

Schizophrenia.

-) Schizophrenia is one of the most challenging & complex psychiatric disorder.
- It represent a heterogenous syndrome of disorganised bizzare thoughts, delusions & Hallucinations.

Types:

- 1) Paranoid.
- 2) Disorganised.
- 3) catatonic.
- 4) schizoaffective.
- 5) childhood onset.

Symptoms:

Positive symptoms:

Delusions.
Hallucinations.
Disorganisation of thought.
Suspiciousness.
Perceptions.

Cognitive:

Impaired attention.
memory.
Executive function.

Negative Symptoms:

inability to speak ← Alogia
inability to feel pleasure in normal. ← Anhedonia.
AVOLITION.
Apathy. Use in motivation to initiate & perform self-directed purposeful activities.
lack of interest & concern.

Pathophysiology:

① Structural / Functional abnormalities in brain:

→ It is associated with structural & functional changes in the cortex, as well as in the connections b/w different cortical regions, structural deficit such as reduced grey volume, & disrupted white matter volume, or integrity.

→ ↑ sized ventricular size.

② Neurotransmitter changes:

① Dopaminergic pathway:

Increased metabolism in. → dopaminergic hyperactivity.
Caudate nucleus.

Decreased blood flow & glucose metabolism in. → dopaminergic hypoactivity.
Frontal & left temporal lobes.

PET studies specific D_2 receptor ligands,

↑ density of D_2 in caudate nucleus.

↓ density of D_2 in frontal & temporal lobes.

using D_1 ligands indicated that,

↓ density in both caudate nucleus & fronto-temporal lobes.

Hypo-frontality: lack of decision making
cognitive dysfunction.
Negative symptom.

DA Hypoactivity in caudate nucleus → Positive symptoms.

Nigrostriatal → Substantia nigra to caudate nucleus.

→ movement.

Mesolimbic → VTA to limbic area → memory & behaviour.

Mesocortical → VTA to frontal/parietal → cognition.

Communication
social function.

Tuberoinfundibular → Hypothalamus to pituitary gland.

→ Regulate prolactin release.

3) Glutamergic Hypothesis:

→ Glutamate system is one of the major excitatory neurotransmitter system in brain.

Hypoactivity/Hyporeactivity can cause toxicities.

when glutamergic inhibition → DA Release.

↑ D₁ ↓

↓
Used DA D₁ neurotransmitter.
↑ Used DA D₂ neurotransmitter.

↓
Impair NMDA transmission via GABAergic neurons.

NMDA Hypofunction: (N-methyl D-Aspartate).

NMDA receptor block → Used DA D₁ neurotransmitter.
by glutamergic inhibition of DA Release.

NMDA transmission via GABAergic neurons

← Excess DA D₂ stimulation
Impair.

3) serotonergic pathway:

- serotonin receptors were found in dopaminergic area.
- stimulation causes ↓ ser DA release.
- serotonin receptors & DA receptors are found in co-localised in cortex.
- Pt with schizophrenia have high blood 5-HT level thus correlated to the

↑ ventricular size.

Diagnosis

- Two or more symptoms. Persistent, at least 1 month.
- social / occupational dysfunction.
- continuous symptoms for 6 months.
- mood disorder is excluded.
- Disorder not due to substance abuse or medical disorder.

Diagnostic texts for Schizophrenia (Diagnostic & Statistical Manual of Mental Disorders, 4th Edition, Revision).

DSM-IV-TR. Diagnostic criteria for schizophrenia.

- Characteristic symptoms: Two & more of the following each persisting for a significant portion for at least 1 month.
 - 1) Delusions.
 - 2) Hallucinations.
 - 3) Disorganized speech.
 - 4) Grossly disorganised / catatonic behaviour.
 - 5) Negative symptoms.
- Disorder not due to medical disorder or substance use.

Treatment for schizophrenia:

① Nonpharmacological Treatment:

- > Psychological Rehabilitation Therapy.
- > Cognitive Therapy.
- > Social Skill Training.
- > Basic Education.
- > Counseling.
- > Personal Therapy.

Diagnostic Statistical manual of mental disorder IV Edition Text division.

② Pharmacological Therapy:

① Antipsychotics:

I generation.

	<u>Dose</u>	<u>Adverse Effects</u>
① Chlorpromazine	50-150mg/day (1000mg/day)	Sedation. Seizures Thermoregulation glaucoma.
② Haloperidol	2-5mg/day (20mg/day)	wt. gain.
③ Fluphenazine	5-20mg/day	orthostatic.
④ Loxapine	50-150mg/day	Hypotension.
⑤ Perphenazine	16-64mg/day	ECG changes.
⑥ Thioridazine	100-800mg/day	↑ sed heart rate.
⑦ Trifluoperazine	5-40mg/day	Prolonged QT-intervals.

II generation:

Aripiprazole	15-30mg/day	Dystonia:
Asenapine	10-20mg/day	A state of abnormal tonic.
Iloperidone	6-24mg/day	severe muscle spasm.
Luxaridone	40-120mg/day	

olanzapine	10-20mg/day	Akathisia - inability to sit Pseudoparkinsonism. ↓ D ₂ blockade in the nigrostriatum resembles idiopathic Parkinsonism.
Quetiapine	300-800mg/day	
Ziprasidone	80-160mg/day	

Extrapyramidal effects treatment
agents to treat these symptoms are.

Symptoms: 4 cardinal symptoms.

- a) akinesia } ↓ sed motor activity.
- ⓐ Bradykinesia } including difficulty initiating movement as well as extreme slowness, masklike facial expression.
- b) Tremor: known as pill rolling type. ↓ sed with movement. usually involving fingers & hands. Tremors also can be seen.
- c) Cogwheel: Rigidity seen as the patients limb yielding in jerky, ratchet like fashion when passively moved by the Examiner.
- d) Postural abnormalities: Stooped posture. Difficulty in maintaining stability when changing body position & a gait that ranges from slow & shuffling to festinating. Fatigue & weakness.

Tardive Dyskinesia:

→ abnormal involuntary movements occurring late in onset in relation to initiation of antipsychotic therapy.

Buccal lingual masticatory Syndrome (d)

- Orfacial movements.
- Tongue thrusting
- Rolling.

ply catching movements. & chewing/lateral jaw movements.

antipsychotic mechanism of action:

→ Exact mechanism is unknown.

- a) typical (traditional (High D_2 antagonism & low $5HT_{2A}$ antagonism)
- b) Atypical. (moderate to high D_2 antagonism? High $5HT_{2A}$ antagonism)
- c) atypical clozapine like. (low D_2 antagonism High $5HT_{2A}$ antagonism).

(SAGs)

All second generation Antipsychotics are having greater affinity for $5HT_{2A}$ ~~receptor~~ receptors than D_2 receptors.

FGAs are DA receptor antagonists with high affinity for D_2 receptors.

→ Transient blockade of DA receptors may be adequate to produce antipsychotic effect.

↓

Antipsychotic drugs binds to.

D_2 receptor. & then blockade of D_2 receptors.