

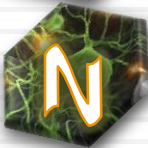


Lecture : 12

Drugs Used in Schizophrenia

Done by: Ibrahim Alqasir

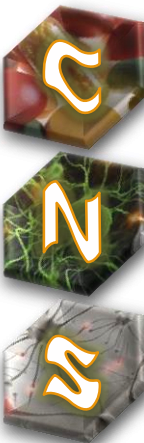
Revised by: Shahd Al-Awwad & Shatha Alshanqeeti





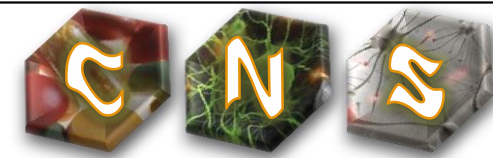
OBJECTIVES

- ❑ List the classification of antipsychotic drugs used in schizophrenia.
- ❑ Describe briefly the mechanism of antipsychotic action of these drugs.
- ❑ Describe the pharmacological actions of antipsychotic drugs.
- ❑ Relate between pharmacological actions & adverse effects of antipsychotic drugs.
- ❑ Enumerate the clinical uses of antipsychotic drugs.
- ❑ Describe the advantages of atypical antipsychotic drugs over typical drugs.
- ❑ **NOTE: this work is based on the objectives, for further understanding of the disease please study the psychiatry lecture first.**





PSYCHOSES



1- Affective Psychoses:

- a- Mania
- b- Depression
- c- Manic-depressive illness
- (bipolar affective disorder)

2- Schizophrenia

- Definition:
- - It is a thought disorder
- characterized by a divorcement from reality in the mind of the patient

- - It may involve hallucinations, delusions, intense suspicion, feelings of controlling by external forces (paranoia)

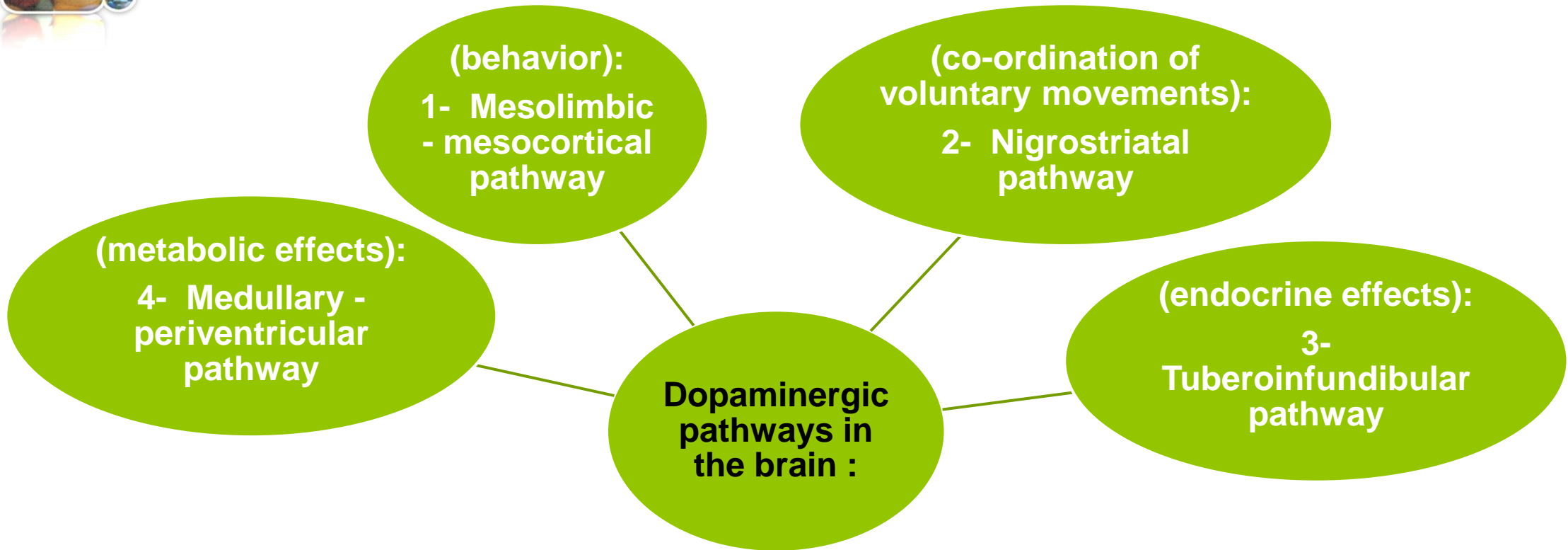
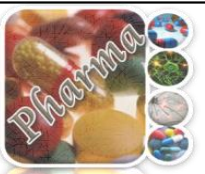
+ve Symptoms:

