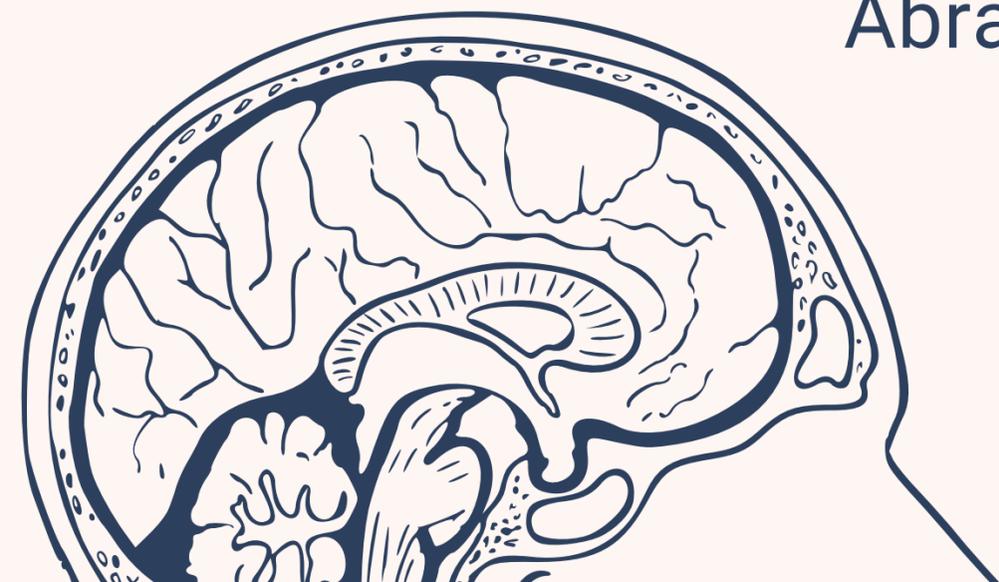
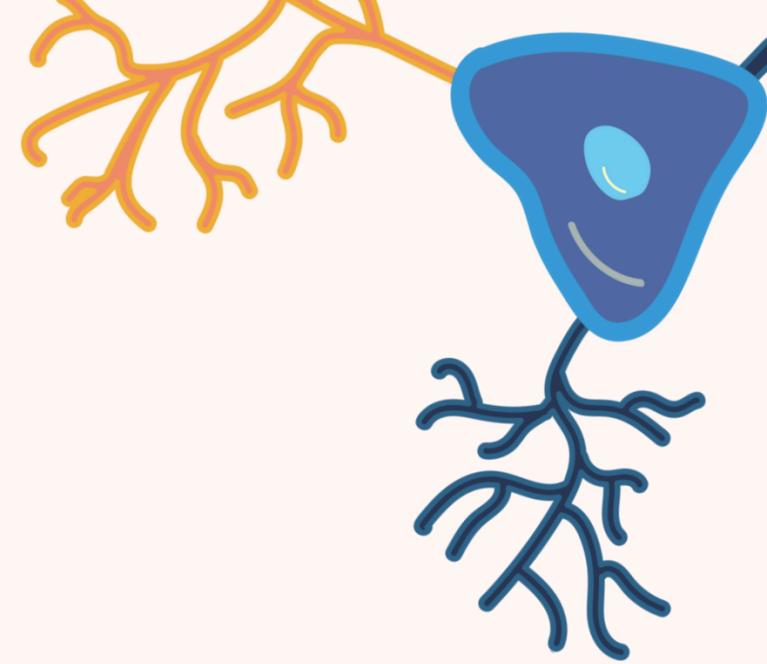
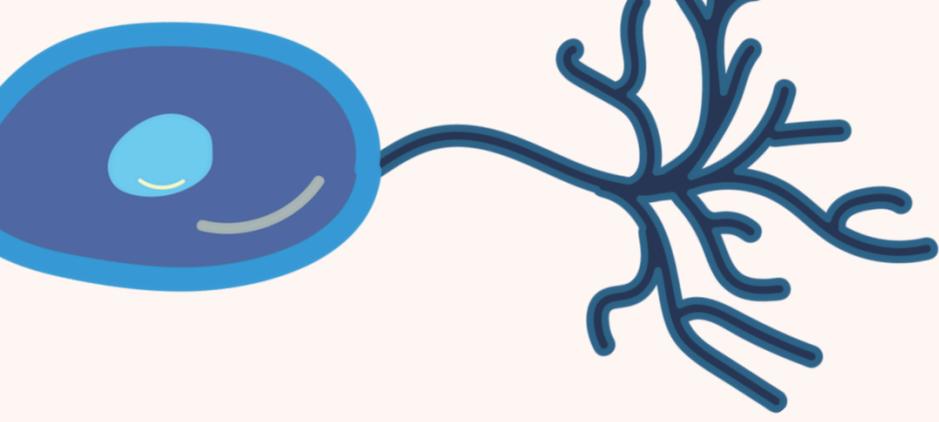


Antipsychotics

By:- Hanan AL-Bayad
Shames AL-Duha
Abrar Amjad



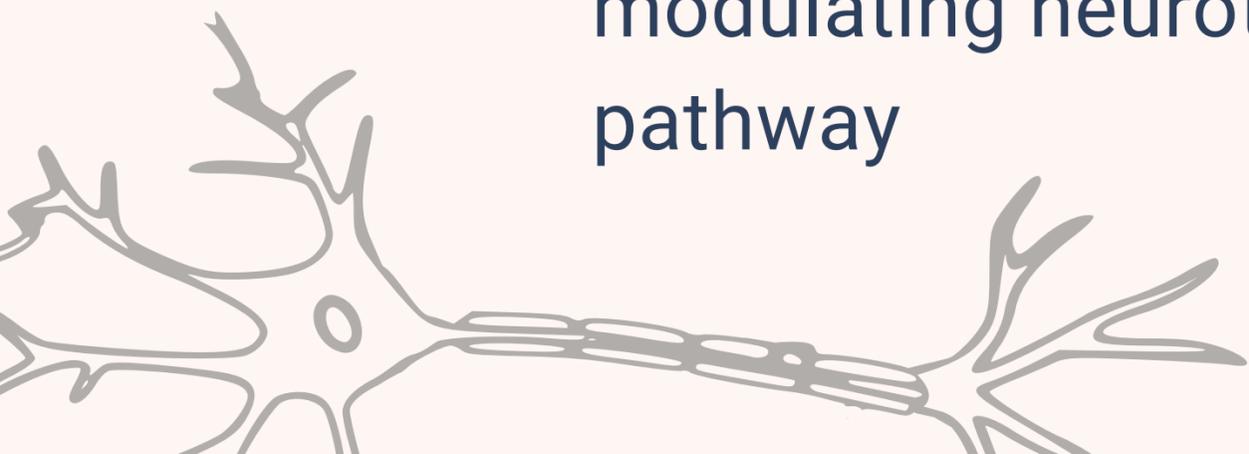


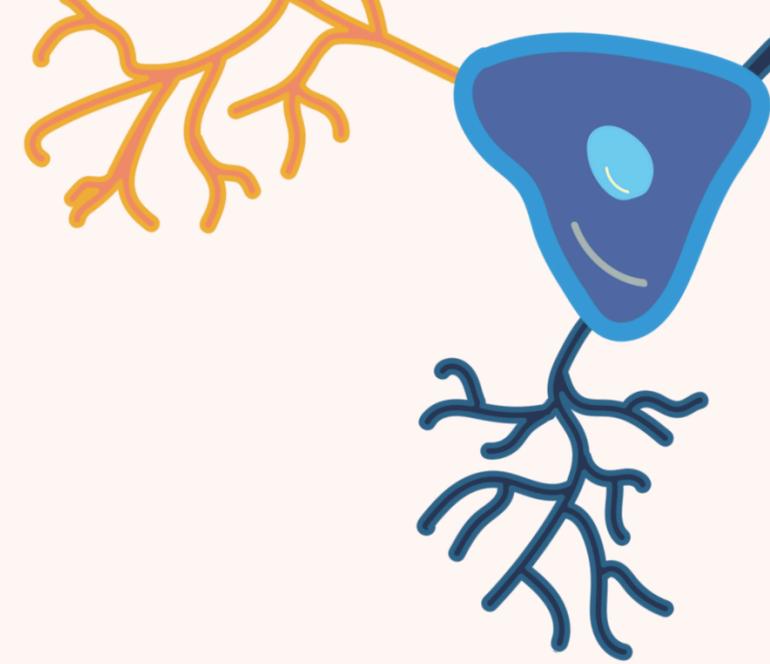
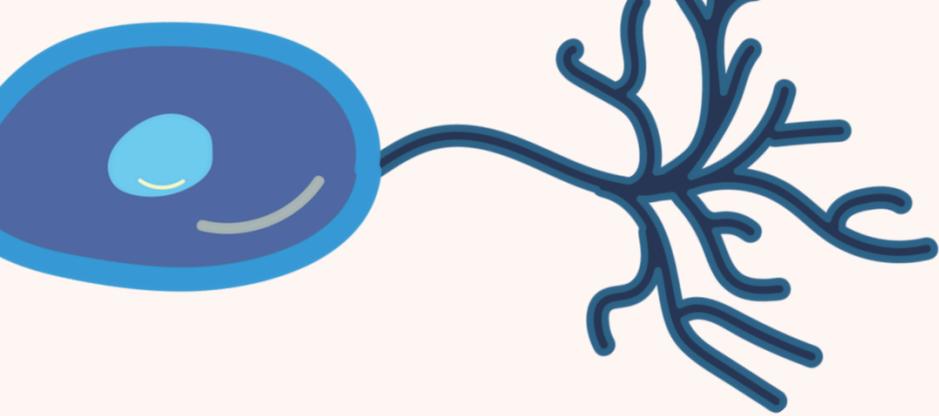
Definition

Medications used to manage psychotic disorders, bipolar disorders and some psychotic symptoms that are associated with other psychiatric and medical illnesses.

Purpose

To reduce or eliminate psychotic symptoms by modulating neurotransmitters activity, mainly dopamine pathway

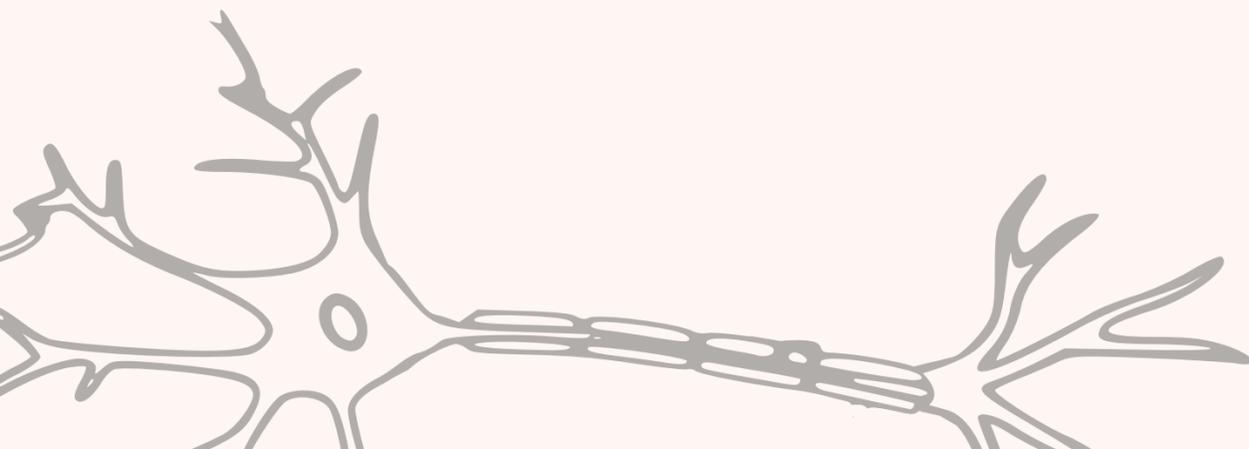


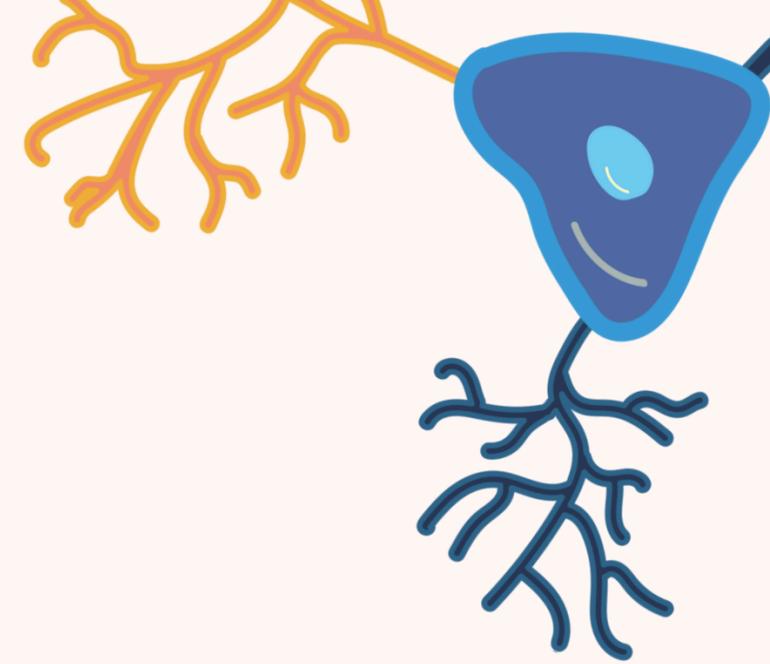
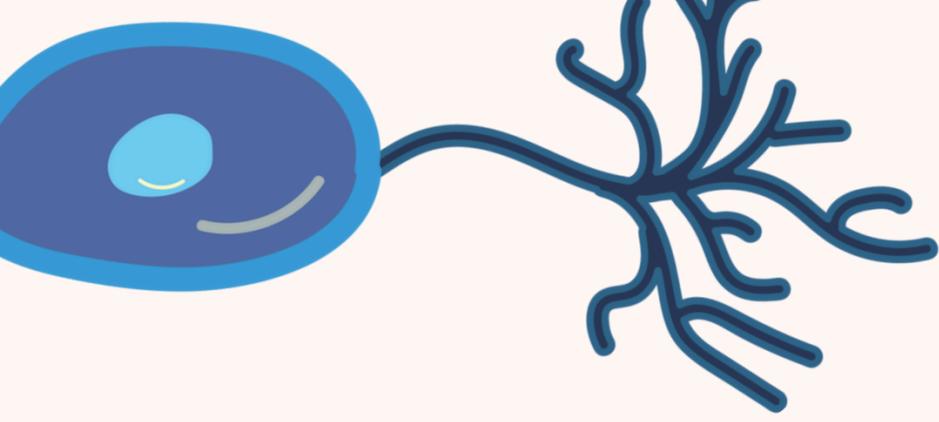


Types

First generation or Typical:- Sometimes referred to as neuroleptics, are classified according to potency and treat psychosis by primarily blocking dopamine (D2) receptors

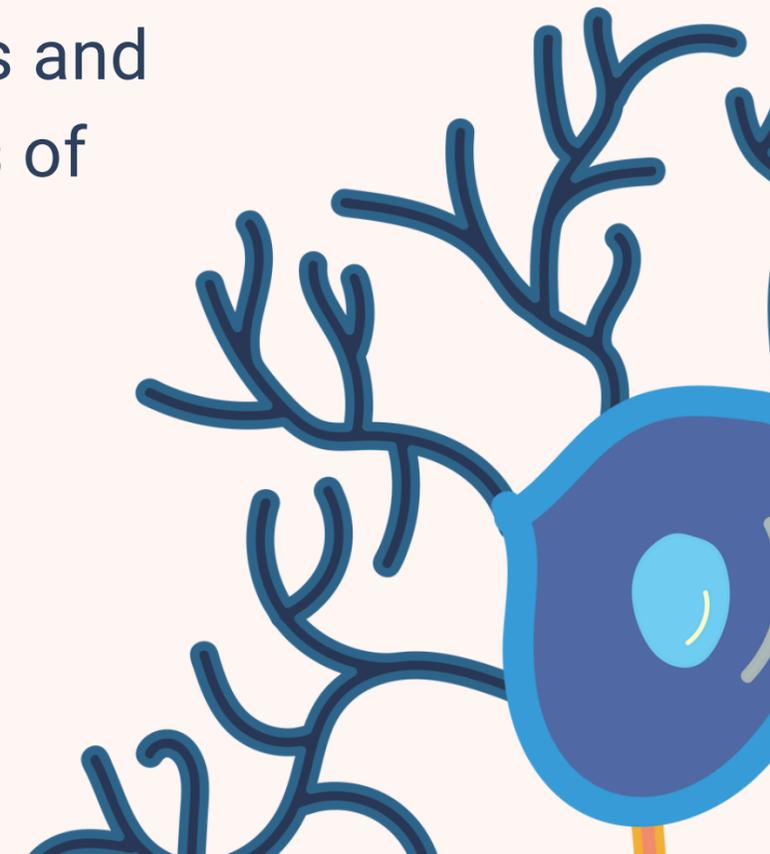
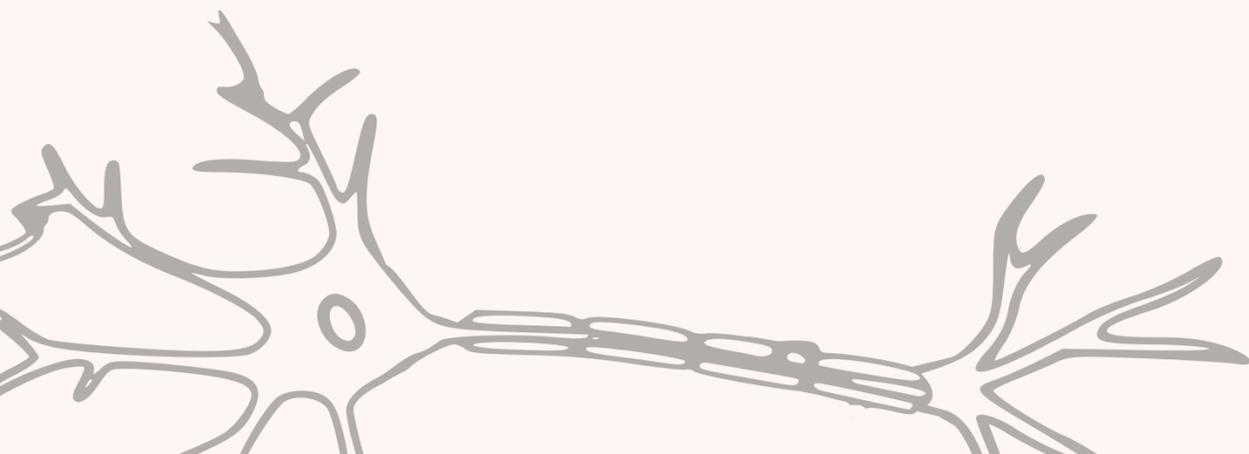
Second generation or Atypical:- Block both Dopamine (D2) and serotonin (5HT-2A) receptors

