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Review Article

Advances in Schizophrenia Treatment: Current Pharmacological Strategies and Emerging Therapies

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ABSTRACT

Schizophrenia is a long-term mental disorder that affects how a person thinks, feels, and behaves, often leading to serious challenges in daily life. Over time, its treatment has improved significantly, moving from older antipsychotic drugs with many side effects to newer medications that are safer and more effective. However, issues like treatment resistance and poor medication adherence still remain. Recent research is exploring new treatment options that target different brain pathways, such as glutamate and acetylcholine systems. There is also growing interest in personalized medicine, where treatment is tailored to each individual. Overall, ongoing advancements offer hope for better management and improved quality of life for people living with schizophrenia

INTRODUCTION

Schizophrenia is a global condition. Schizophrenia's severe symptoms and chronic, long-lasting pattern frequently result in a significant level of disability (1). When taken consistently and as directed, medications and other therapies for schizophrenia can help lessen and manage the illness's upsetting symptoms (2). However, some patients may not benefit much from the medicines that are currently available, or they may stop treatment too soon due to unpleasant side effects or other reasons (3). Even with successful treatment, the illness's aftereffects, such as missed chances, stigma, lingering symptoms, and adverse drug reactions, can be extremely upsetting (4).

Delusions are erroneous personal ideas that cannot be supported by logic, contradicting data, or one's typical societal conceptions (5). Different topics can be found in delusions. For instance, patients with paranoid-type symptoms, which affect about one-third of individuals with schizophrenia, frequently experience delusions of persecution, which are illogical and false ideas that they are being betrayed, harassed, poisoned, or the target of a conspiracy (6,7).

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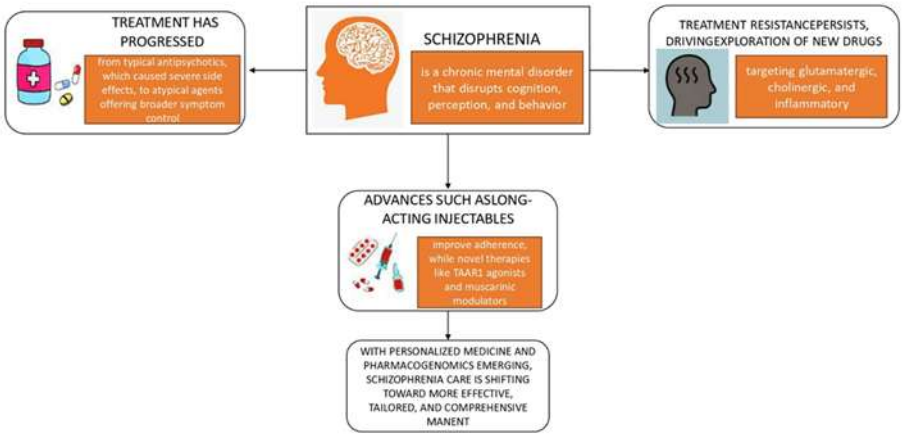

MYOLOGY

A severe, long-lasting, and incapacitating brain disorder is schizophrenia. Schizophrenia affects about 1 percent of people in their lifetime; in any given year, over 2 million Americans have the disorder (2). Even while schizophrenia affects both men and women equally, men typically experience symptoms in their late teens or early twenties, while women typically experience symptoms in their twenties to early thirties (8). Schizophrenia patients frequently have frightening symptoms including hearing voices inside their heads that others cannot hear or thinking that others are reading their minds, manipulating their thoughts, or planning an attack (5). Due to these symptoms, they could become reclusive and afraid. They may behave and speak in such a disorganised manner that others may find them frightening or unintelligible (9). Most persons with schizophrenia experience some symptoms throughout their lives, even though many of them can be relieved by current medications; it has been predicted that just one in five people fully recover (10).

ETIOLOGY

EXTERNAL INFLUENCES

Schizophrenia is aetiologically related to certain features of one or both parents' conduct, dispositions, or attitudes, or to specific ways of family interactions (11).

