

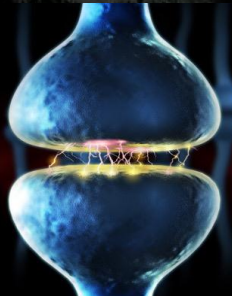
King Saud University
College of Medicine
2nd Year, 1st Block



L12- DRUGS USED IN SCHIZOPHRENIA



CNS Block

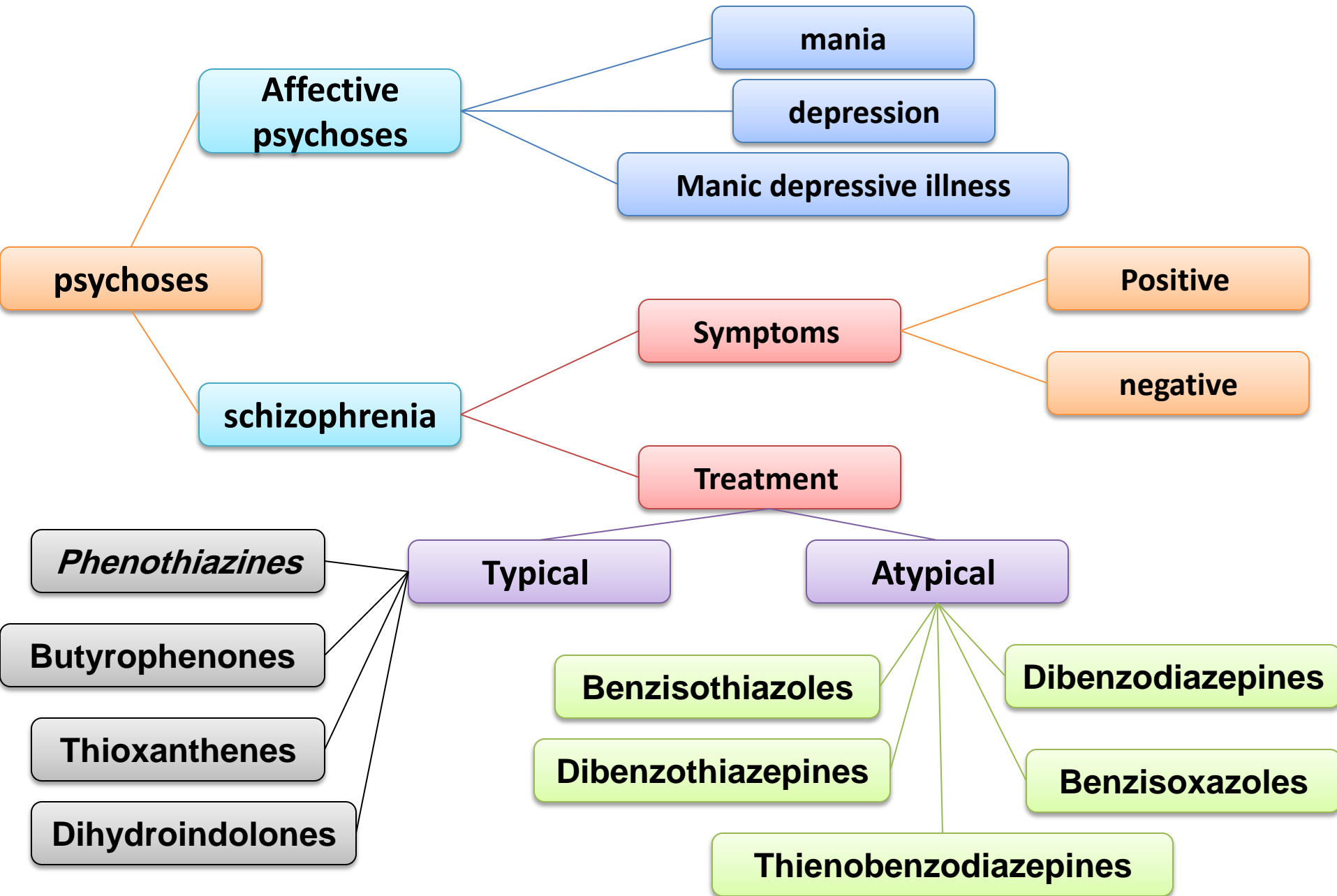




Objectives :