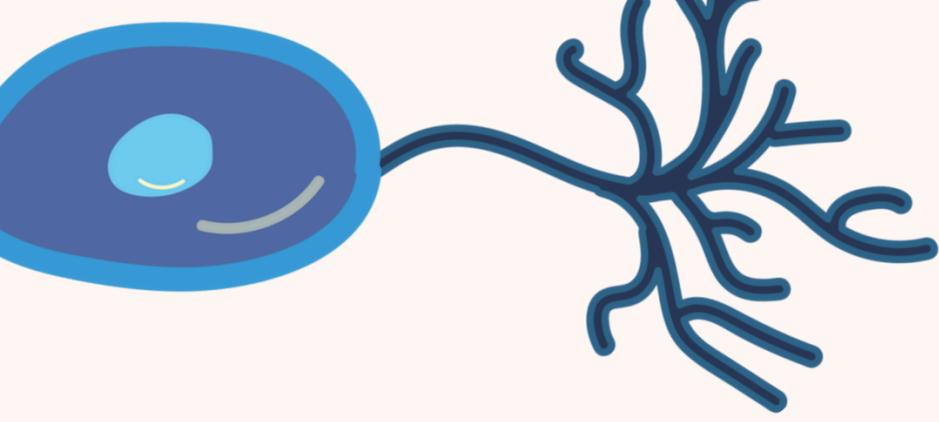




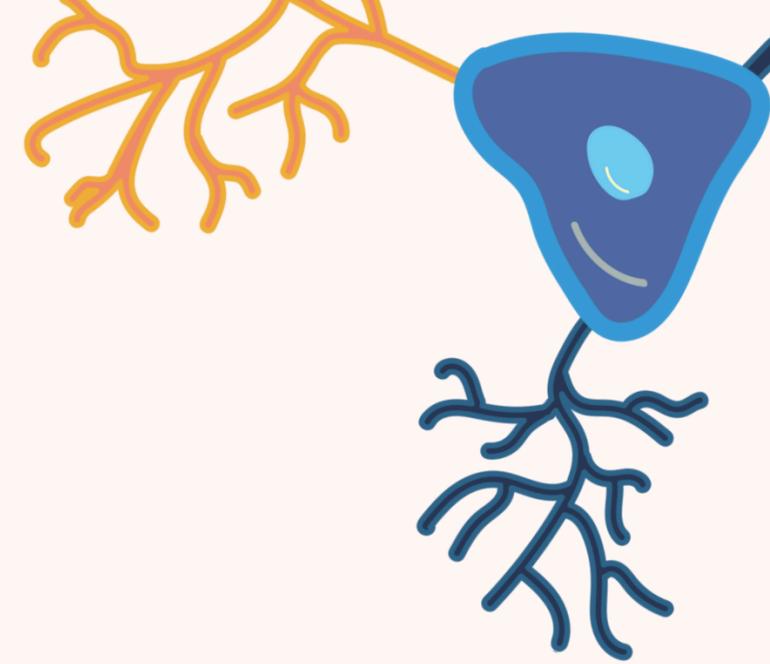
Dopamine

Dopamine is a neurotransmitter and hormone produced in the brain that plays a crucial role in various body functions, including memory, movement, motivation, mood, and attention. It acts as a chemical messenger, transmitting signals between nerve cells and is involved in the brain's reward system, influencing feelings of pleasure and satisfaction.





Dopamine pathways

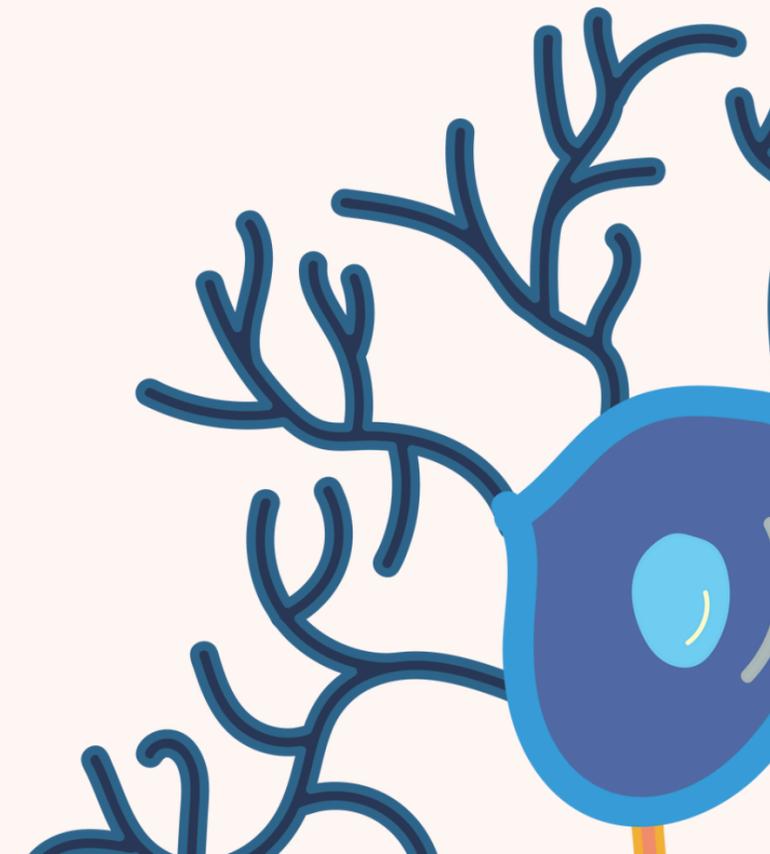
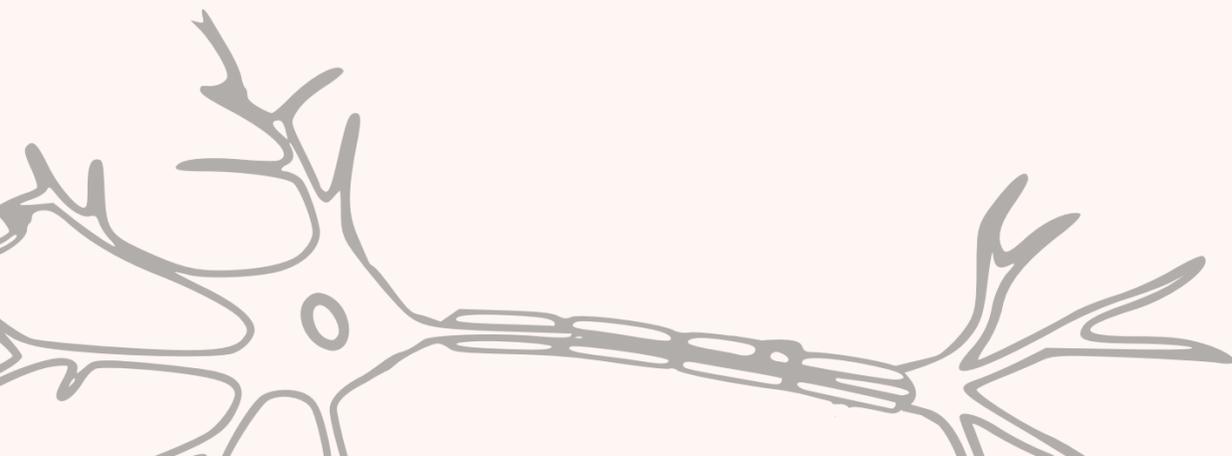


1) The mesolimbic (“The reward”) Pathway

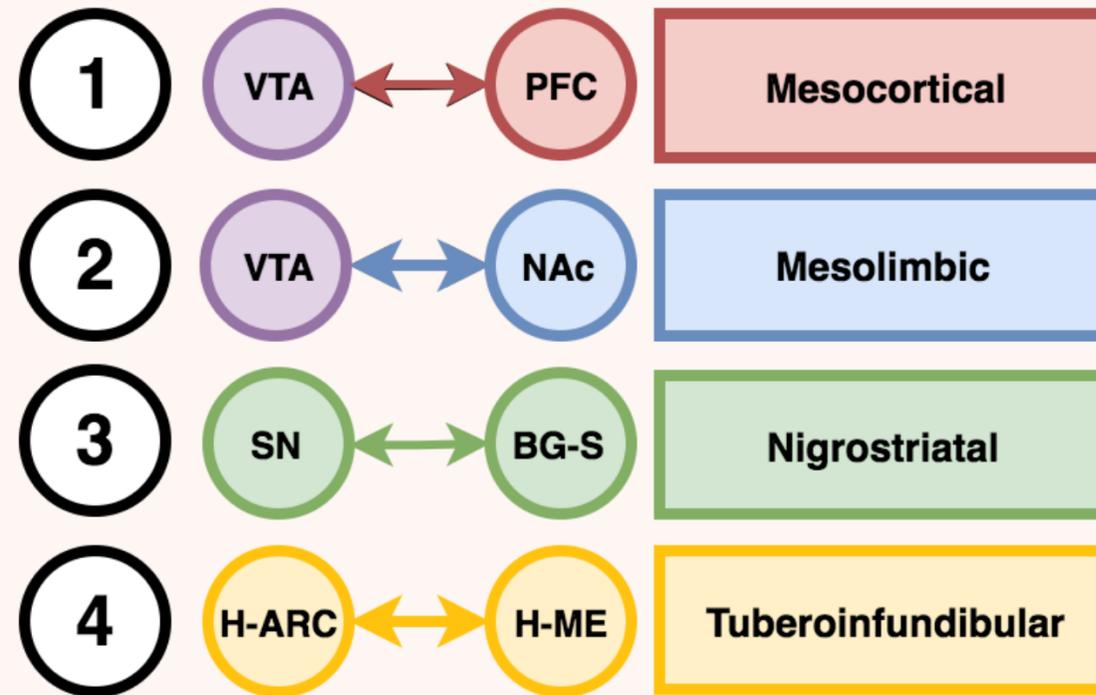
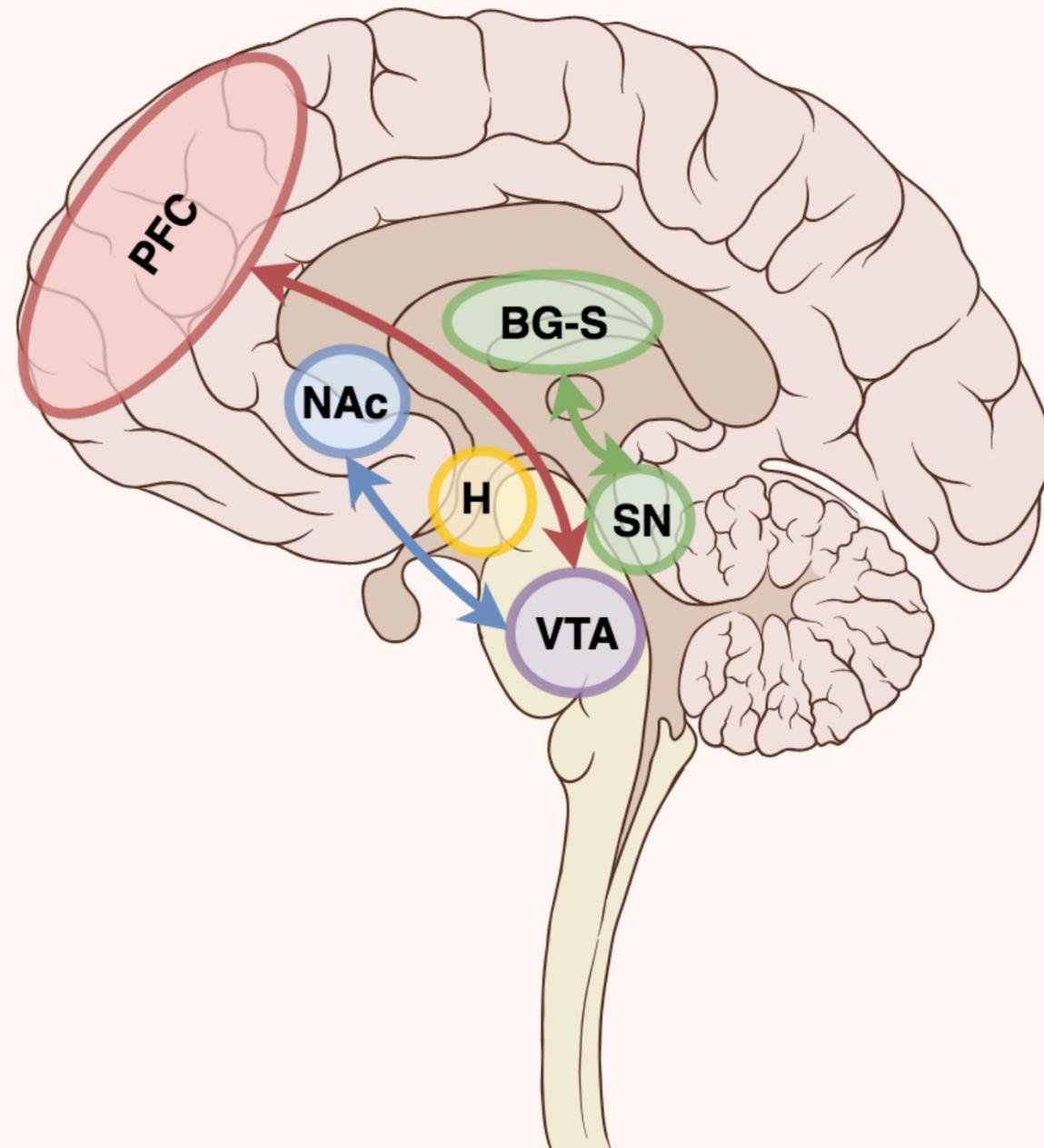
2) the Mesocortical Pathway

