

# ANTIDEPRESSANTS





- Symptoms of depression:

- Intense feelings of sadness, hopelessness and despair
- Inability to experience pleasure in usual activities
- Change in sleep patterns
- Suicidal thoughts

# Depression may be secondary to:

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- Organic problems like hypothyroidism, dementia, anemia
- Psychiatric problems like schizophrenia, drug abuse, anxiety disorders
- Use of depressants drugs such as alcohol

# Depression in the Elderly:

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- Not natural part of aging
- Underdiagnosed and misdiagnosed in elderly
- 10-15% of elderly have clinically significant depression
- Drug responsiveness similar to younger patients

# Mechanisms of antidepressant drugs

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- Potentiate the actions of **norepinephrine** and/or **serotonin**
  
- Antidepressant benefit requires 2-3 weeks or more

# Drug classes used in depression

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1. Tricyclic antidepressants
2. Monoamine oxidase inhibitors
3. Selective serotonin reuptake inhibitors (SSRI)
4. Serotonin/Norepinephrine reuptake inhibitors (SNRIs)
5. Atypical antidepressants

# Tricyclic antidepressants

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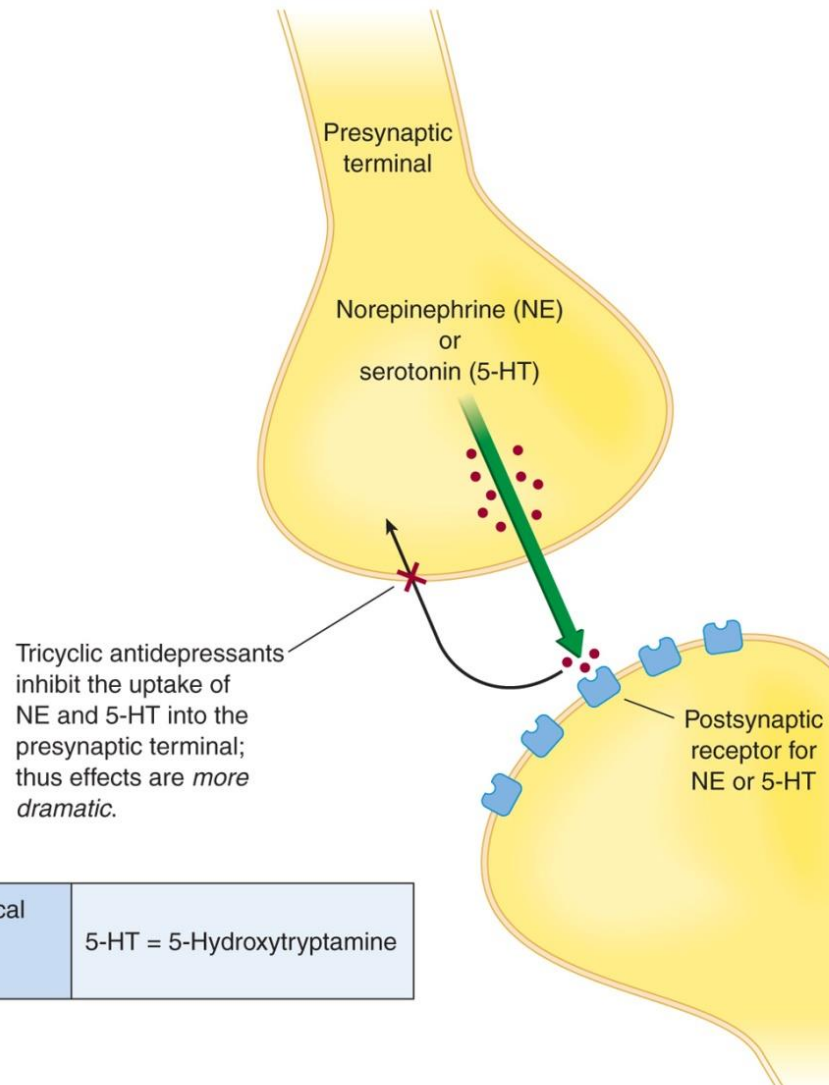
- Imipramine
- Clomipramine
- Amitriptyline
- Maprotiline

# Tricyclic antidepressants (TCA)

- Mechanism of action: inhibit the reuptake of norepinephrine and serotonin (nonselectively) into the neuron, increasing the concentration of these neurotransmitters in the synapse resulting in antidepressant effects
- Have anti-muscarinic activity
  - ▣ Cause side effects like dry mouth and blurred vision
- $\alpha$ -receptor blocking activity
  - ▣ Cause side effects like orthostatic hypotension
- Block histamine H<sub>1</sub> receptors
  - ▣ Cause sedation (side effect)



Tricyclic antidepressants produce their effects by inhibiting the reuptake of neurotransmitters into presynaptic nerve terminals. The neurotransmitters particularly affected are norepinephrine and serotonin.



