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- IMPORTANT
- NOTES
- EXTRA INFO

**SCHIZOPHRENIA**

## Definition:

Is a mental disorder characterized by a breakdown of thought processes and by poor emotional responsiveness.

*Thought is the first & important part affected then behavior & emotion. They start with stress and loss of focusing*

It is not a single disease but a group of disorders with heterogeneous etiologies  
Found in all societies and countries with equal prevalence & incidence worldwide.

A life prevalence of 0.6 – 1.9 %.

Peak ages of onset are 10-25 years for ♂ & 25-35 years for ♀.

Etiology: Exact etiology is unknown.

### **1- Stress-Diathesis Model:**

- Integrates biological, psychosocial and environmental factors in the etiology of schizophrenia.
- Symptoms of schizophrenia develop when a person has a specific vulnerability that is acted on by a stressful influence

*A specific vulnerability = Genetic vulnerability.  
In a simple way: it's an interaction between genetic and environmental influences*

### **2- Neurobiology**

Certain areas of the brain are involved in the pathophysiology of schizophrenia: the limbic system, the frontal cortex, cerebellum, and the basal ganglia.

#### **a- Dopamine Hypothesis;**

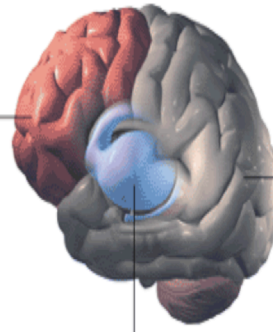
Too much dopaminergic activity ( whether it is ↑ release of dopamine, ↑ dopamine receptors, hypersensitivity of dopamine receptors to dopamine, or combinations is not known ).

#### **b- Other Neurotransmitters;**

Serotonin, Norepinephrine, GABA, Glutamate & Neuropeptides

## DIFFERENT NEUROTRANSMITTERS, SAME RESULTS

SOME SCIENTISTS have proposed that too much dopamine leads to symptoms emanating from the basal ganglia and that too little dopamine leads to symptoms associated with the frontal cortex. Insufficient glutamate signaling could produce those same symptoms, however.



IN THE REST OF THE CORTEX, glutamate is prevalent, but dopamine is largely absent.

IN THE FRONTAL CORTEX, where dopamine promotes cell firing (by acting on D1 receptors), glutamate's stimulatory signals amplify those of dopamine; hence, a shortage of glutamate would decrease neural activity, just as if too little dopamine were present.

IN THE BASAL GANGLIA, where dopamine normally inhibits cell firing (by acting on D2 receptors on nerve cells), glutamate's stimulatory signals oppose those of dopamine; hence, a shortage of glutamate would increase inhibition, just as if too much dopamine were present.

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## c- Neuropathology:

Neuropathological and neurochemical abnormalities have been reported in the brain particularly in the limbic system, basal ganglia and cerebellum. Either in structures or connections.

*It affects the neurons gradually.*

## THE BRAIN IN SCHIZOPHRENIA

MANY BRAIN REGIONS and systems operate abnormally in schizophrenia, including those highlighted below. Imbalances in the neurotransmitter dopamine were once thought to be the prime cause of schizophrenia. But new findings suggest that

impoverished signaling by the more pervasive neurotransmitter glutamate—or, more specifically, by one of glutamate's key targets on neurons (the NMDA receptor)—better explains the wide range of symptoms in this disorder.

### BASAL GANGLIA

Involved in movement and emotions and in integrating sensory information. Abnormal functioning in schizophrenia is thought to contribute to paranoia and hallucinations. (Excessive blockade of dopamine receptors in the basal ganglia by traditional antipsychotic medicines leads to motor side effects.)

### AUDITORY SYSTEM

Enables humans to hear and understand speech. In schizophrenia, overactivity of the speech area (called Wernicke's area) can create auditory hallucinations—the illusion that internally generated thoughts are real voices coming from the outside.

### OCCIPITAL LOBE

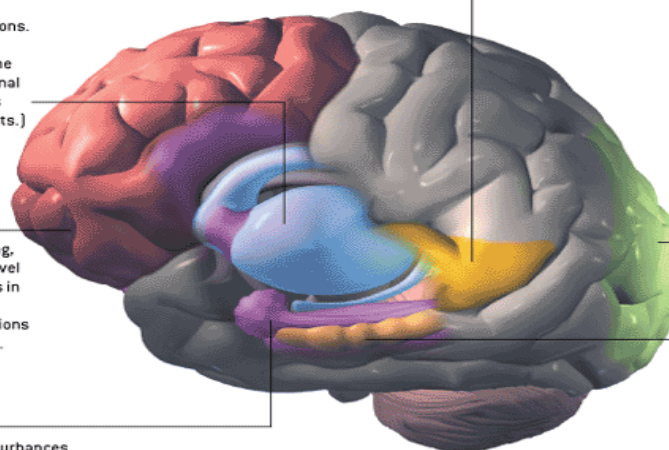
Processes information about the visual world. People with schizophrenia rarely have full-blown visual hallucinations, but disturbances in this area contribute to such difficulties as interpreting complex images, recognizing motion, and reading emotions on others' faces.