3) The Nigrostriatal Pathway

4) The Tuberoinfundibular Pathway

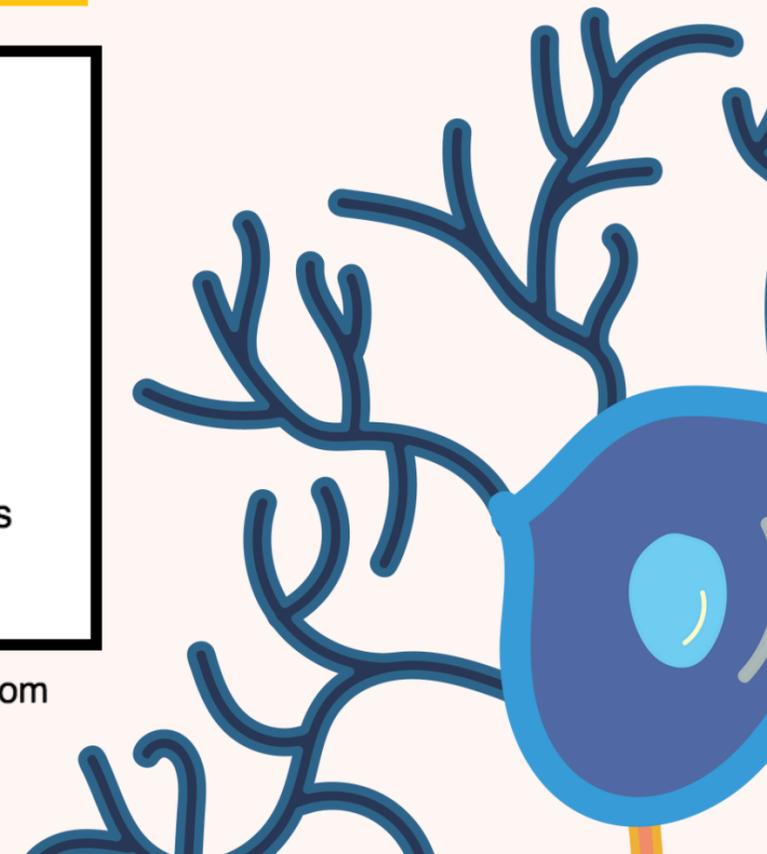


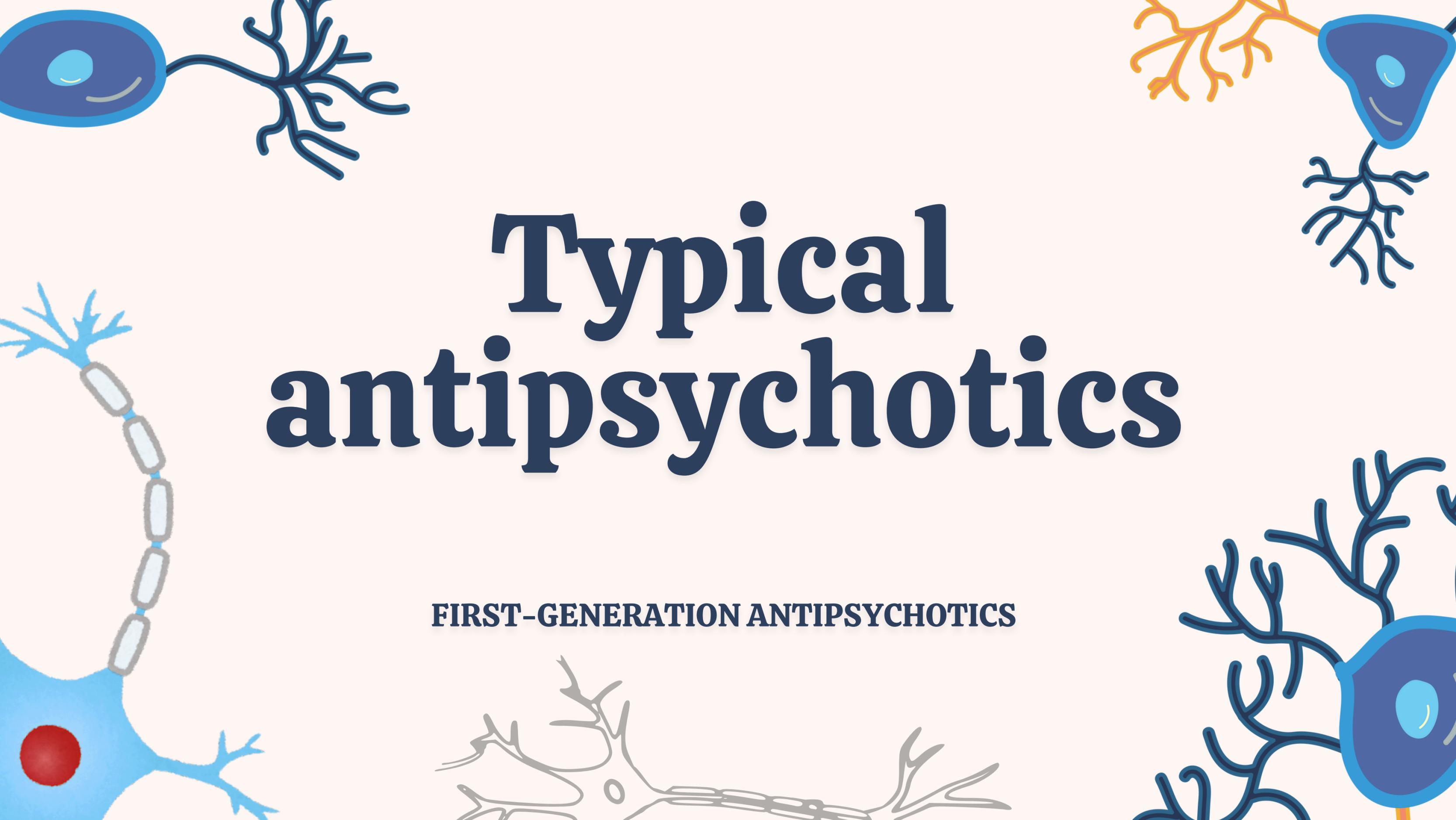
DOPAMINERGIC PATHWAYS IN THE BRAIN



LEGEND

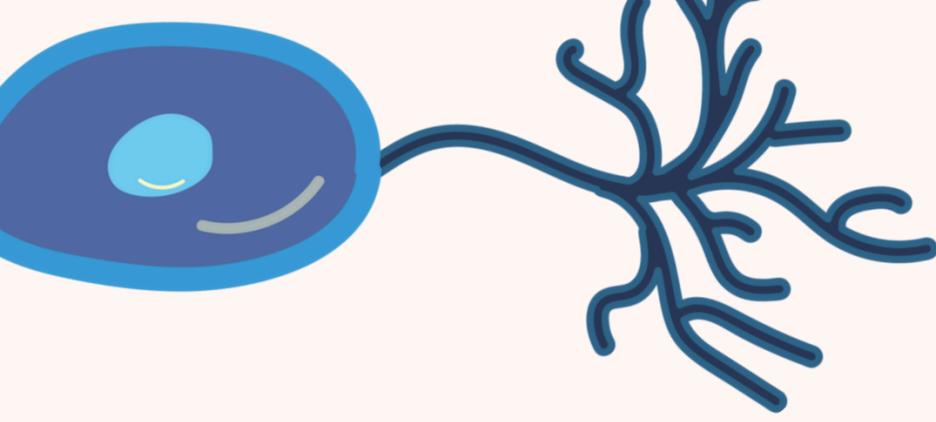
- VTA** = Ventral tegmental area
- PFC** = Prefrontal cortex
- NAc** = Nucleus accumbens
- SN** = Substantia nigra
- BG-S** = Basal ganglia (striatum)
- H-ARC** = Hypothalamus, arcuate (infundibular) nucleus
- H-ME** = Hypothalamus, median eminence



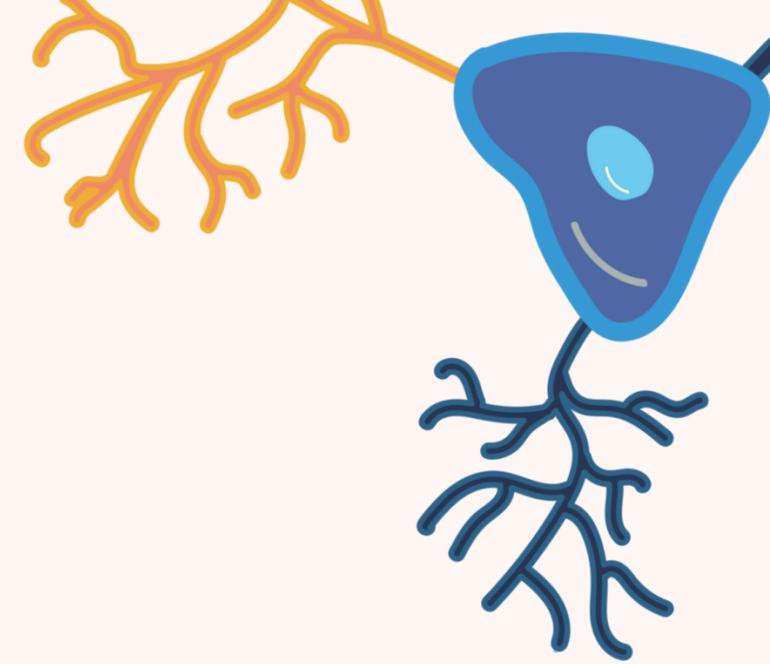


Typical antipsychotics

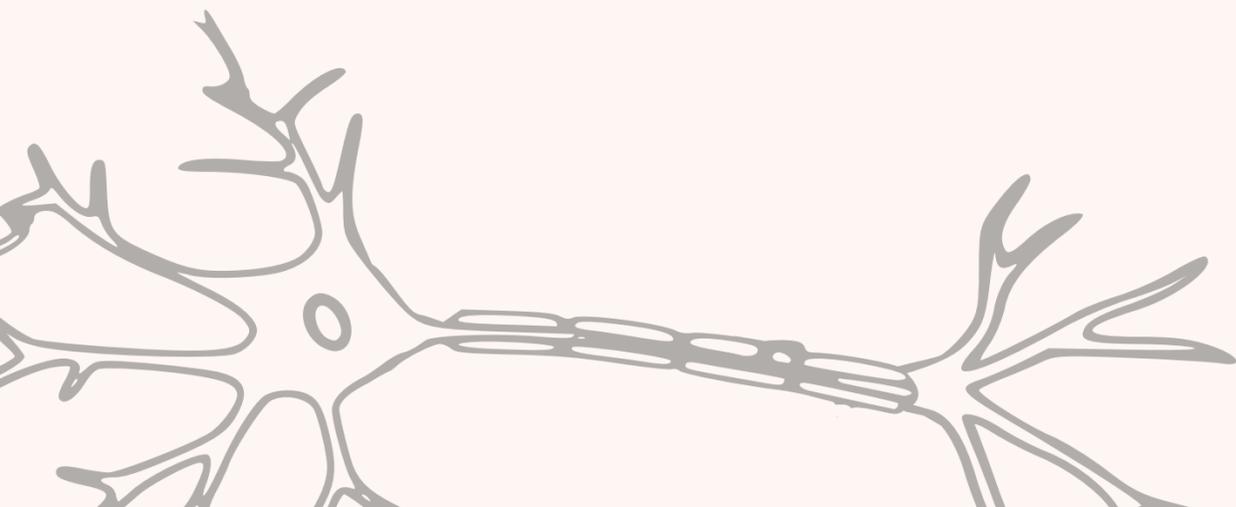
FIRST-GENERATION ANTIPSYCHOTICS

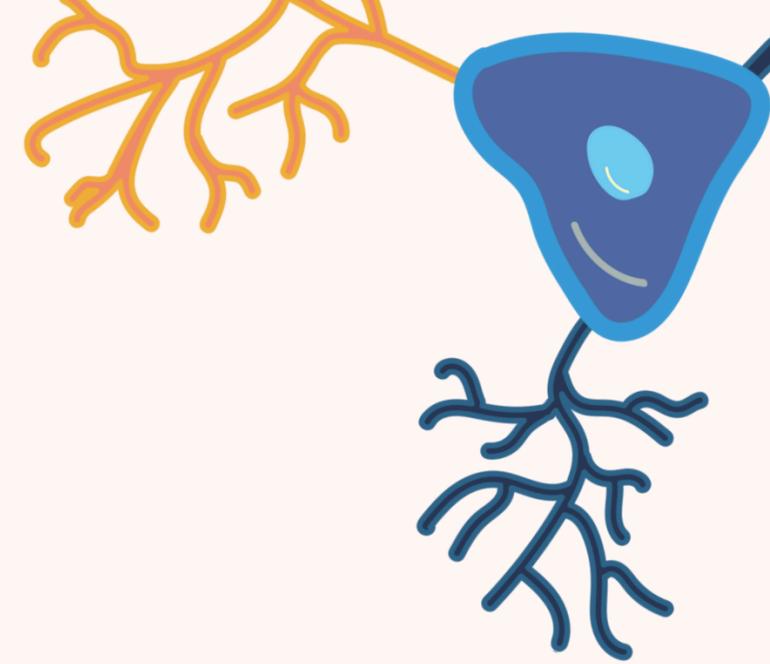
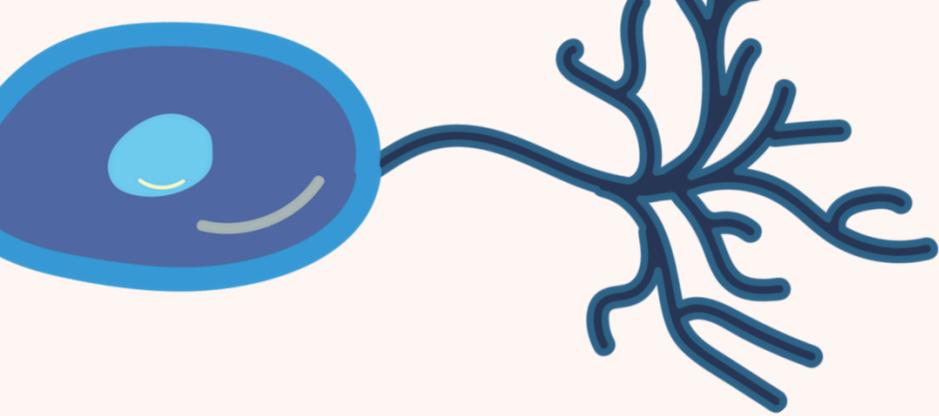


All have similar efficacy, but vary in potency

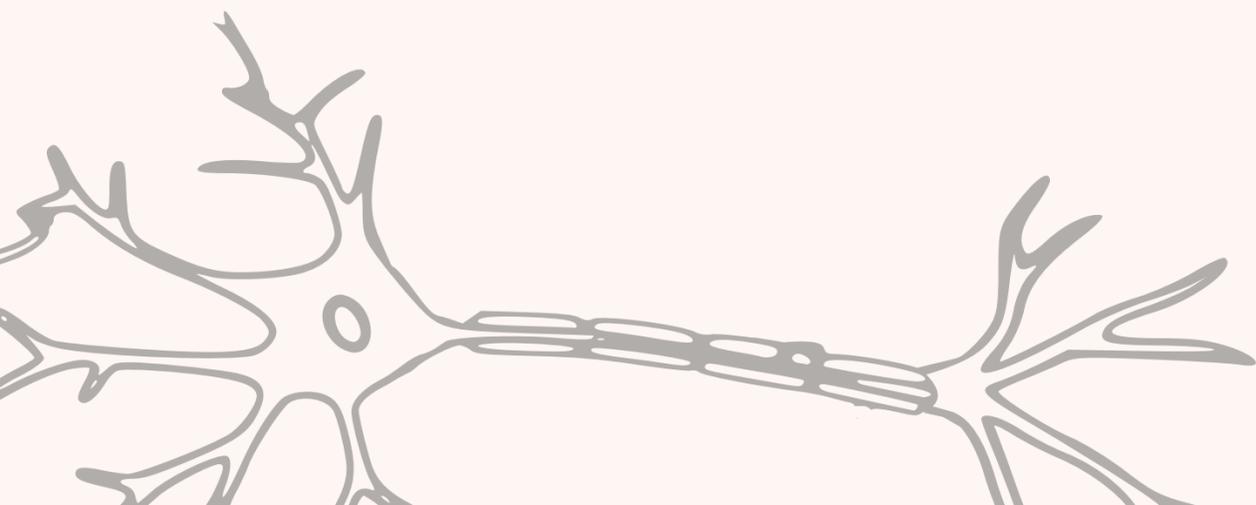


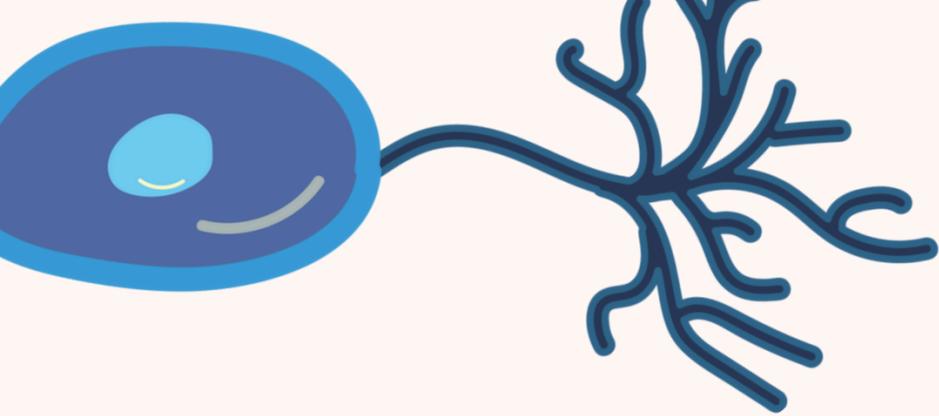
- Low Potency:- **Chlorpromazine / Thioridazine**
- Mid-Potency:- **Loxapine / Thiothixene / Molindone / Perphenazine**
- High Potency:- **Haloperidol / Fluphenazine / Trifluoperazine / Pimozide**



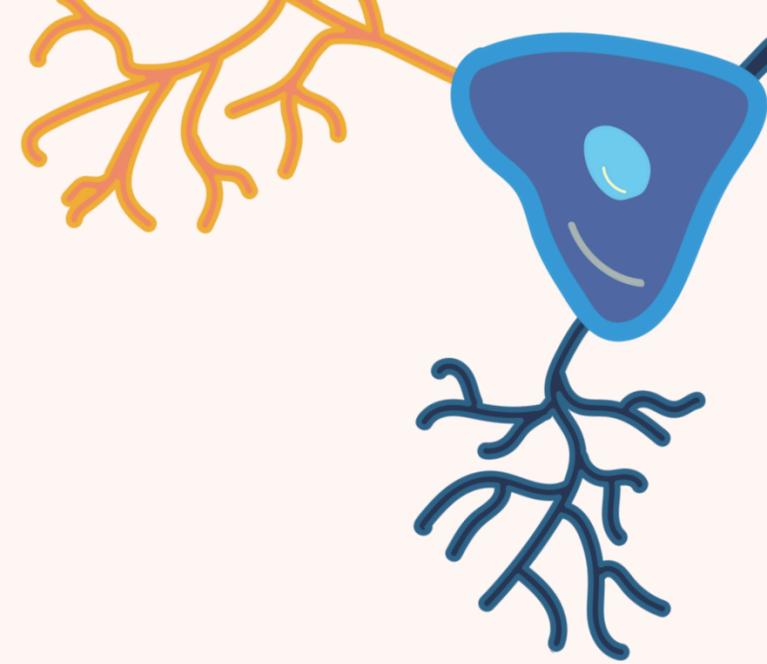


- They primarily work by broadly blocking dopamine D2 receptors across the brain. This non-selective action is both their therapeutic strength and the source of their significant side effects.
- Secondarily work as Anti-cholinergic, Anti-adrenergic and Anti-histaminic





Effects of D2 receptor blockade

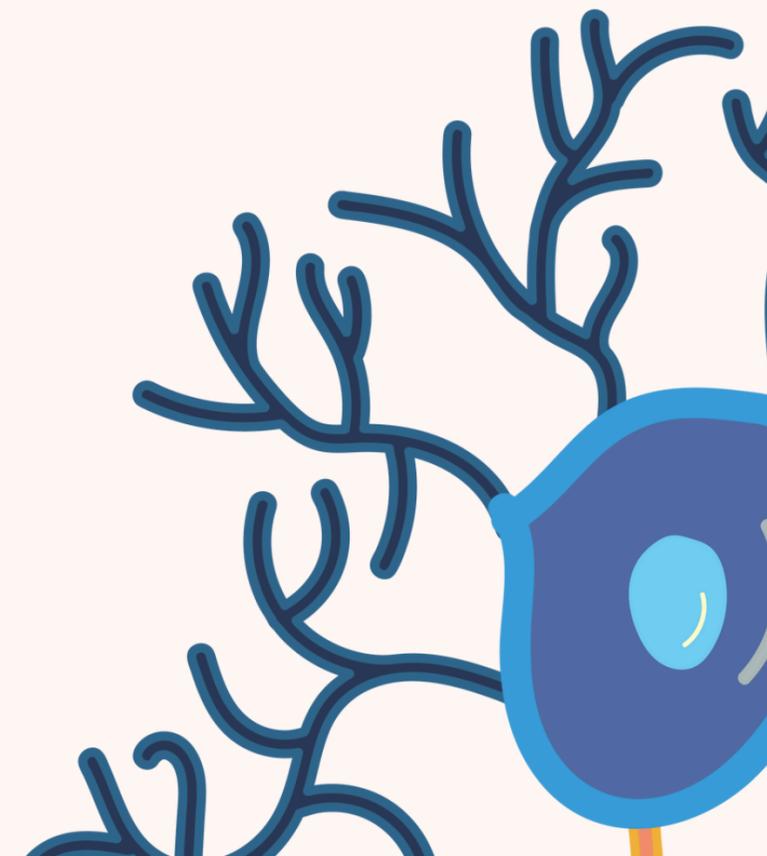
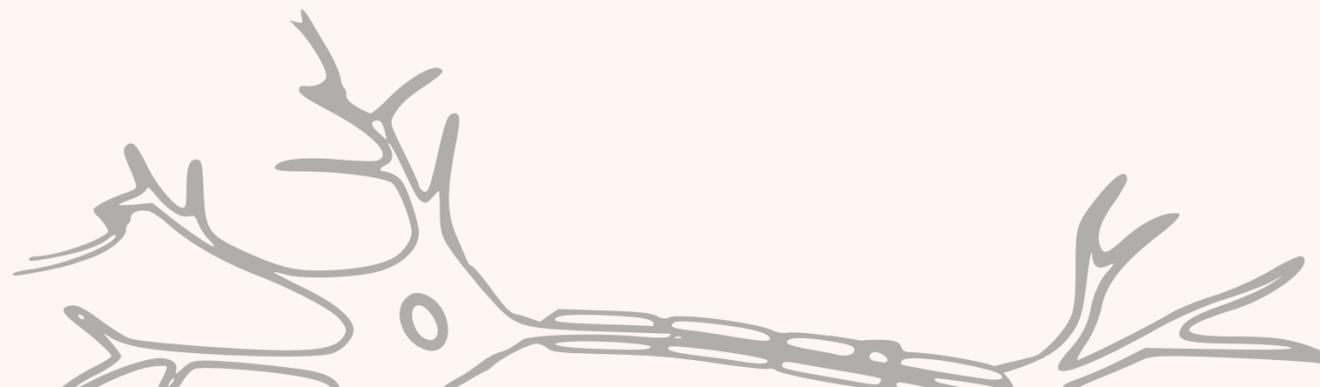


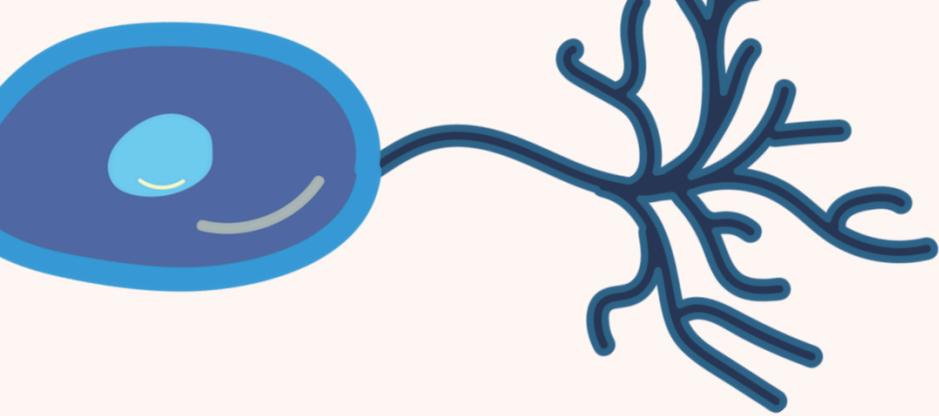
1) Mesolimbic Pathway:-

Reduction in the “positive” symptoms of Psychosis, such as hallucinations, delusions and disorganized thinking. By Dampening this hyperactive circuit, the drug helps bring the patient’s perception of reality closer to normal.