- 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.**

Mind Map



Psychosis

Affective Psychoses:

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

Dopamine system

-Dopaminergic pathways in the brain:

- 1- **Mesolimbic - mesocortical pathway:** responsible for behavior.
- 2- **Nigrostriatal pathway:** responsible for co-ordination of voluntary movements.
- 3- **Tuberoinfundibular pathway:** responsible for endocrine effects.
- 4- **Medullary - periventricular pathway:** responsible for metabolic effects.

-Dopamine receptors:

There are at least five subtypes of receptors:

D 1, D 2, D 3, D 4, D 5

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 persecution or control by external forces (paranoia).

positive symptoms:*1

- Hallucinations.
- Delusions.
- Paranoia.

negative symptoms:*2

- Social withdrawal
- Anhedonia (absence of pleasure)
- Emotional blunting

1***positive symptoms:** are psychotic behaviors not seen in healthy people.

2***negative symptoms:** are associated with disruptions to normal emotions and behaviors.

Classification of Antipsychotic drugs

According to chemical structure

Typical Antipsychotic Drugs:

1- Phenothiazine derivatives

- Chlorpromazine.
- Thioridazine.

2- Butyrophenones

- Haloperidol.

3- Thioxanthene

- Thiothixene.

Atypical Antipsychotic Drugs:

1- Dibenzodiazepines

- Clozapine.

2- Benzisoxazoles

- Risperidone.

3- Thienobenzodiazepines

- Olanzapine.

4- Dibenzothiazepines

- Quetiapine.

5- Benzisothiazoles

- Ziprasidone.

PHARMACOKINETICS

-Incompletely absorbed.

Highly bound to plasma proteins.

Undergo extensive first-pass hepatic metabolism .

Excretion by the kidney.

-Highly lipid soluble.

Pharmacological Actions

C.N.S

A.N.S

C.N.S

1- Antipsychotic effect:

- Produce emotional quieting and psychomotor slowing.
- Decrease hallucinations, delusions and agitation.

Mechanism:

- Blockade of dopamine receptors in the mesolimbic system.

-Atypical drugs exert their antipsychotic action through blocking serotonergic (5HT₂) & dopaminergic receptors.

2- Extrapyramidal Symptoms:

- Abnormal involuntary movements such as tremors, parkinsonism & tardive dyskinesia*.

Mechanism:

Blockade of dopamine receptors in the nigrostriatum.

3- Endocrine effects

- Galactorrhea, amenorrhea, gynecomastia* & impotence.

Mechanism:

Prevent dopamine inhibition of prolactin release from pituitary → Hyperprolactinemia.

4- Metabolic effects:

- Changes in eating behavior and weight gain.

Mechanism:

-Blockade of dopamine receptors in the medullary-periventricular pathway.

5- Anti-emetic effect:

- Effective against drug & disease-induced vomiting (not-motion sickness).

Mechanism:

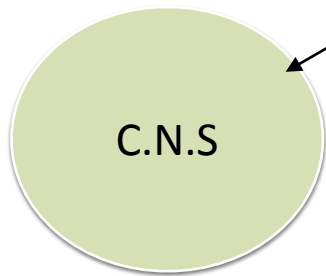
Blockade of dopamine receptors in the CTZ of the medulla.

*tardive dyskinesia: is a mostly irreversible neurological disorder of involuntary movements caused by long-term use of antipsychotic drugs.

*galactorrhea: is the secretion of breast milk in women who are not breastfeeding an infant.

*amenorrhea: The absence of menstrual periods. * gynecomastia: is excess growth of the adipose tissue in a male breast.

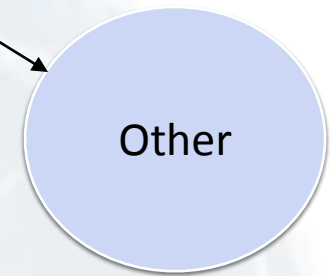
Pharmacological Actions



C.N.S.



