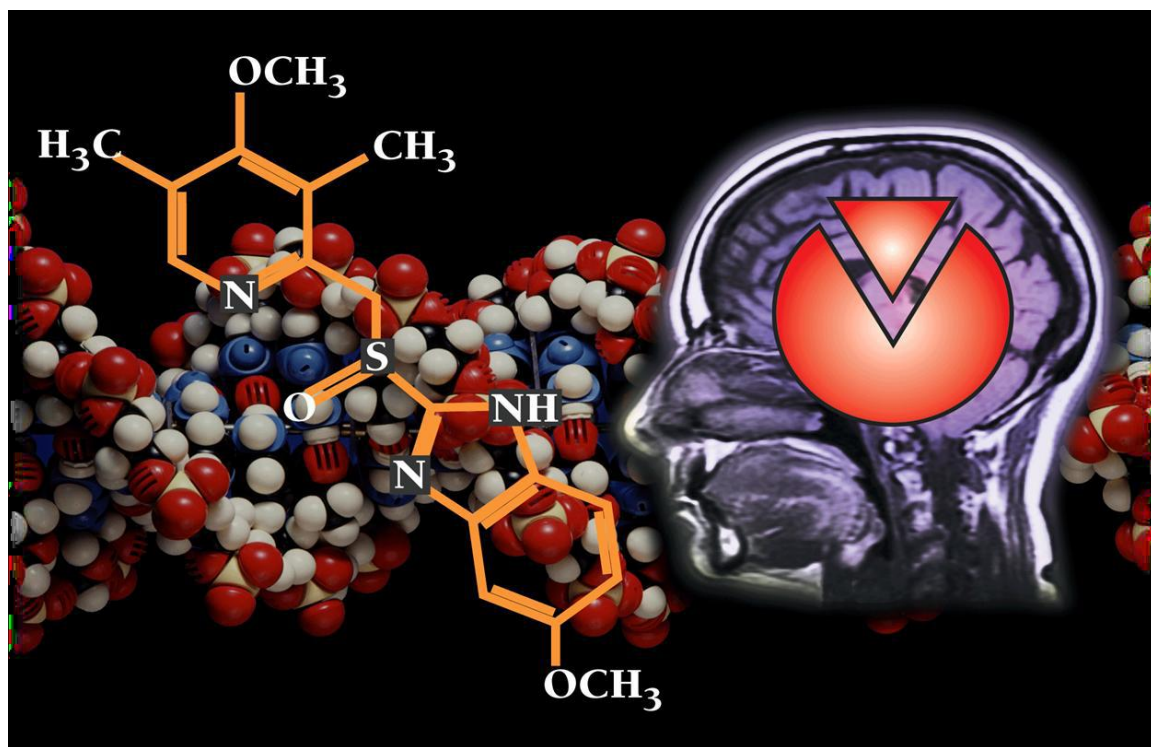


Drugs used in schizophrenia

Drugs Used in Schizophrenia



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Introduction

PSYCHOSIS:

1- Affective Psychoses:

- Mania
- Depression
- Manic-depressive (bipolar affective disorder)

2- Schizophrenia

Symptoms of Schizophrenia :

Positive Symptoms : 1st generation drugs was used to treat these symptoms , and it was not that much effective because treatment of schizophrenia also require treatment of –ve symptoms

- Hallucinations
- Delusions
- Paranoia

Negative Symptoms

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

Antipsychotic drugs

Classification :

Typical Antipsychotic Drugs

According to chemical structure into :

- Phenothiazine : Chlorpromazin still used - Thioridazine
- Butyrophenones : Haloperidol still used
- Thioxanthene : Thiothixene not used now a days

Atypical Antipsychotic Drugs

- Dibenzodiazepines: Clozapine
 - Benzisoxazoles : Risperidone
 - Thienobenzodiazepines : Olanzapine
 - Dibenzothiazepines: Quetiapine
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Schizophrenia – Dopaminergic receptor Systems

- Five sub-types of dopamine receptors
- D1- D5 are widely distributed throughout both the cerebral cortex and limbic system.
- D1 & D2 are found also in corpus striatum