- Hallucinations
- Delusions
- Paranoia
- * Easy to detect

-ve Symptoms:

- Social withdrawal
- Anhedonia (absence of pleasure)
- Emotional blunting
- * hard to detect & treat ,& could happen in normal people.

Dopaminergic pathways in the brain :



There are 5 types : D1,D2,D3,D4,D5 * most of drugs act on D5

The action of the drug depend on the location of the Dopamenergic receptors” as mentioned the pathway above either its clinical use or side effect.



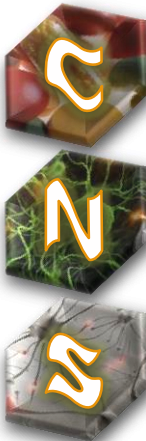


Antipsychotic drugs

Act (Block) on the following receptors :

- 1- Dopaminergic
 - 2- α_1 - adrenergic
 - 3- Muscarinic
 - 4- H_1 – histaminic
 - 5- Serotonergic (5-HT₂)
- * I expect side effect.

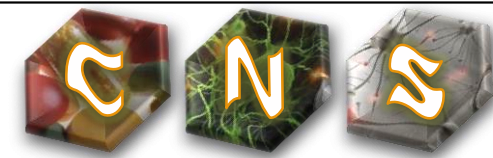
- What is Tardive dyskinesia: * see page 7
- Is the symptom that may occur after prolonged Therapy with neuroleptic (4 months – 1 year) it is characterized by rhythmic involuntary movement of tongue , lips , or jaw.
- Patient may also demonstrate puckering of the mouth or even chewing movement.





Classification of Anti psychotic drugs

According to chemical structure:

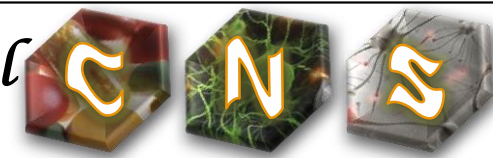


Typical	Atypical	Pharmacological actions
<ul style="list-style-type: none"> ➤ 1-Phenothiazine derivatives : <ul style="list-style-type: none"> ➤ Chlorpromazine ➤ Thioridazine 2- Butyrophenones: <ul style="list-style-type: none"> ➤ Haloperidol 3- Thioxanthene: <ul style="list-style-type: none"> ➤ Thiothixene 4- Dihydroindolones: <ul style="list-style-type: none"> Molindone 	<ul style="list-style-type: none"> 4- Dibenzodiazepines <ul style="list-style-type: none"> ➤ Clozapine 5- Benzisoxazoles <ul style="list-style-type: none"> ➤ Risperidone 6- Thienobenzodiazepines <ul style="list-style-type: none"> ➤ Olanzapine 7- Dibenzothiazepines <ul style="list-style-type: none"> ➤ Quetiapine 8- Benzisothiazoles <ul style="list-style-type: none"> ➤ Ziprasidone 	<p>On the CNS * in general , next slides will discuss in details</p> <p>To be considered Antipsychotic drugs they :</p> <ul style="list-style-type: none"> ➤ Produce emotional quieting and psychomotor slowing ➤ Decrease hallucinations, delusions and agitation. <p>They produce these two actions by bloking dopamine receptors in the mesolimbic system.</p>

Atypical drugs exert their antipsychotic action through blocking both serotonergic & dopaminergic receptors. * so, it's the preferable group " first line of treatment" because it treats the +ve & -ve symptoms .



