vision, urine retention CNS **sedation**
- **Cardiac arrhythmia** Most lethal in overdose due to cardiac arrhythmias Can aggravate prolonged QTc syndrome
- **Serotonin syndrome**
- **Weight gain**
- **Sexual dysfunction:** (erectile dysfunction in men and anorgasmia in women)

TCA Toxicity

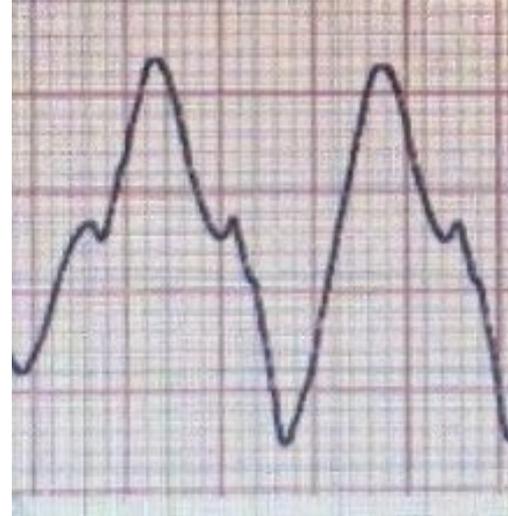
Manifestations :

- **1. Atropine-like action** : dry mouth , blurred vision , urine retention
- **2. Metabolic acidosis**
- **3. Cardiac arrhythmia** : tachy cardia - wide QRS - long QT interval

Treatment:

- **1. IV NaHCO₃**: is the 1st line
- 2. IV lidocaine

- N.B. Hemodialysis is not effective because TCAs have large Vd



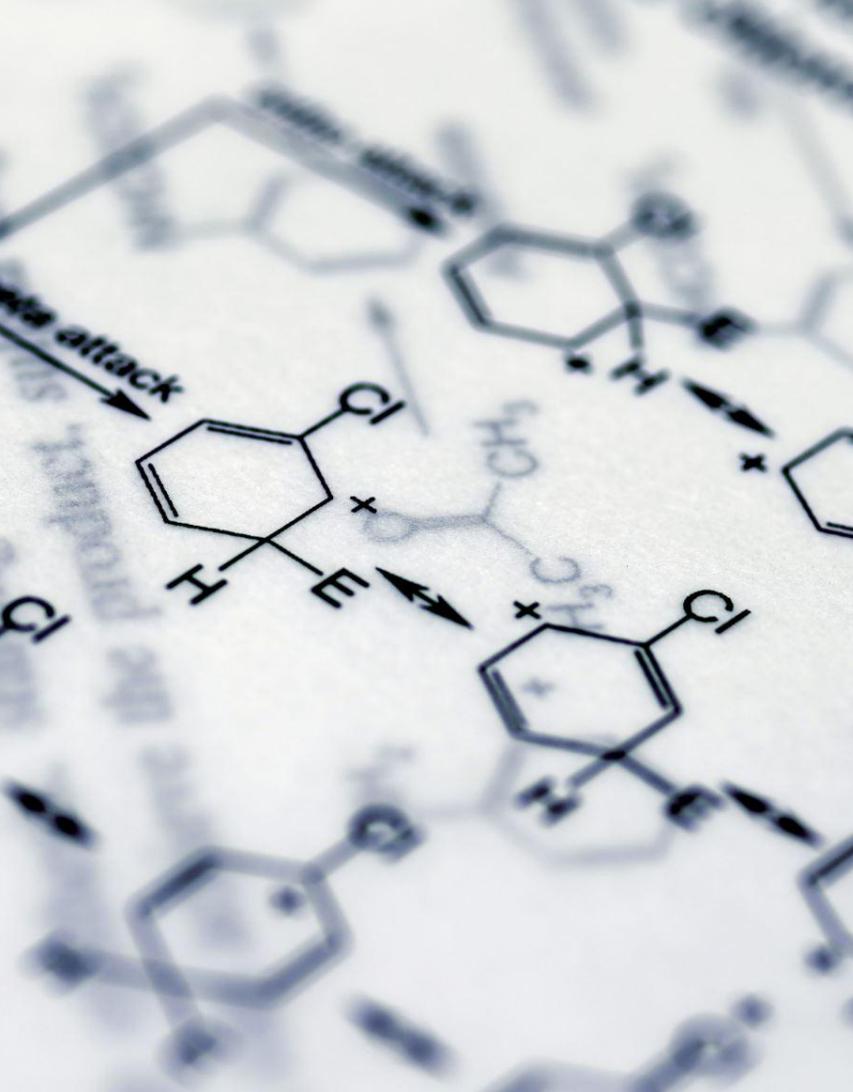
4. ATYPICAL ANTIDEPRESSANTS

□ The atypical antidepressants are a mixed group of agents that have actions at several different sites

Include

1. bupropion,
2. mirtazapine,
3. nefazodone, and
4. trazodone





CLASS (A) –reuptake inhibitors

Serotonin/norepinephrine re-uptake inhibitors (SNRIs)

Effective in depressed patients in which SSRIs are ineffective

- **Venlafaxine** is especially treating refractory depression.
- **Duloxetine**: used more for autonomic neuropathy

Class B : Receptor blockers:

	NA reuptake	5-HT reuptake
TCA		
SSRI		
Atypical		

Trazodone:

-Highly sedating

useful in treatment of refractory major .

Mirtazapine:

- Useful in the treatment of refractory major depression
- Causes less GIT upset and sexual dysfunction than SSRIS



MONOAMINE OXIDASE INHIBITORS



- **There are 2 isotope of MAO enzyme:**
- **MAO-A** : present in the cytoplasm of neurons (CNS) and peripheral tissue such as liver
- It act on NA,5-HT, AND dopamine
- **MAO-B enzyme** : present mainly in the CNS and act more on dopamine



Mechanism of action

- They inhibit MAO enzyme leading to accumulation of active monoamine (NA,5-HT,dopamine)in neuronal tissue
- Most MAOIs are irreversible inhibitors so the recovery take several weeks



Therapeutic uses

1. Major depression: unresponsive to other drugs

N.B. Clinical improvement occurs after 2-3 weeks

2. Parkinsonism: orgasm

Adverse effects

1. **Orthostatic hypotension**
2. **Sexual dysfunction:** delayed organising
3. **Serotonin syndrome :** if combined with TCA or SSRIS
4. **CNS stimulation :** irritability, insomnia, tremors, hyperthermia, convulsion.
5. **Cheese reaction :** (hypertensive crisis) occur when eating tyrosine rich food such as yogurt , old cheese.





THANK

Done BY : YOU

Batool Kasasbeh

Yaqout Mriyan

Esraa Hawawreh