### FRONTAL LOBE

Critical to problem solving, insight and other high-level reasoning. Perturbations in schizophrenia lead to difficulty in planning actions and organizing thoughts.

### LIMBIC SYSTEM

Involved in emotion. Disturbances are thought to contribute to the agitation frequently seen in schizophrenia.



### HIPPOCAMPUS

Mediates learning and memory formation, intertwined functions that are impaired in schizophrenia.

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*Hippocampus involvement appears in advanced cases*

## d- Psycho-neuro-immunology;

↓ T-cell interleukin-2 & lymphocytes, abnormal cellular and humoral reactivity to neurons and presence of antibrain antibodies.

These changes are due to neurotoxic virus ? or endogenous autoimmune disorder ?

## e- Psycho-neuro-endocrinology;

Abnormal dexamethasone-suppression test ↓ LH/FSH

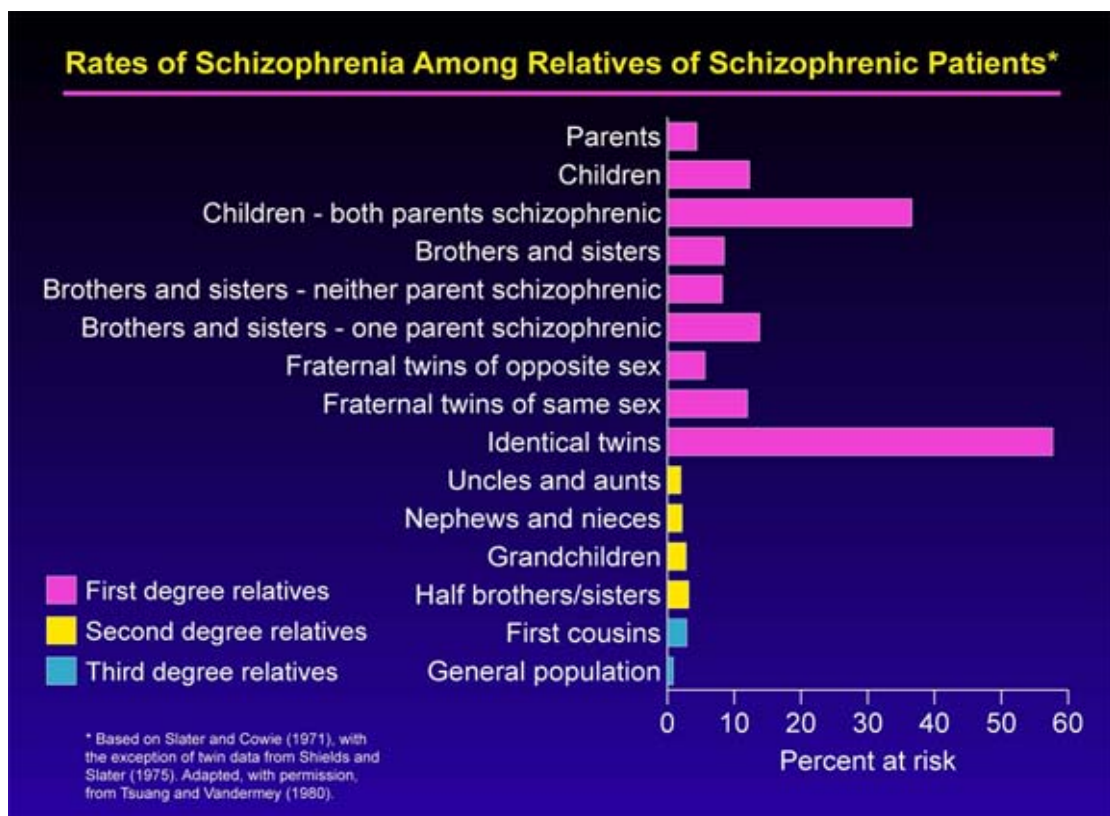
A blunted release of prolactin and growth hormone on stimulation.