Pharmacological actions for Both Typical & Atypical

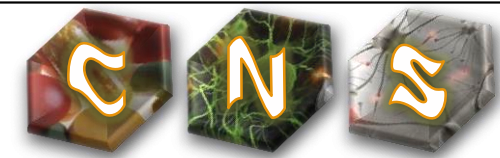


Actions On The CNS

<u>Extrapyramidal</u>	<u>Endocrine</u>	<u>Metabolic</u>	<u>Anti-emetic</u>
<p>Abnormal involuntary movements such as tremors, parkinsonism & tardive dyskinesia. See page 5*</p>	<p>Galactorrhea, amenorrhea, for the females, gynecomastia & impotence(males.)</p>	<p>Changes in eating behavior and weight gain</p>	<p>Effective against drug & disease- induced vomiting (not- motion sickness)</p>
<p><u>Mechanism:</u> Blockade of dopamine receptors in the nigrostriatum</p>	<p><u>Mechanism:</u>Blocking dopamine receptors in tuberoinfundibular area → Preventing the dopamine inhibition of prolactin release from pituitary → Hyperprolactinemia</p>	<p><u>Mechanism:</u> Blockade of dopamine receptors in the medullary – periventricular pathway</p>	<p><u>Mechanism:</u> Blockade of dopamine receptors in the CTZ of the medulla</p>



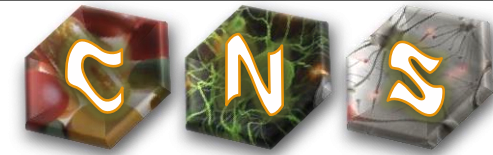
Pharmacological actions



On The ANS		Other			
<p><u>Anticholinergic:</u></p> <ul style="list-style-type: none"> - Blurred vision “cause of mydriasis” - Dry mouth - Urinary retention - Constipation 	<p><u>Antiadrenergic</u></p> <ul style="list-style-type: none"> - Postural hypotension - Impotence - Failure of ejaculation 	<p><u>Temperature regulation</u></p> <p>lowering of body temperature (Chlorpromazine) Good in operation & surgery .</p>	<p><u>ECG changes</u></p> <p>Prolongation of QT interval, Abnormal configuration of ST- segment & T wave.</p>	<p><u>Antihistaminic effect</u></p> <p>Sedation</p>	<p><u>Quinidine – like actions</u></p>
<p><u>Mechanism:</u> Blockade of muscarinic receptors</p>	<p><u>Mechanism:</u> Blockade of α-adrenergic receptors</p>	<p><u>Mechanism:</u> Heat loss as a result of vasodilation (α- blocking) Or due to central effect</p>	<p>...</p>	<p><u>Mechanism:</u> H1 receptor blockade</p>	



Therapeutic Uses



Psychiatric

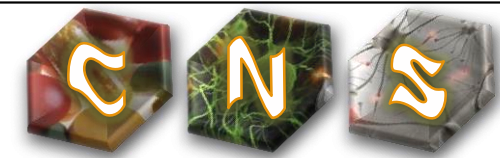
- ▶ **Schizophrenia** (**primary indication**)
- ▶ Acute mania
- ▶ Manic-depressive illness (bipolar affective disorder) during the manic phase

Non-Psychiatric

- 1- Drug and disease induced nausea and vomiting
 - **prochlorperazine and benzquinamide are only used as antiemetics**
 - **not used in motion sickness**
- 2- Pruritis
- 3- Preoperative sedation (rare use)