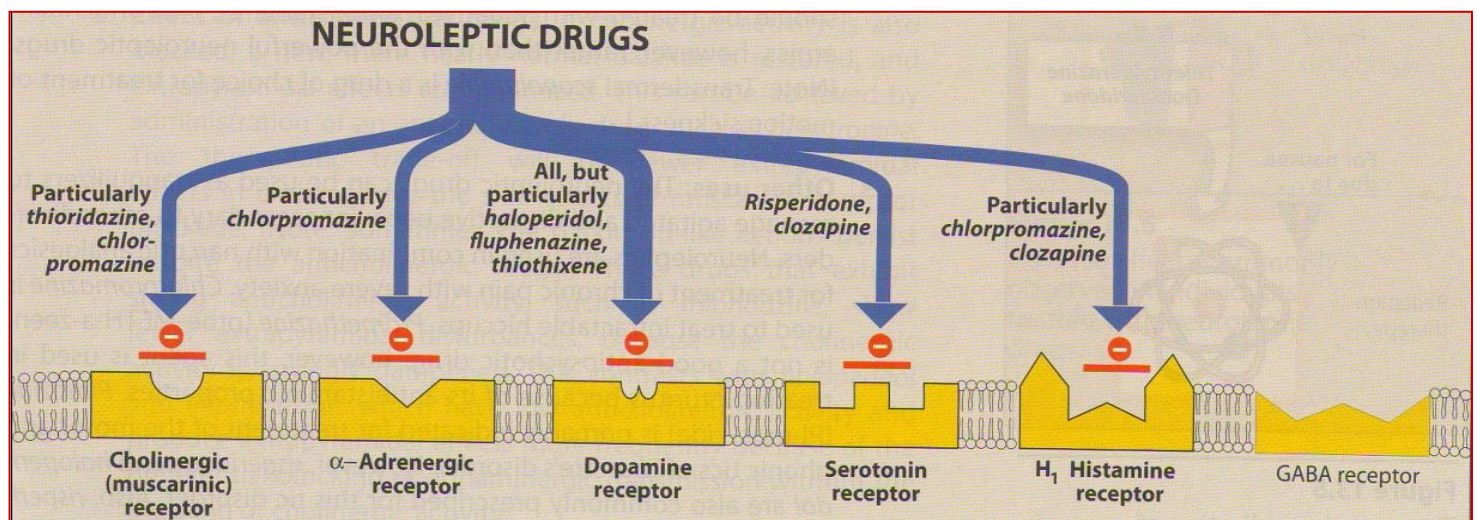
Dopamine System:

Dopaminergic pathways in the brain :

- Mesolimbic - mesocortical pathway → (behavior) **blocking dopamine here lead to treatment of schizophrenia**
- Nigrostriatal pathway → (co-ordination of voluntary movements)
- Tuberoinfundibular pathway → (endocrine effects)
- Medullary - periventricular pathway → (metabolic effects)

Pharmacological actions :

Due blocking effects on different types of receptors



CNS : by blocking **dopamine** receptors

Antipsychotic effect

- Produce emotional quieting
- psychomotor slowing
- Decreases hallucination

Mechanism: Blockade of dopamine receptors in the mesolimbic system.
this mechanism is only responsible for the +ve manifestation , which is known as a action of the 1st generation / typical drugs

Atypical drugs exert their antipsychotic action through blocking serotonin (5HT₂) & dopamine receptors.

Extrapyramidal Symptoms (SE)

Abnormal involuntary movements such as tremors, parkinsonism & tardive dyskinesia
(appears late, and more common in female : involuntary movement of the lips, tong, face , limbs and trunk)

Mechanism : Blockade of dopamine receptors in the nigrostriatum system

Endocrine (SE)

- Galactorrhea, amenorrhea , impotence in female
 - Gynecomastia in male
- (Hyperprolactinemia)

Mechanism: Prevent inhibiting effect of dopamine on prolactin release from pituitry (tuberoinfundibular system)

Metabolic effects (SE)

Changes in eating behavior and weight gain

Mechanism : Blockade of dopamine receptors in the medullary – periventricular pathway

Anti-emetic effect (theapeutic use)

Drug & disease-induced vomiting (not in motion sickness)

Mechanism : Blockade of dopamine receptors in the CRTZ of the medulla

ANS : by blocking adrenergic and colnergic receptors

muscarinic receptors (SE)