## 3- Genetic Factors:

A wide range of genetic studies strongly suggest a genetic component to the inheritance of schizophrenia that out weights the environmental influence

These include: family studies, twin studies and chromosomal studies

*This is the most important factor.*



*The most important risk factors are identical twins and both parents schizophrenic.*

## Schizophrenia: genes plus stressors:

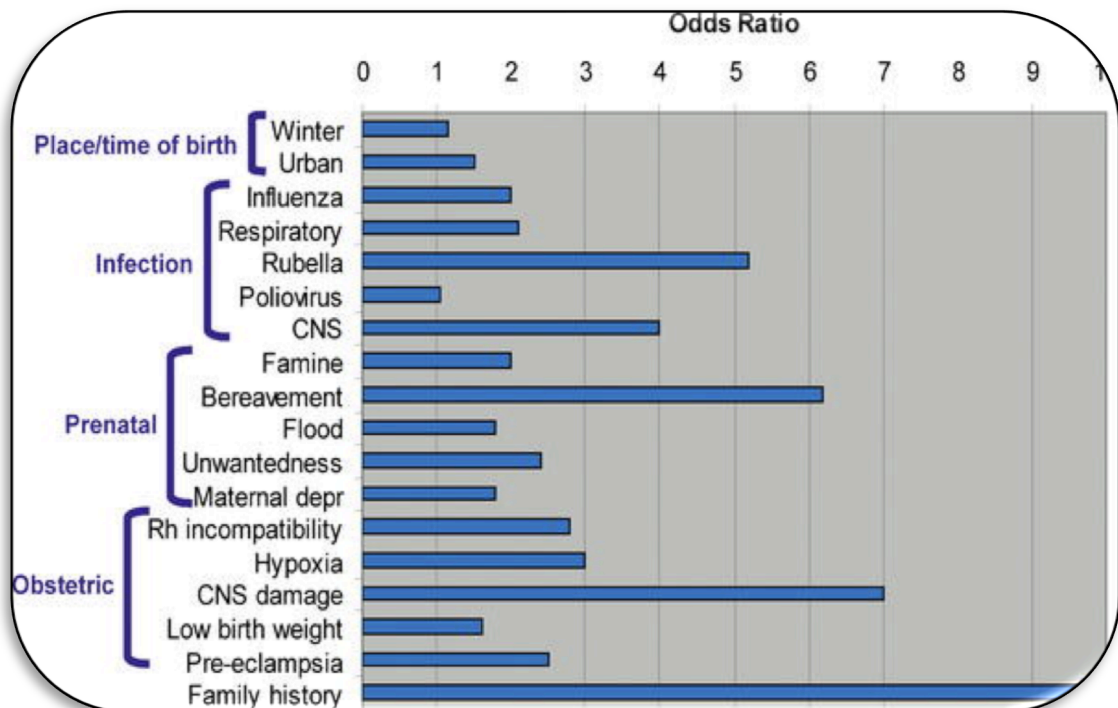
Schizophrenia is mostly caused by various possible combinations of many different genes (which are involved in neurodevelopment, neuronal connectivity and synaptogenesis) plus stressors from the environment conspiring to cause abnormal neurodevelopment.

There is also abnormal neurotransmission at glutamate synapses, possibly involving hypofunctional NMDA receptors.

### 4- Psychosocial Factors:

- In family dynamics studies, no well-controlled evidence indicates specific family pattern plays a causative role in the development of schizophrenia.
- **High Expressed Emotion family: increase risk of relapse.**

*The increase is because the family expects a full recovery from the patient which in that case is very rare so that puts him in high stress.*



This chart represents the risk factor 😊



## DIAGNOSIS: (based on Diagnostic and Statistical Manual of Mental Disorders)

DSM-IV-TR Diagnostic Criteria for Schizophrenia:

### A- ≥ two characteristic symptoms

- 1- Delusions
- 2- Hallucinations
- 3- Disorganized speech
- 4- Disorganized behavior
- 5- Negative symptoms

} Positive symptoms

*Delusions: are False Fixed beliefs.*

*Hallucinations: are false perceptions.*

*\*Negative symptoms are deficits of normal emotion responses.. They respond less well to medication. (Ex: AntiSocial personality).*

*sometimes there is a physical involvement (means not only mentally).*

### B- Social / Occupation dysfunction

*Never diagnose an individual with Schizophrenia without the fact that there is a social/occupational dysfunction*

### C- Duration of at least 6 months

### D- Schizoaffective & mood disorder exclusion

*Schizoaffective: has both features of Schizophrenia and features of a mood disorder.*

## E- Substance / General medical condition exclusion

We should do a CT scan to exclude any other diseases that could present as schizophrenia; diseases such as: Frontal lobe epilepsy or frontal lobe tumors.