2) Mesocortical Pathway:-

Worsening or lack of improvement in “negative” symptoms like apathy, social withdrawal and blunted emotions. It can also impair cognitive function



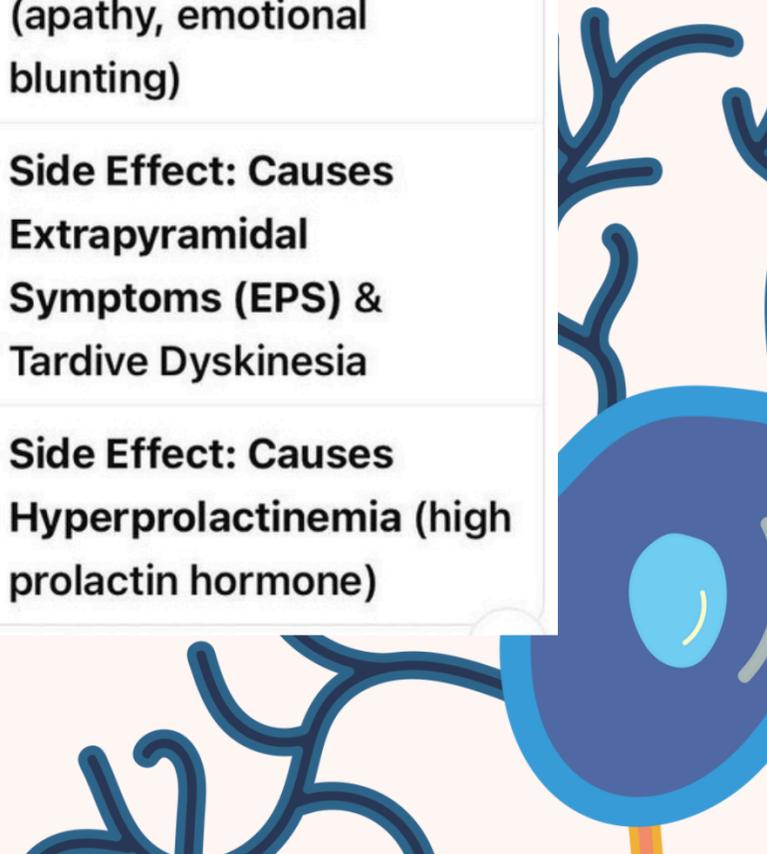
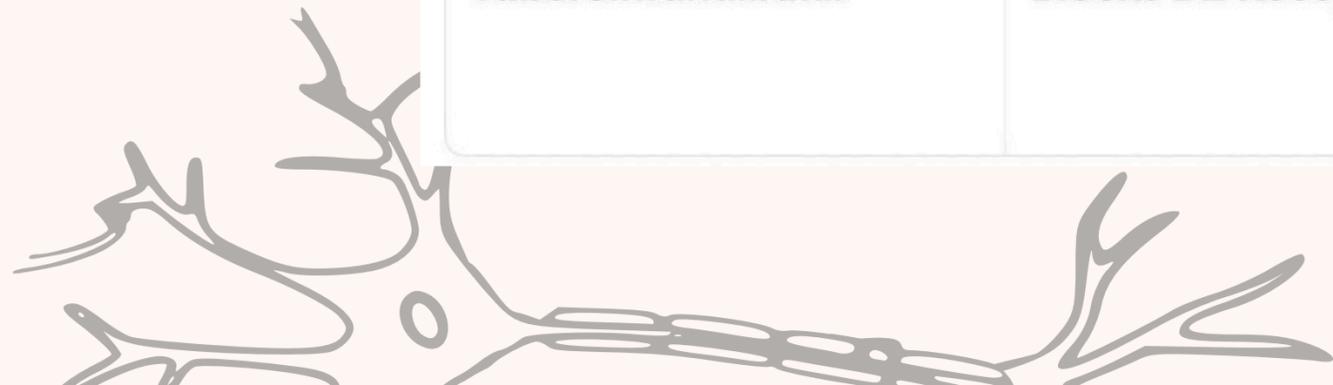


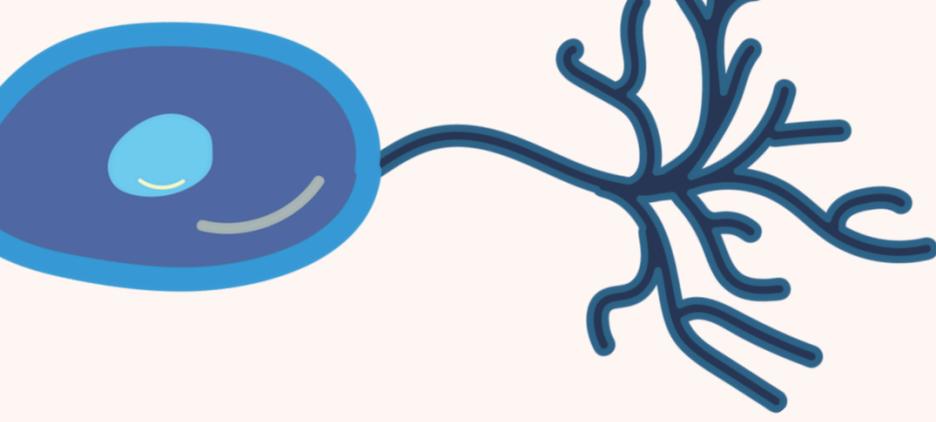
Effects of D2 receptor blockade

3) Nigrosriatal Pathway:-
Result in EPS

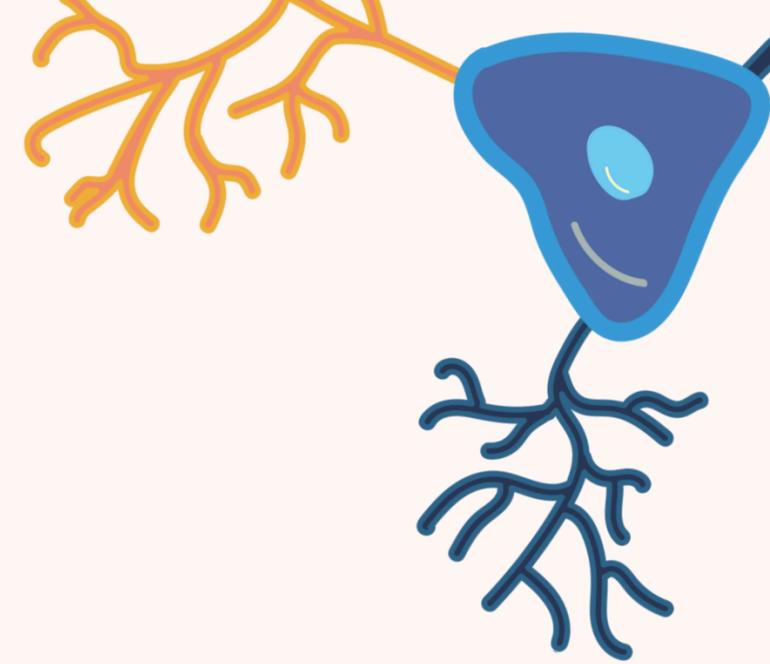
4) Tuberoinfundibular Pathway:-
Results in Hormonal side effects

Dopamine Pathway	Effect of Typical Antipsychotic	Clinical Consequence
Mesolimbic	Blocks D2 Receptors	Therapeutic: Reduces positive symptoms (hallucinations, delusions)
Mesocortical	Blocks D2 Receptors	Side Effect: Can worsen negative symptoms (apathy, emotional blunting)
Nigrostriatal	Blocks D2 Receptors	Side Effect: Causes Extrapyrimal Symptoms (EPS) & Tardive Dyskinesia
Tuberoinfundibular	Blocks D2 Receptors	Side Effect: Causes Hyperprolactinemia (high prolactin hormone)

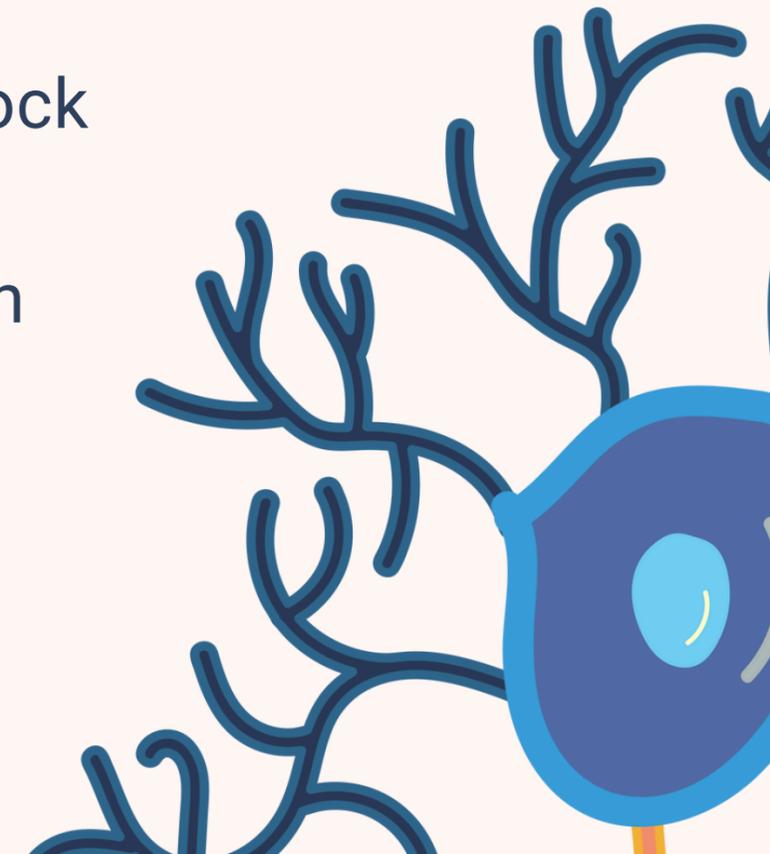
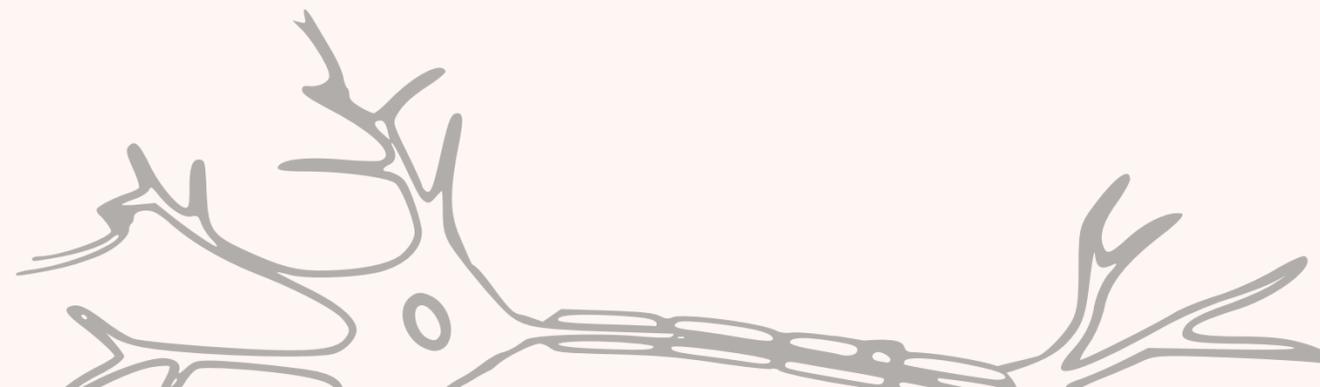


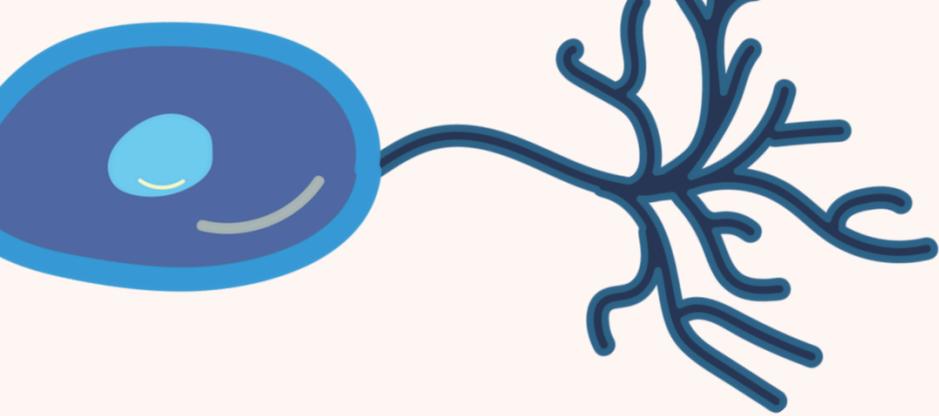


Low Potency Anti-psychotics

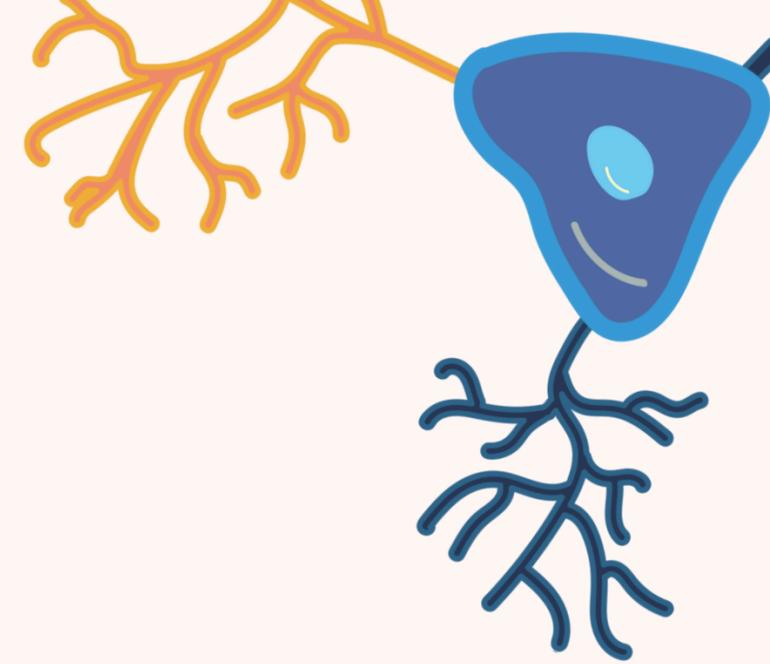


- Lower affinity for dopamine receptors and therefore a higher dose is required
- Higher incidence of antiadrenergic, anticholinergic and antihistaminic side effects.
- Lower incidence of EPS and NMS
- Lethal in overdose due to QT prolongation and the potential for heart block and ventricular tachycardia.
- Rare risk of agranulocytosis and slightly higher risk of seizures than high potency antipsychotics



