



## Review - Schizophrenia: Current Research and Observations

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### Abstract

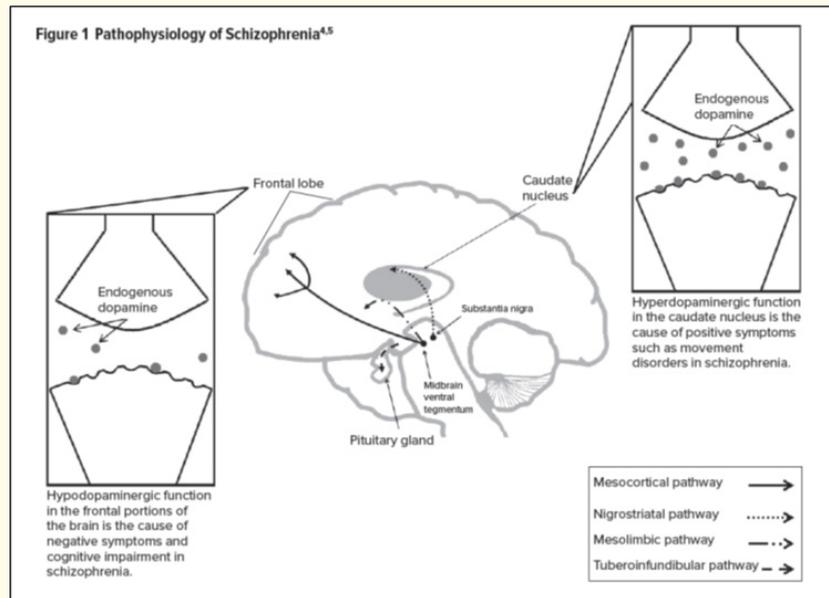
Schizophrenia is significant mental illness that impairs person's ability to think, feel, and act. Schizophrenia patients may appear to be out of touch with reality. They may hear voices that others do not. Positive, Negative, and Cognitive symptoms are three types of schizophrenia symptoms. Schizophrenia can be caused by variety of factors, including genes, environment, or changes in brain structure. Schizophrenia affects less than 1% of general population, but 10% of those who have first-degree relatives with condition, such as parents, brothers, or sisters, are affected. Majority of people suffering with schizophrenia are not that aggressive; nonetheless, when schizophrenia is left untreated, risk of violence also increases. Neurodevelopment Hypothesis, Dopamine Hypothesis, and Glutamate Hypothesis are three possible biological theories for Schizophrenia. It's critical to assist someone with schizophrenia symptoms in receiving treatment as soon as feasible. Here Antipsychotic medicines and psychosocial therapy are two types of therapy that can help with symptoms. Family and friends may assist their loved ones with schizophrenia by assisting them in obtaining treatment and encouraging them to adhere to it.

**Keywords:** Schizophrenia; Current Research; Hallucination; Glutamate Hypothesis

### Introduction

Schizophrenia is most common mental condition nowadays. Kraepelin in 1896 coined term "dementia praecox," which was later renamed to "schizophrenia" by the other scientist named Bleuler in 1911. Disturbances in thinking, perception, and mood are all symptoms of this illness. These problems "involve most basic activities that provide normal person sense of identity, distinctiveness, and self-direction," according to researchers. German Psychiatrist found first rank signs of schizophrenia in 1959. Schneider classified symptoms into three basic groups: auditory hallucinations, passivity experience, and delusional thought. Schizophrenia patients hear hallucinating "voices" that may offer running commentary on their actions or direct them to perform certain activities. Some people hear voices that are rude or offensive. Passivity emotions are those sentiments, ideas, or behaviours that individual has while being influenced by third person. Delusional thinking is re-