## F- Relationship to pervasive developmental disorders

### Types:

1-Paranoid type : (Best diagnosis – high cognitive abilities – good judgment)

2-Disorganized type : (Disorganized speech and behavior)

Catatonic type (A marked psychomotor disturbance that may involve stupor or mutism, negativism, rigidity, purposeless excitement, and inappropriate or bizarre posturing) (Now rarely seen)

3-Undifferentiated type (Hardest diagnosis)

4-Residual type (characterized by a past history of at least one episode of schizophrenia, but the person currently has no positive symptoms)

## Clinical Features:

- No clinical sign or symptom is pathognomonic for schizophrenia
- Patient's history & mental status examination are essential for diagnosis.
- Premorbid history includes schizoid or schizotypal personalities, few friends & exclusion of social activities. (Odd behaviors)
- Prodromal features include obsessive-compulsive behaviors. (Prodromal = an early symptom)
- Picture of schizophrenia includes positive and negative symptoms.
- Positive symptoms like: delusions & hallucinations.
- Negative symptoms like: affective flattening or blunting, poverty of speech, poor grooming, lack of motivation, and social withdrawal.

## Mental state examination:

- Appearance & behavior ( variable presentations).
- Mood, feelings & affect ( reduced emotional responsiveness, inappropriate emotion).
- Perceptual disturbances ( hallucinations, illusions ).
- Thought: Thought content ( delusions).
- Form of thought ( looseness of association).



-Thought process ( thought blocking, poverty of thought content, poor abstraction, perseveration ) .

- Impulsiveness, violence, suicide & homicide.

- Cognitive functioning (poor)

- Poor insight and judgment.

## Course:

- Acute exacerbation with increased residual impairment
- Full recovery: very rare
- Longitudinal course: downhill

## Prognosis:

<b>Good P.F</b> <u>not a cure just an improvement</u>	<b>Poor P.F</b>
Late age of onset	Young age of onset
Acute onset	Insidious onset
Obvious precipitating factors	Lack of an obvious precipitating factor
Presence of mood component	Multiple relapses
Good response to treatment	Low IQ
Good supportive system	Poor premorbid personality *(before the disorder)
	Negative symptoms Positive family history

## Differential Diagnosis:

### 1-Nonpsychiatric disorders:

- Substance-induced disorders : substance abuse
- Epilepsy (Temporal lobe epilepsy)
- CNS diseases
- Trauma
- Others :like SLE

### 2-Psychiatric disorders:

- Schizophreniform disorder. (the difference between schizophrenia and schizophreniform is the duration ; schizophreniform is presented within a month or five months..."not more than 6 months")
- Brief psychotic disorder.
- Delusional disorder.
- Affective disorders.
- Schizoaffective disorder. (Accompanied by a mood disorder)
- Personality disorders (schizoid, schizotypal & borderline personality)

-Malingering & Factitious disorders. (Types of personalities).

## Treatment:

### What are the indications for hospitalization?

Diagnostic purpose.

Patient & other's safety.

Initiating or stabilizing medications.

Establishing an effective association between.

Patient & community supportive systems.

## Biological therapies:

**Antipsychotic** medications are the mainstay of the treatment of schizophrenia.

Generally, they are remarkably safe.

### Two major classes:

-Dopamine receptor antagonists ( haloperidol, chlorpromazine )

-Serotonin-dopamine receptor antagonists ( Risperidone, clozapine, olanzapine ).

### Other drugs:

-Anticonvulsants

-Lithium

-Benzodiazepines

Depot forms of antipsychotics e.g. Risperidone Consta is indicated for poorly compliant patients.

Electroconvulsive therapy (ECT) for **catatonic or poorly responding patients** to medications.

<i>First generation antipsychotics</i>	<i>Second generation antipsychotics</i>	<i>Clozapine</i>
Extrapyramidal effects Dystonia Pseudoparkinsonism Akathisia Tardive dyskinesia	Olanzapine Weight gain Sedation Glucose intolerance and frank diabetes mellitus Hypotension	Sedation
Sedation Hyperprolactinaemia	Risperidone Hyperprolactinaemia Hypotension EPS at higher doses Sexual dysfunction	Hypersalivation Constipation
Reduced seizure threshold Postural hypotension	Amisulpiride Hyperprolactinaemia Insomnia Extrapyramidal effects	Reduced seizure threshold Hypo & hypertension
Anticholinergic effects Blurred vision Dry Mouth Urinary Retention	Quetiapine Hypotension Dyspepsia Drowsiness	Tachycardia
Neuroleptic malignant syndrome		Pyrexia
Weight gain		Weight gain
Sexual dysfunction		Glucose intolerance and diabetes mellitus
Cardio-toxicity (including prolonged QTc)		Nocturnal enuresis
		Rare serious side effects Neutropenia 3% Agranulocytosis 0.8% Thromboembolism Cardiomyopathy Myocarditis Aspiration pneumonia

**CLOZAPINE:** causes agranulocytosis (lowered WBC count)

## Psychological therapies:

- Social skills training.
- Family oriented therapies.
- Group therapy.
- Individual psychotherapy.
- Assertive community treatment.