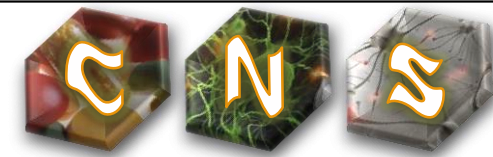
Adverse Effects



CNS	ANS	Endocrine	Miscellaneous Effects
<p>1- Sedation, drowsiness, fatigue (haloperidol , Risperidone)</p> <p>2- Extrapyramidal symptoms :</p> <p>Early occurring: Parkinson's syndrome</p> <p>late – occurring :</p> <p><u>1-Tardive Dyskinesia:</u> Involuntary movements of lips, jaws, face, limbs, and sometimes trunk</p> <p><u>2- Neuroleptic Malignant Syndrome :</u> leukocytosis, fever, muscle rigidity</p> <p>Right click, open hyperlink on the words above for more information, it's really interesting and important!</p>	<p>1- Anticholinergic Effects</p> <ul style="list-style-type: none"> - Blurred vision - Dry mouth - Urinary retention - Constipation <p>(Clozapine, Chlorpromazine)</p> <p>2- Antiadrenergic Effects</p> <ul style="list-style-type: none"> - Postural hypotension - Impotence - Failure of ejaculation <p>(Chlopromazine , Thioridazine)</p>	<ol style="list-style-type: none"> 1. Gynecomastia 2. Galactorrhoea 3. Amenorrhoea 	<ol style="list-style-type: none"> 1. Obstrucive jaundice 2. Granular deposits in cornea 3. Retinal deposits (thioridazine) 4. Weight gain 5. Agranulocytosis (Clozapine) 1-2% usually happen after 6-18 weeks Weekly WBC is mandatory 6. Seizures (Clozapine)



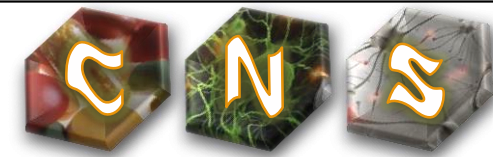
Pharmacokinetics



- ▶ **Incompletely absorbed**
- ▶ **Highly lipid soluble**
- ▶ **Highly bound to plasma proteins**
- ▶ **Undergo extensive first-pass hepatic metabolism.**
- ▶ **Excretion by the kidney**



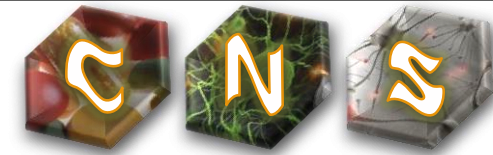
Atypical Antipsychotics



- ▶ **2nd Generation antipsychotics**
- ▶ **Are now considered to be first line treatments for schizophrenia**
- ▶ **Little or no extrapyramidal side effects**
- ▶ **Effective in treatment of resistant schizophrenia**
- ▶ **Are effective on both positive & negative symptoms.**
- ▶ **Block both dopaminergic & serotonergic receptors.**
- **Clinical uses:**
 - **Refractory cases of schizophrenia.**
 - **To reduce the risk of recurrent suicidal behavior in patients with schizophrenia**



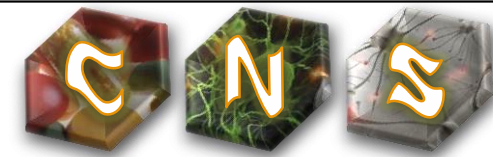
Atypical Antipsychotics



CLOZAPINE	RISPERIDONE	OLANZAPINE	QUETIAPINE	Ziprasidone
Blocks both D₄ & 5HT₂ receptors	Blocks D₂ & 5HT₂ receptors	Blocks D₁- D₄ & 5HT₂ receptors	Blocks D₁-D₂ & 5HT₂ receptors	- Blocks D₂ & 5HT₂ receptors
Side Effects: -Agranulocytosis -Seizures -Myocarditis - Excessive salivation (during sleep)	Side Effects: - Postural hypotension - QT prolongation - Weight gain Contraindicated in patients with long QT interval	Side Effects: - Weight gain - Sedation - Flatulence , increased salivation & thirst - Postural hypotension	Side Effects: - Sedation - Hypotension - Sluggishness - Dry mouth - Increased appetite (weight gain) - Abdominal pain - Constipation	Side Effects: - Drowsiness - Akathisia - Headache - Dizziness - Weight gain