sult of erroneous perceptions [1]. Delusional thinking is frequently devoid of understanding and impervious to logic. Although these symptoms are no longer employed as solitary diagnostic tool, they are nevertheless useful. Schneider's classification of symptoms offers idea of amount of distress that people with schizophrenia go through. Schizophrenia, on other hand, is connected with wide variety of additional symptoms, such as social withdrawal, incongruent emotions, and thinking disorders, all of which add to person's debilitating consequences. Schizophrenia has high human cost as well as high economic cost to country. In addition to symptoms listed above, sickness is frequently accompanied by loss of social relationships and professional opportunities. Cost of schizophrenia to country, according to Davies, is £397 million, or 1.6 percent of entire health-care expenditure. This study will aim to analyse current advancements in categorization, aetiology, and treatment of schizophrenia, with goal of drawing some inferences from literature about future advancements in schizophrenia therapy [2].



**Figure 1:** Pathophysiology of Schizophrenia [4,5].

### Characteristics of clinic

Schizophrenia manifests itself in variety of ways that usually begin in early adulthood and last for rest of one's life. Majority of patients have history of behavioural problems, especially social and learning issues. Auditory hallucinations and delusions are the common type of symptoms of schizophrenia. Patients may have seen these signs, however these phenomena may or may not be real, and it is now causing concern. Positive, Negative, and Cognitive symptoms are three primary symptoms of schizophrenia, which may be separated into three stages. Positive symptoms are those that can be easily recognized and are not generally seen in healthy persons. Hallucination, delusion, and aberrant motor behaviour are the common examples of symptoms with varying degrees of severity. Negative symptoms are difficult to recognise and are linked to high risk of morbidity. Avolition, Alogia, Anhedonia, and reduced emotional expressiveness were most prevalent Negative symptoms. most recent categorization is Cognitive Symptoms. As result, individual's communication abilities are harmed as his speech and attention are disrupted [3].

### Pathophysiology

Theories on pathogenesis of schizophrenia have been based on abnormalities in neurotransmission. Majority of these ideas

revolve upon neurotransmitter imbalances, such as dopamine, serotonin, and glutamate. Other ideas link aspartate, glycine, and gamma-aminobutyric acid (GABA) to schizophrenia's neurochemical imbalance. Many of symptoms of schizophrenia are considered to be linked to abnormal activation at dopamine receptor sites (particularly D2). There are four dopaminergic pathways that have been identified. substantia nigra is start of nigrostriatal pathway, which leads to caudate nucleus. Low dopamine levels in this pathway are considered to cause motor symptoms through affecting extrapyramidal system. In presence of excess dopamine, mesolimbic pathway, which extends from ventral tegmental area (VTA) to limbic regions, may have role in positive symptoms of schizophrenia. From VTA to cortex, mesocortical circuit runs. Low mesocortical dopamine levels are hypothesised to be source of negative symptoms and cognitive difficulties in schizophrenia. From hypothalamus to pituitary gland, tuberoinfundibular route runs. Increased prolactin levels, galactorrhea, ammenorrhea, and lower libido arise from reduction or blocking of tuberoinfundibular dopamine. finding that lysergic acid diethylamide amplified effects of serotonin in brain led to establishment of serotonin hypothesis for schizophrenia. In contrast to prior drugs that solely targeted dopamine receptors, subsequent research led to discovery of pharma-

cological molecules that inhibited both dopamine and serotonin receptors. Newer chemicals have been discovered to help with both positive and negative symptoms of schizophrenia [4].

### Aetiology

Studies have discovered number of variables that increase likelihood of developing schizophrenia. Scientists have known for long time that schizophrenia may run in families. sickness affects less than 1% of general population, but 10% of those who have first-degree relatives with condition, such as parents, brothers, or sisters, are affected. Many environmental variables, such as virus infection or starvation prior to delivery, complications during birth, and other unidentified psychological variables, may all have role (Schizophrenia). Scientists also believe that persons with schizophrenia have somewhat different brain structure than healthy people. Some persons with schizophrenia, for example, have bigger ventricles, which are fluid-filled holes in middle of brain. Another prevalent cause of schizophrenia has been shown to be increase in dopamine levels in most persons diagnosed with schizophrenia, however it is yet unknown how everyone diagnosed with schizophrenia has too much dopamine [5].