A.N.S.



Other

1- Anticholinergic Effects:

- Blurred vision
- Dry mouth
- Urinary retention
- Constipation

Mechanism:

Blockade of muscarinic receptors.

2- Antiadrenergic Effects:

- Postural hypotension.
- Impotence.
- Failure of ejaculation.

Mechanism:

Blockade of α - adrenergic receptors.

Pharmacological Actions

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graph TD; A[Pharmacological Actions] --> B((C.N.S.)); A --> C((A.N.S.)); A --> D((Other));
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C.N.S

1- Temperature regulation:
-May cause lowering of body temperature.

Mechanism:

-Heat loss as a result of vasodilation (α - blocking) Or due to central effect.

2- ECG changes:

-Prolongation of QT interval
Abnormal configuration of ST- segment & T wave.

A.N.S

3- Antihistaminic effect:

-Sedation due to H1 receptor blockade.

4- Quinidine –like actions.

Other

Therapeutic action

PSYCHIATRIC

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

NON-PSYCHIATRIC

- Nausea and vomiting:
 - **prochlorperazine and benzquinamide are only used as antiemetics**
- Pruritus “severe itching of the skin”
- Preoperative sedation (rare)

Tardive Dyskinesia

it is a disorder of involuntary movements.

(choreoathetoid movements of lips, tongue, face, jaws, and limbs)

Choreoathetosis :

combination of chorea (irregular migrating contractions) and athetosis (twisting)

Neuroleptic Malignant Syndrome

Rare but life threatening.

Symptoms are muscle rigidity and high fever (clinically similar to anaesthetic malignant hyperthermia).

The stress leukocytosis and high fever associated with this syndrome may wrongly suggest an infection.

Adverse Effects

CNS

1- Sedation, drowsiness, fatigue : (with haloperidol , Risperidone)

2. Extrapyramidal symptoms (haloperidol):

Early in treatment with parkinson disease

Late in :

- a. Tardive Dyskinesia * (IN PERVIOUS SLIDE)
- b. Neuroleptic Malignant Syndrome ** (IN PERVIOUS SLIDE)

ANS

1- Anticholinergic Effects: (with Chlorpromazine , Clozapine)

Blurred vision, Dry mouth, Urinary retention, Constipation

2- Antiadrenergic Effects: (with Chlopromazine , Thioridazine)

Postural hypotension, Impotence, Failure of ejaculation

ENDOCRINE effects:

Others

- Gynecomastia
- Galactorrhoea
- Amenorrhoea

- Obstrucive jaundice
- Granular deposits in cornea
- Retinal deposits (thioridazine)
- Weight gain

- Agranulocytosis
(Clozapine) about 1-2%
Usually happen after 6-18 weeks
Weekly WBC is mandatory

- Seizures (Clozapine)

Atypical Antipsychotics

2ND Generation!

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

Drug	Mechanism of action	Adverse effects
Clozapine	Blocks both D ₄ & 5HT ₂ receptors	Agranulocytosis, Seizures , Myocarditis, Excessive salivation (during sleep)
Risperidone	Blocks D ₂ & 5HT ₂ receptors	- Postural hypotension, QT prolongation , Weight gain Contraindicated in patients with long QT interval
Olanzapine	Blocks D ₁ - D ₄ & 5HT ₂ receptors	Weight gain, Sedation , Flatulence, increased salivation & thirst, Postural hypotension
Quetiapine	Blocks D ₁ -D ₂ & 5HT ₂ receptors	Sedation, Hypotension, Sluggishness , Dry mouth, Increased appetite (weight gain), Abdominal pain, Constipation
Ziprasidone	Blocks D ₂ & 5HT ₂ receptors	Drowsiness , Akathisia “inability to sit”, Headache, Dizziness & Weight gain. *Drug interactions: -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). <u>WARNING: INCREASE MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS.</u>