The chemical name for serotonin	5-HT = 5-Hydroxytryptamine
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# Tricyclic antidepressants (TCA)

- Onset of mood elevation is slow requiring 2 weeks or longer
- Discontinuation syndrome occurs if drug is stopped abruptly
- Narrow therapeutic index, overdose is lethal
- Adverse effects:
  - Antimuscarinic (Blurred vision, dry mouth, urinary retention, tachycardia, constipation)
  - Arrhythmia (Prolonged QT intervals)
  - Orthostatic hypotension (due to blocking of  $\alpha$ -receptors)
  - Sedation (due to blocking of H1 histamine receptors)

# Monoamine oxidase inhibitors

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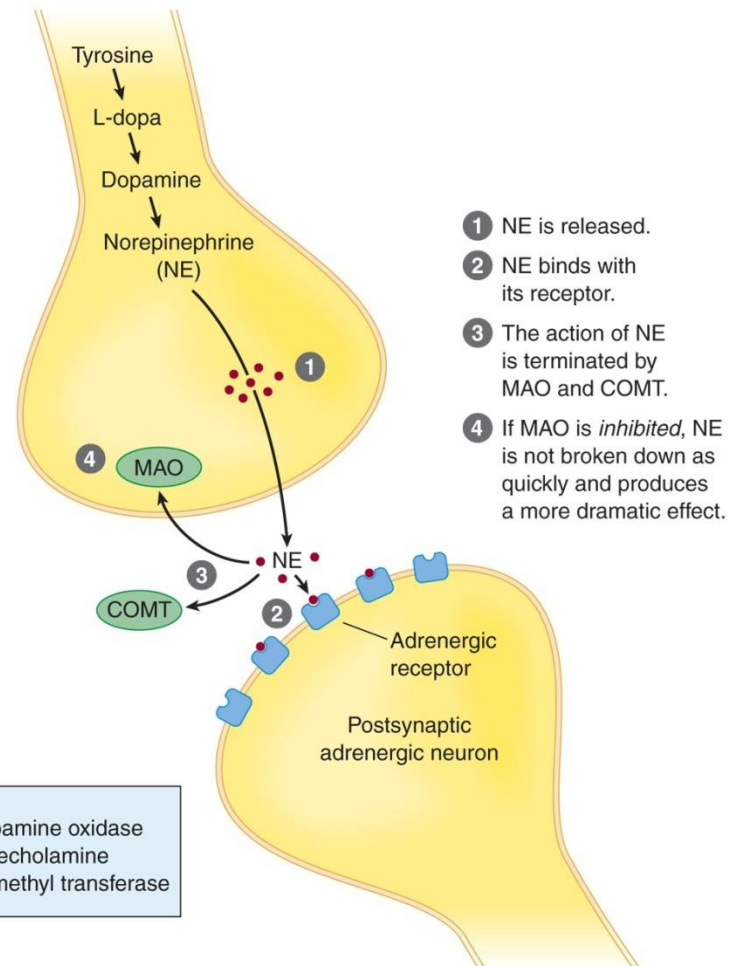
- Phenzelzine
- Selegiline

# Monoamine oxidase inhibitors

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- The enzyme monoamine oxidase (MAO) inactivates norepinephrine, serotonin and dopamine
- Monoamine oxidase inhibitors inhibit this enzyme and increases the levels of norepinephrine, serotonin and dopamine in the synapse
- Antidepressant effects require 2-4 weeks of treatment

## Termination of the norepinephrine activity through enzyme activity in the synapse.



# Monoamine oxidase inhibitors

- Adverse effects
  - Due to inhibition of MAO enzyme in the liver and gut, severe drug-food interaction occur, leading to accumulation of substances like tyramine which is found in cheese and meat, and its accumulation lead to release of large amounts of catecholamines causing “**hypertensive crisis**” (headache, hypertension, tachycardia, arrhythmia, seizures)

# Selective serotonin reuptake inhibitors (SSRI)

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- Citalopram
- Fluoxetine
- Paroxetine
- Sertraline