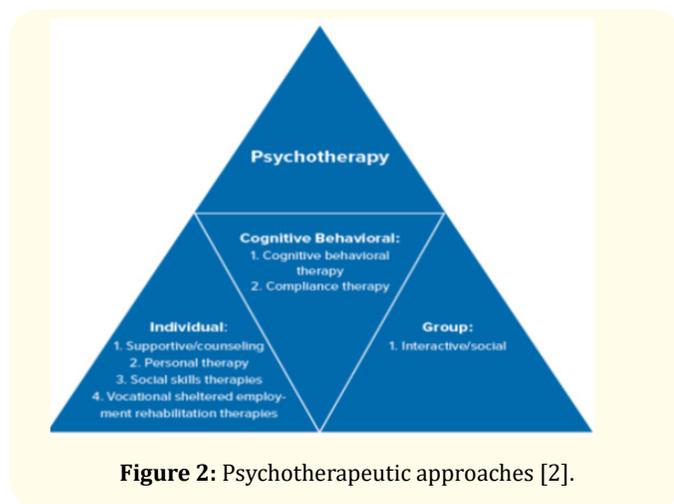
### Epidemiology

Schizophrenia affects people all throughout world. Schizophrenia affects about one percent of world's population. rate of occurrence is around 1.5 per 10,000 persons. Men are diagnosed with schizophrenia at younger age than women, although women are more prevalent as they become older. For men, typical age of onset is 18 to 25, while for women, it is 25 to 35. However, more recent study that included data from 33 nations found that prevalence of schizophrenia varied by geographic location [6].

### Diagnostic criteria and classification

Psychiatrists have generally defined how schizophrenia is classified. While there are many diagnostic textbooks for mental illness, many are only utilised for study and are seldom utilised in clinical practise. As result, focus of this research will be on those that are employed in clinical practise. There are now two primary textbooks used in clinical settings to define and describe mental diseases, including schizophrenia, for diagnostic reasons. International Classification of Diseases-10 (ICD-10) and Diagnostic and Statistical Manual of Mental Disorders-IV are two systems in question (DSM-IV) [7]. For mental diseases, such as schizophrenia,

International Classification of Diseases-10 gives diagnostic categories. "Syndrome with range of causes and results, depending on balance of genetic, physical, social, and cultural influences," according to definition of schizophrenia. ICD-10 classification system divides schizophrenia into variety of sub-categories. These include paranoid schizophrenia, hebephrenic schizophrenia, catatonic schizophrenia, undifferentiated schizophrenia, residual schizophrenia, simple schizophrenia, and post-schizophrenic depression. In most regions of globe, paranoid schizophrenia is most frequent kind of schizophrenia, according to ICD-10. It is defined as "stable, frequently paranoid delusions that are generally accompanied by hallucinations and perceptual disturbances". Hebephrenic schizophrenia is kind of schizophrenia that generally begins in late adolescence or early adulthood and has bad prognosis. Affective shifts, brief delusions and hallucinations, and reckless or unpredictable behaviour are all symptoms. For reasons that are still unknown, catatonic schizophrenia is uncommon in industrialised countries [8]. It is characterised by movement and volitional problems. There have been many reports which states that patients had experienced drowsiness and sudden explosive excitation. Residual schizophrenia is most prevalent of different kinds of schizophrenia. It is characterised by substantial negative-type symptoms that develop after initial period of sickness marked by florid symptoms. intensity of these florid symptoms should have been significantly decreased for at least year in person. ICD-10 recommends one-month interval between start of symptoms and diagnosis of schizophrenia. This is to distinguish schizophrenia from acute psychotic episodes, which can last for up to two weeks without treatment. For purposes of diagnosis, Diagnostic Statistical Manual of Mental Disorders-IV (DSM-IV) divides schizophrenia into four categories. DSM-IV diagnostic criteria differ somewhat from ICD-10 diagnostic criteria. Evidence and symptoms of schizophrenia must be present for "a major percentage of time over one-month period, with certain signs of condition continuing for at least six months," according to DSM-IV criteria. ICD-10 criteria, on other hand, require symptoms to be present for at least one month. DSM-IV and ICD-10 classifications of schizophrenia subgroups are quite similar. It divides people into five subtypes: paranoid, disorganised, catatonic, undifferentiated, and residual. In both books, descriptions of subtypes are substantially same. commonalities are product of extensive international collaboration between two texts, as well as desire for comparable descriptions to enable research compatibility [9].