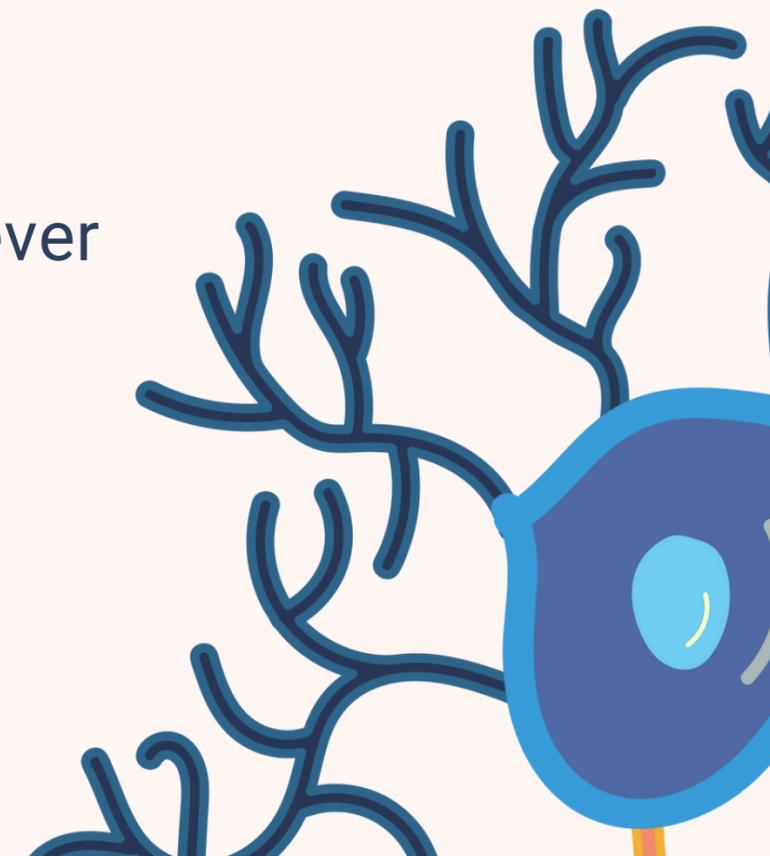


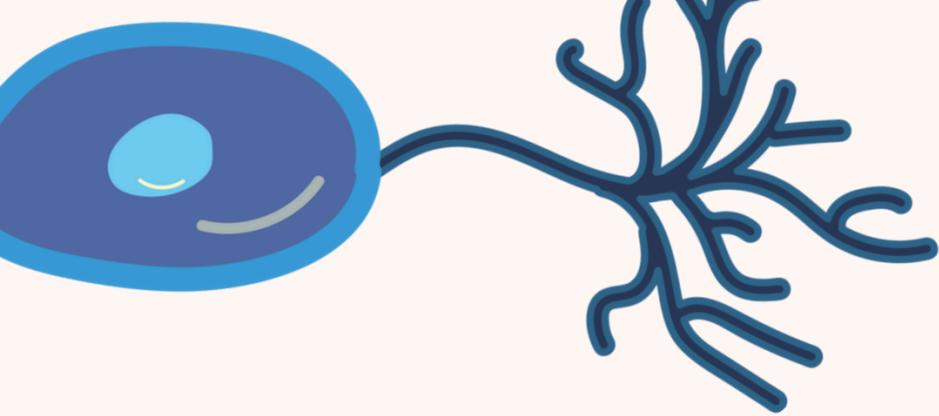
Low Potency Anti-psychotics



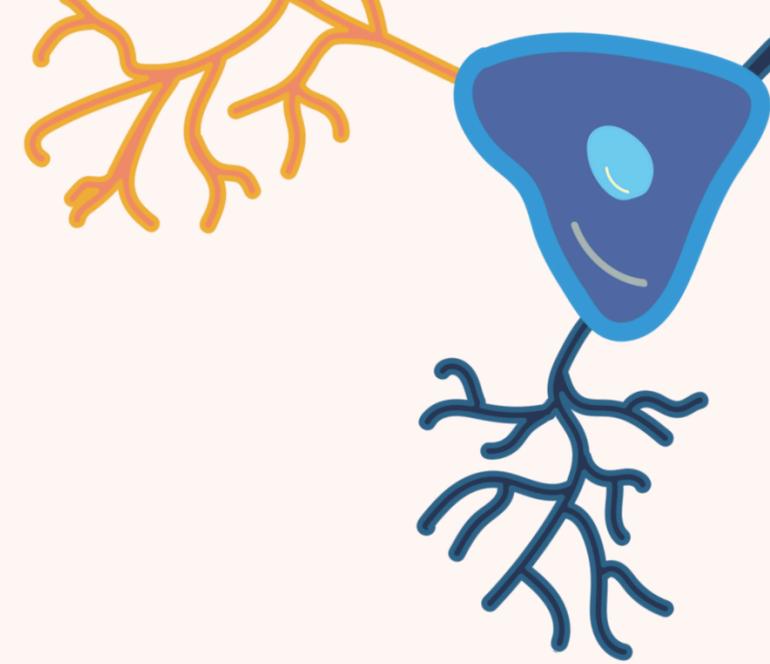
Chlorpromazine (Thorazine):-

- Use in psychiatry was first recognized by Henri Laborit (1952)
- Sedative
- Effect $\rightarrow \alpha_1 = 5HT > D2$
- Commonly causes Orthostatic hypotension
- Can cause blue-grey skin discoloration as well as corneal and lens deposits
- Can lead to photosensitivity
- For Schizophrenia and Schizoaffective Disorder
- Effective in treating agitations and psychotic symptoms that occur in severe manic episodes
- Also used in treating nausea/vomiting and intractable hiccups
- Comes in PO and IM formulations



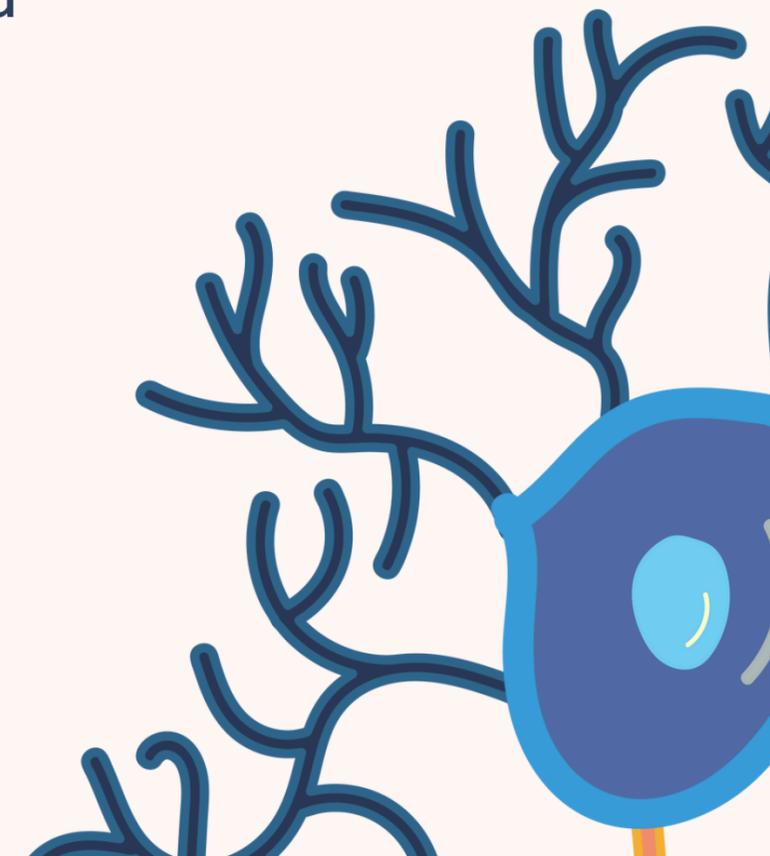


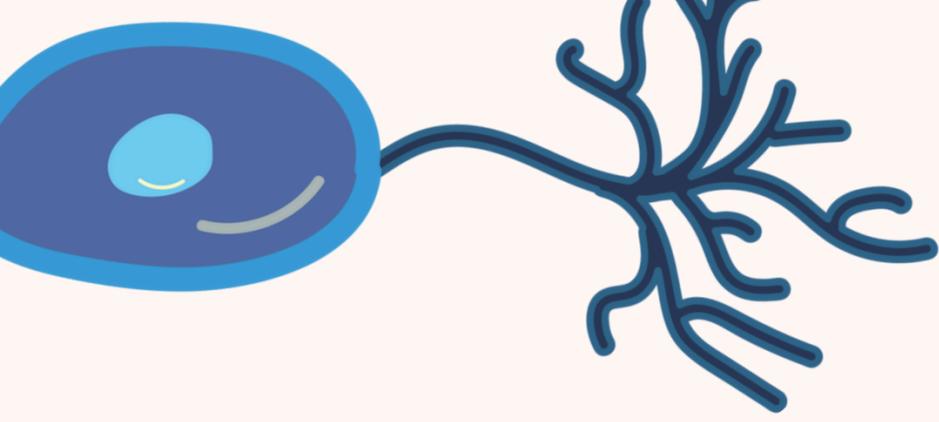
Low Potency Anti-psychotics



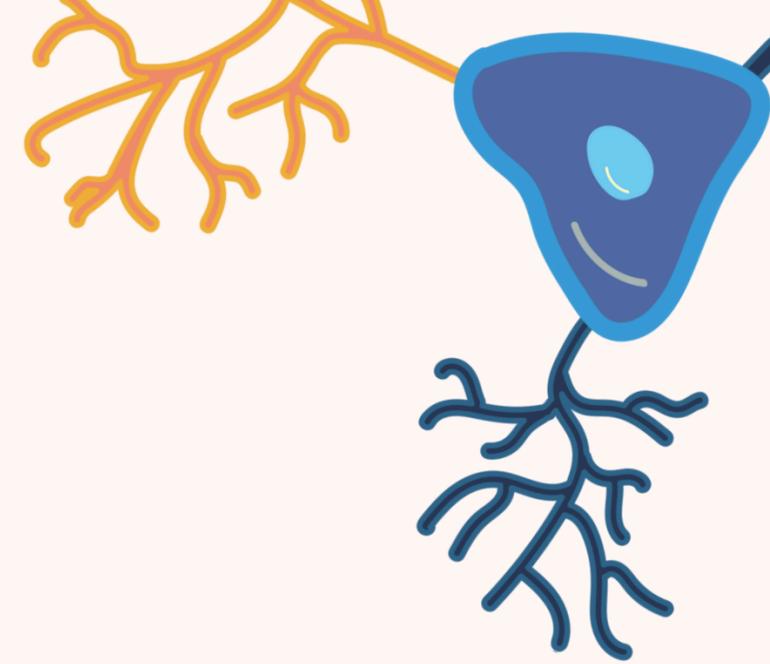
Thioridazine (Mellari):-

- Atypical Typical Anti-psychotic / Low-EPS typical
- For Schizophrenia and other psychotic D.
- Effect → like Chlorpromazine
- Very low risk of EPS, drug of choice for who cannot tolerate drug caused tremors and stiffness
- Pronounced sedation, sever orthostatic hypotension, significant anticholinergic side effects
- Torsades de pointes → sudden cardiac death
- Associated with retinitis pigmentosa





Mid Potency Anti-psychotics



Loxaoine (Loxitane):-

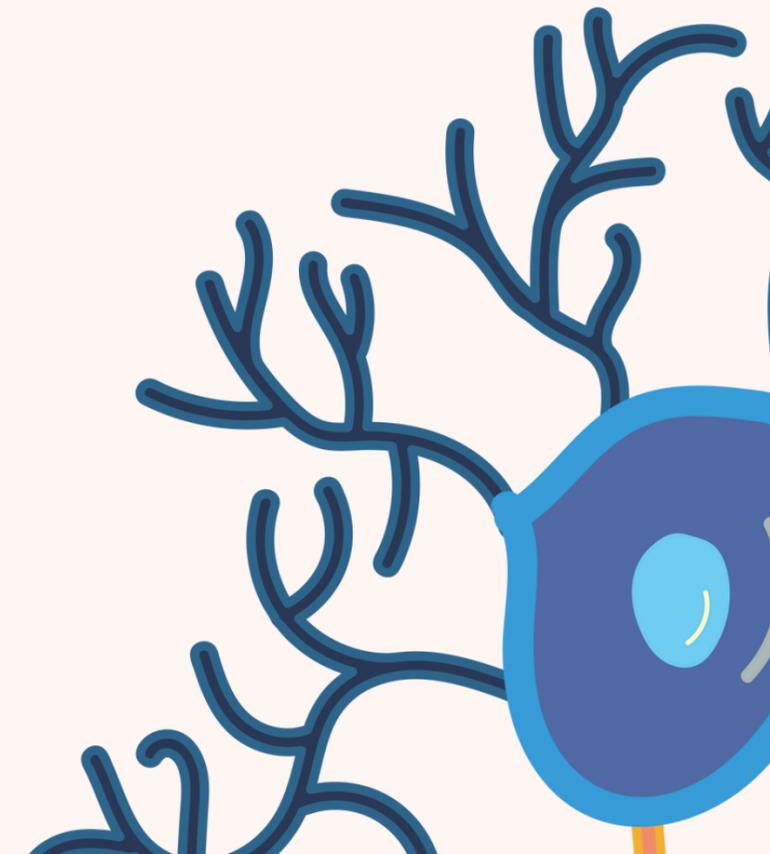
- High risk of seizures
- Metabolite acts as an antidepressant

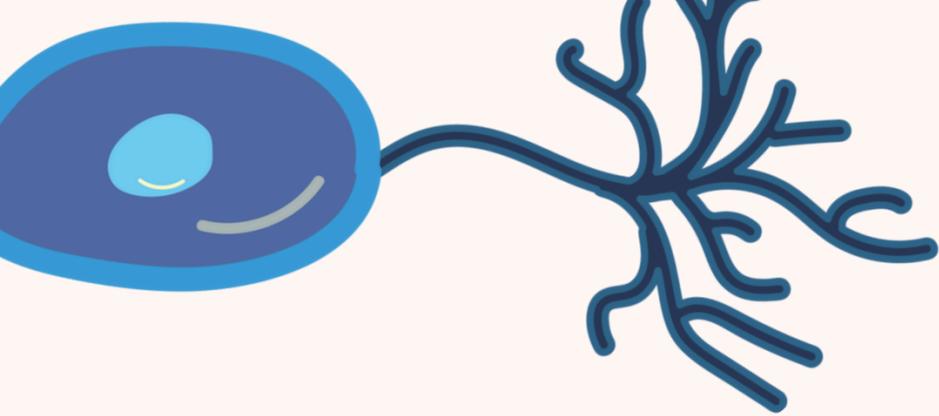
Thiothixene (Navane) :-

- Causes ocular pigment changes

Molindone (Moban)

Perphenazine (Trilafon)





High Potency Anti-psychotics



- Greater affinity for dopamine receptors; therefore, a relatively low dose is needed to achieve the effect
- Effect → D2 > α1 > 5HT > H1
- Less sedation, orthostatic hypotension, Anticholinergic effects
- Greater risk for EPS and TD (likely)

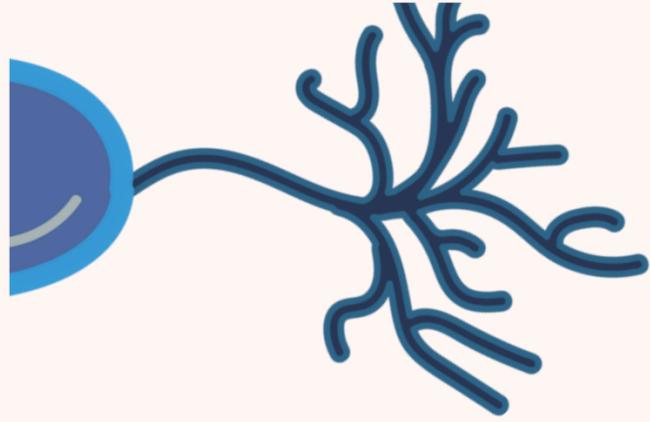
Haloperidol (Haldol):- Given PO/IM/IV (available long acting)

Fluphenazine (Prolixine):- Given PO/IM (available long acting)

Trifluoperazine (Stelazine):- Approved for nonpsychotic anxiety

Pimozide (Orap):- Associated with QT prolongation and ventricular tachycardia

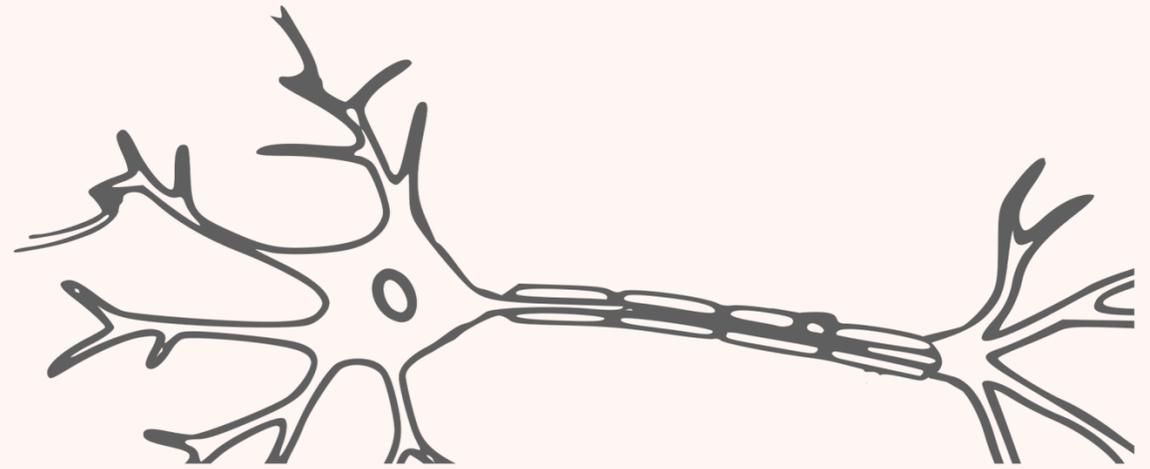
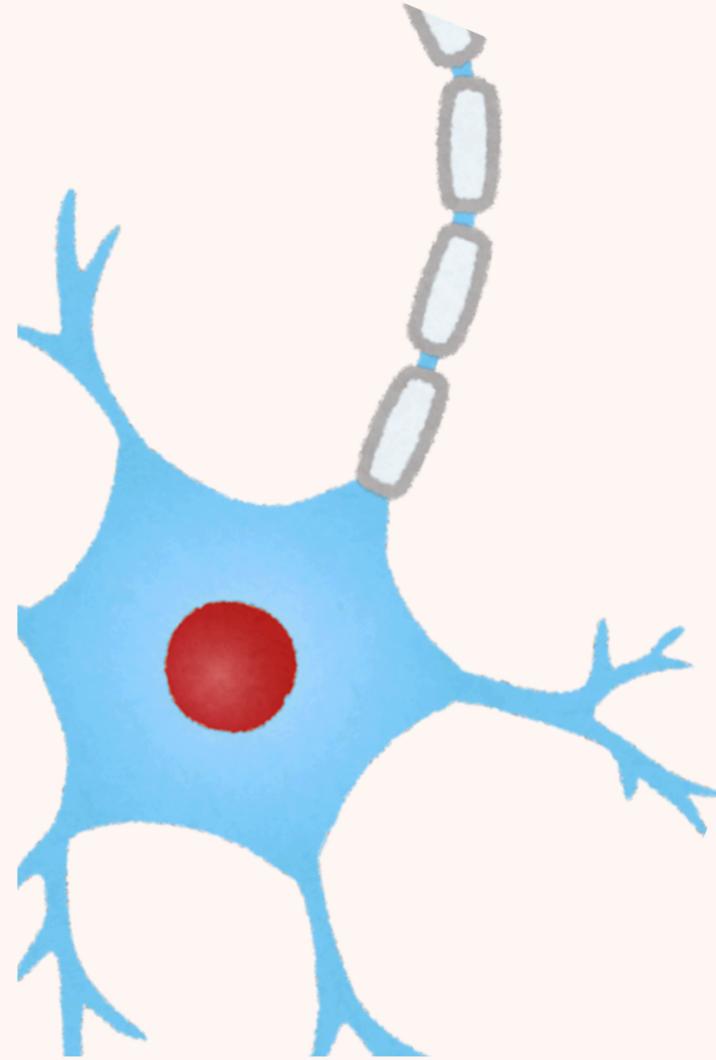