NEUROLOGICAL FACTORS

Postmortem examinations, cranial CT scans, and MRI scans reveal enlarged ventricles and modest cortical atrophy in certain schizophrenia patients. PET (Positron Emission Tomography) reveals reduced glucose utilisation and hypo frontality in the dominant temporal lobe (12). Positron Emission Tomography (PET) scans have revealed reduced glucose utilization and hypo frontality (reduced activity in the frontal lobes) in the dominant temporal lobe (13). Additionally, conditions such as Huntington's chorea and chronic temporal lobe epilepsy are associated with an increased risk of schizophrenia-like symptoms. Electroencephalogram (EEG) studies have also shown that individuals with schizophrenia often exhibit higher levels of theta activity, rapid activity, and paroxysmal activity compared to healthy controls (14).

PRECIPITATING FACTORS: -

STRESS: A sensitive person's vulnerability to the beginning of schizophrenia is likely triggered by a

greater number of stressful events in their life prior to the onset or relapse (15).

1. **PHYSICAL ILLNESS:** In most cases, the correlation between schizophrenia and physical sickness or childbearing appears to be caused by general stressful psychological and physiological variables rather than a specific causal agent.

2. **SUBSTANCE ABUSE:** sing mind-altering substances such as cannabis, amphetamines, LSD, or alcohol can trigger or intensify psychotic symptoms in some individuals. Among these, cannabis use—particularly during the teenage years—has been linked to an earlier development of schizophrenia, especially in people who are already genetically vulnerable to the condition.

MAINTAINING FACTORS:

1. Social Factors

Schizophrenia was found to be more prevalent among those with lower socioeconomic position, even though its prevalence is rather consistent throughout cultures. Instead of being the cause of schizophrenia, this is now explained by a downward social drift (16). There have been reports of high rates of schizophrenia among migrants. Unsettled individuals who are growing mentally sick may be the source of this excessive movement. In susceptible individuals, the impact of a new environment may potentially contribute to the development of sickness (17). Living alone, unmarried, and having few friends are examples of social isolation that may lead to schizophrenia, according to a retrospective study that compared schizophrenics with controls (18).

2. Deviant Role Relationships

There were reports of two different kinds of aberrant family patterns.

(i) A skew in marriage where one parent gave in to the idiosyncrasies of the other, which took over the family

(ii) A marital fracture where the parents held divergent opinions, causing the chills to have conflicting allegiances (19).

3. Disordered Family Communication

Amorphous (vague, indeterminate, loose) and fragmented (early interrupted, poorly integrated, and without closure) parents have been shown to have a higher risk of schizophrenia in their offspring.

Schizophrenia has no single recognised cause. Many illnesses, like heart disease, are caused by a combination of behavioural, genetic, and other variables; schizophrenia might be one of them. Although the exact causes of schizophrenia are still unknown, scientists are using every resource available in contemporary biomedical research to look for genes, crucial stages in brain development, and other potential contributing factors(20).

DISEASE MECHANISMS

Magnetic resonance imaging (MRI) and computerised axial tomography (CAT) scans reveal larger ventricles, especially in the lateral and third ventricles, in schizophrenia subtypes. In comparison to matched controls, current research also demonstrates a little but noticeable reduction in brain size. The ventricular expansion is most noticeable in the left temporal horn, while the decreased cortical size is most noticeable in the left temporal lobe. These changes seem to be consistent with brain asymmetry. These alterations seem to align with modifications in

neuropsychological assessments, and these patients might not respond well to conventional antipsychotic drugs. Instead of reflecting a reduction in the quantity of neurons in the prefrontal lobe cortex, decreasing cortical thickness indicates a decrease in the distance between neurons. This may result in fewer axonal and dendritic connections between cells, which could lead to a loss of connectivity that is crucial for neuronal adaptability and central nervous system homeostasis. It is probable that these alterations align with the effectiveness of aberrant neural pruning(21).