**Figure 2:** Psychotherapeutic approaches [2].

### Schizophrenia molecular mechanisms

The following are many processes linked to schizophrenia.

#### Hypothesis of neurodevelopment

The neurodevelopment theory of schizophrenia proposes that impacts on brain development during embryonic or foetal stages lead to abnormal neural activity and neuronal functioning later in life. Neuro developmental abnormalities mostly connected to hippocampus formation and superior temporal lobe were discovered in post mortem of schizophrenia patient. Neurodevelopment anomalies arise in utero as early as late first or early second trimester, leading to appearance of positive and negative symptoms, or both, in young adulthood [10].

#### Hypothesis of dopamine

The dopamine hypothesis, which theorises that symptoms of schizophrenia are caused by excessive dopaminergic neurotransmission, particularly in mesolimbic and striatal brain regions, which leads to positive symptoms and eventually schizophrenia, is most widely considered neurochemical hypothesis of schizophrenia. There are several clinical shards of data that support dopamine theory in schizophrenia. Different evidence has surfaced in support of this concept. Amphetamine users provided first proof that dopamine was present in schizophrenic patients. Amphetamine has been shown to increase dopamine production and cause psychotic symptoms similar to schizophrenia [11].

#### Hypothesis of glutamate

It is emphasised in this Hypothesis that dopaminergic dysfunction may be linked to glutamatergic dysfunction. According to this

theory, glutamate malfunction generates opening effect in thalamocortical loop, resulting in psychotic symptoms and well-known dopamine concentration fluctuations. Glutamatergic receptors are divided into two groups, each of which can perform various roles, eventually leading to onset of schizophrenia symptoms. NMDA (N-methyl, D-aspartate) receptor is key receptor in these receptors that causes schizophrenia in most people by shifting dopamine levels outside of usual range [12].

### Schizophrenia therapy methods currently available

Recently, various therapy alternatives for treatment of schizophrenia have become available and are being employed in practise. Typically, schizophrenia treatment is indicated through clinical reports and their ranges or severity levels. Patients with schizophrenia who are unable to take their medications are more likely to relapse, which can result in hospitalisation. As result, it is critical to tell patient about his sickness and current disease status. As you may be aware, schizophrenia is serious chronic condition that needs lifetime treatment, thus it is your responsibility to keep this up to date [13].

#### Antipsychotic drugs are used to treat schizophrenia

Chlorpromazine, first-generation antipsychotic medication developed in 1950 and widely utilised since it was only antipsychotic medicine available at time for treatment of schizophrenia. potency of chlorpromazine will lessen severity of schizophrenia. Other medicines of this family, including as loxapine, fluphenazine, perphenazine, and haloperidol, were identified by modifying their structure and activity, however they all have serious side effect, extrapyramidal symptoms, which should not be overlooked. As result, these drugs are no longer in use. These FGAs medications are also known as traditional or traditional medications. Clozapine is second-generation antipsychotic drug that was developed in 1970 and is far superior to previous drugs. Its dopamine receptor agonist, but it works in different way. Second-generation antipsychotics are commonly used as first-line therapy for schizophrenia, and they are effective. Following this, number of SGAs has been found that may also be effective in reducing severity of this condition. This family of medications, formerly classified as atypical antipsychotics but now referred to as second generation antipsychotics, was touted as first substantial development in schizophrenia treatment in 40 years. Drugs appear to have edge over first-generation antipsychotics. It is difficult to establish successful rehabilitation programmes in most schizophrenia patients without use of anti-