Pyramidal vs. Extrapyramidal

Pyramidal System: Includes: Corticospinal tract Pathway:
Runs through the pyramids of the medulla Function:
Controls voluntary movements Damage leads to: Weakness
or paralysis

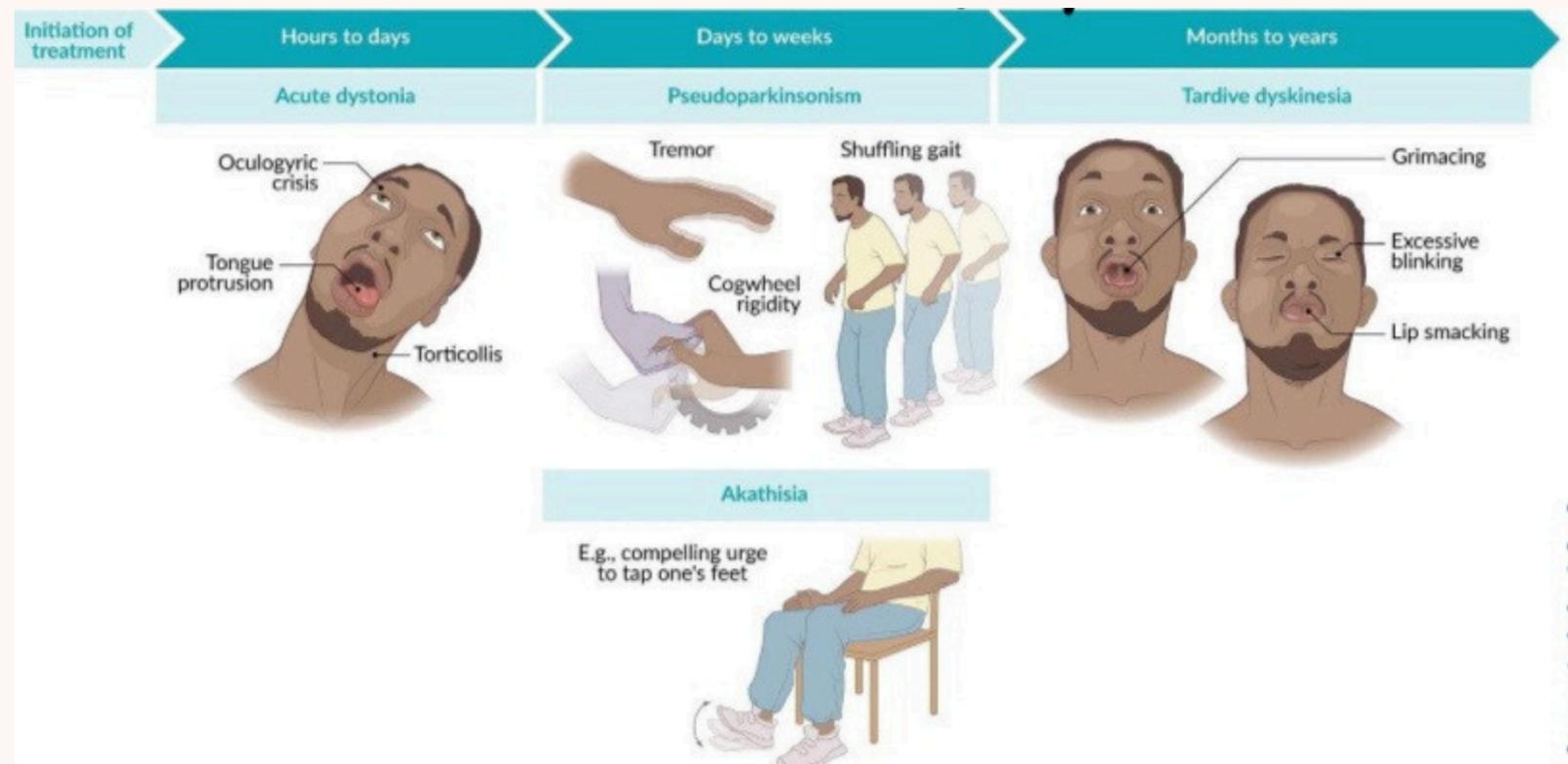
Extrapyramidal System: Includes: Basal ganglia and associated
tracts Function: Coordinates involuntary movements, posture,
and muscle tone Damage leads to: Movement disorders(e.g.
dystonia, tremors, rigidity)



Side effects ass. with typical antipsychotic drugs

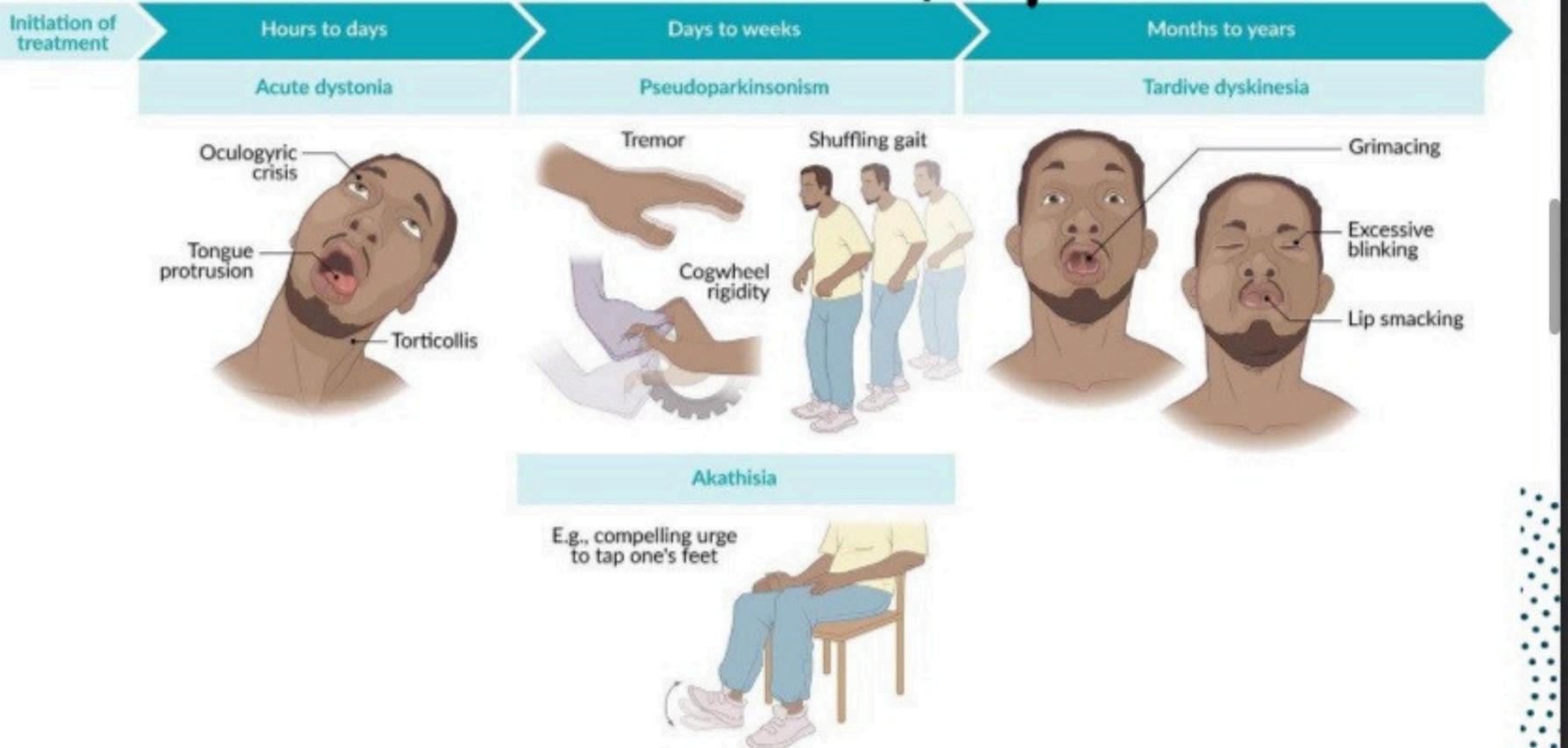
1- Antidopaminergic effects:

- EPS: - **Dystonia**—Sustained painful contraction of muscles of neck (torticollis), tongue, eyes (oculogyric crisis). It can be life threatening if it involves the airway or diaphragm. Treat with benztropine (Cogentin) or diphenhydramine (Benadryl), or lower the dose if appropriate.



1- Antidopaminergic effects:

- EPS: - **Parkinsonism**—Bradykinesia, mask-like face, cogwheel rigidity, pill-rolling tremor. Treat with **benztropine** (Cogentin) or lower dose if appropriate.

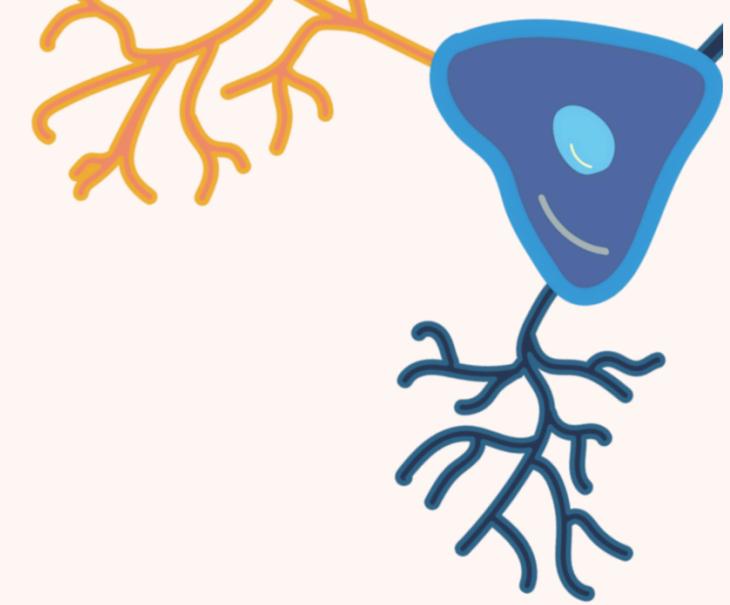
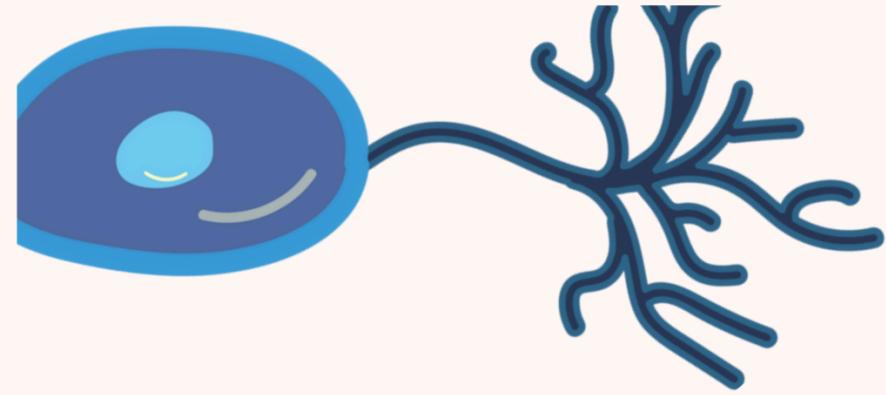


1- Antidopaminergic effects:

- EPS: - **Akathisia**—Subjective anxiety and restlessness, objective fidgetiness. Patients may report a sensation of inability to sit still. Best treated with dose reduction (if appropriate), **b-blockers**, or **benzodiazepines**. -



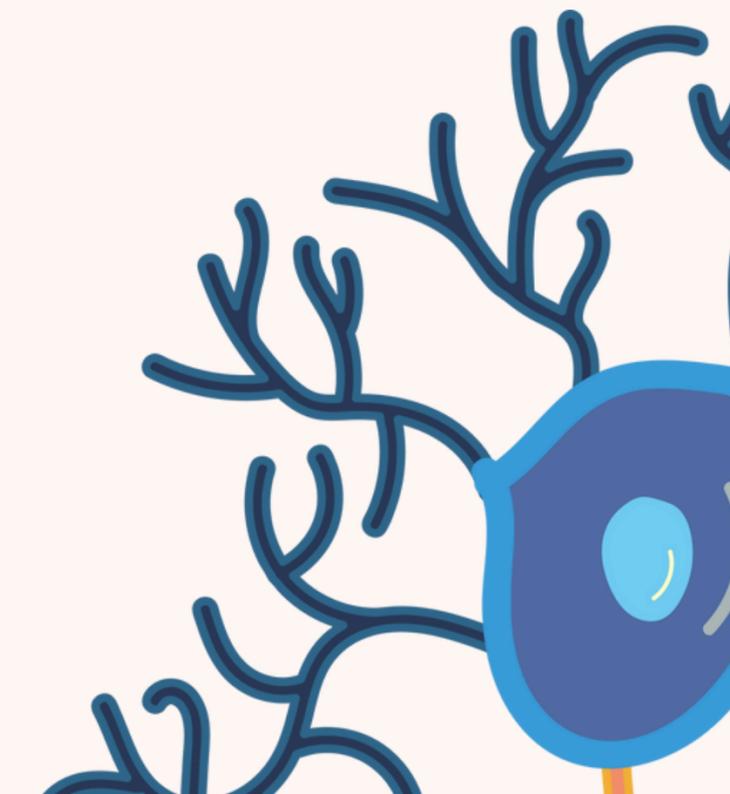
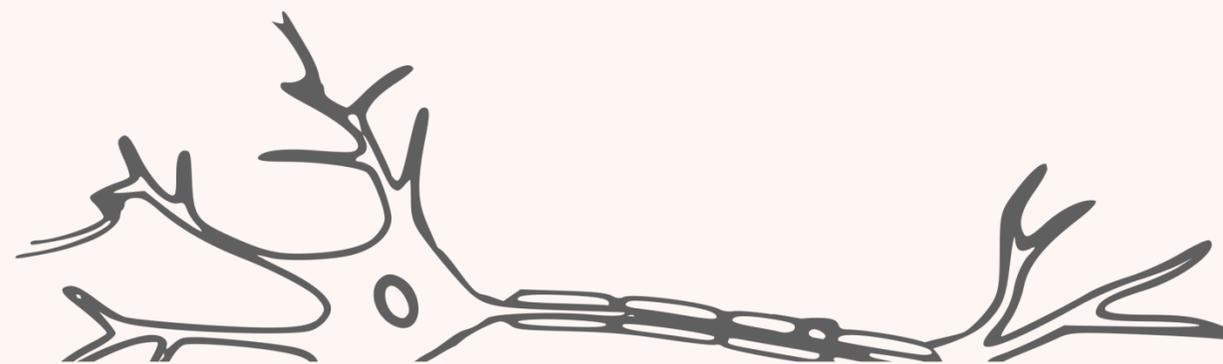
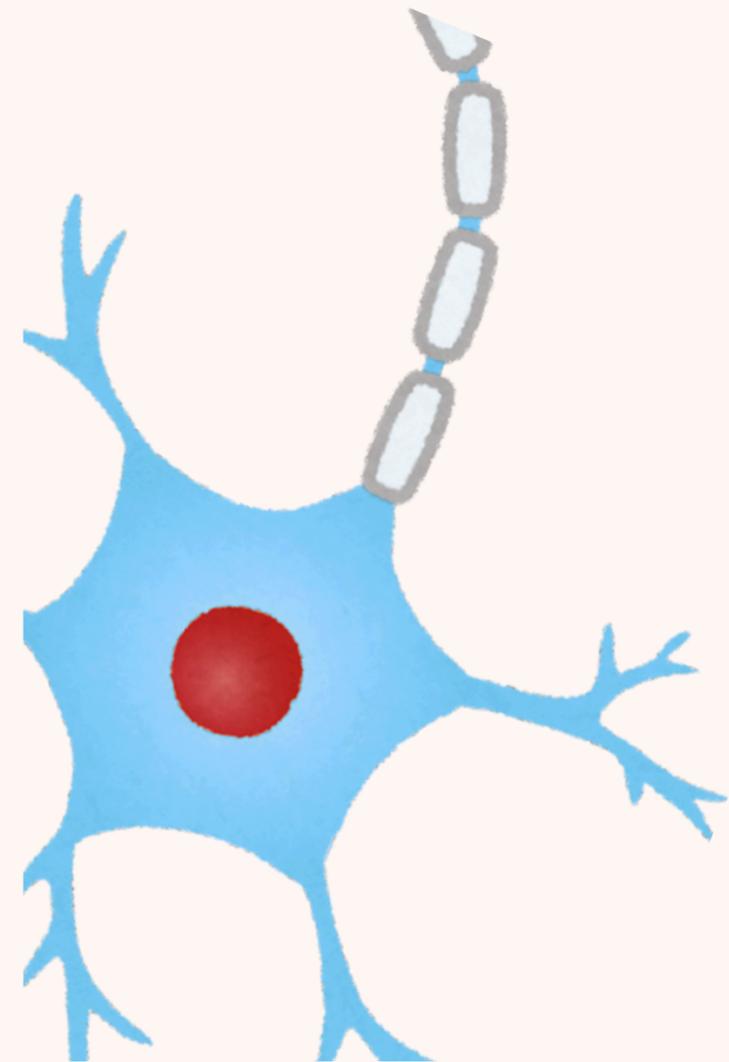
- **Hyperprolactinemia**— Leads to decreased libido, galactorrhea, gynecomastia, impotentes, amenorrhea.