The presence of serotonergic receptors on dopaminergic axons is known to reduce dopamine release, at least in the striatum, when these receptors are stimulated. Because serotonergic and dopaminergic neurones have similar distributions, although being somewhat more diffuse, these two neurotransmitter systems can innervate the same region. In the cortex, serotonin and the D4 receptor have been identified to colocalize(22).

Abnormal brain scans in patients with schizophrenia show greater levels of whole blood 5HT, which are associated with larger ventricles. Schizophrenic patients' symptoms worsened by 5HT antagonists are reversed by common antipsychotics with strong 5HT2 receptor antagonist activity(22).

There is mounting evidence that schizophrenia is associated with a DA receptor deficiency. Numerous PET investigations have revealed localised abnormalities in the brain, such as elevated glucose metabolism in the left temporal lobe and frontal lobe. Both dopaminergic hypofunction in the frontal emporia areas and the head of the nucleus may be indicated by this. The subpopulation of the schizophrenic may have lower densities of D1 receptors in the carotid nucleus and pre fontal cortex, according to PET studies evaluating dysfunction. Considering the heterogeneity of the traditional presentation of schizophrenia, it has also been proposed that the DA hypothesis might apply more to neuroleptic response psychosis, with schizophrenia potentially resulting from a variety of aetiologies(23).

It is generally thought that the antipsychotic action of antipsychotic medications is due to the inhibition of dopamine receptors, which are primarily found in the mesolimbic regions, whereas the extrapyramidal adverse effects are caused by the blocking of the D2 receptor. SHT2 receptors are specifically impacted by the more recent or conventional antipsychotics. While normal medications are effective in treating both positive and negative systems of schizophrenia with fewer side effects, typical antipsychotics are effective in treating positive symptoms of the disorder. When it comes to treating resistant schizophrenia, clozapine works well(23).

Researchers are looking into hereditary components of schizophrenia. It seems likely that a predisposition to develop the disorder is created by a combination of genes. Furthermore, neonatal problems, a variety of nonspecific stresses, and prenatal challenges such intrauterine malnutrition or viral infections appear to have an impact on the development of schizophrenia. Nevertheless, the mechanism of transmission of the genetic predisposition remains unclear, and it is now impossible to predict with any degree of accuracy whether a particular individual would acquire the condition or not(24).

Researchers are looking into several human genome regions to find genes that might increase a person's risk of developing schizophrenia. Although it hasn't been verified, the strongest evidence to far points to chromosomes 13 and 6. The fundamental understanding of brain chemistry and how it relates to schizophrenia is quickly

growing. It has long been believed that neurotransmitters—substances that facilitate communication between nerve cells—play a role in the onset of schizophrenia. Though not yet confirmed, it is believed that the condition is linked to an imbalance in the brain's intricately linked chemical processes, possibly involving the neurotransmitters glutamate and dopamine. There is promise in this field of study(25).

Schizophrenia may be a developmental illness caused by neurones forming improper connections during foetal development, according to developmental neurobiologists supported by the National Institute of Mental Health (NIMH). Until puberty, when normal brain changes that take place during this crucial stage of maturation interact negatively with the defective connections, these errors may remain dormant. Finding prenatal variables that might be somewhat responsible for the apparent developmental abnormalities has been prompted by this research(24).

SIGNS AND SYMPTOMS

The initial symptoms of schizophrenia frequently manifest as perplexing or even startling behavioural abnormalities. Family members may find it more challenging to deal with the symptoms of schizophrenia if they recall how active or involved the individual was prior to their illness. An "acute" phase of schizophrenia occurs when severe psychotic symptoms appear suddenly. Hallucinations, which are disruptions of sensory perception, and/or delusions, which are erroneous but deeply held personal beliefs that arise from an inability to distinguish between real and unreal events, are hallmarks of "psychosis," a prevalent symptom in schizophrenia. The psychotic symptoms may be preceded, observed alongside, or followed by less evident symptoms such social disengagement or withdrawal, or by aberrant speech, thought, or behaviour(25).