psychotic medications. In event of acute psychotic episode, medication should be started right away. Clozapine's efficacy may be enhanced when used in conjunction with other medications, such as risperidone. Clozapine is more effective antipsychotic than other antipsychotics. Clozapine was first provided with count of white blood cells being monitored. If agranulocytosis develops as result of high dose, clozapine must be stopped. If schizophrenia is severe, then combination therapy, such as SGAs combined with FGAs or other medicines may be beneficial [14].

### Combination and augmentation therapy

Combination therapy is administered with different antipsychotic drugs, whereas augmentation therapy is provided with second generation antipsychotics along with electroconvulsive treatment (ECT) or mood stabilising medicines. Lithium is mood stabiliser that is widely used. Lithium may enhance mood and behaviour, although it has no antipsychotic properties.

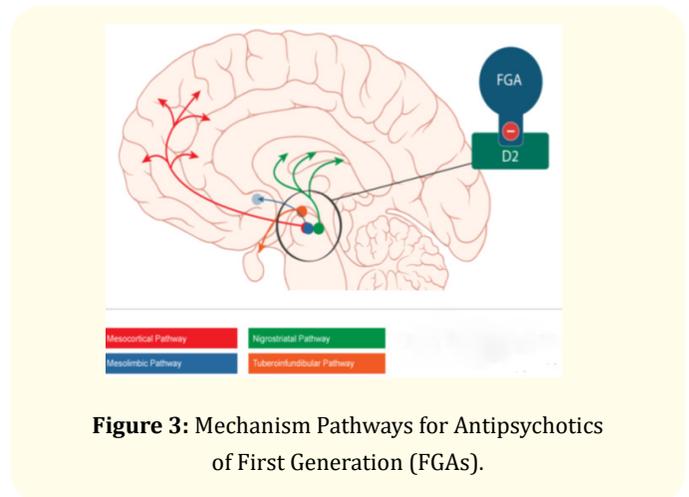
### Commonly used medications in schizophrenia mechanisms

There is variety of medicines used to treat schizophrenia, each with its own mode of action for producing effect in body. Antipsychotics, in particular, are used to treat schizophrenia, thus here are some processes associated to antipsychotics.

### Antipsychotics of first generation

Antipsychotics of first generation (FGAs) are also known as conventional antidepressants, dopamine antipsychotics, and classic antipsychotics. specific mechanism of action is unknown, although they are phenothiazines derivatives that suppress release of hypothalamic and hypophyseal hormones by interacting with D2 receptors in brain and acting as antagonizers, as well as inhibiting mesolimbic dopamine receptors.

FGAs inhibit dopamine receptors through these pathways. Positive symptoms are caused by over activity of several pathways such as mesolimbic, mesocortical, and nigrostriatal pathways, among others... When dopamine neurotransmitter system is active, over activity of dopamine activates these circuits, resulting in positive schizophrenia symptoms. However, FGAs inhibit neurotransmitter dopamine receptor 2 activities, preventing these pathways from activating and inhibiting schizophrenia [15].