Anticholinergic Effects :
atropine like actions

- Blurred vision
- Dry mouth
- Urinary retention
- Constipation

α - adrenergic receptors (SE)

Antiadrenergic Effects :

- Postural hypotension
- Impotence
- Failure of ejaculation

Other actions

Temperature regulation (SE)

Temperature regulation : May cause lowering of body temperature

Mechanism : Heat loss as a result of vasodilation

(α - blocking) Or due to central effect

ECG changes (SE)

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

Antihistaminic effect

(it is maybe consider as SE or as a therapeutic use according to the patient status as in case of purities) :

Sedation due to H1 receptor blockade

Therapeutic Uses :

• Psychiatric :

- Schizophrenia
- Acute mania
- Manic-depressive illness

• Non-Psychiatric :

- Nausea and vomiting
- Pruritis [due to their anti histaminic effect](#)
- Preoperative sedation [due to H1 effect](#)

ADVERSE EFFECTS:

- **Sedation, drowsiness, fatigue** : haloperidol , Risperidone

- Extrapyramidal symptoms :

Occurring early in the treatment as : Parkinson's syndrome [to treat this symptoms we give Parkinson's drugs](#)
occurring late in the treatment as :

- * Tardive Dyskinesia [There is no specific treatment for this manifestations , we only treat its symptoms + gradual withdrawal of the antipsychotic drug](#)
- * Neuroleptic Malignant Syndrome . [due to excessive blocking of dopamine receptors \(fever , leucocytosis , ms spasm \) treatment : dantrolene , Fatal if not treated earlier](#)

- A.N.S effects. :

- * Anticholinergic effects : Clozapine, Chlorpromazine
- * Antiadrenergic effects : Chlorpromazine , Thioridazine

- Endocrine effects : Hyperprolactinemia

- Miscellaneous Effects :

- * Obstructive jaundice : [due to allergic reaction](#)
- * Granular deposits in cornea
- * Retinal deposits (thioridazine) [not used anymore.](#)
- * Weight gain
- * **Agranulocytosis**(means a failure of the bone marrow to make enough white blood cells (neutrophils)) : **Clozapine** (Weekly CBC is done if we use Clozapine)
- * **Seizure** : Clozapine [better to be avoided with epilepsy patient](#)

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 [because it is effective on –ve symptoms which make the case to be resistant.](#)
- Are effective on both positive & negative symptoms.
- **Block both dopaminergic & serotonergic receptors.**
- To reduce the risk of recurrent suicidal behavior in patients with schizophrenia [which is a –ve symptom treated by these drugs](#)

1-CLOZAPINE :

- Blocks both D_4 & $5HT_2$ receptors

Main adverse effects

- Agranulocytosis
- Seizures (better avoided in epileptic patients)
- Excessive salivation (during sleep) , unknown cause

2-RISPERIDONE :

- Blocks D_2 $5HT_2$ receptors

Main adverse effects

- Postural hypotension due to alpha blocking effect
- QT prolongation , so it is Contraindicated in cardiac pt. esp. in case of cardiac arrhythmia
- Sedation -> due to the Anti-histamine effect & high $5HT_1$
- Contraindicated in patients with cardiac problems

3-OLANZAPINE :

- dopamine + serotonin + H_1 + muscarinic + alpha blocking effect

Main adverse effects

- Weight gain
- Postural hypotension
- Flatulence
- sedation
- ↑ Salivation (not only during the sleep) & thirst

4-QUETIAPINE :

- Blocks D_1, D_2 & $5HT_2$ receptors

Main adverse effects

- Sedation
- Hypotension
- sluggishness (Lacking of alertness)
- Increase appetite
- weight gain
- Abdominal pain
- Constipation

Summary

- Drugs used in schizophrenia are classified according to chemical structures.

- **The advantages of atypical drugs includes :**

- They block both dopaminergic & serotonergic drugs.
- They are effective in refractory cases of schizophrenia
- They produce few extrapyramidal effects

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**. Also , due to blockading H1, muscarinic & α - adrenergic receptors.
- The main clinical uses is in schizophrenia
- **Examples of atypical drugs includes : Clozapine - Risperidone - Olanzapine- Quetiapine**