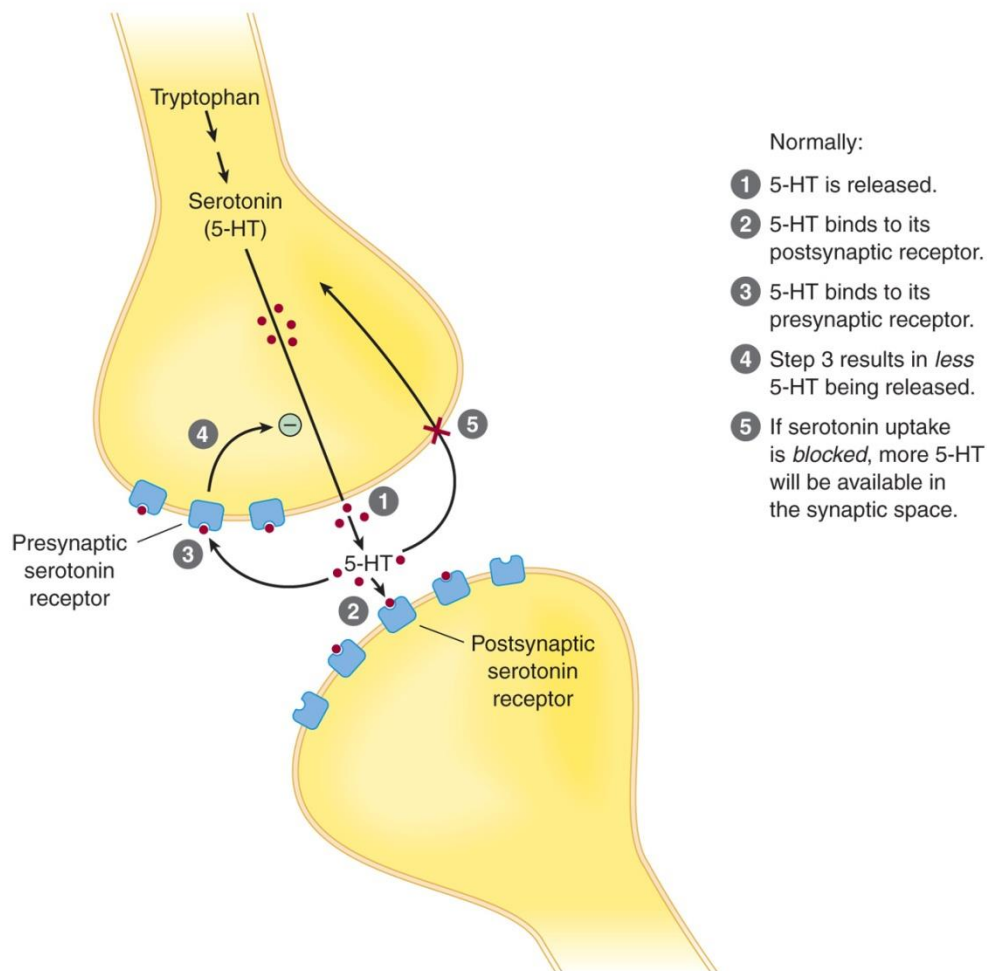
# Selective serotonin reuptake inhibitors (SSRI)

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- Mechanism of action: inhibit serotonin reuptake increasing the concentration of the neurotransmitter in the synaptic cleft and increasing its activity
- The drug of choice for treating depression
- Fewer adverse effects than tricyclic antidepressants  
(no blocking effects on muscarinic,  $\alpha$ - and histamine H1 receptors)
- Take about 2 weeks to produce effects
- Not all patients respond well to antidepressant drugs



SSRIs block the reuptake of serotonin into presynaptic nerve terminals. Increased levels of serotonin induce complex changes in presynaptic and postsynaptic neurons of the brain. Presynaptic receptors become less sensitive and postsynaptic receptors become more sensitive.



# Selective serotonin reuptake inhibitors (SSRI)

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- Therapeutic uses
  - ▣ Depression
  - ▣ Obsessive compulsive disorder
  - ▣ Generalized anxiety disorder
- Adverse effects
  - ▣ Gastrointestinal: Nausea, vomiting
  - ▣ Sleep disturbances
  - ▣ Sexual dysfunction
- Discontinuation syndrome occurs with abrupt discontinuation (headache, agitation, nervousness)

# Serotonin/Norepinephrine reuptake inhibitors (SNRI)

- Venlafaxine
- Duloxetine

# Serotonin/Norepinephrine reuptake inhibitors (SNRI)

- Mechanism of action: Inhibit reuptake of both norepinephrine and serotonin
- Have fewer adverse effects than TCA as they have less effects on adrenergic, cholinergic and histamine receptors
- Adverse effects
  - ▣ Nausea
  - ▣ Dizziness
  - ▣ Sexual dysfunction
- Discontinuation syndrome occurs if treatment is stopped abruptly

# Atypical antidepressants

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- Bupropion
  - ▣ Dopamine and norepinephrine reuptake inhibitor
  - ▣ Used for
    - Depression
    - Attenuate withdrawal symptoms for quitting smoking

# BIPOLAR DISORDER AND MANIA



- In bipolar disorder patients go through episodes of an elevated or agitated mood known as mania alternating with episodes of depression.
- Mania is characterized by enthusiasm, rapid thought and speech pattern, extreme self confidence and impaired judgment

# Lithium

- Used as salt: lithium carbonate
- Mechanism of action: unknown
- Used prophylactically for manic episodes in manic-depressive patients (mood stabilizer)
- A partial sodium substitute
- Indications: all kinds of bipolar and other psychiatric problems secondary to mood disorders
- Narrow therapeutic index
  
- Adverse effects:
  - Dry mouth,
  - Polydipsia
  - Polyuria
  - Tremor
  - Dizziness
  - Fatigue
  - Convulsions



# Antiepileptics for Mania:

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- Valproate
- Gabapentin
- Carbamazepine
  
- Mood stabilizers