2- Anti-HAM effects:

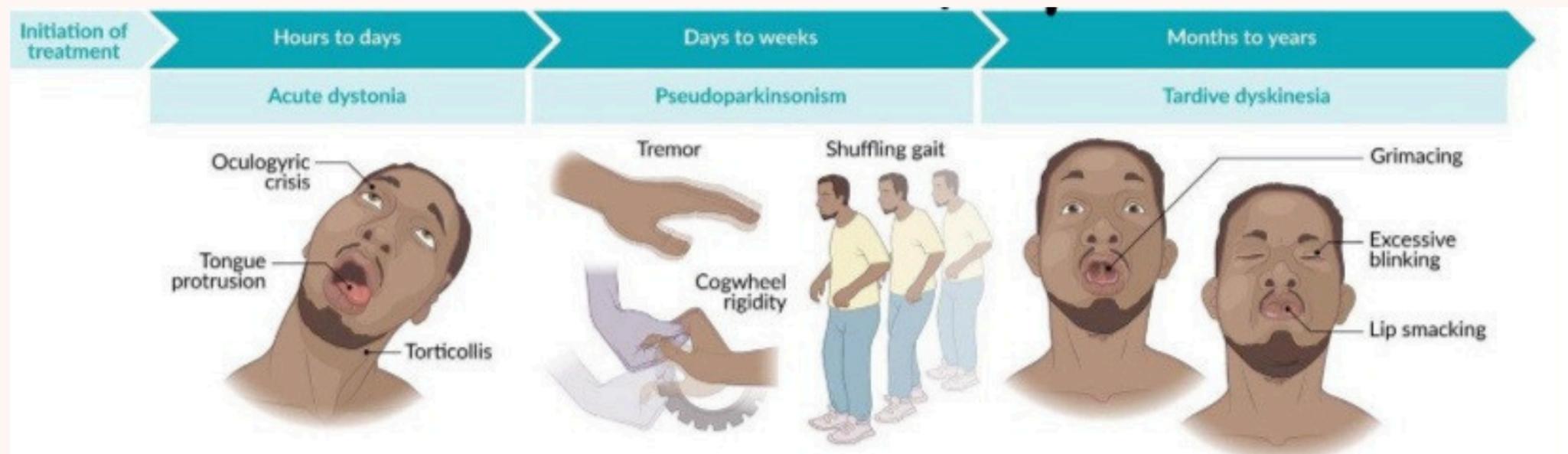
Caused by actions on Histaminic, Adrenergic, and Muscarinic receptors:

- **Antihistaminic**—Results in sedation, weight gain.
- **Anti- α_1 adrenergic**—Results in orthostatic hypotension, cardiac abnormalities, and sexual dysfunction.
- **Antimuscarinic**—Anticholinergic effects, resulting in dry mouth, tachycardia, urinary retention, blurry vision, constipation, and precipitation of narrow-angle glaucoma.



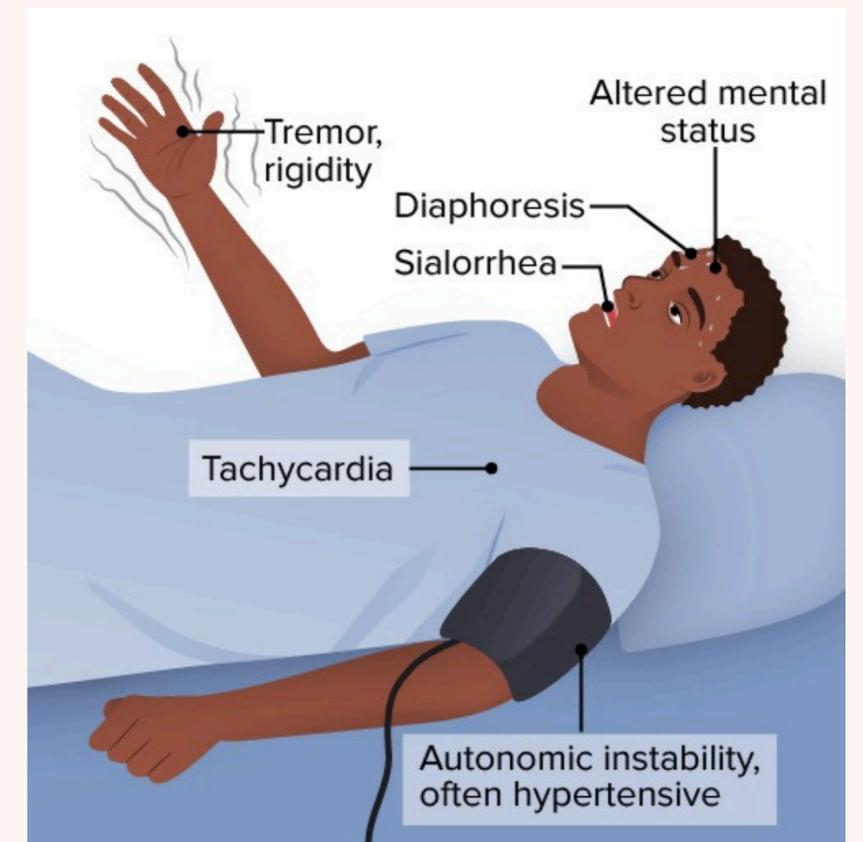
3- Tardive dyskinesia:

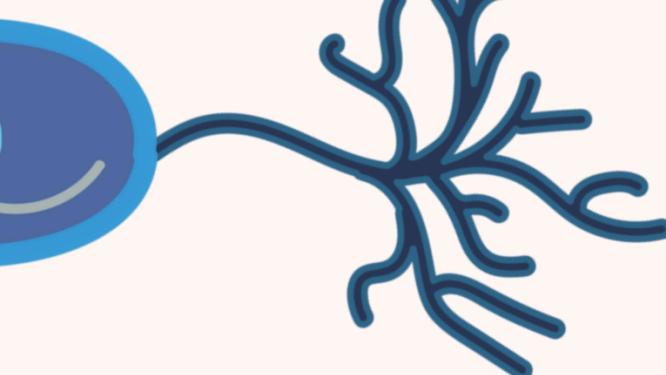
- Choreoathetoid (writhing, irregular) movements of mouth and tongue (or other body parts) that may occur in patients who have used antipsychotics for more than 6 months.
- **Older age** is a risk factor.
- **Women and patients with affective disorders** may be at an increased risk.
- Although up to 50% of cases will remit (without further antipsychotic use), most cases are permanent.
- Treatment involves discontinuation of current antipsychotic if clinically possible and changing to a medication with less potential to cause TD.



4- neuroleptic malignant syndrome

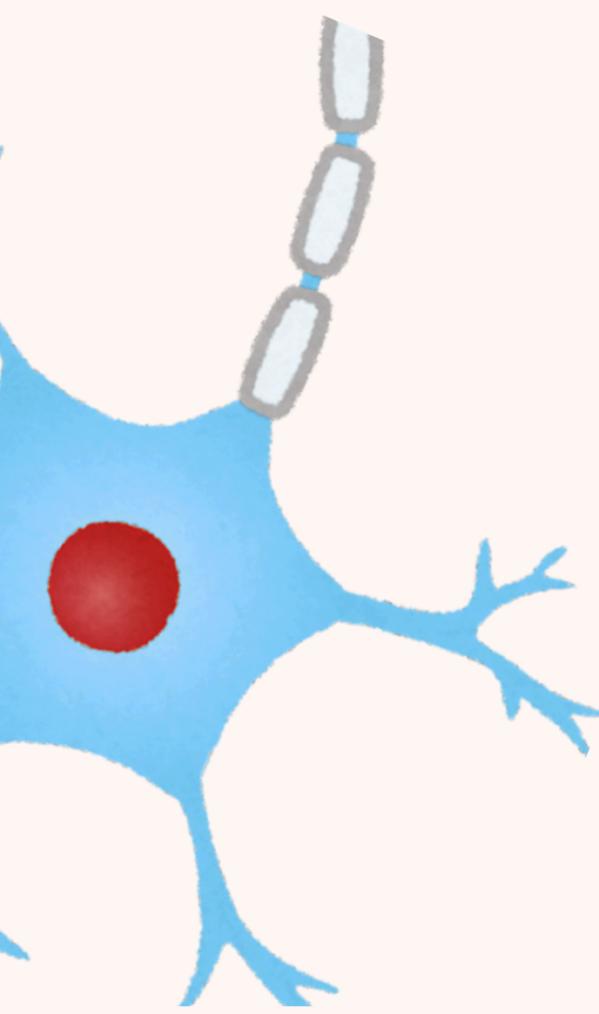
- Less common side effects include neuroleptic malignant syndrome (NMS):
- **Though uncommon, occurs more often in young males early in treatment with high-potency typical antipsychotics.**
- **It is a medical emergency and has up to a 20% mortality rate if left untreated.**
- **It is characterized by FALTERED:**
 - **Fever** (most common presenting symptom).
 - **Autonomic instability** (tachycardia, labile hypertension, diaphoresis)
 - **Leukocytosis.**
 - **Tremor.**
 - **Elevated CPK.**
 - **Rigidity** (lead pipe rigidity is considered almost universal)
 - **Excessive sweating** (diaphoresis).
 - **Delirium** (mental status changes).





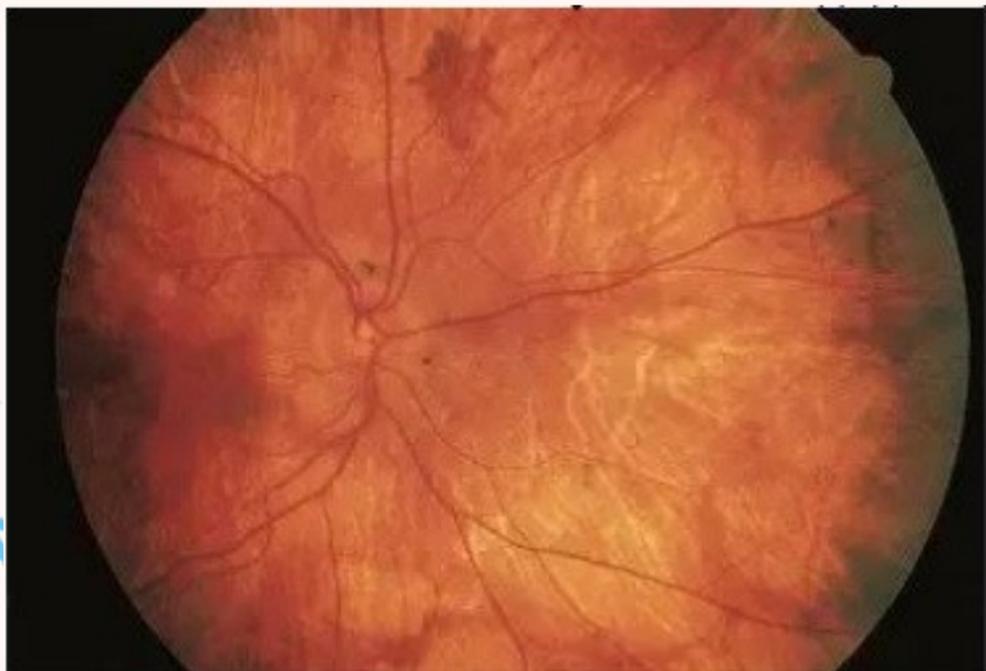
NMS :

Treatment involves discontinuation of current medications and administration of supportive medical care (hydration, cooling, etc.).

- **Sodium dantrolene, bromocriptine, and amantadine** may be used but have their own side effects and unclear efficacy. ECT can also be effective.
 - This is not an allergic reaction.
 - Patient is not prevented from restarting the same antipsychotic at a later time, but will have an increased risk for another episode of neuroleptic malignant syndrome.
- 

Side effects...

- 5- Elevated liver enzymes, jaundice (cholestatic)
- 6- Ophthalmologic problems (irreversible retinal pigmentation with high doses of **thioridazine**, deposits in lens and cornea with **chlorpromazine**).

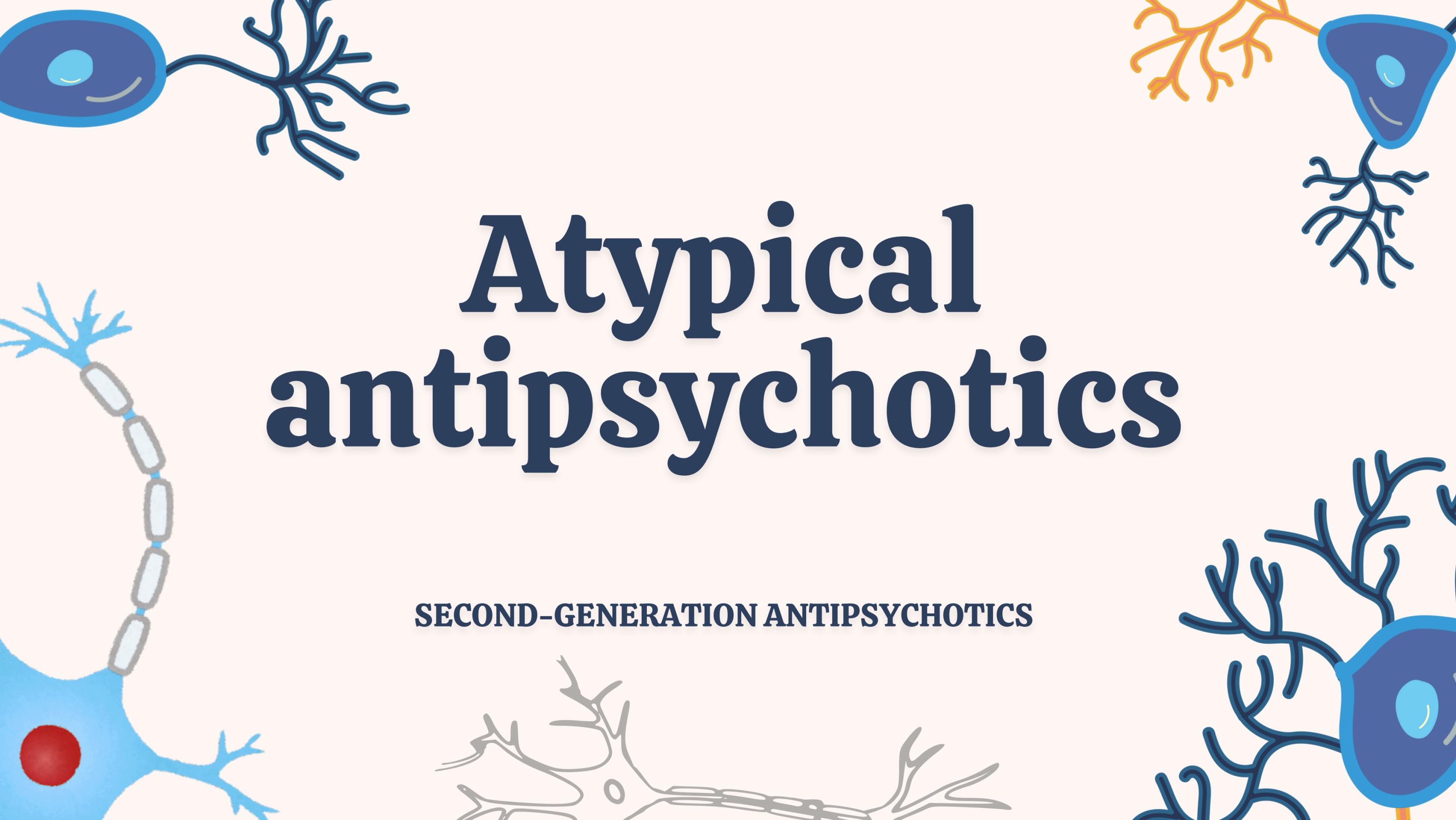


Side effects ...

7- Dermatologic problems, including rashes and photosensitivity (blue-gray skin discoloration with chlorpromazine).



8- Seizures: All antipsychotics lower the seizure threshold, although low-potency antipsychotics are more likely.

The slide features four stylized neuron illustrations in the corners. Top-left: a blue neuron with a central nucleus and branching dendrites. Top-right: a blue neuron with a central nucleus and branching dendrites, with orange dendrites extending upwards. Bottom-left: a blue neuron with a central nucleus, a red nucleus, and a long, segmented axon extending upwards. Bottom-right: a blue neuron with a central nucleus and branching dendrites. Center: The title 'Atypical antipsychotics' is written in a large, bold, dark blue serif font. Below the title, the text 'SECOND-GENERATION ANTIPSYCHOTICS' is written in a smaller, bold, dark blue sans-serif font.

Atypical antipsychotics

SECOND-GENERATION ANTIPSYCHOTICS

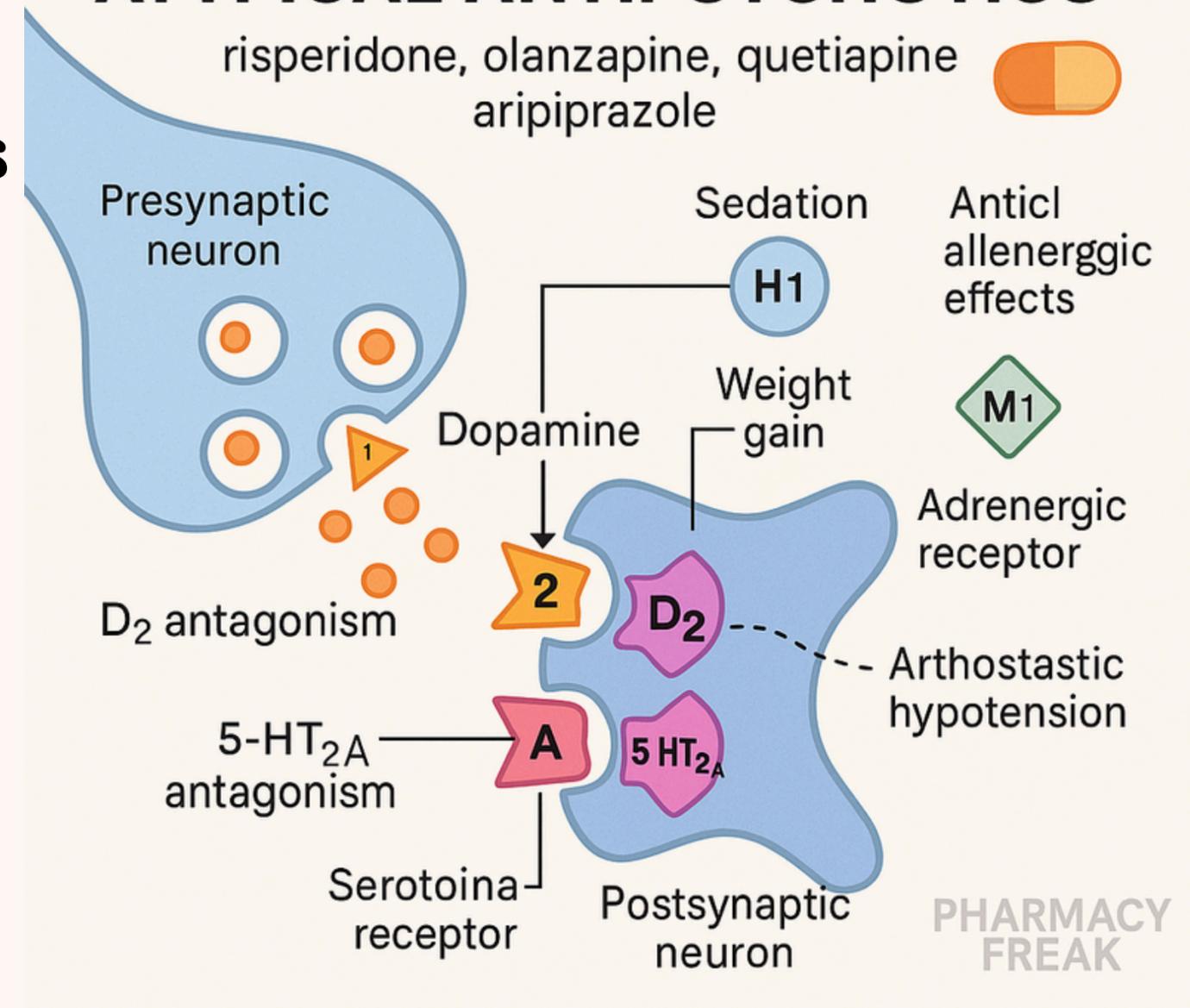
Atypical antipsychotics block both dopamine and serotonin receptors and are associated with different side effects than typical antipsychotics.