Ziprasidone



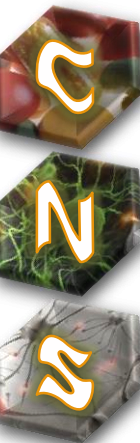
Contraindications:

- Should not be used **with any drug that prolongs the QT interval**
- Activity decreased by **carbamazepine** (inducer of CYP3A4)
- Activity increased by **ketoconazole** (inhibitor of CYP3A4)
- Elderly Patients **With Dementia-related Psychosis**



SUMMARY

- Drugs used in schizophrenia are classified according to chemical structures.
- **The advantages of atypical drugs include :**
- They block both dopaminergic & serotonergic drugs.
- They are effective in refractory cases of schizophrenia
- They produce few extrapyramidal effects





SUMMARY

- The pharmacological actions of antipsychotic drugs result from :
- Blocking dopamine receptors at different areas in the brain.
- Blocking muscarinic receptors
- Blocking α -adrenergic receptors
- Blocking H1 receptors
- Adverse effects on CNS are due to blocking dopamine receptors at areas other than mesolimbic area
- Blockade of H1, muscarinic & α - adrenergic receptors.

The main clinical use is in schizophrenia





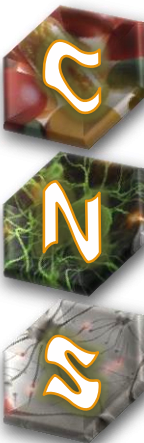
SUMMARY

Clozapine	Thiroidazone	Haloperidol	Zeprasideone
Agranulocytosis and seizures	Retinal deposits	Extrapyramidal side effects	Affected by CYT P _{34A} inducers and inhibitors + mortality in dementia-related psychosis in Iderly

- Drugs that prolong Q-T interval:
Risperidone, Ziprasidone

Drugs not used with Zeprasideone:

- Carbamazepine >> decreases effect
- Ketoconazole >> toxicity





QUESTIONS

- 1- The mechanism of Atypical Antipsychotics :
 - A) Block Dopamine Receptors
 - B) Block Serotonin Receptors
 - C) A&B

- 2- The mechanism of Ziprasidone :
 - A) Blocks D₁-D₂ & 5HT₂ receptors
 - B) Blocks D₂ & 5HT₂ receptors
 - C) Blocks D₁- D₄ & 5HT₂ receptors

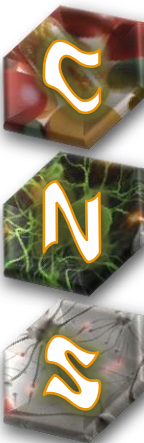
- 3- Excessive salivation during sleep is a side effect of:
 - A) CLOZAPINE
 - B) RISPERIDONE
 - C) Ziprasidone

Answers:

1- C

2- B

3- A

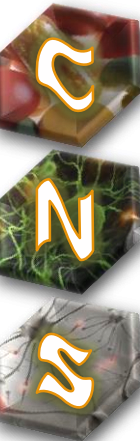




QUESTIONS

Questions from pharmacology book:

- ❑ What distinctive side effects does thioridazine cause?
Pigmentary retinopathy may cause cardiac arrhythmias & conduction block.
- ❑ What type of side effect is especially pronounced with haloperidol?
Extra pyramidal side effect .



THE END



Leaders

Abullah AL-Anazi & Tuqa Alkaff

E-Mail

pharmacologyteam1@gmail.com