**Figure 3:** Mechanism Pathways for Antipsychotics of First Generation (FGAs).

### Antipsychotics of second generation

Atypical antipsychotics are sometimes also specified as generation antipsychotics or SGA, SGAs were recently developed and have been shown to enhance schizophrenia therapy while posing fewer dangers. Many schizophrenia drugs have higher risk of side effects and are ineffective. Clozapine, for example, is powerful serotonin antagonist that binds to 5-HT<sub>2A/2C</sub> receptor subtypes. It also has some affinity for dopaminergic (D<sub>2</sub>) receptors, although only to minor degree. Clozapine has antagonistic impact on D<sub>2</sub> receptors in mesolimbic pathway and 5-HT<sub>2A</sub> receptors in frontal cortex when used in combined form. activation of mesolimbic pathways and frontal cortex respectively is reduced when D<sub>2</sub> and 5-HT receptors are blocked. Positive feelings are relieved by D<sub>2</sub> antagonists, whereas negative sensations are relieved by 5-HT<sub>2A</sub> antagonists. difficulty is that frequent use of these drugs at regular dosages generates super-sensitivity in patients, resulting in no additional impact. As result, we must raise dose in order to cure or have effect. There are several substances that increase dopamine levels in body and cause schizophrenia in individuals, including as cocaine, amphetamines, and other stimulants [16].

### Adverse reactions of various types

Medications for schizophrenia can have number of side effects, including following:

- antipsychotics with anticholinergic effects have been reported to exacerbate narrow-angle glaucoma, thus patients should be closely watched. most prevalent side effect of chlor-

promazine is opaque deposits in cornea and lens. Patients using quetiapine should have their eyes examined because of possibility of cataracts. Those who take more than 800 mg of thioridazine per day are at risk of getting retinitis pigmentosa.

- Urinary hesitancy and retention have been linked to low-potency FGAs and clozapine. Urinary incontinence can affect up to 44% of clozapine users, and it can last up to year in 25% of cases.
- When compared to SGAs, FGAs and risperidone have higher risk of causing sexual dysfunction.
- Antipsychotic medication can induce temporary leukopenia. Clozapine, chlorpromazine, and olanzapine are three antipsychotics having highest risk of haematological problems. Clozapine is linked to higher risk of neutropenia or agranulocytosis than other antipsychotics.
- Both FGAs and SGAS can induce photosensitivity, resulting in severe sunburn.
- Dermatological allergic responses have occurred on rare instances, typically eight weeks following commencement of antipsychotic medication.
- Clozapine has been linked to sialorrhoea in roughly 54 percent of schizophrenia patients. This effect's mechanism is unclear.

Antipsychotic medicines' differing safety profiles may be attributable to their actions on different neuroreceptor systems [17].

### Evaluation of progress

Recovery from schizophrenia therapy is defined empirically and subjectively, as it is in other medical specialities. Remission of symptoms and patient's return to full-time job or college enrolment are objective measures of recovery. There are several ways for assessing progress of schizophrenia patients. As numerical indices of progress, Brief Psychiatric Rating Scale (BPRS) and Positive and Negative Syndrome Scale (PANSS) were established, for example. Positive Symptom Rating Scale and Brief Negative Symptom Assessment is two four-item measures used by clinicians. patient's subjective aspects of recovery are measured in terms of life satisfaction, hope, understanding of his or her mental disease, and empowerment. Despite ongoing treatment improvements, life expectancy of patients with schizophrenia is lowered by 10 to 25 years when compared to that of healthy people. Management-related adverse events, inadequate treatment of associated medical disorders, and suicide have all been linked to higher mortality among people with schizophrenia [18].

### Conclusion

Schizophrenia is complicated, chronic mental health illness marked by wide range of symptoms, including delusions, hallucinations, and disordered speech or behaviour, according to findings of this study. Schizophrenia is difficult illness that need immediate treatment. Although present pharmaceutical and nonpharmacological therapy options can help patients improve adaptive functioning, it is hoped that future research will address treatment gaps and maybe lead to cure for schizophrenia. articles examined here are all authored by professionals who have been trained in system that effectively perpetuates itself. Although there may be disagreement among those professions, they all approach problem from medico-social perspective. As result, different viewpoints are rarely heard or even recognised.

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