A person with "chronic" schizophrenia, or a persistent or recurrent pattern of illness, usually needs long-term care, usually including medication, to manage their symptoms. They also frequently do not entirely recover to their normal functioning(25).

1. CHARACTERISTIC SYMPTOMS:

Two or more of the following each persisting for a significant portion of at least a 1-month period.

1) Delusion

2) Hallucination

3) Disorgnized speech

4) Grossly disorganized or cationic behavior

5) Negative symptoms

2. SOCIAL/ OCCUPATIONAL DYSFUCTION:

One or more key areas of functioning, including interpersonal relationships at work or self-care, have been much lower than before the condition began for a considerable amount of time(21).

DURATION

At least six months of consistent symptoms of the illness. This needs to include symptoms that meet the requirement for at least one month. Prodromal or lingering symptoms may be present during this six-month period(21).

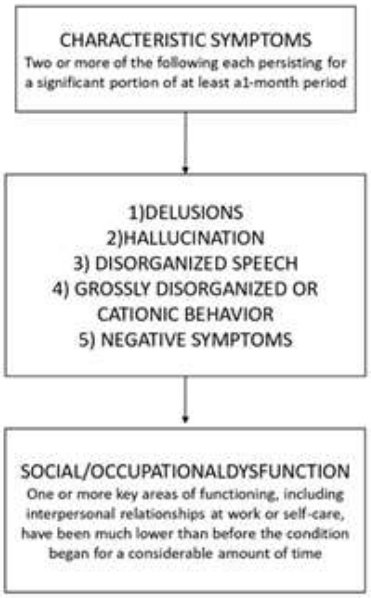

Fig.1. Signs and symptoms

Current treatment approaches are based on both clinical study and experience because schizophrenia may not be a single disorder, and its causes are still unknown. These methods are selected based on their capacity to minimise schizophrenia symptoms and the likelihood that they will recur(26).

Recommended Duration for Antipsychotic Medication Use in Individuals with Schizophrenia

Since the middle of the 1950s, antipsychotic drugs have been on the market. They have significantly improved each patient's prognosis. These drugs typically enable the patient to perform more appropriately and successfully while lowering the psychotic symptoms of schizophrenia. Although antipsychotic medications are now the best treatment for schizophrenia, they neither "cure" the disorder nor guarantee that psychotic episodes won't occur again. Only a licensed medical professional with extensive training in treating mental illnesses can decide on the best course of action and dosage. Each patient receives a customised dosage of medication because individuals may differ greatly in the amount of medication required to alleviate symptoms without causing problematic side effects(27).

Most individuals with schizophrenia exhibit significant improvement after using antipsychotic medications. Nonetheless, some people do not appear to require the drugs, while others do not benefit much from them. Which patients will fit into these two categories and how to differentiate them from most patients who do benefit from antipsychotic medication treatment are both challenging tasks(27).

Since 1990, several novel antipsychotic medications (referred to as "atypical antipsychotics") have been become available. Although the first of these, clozapine (Clozaril®), has been demonstrated to be more effective than other antipsychotics, patients must be monitored with blood tests every one or two weeks due to the possibility of serious side effects, particularly agranulocytosis (loss of the white blood cells that fight infection). Even more recent antipsychotic medications, like aripiprazole (Abilify), ziprasidone (Geodon), quetiapine (Seroquel), olanzapine (Zyprexa®), and risperidone (Risperdal®), are safer than clozapine and may also be better tolerated. However, they might or might not be as effective at treating the condition as clozapine. A number of other antipsychotics are presently being developed(28).

Antipsychotic medications are frequently highly successful in treating some symptoms of schizophrenia, especially delusions and hallucinations; however, they may not be as beneficial for other symptoms, like decreased motivation and emotional expressiveness. Indeed, the adverse effects of the older antipsychotics (also known as "neuroleptics"), such as haloperidol or chlorpromazine, might even mimic the more challenging symptoms. Lowering the dosage or

changing medications can frequently lessen these side effects; newer medications, such as risperidone, quetiapine and olanzapine seem to be less prone to cause this issue. Other symptoms may seem to get worse when persons with schizophrenia experience depression. Adding an antidepressant prescription may help with the symptoms(29).