■ **In particular, they are less likely to cause EPS, TD, or neuroleptic malignant syndrome.**

■ **They may be more effective than typical antipsychotics in treating negative symptoms of schizophrenia.**

MECHANISM OF ACTION OF ATYPICAL ANTIPSYCHOTICS

risperidone, olanzapine, quetiapine
aripiprazole



Serotonin and dopamine pathways

Pathway	Effect of D2 Blockade	Clinical Manifestation (Dopamine)	Effect of 5-HT _{2A} Blockade	Clinical Manifestation (Serotonin)
Mesolimbic	↓ Dopamine	↓ Positive symptoms (hallucinations, delusions)	Minor effect	Maintains control of positive symptoms
Mesocortical	↓ Dopamine	May worsen negative & cognitive symptoms	↑ Dopamine in cortex	Improves negative & cognitive symptoms
Nigrostriatal	↓ Dopamine	EPS (parkinsonism, dystonia, akathisia)	↑ Dopamine release	↓ EPS
Tuberoinfundibular	↓ Dopamine	↑ Prolactin → galactorrhea, amenorrhea, gynecomastia	Reduces serotonin inhibition on dopamine	↓ Prolactin levels
Limbic & Hypothalamic regions	—	—	Alters appetite, arousal regulation	↑ Appetite, weight gain, sedation

Atypical antipsychotics

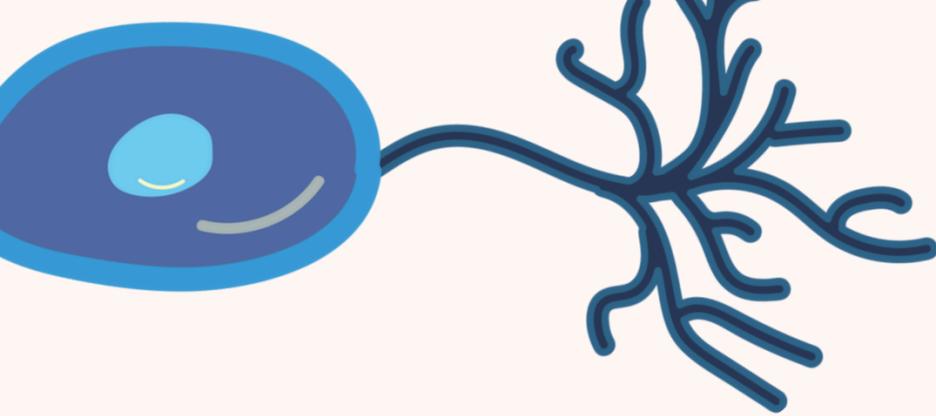
Drug	Key Features / Indications	Side Effects	Special Notes
Clozapine (Clozaril)	<ul style="list-style-type: none">• Most effective antipsychotic; used in treatment-refractory schizophrenia.• Only antipsychotic proven to reduce suicide risk.• Less likely to cause tardive dyskinesia (TD).	<ul style="list-style-type: none">• Anticholinergic effects: tachycardia, constipation, hypersalivation.• 1% risk of agranulocytosis.• 4% risk of seizures.• Small risk of myocarditis.	<ul style="list-style-type: none">• Stop if ANC <1500/μL.• ANC monitoring: weekly \times 6 mo \rightarrow biweekly \times 6 mo \rightarrow monthly.• More anticholinergic than other atypicals or high-potency typicals.

Atypical antipsychotics

Drug	Key Features / Indications	Side Effects	Special Notes
Risperidone (Risperdal)	<ul style="list-style-type: none">• Effective atypical antipsychotic.	<ul style="list-style-type: none">• ↑ Prolactin.• Orthostatic hypotension.• Reflex tachycardia.	<ul style="list-style-type: none">• Long-acting injectable (LAI) form: Risperdal Consta.
Quetiapine (Seroquel)	<ul style="list-style-type: none">• Low risk of EPS.• Often used when sedation is desired.	<ul style="list-style-type: none">• Sedation.• Orthostatic hypotension.• Weight gain.	<ul style="list-style-type: none">• Preferred for Parkinson's or movement disorder patients due to low EPS risk.
Olanzapine (Zyprexa)	<ul style="list-style-type: none">• Broad efficacy; available in multiple forms.	<ul style="list-style-type: none">• Significant weight gain.• Sedation.• Dyslipidemia.	<ul style="list-style-type: none">• Available as PO, IM, and LAI formulations.

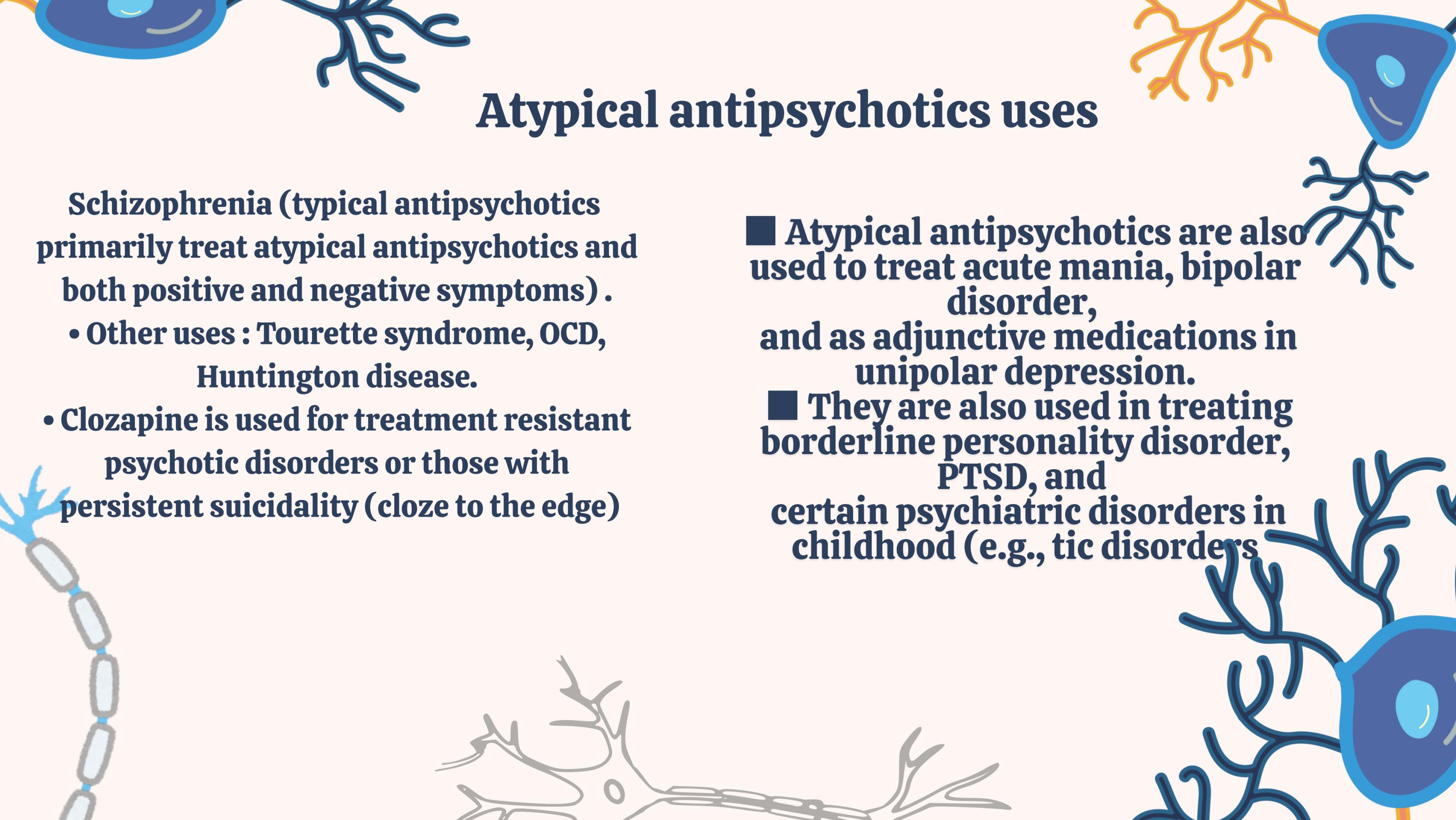
Atypical antipsychotics

Drug	Key Features / Indications	Side Effects	Special Notes
Ziprasidone (Geodon)	<ul style="list-style-type: none">• Less weight gain than others.	<ul style="list-style-type: none">• QTc prolongation.	<ul style="list-style-type: none">• Must be taken with food (≥ 300 calories); absorption \downarrow 50% without it.• Available as PO and IM forms.
Aripiprazole (Abilify)	<ul style="list-style-type: none">• Partial D₂ agonist (unique mechanism).	<ul style="list-style-type: none">• Akathisia (activating).• Less sedating.• Less weight gain.	<ul style="list-style-type: none">• Available as PO, IM, and LAI forms.



Newer (more expensive) antipsychotics:

Drug Name (Brand)	Key Features / Notes	Special Form / Use
Paliperidone (Invega)	- Active metabolite of risperidone.	- Long-acting injectables: • Invega Sustenna → monthly • Invega Trinza → every 3 months
Asenapine (Saphris)	- Orally dissolving (sublingual) tablet.	- Useful for patients who have difficulty swallowing pills.
lloperidone (Fanapt)	- Similar to risperidone but newer and more expensive.	- No special administration form.
Lurasidone (Latuda)	- Must be taken with food for proper absorption.	- Also used in bipolar depression.



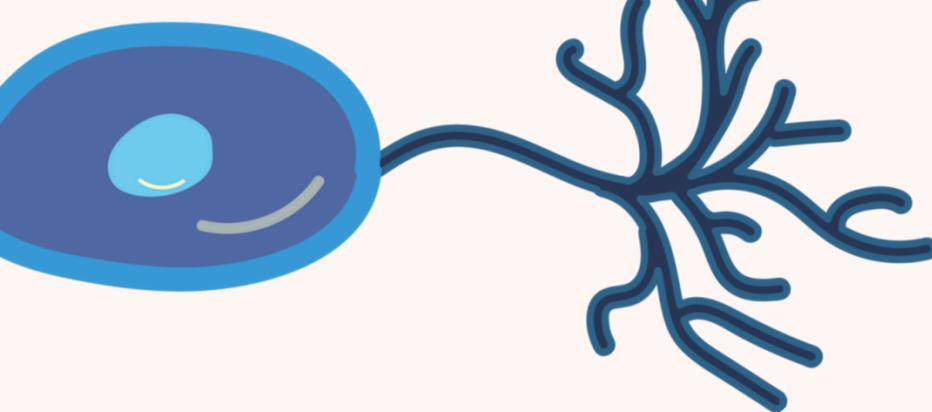
Atypical antipsychotics uses

Schizophrenia (typical antipsychotics primarily treat atypical antipsychotics and both positive and negative symptoms) .

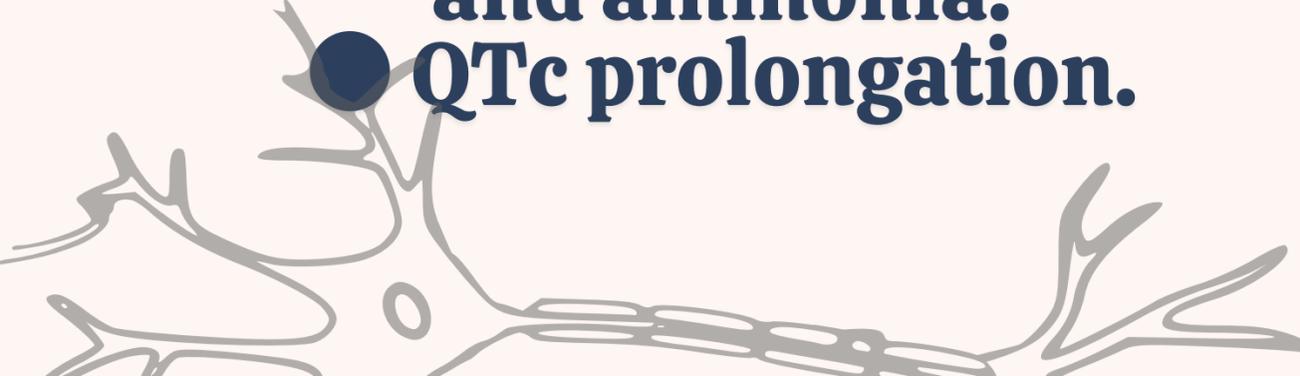
- **Other uses : Tourette syndrome, OCD, Huntington disease.**
- **Clozapine is used for treatment resistant psychotic disorders or those with persistent suicidality (cloze to the edge)**

■ **Atypical antipsychotics are also used to treat acute mania, bipolar disorder, and as adjunctive medications in unipolar depression.**

■ **They are also used in treating borderline personality disorder, PTSD, and certain psychiatric disorders in childhood (e.g., tic disorders)**



■ Side Effects

- **Metabolic syndrome.**
 - **This must be monitored with baseline weight, waist circumference (measured at iliac crest), BP, HbA1c, and fasting lipids.**
 - **Weight gain: Metformin can be used to reduce or prevent.**
 - **Hyperlipidemia.**
 - **Hyperglycemia—Rarely, diabetic ketoacidosis has been reported.**
 - **Some anti-HAM effects (antihistaminic, antiadrenergic, and antimuscarinic).**
 - **Elevated liver function tests (LFTs)—Monitor yearly for elevation in LFTs and ammonia.**
 - **QTc prolongation.**
- 
- 
- 

Atypical antipsychotics



WARDSTIP

Thirty percent of patients with treatment-resistant psychosis will respond to clozapine.



WARDSTIP

Patients on clozapine must have weekly blood draws for the first 6 months to check WBC and absolute neutrophil counts because of the risk of agranulocytosis. With time, the frequency of blood draws decreases.



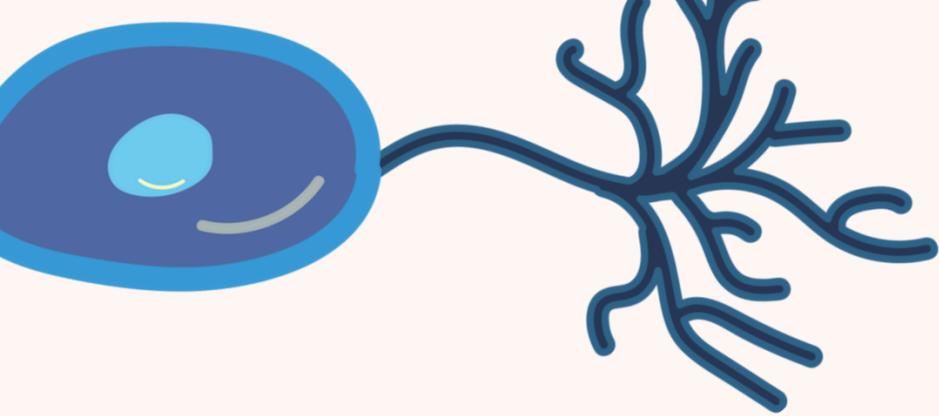
WARDSTIP

Quetiapine, olanzapine, aripiprazole, risperidone, asenapine, and ziprasidone have FDA approval for treatment of mania.

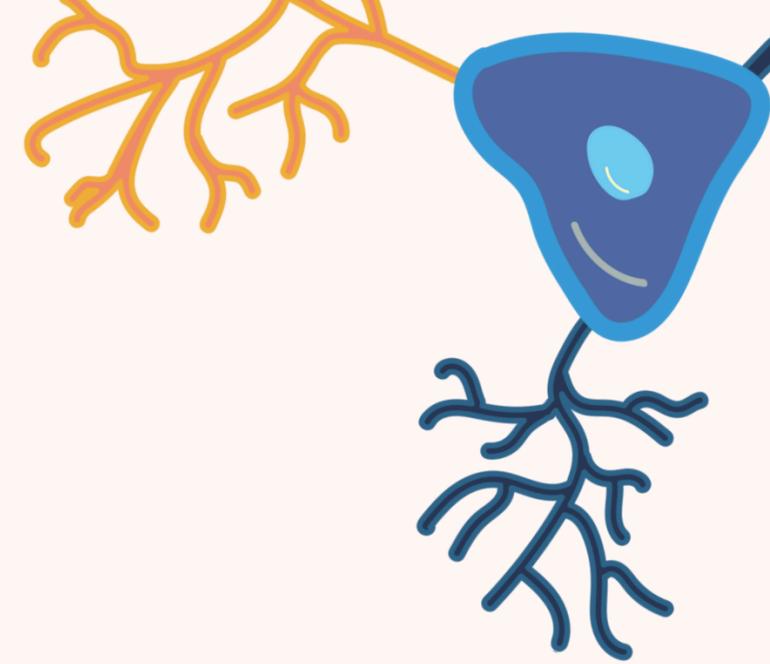


WARDSTIP

Antipsychotics may be used as adjuncts to mood stabilizers early in the course of a manic episode. Atypical antipsychotics are often prescribed as monotherapy in the acute or maintenance treatment of bipolar disorder.



WHO mhGAP 2023 Antipsychotic use in psychosis



First-line:- Haloperidol or Chlorpromazine

Strong recommendation; effective, Affordable, widely available

Second-line:- Atypical antipsychotics (e.g. risperidone, olanzapine) Use if Available/affordable or if first-line not tolerated

Third-line: Clozapine for treatment-resistant psychosis

Requires specialist oversight + lab monitoring

Use minimum effective dose to reduce side effects Low-dose haloperidol or CPZ may be used in pregnancy

Source: WHO mhGAP Guidelines 2023 <https://www.who.int/teams/mental-health-and-substance-use>



**Thank
You**