summary

Drug	Adverse effects	Pharmacological actions	Therapeutic uses
CLOZAPINE Blocks both D ₄ & 5HT ₂ receptors	Agranulocytosis Seizures Myocarditis Excessive salivation (during sleep)	On cns : 1-anti-sychotic effects 2-extrapyramidal 3-endocrine effects 4-metabolic effects 5-anti-emetic effects	1-psychiatric use: -schizophrenia -mania -manic depressive illness
RISPERIDONE Blocks D ₂ & 5HT ₂ receptors	- Postural hypotension - QT prolongation - Weight gain Contraindicated in patients with long QT interval	On ans : 1-anti-cholinergic effects 2-anti-adrenergic effects	2-non-sychiatric use: -preoperative sedation (rare use) -nausea and vomiting (prochlorporazine and bezquinamide)
OLANZAPIN Blocks D ₁ - D ₄ & 5HT ₂ receptors	Weight gain Sedation Flatulence increased salivation & thirst Postural hypotension	Other actions: 1-tempreture regulation 2-ECG changes 3-anti-histamic effects 4-QUNIDINE like actions	3-pruritis
QUETIAPIN Blocks D ₁ -D ₂ & 5HT ₂ receptors	Sedation Hypotension Sluggishness Dry mouth Increased appetite (weight gain) Abdominal pain Constipation		
ZIPRASIDONE - Blocks D ₂ & 5HT ₂ receptors	- Drowsiness - Akathisia - Headache - Dizziness - Weight gain	WARNING : INCREASE MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA RELATED PSYCHOSIS.	

Quiz yourself

1-which one of the dopaminergic pathways responsible for endocrine effects:

- A-Nigrostriatal pathway.
- B-Medullary - periventricular pathway.
- C-Tuberoinfundibular pathway.
- D-Mesolimbic - mesocortical pathway.

2- which one of the following is positive symptom:

- A-Anhedonia.
- B-Social withdrawal.
- C-Emotional blunting.
- D-Paranoia.

3-which one of the following drugs is atypical:

- A- Thiothixene.
- B- Chlorpromazine.
- C- Thioridazine.
- D- Clozapine.

4-Atypical drugs exert their antipsychotic action through blocking:.....

- A- dopamine receptors.
- B- serotonin and dopamine receptors
- C- dopamine and adrenalin receptors.
- D- serotonin receptors .

5-Prevent dopamine inhibition of prolactin release from pituitary lead to:

- A- Hyperprolactinemia.
- B- Hyperprolactinurea.
- C- Hypoprolactinemia.
- D- Hypoprolactinurea.

6. A patient comes in cardiology clinic. With routinely investigation in ECG, the cardiologist suspects the patient has hypercalcemia, but in History, the patient take medication that shows wrong diagnosis. What is the drug?

- A. Chlopromazine
- B. Clozapine
- C. Olanzapine
- D. Risperidone

7. Which one of the following of the drug can cause seizure and agranulocytosis ?

- A. Ziprasidone
- B. Risperidone
- C. Clozapine
- D. thioridazine

8. Which one of the following drugs are antiemetic drugs?

- A. prochlorperazine
- B. haloperidol
- C. benzquinamide
- D. Olanzapine
- E. A & C

9. All the following drugs are Block D2 except:

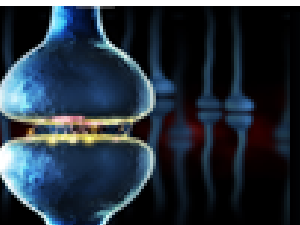
- A. Ziprasidone
- B. Risperidone
- C. Quetiapine
- D. Olanzapine

10: A patient with Schizophrenia, he took medication. Some times, he feels headache, and drowsing & he can't sit , so what is the drug?

- A. Risperidone
- B. Ziprasidone
- C. Olanzapine
- D. Clozapine

Answers:

1-C -2 , D , 3- D , 4- B , 5- A 6-D 7-C 8-E 9-D 10-B



CNS Block

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We hope that we made this lecture easier for you
Good Luck!



CNS Block