Antipsychotic drugs used to treat schizophrenia can occasionally cause anxiety in patients and their families. They might be worried about the potential for addiction in addition to the negative effects. However, those who take antipsychotic drugs do not experience an addictive behaviour(29).

Another myth regarding antipsychotic medications is that they function as a "chemical straitjacket" or a form of mind control. Proper dosage of antipsychotic medications does not "knock out" or take away a person's free will. While sedation is a side effect of these medications, and this effect may be helpful when starting treatment, especially if the patient is very agitated, the drugs' main benefit is their capacity to lessen the hallucinations, agitation, confusion, and delusions that accompany a psychotic episode. Antipsychotic drugs should therefore gradually enable a person with schizophrenia to act more logically in the world(28).

Duration of Antipsychotic Medication Use for Individuals with Schizophrenia

After recovering from an acute episode, people who use antipsychotic drugs are less likely to experience psychotic episodes in the future. Some persons who have recovered will relapse even after receiving ongoing pharmacological treatment. When medicine is stopped, recurrence rates are significantly greater. Most of the time, ongoing drug treatment just lessens the severity and frequency of relapses, not "prevents" them. Higher dosages are typically needed to treat severe psychotic symptoms than for maintenance treatment. A brief dosage increase could stop a full-blown relapse if symptoms return on a lesser dosage(30).

It is crucial that individuals with schizophrenia collaborate with their physicians and family members to follow their treatment plan because stopping antipsychotic drugs or taking them irregularly increases the risk of relapse. The degree to which individuals adhere to the treatment regimens that their physicians propose is known as adherence to treatment. Attending clinic appointments, taking prescribed medications at the appropriate times and doses every day, and/or closely adhering to other treatment protocols are all components of good adherence. People with schizophrenia frequently struggle to stick to their treatment plans, but there are several measures that can help and enhance their quality of life(30).

Schizophrenia patients may not follow their treatment plans for a number of reasons. Patients may not think they are sick and hence refuse to take their medication, or they may think so haphazardly that they forget to take their daily doses. Friends or family who don't understand schizophrenia could give the person with schizophrenia improper advice about stopping treatment once they're feeling better. Although doctors are crucial in helping their patients stick to their treatment plans, they might not ask their patients how frequently they take their prescriptions or might not be ready to comply with a patient's request to attempt a new treatment or change dosage. Some individuals claim that their drug side effects are greater than their actual ailment. Substance misuse can also reduce the efficacy of treatment by causing patients to stop taking their medications. Good adherence may

become much more difficult when any of these issues are combined with a complex treatment plan(31).

Thankfully, there are a variety of tactics available to patients, physicians, and families to enhance adherence and stop the condition from getting worse. Long-acting injectable versions of certain antipsychotic drugs, such as fluphenazine, perphenazine, and haloperidol are available, negating the requirement for daily pill intake. Creating a greater range of long-acting antipsychotics, particularly the more recent ones with less severe side effects that may be administered by injection, is a primary objective of current research on therapies for schizophrenia. Patients and carers can keep track of when prescriptions have been taken or not by using medication calendars or pill boxes labelled with the days of the week. Patients may find it easier to remember and follow their medication schedule if they use electronic timers that sound an alert when it's time to take their prescriptions or if they arrange their medication taking with regular daily activities like eating. Encouraging family members to see patients take their oral medications can help guarantee adherence. Doctors can also determine when pill intake is causing problems for their patients and work with them to make adherence simpler by using a range of additional adherence monitoring techniques. Helping people stay motivated to take their medications as prescribed is crucial(31).

A crucial component of treatment is educating patients and their families about schizophrenia, its symptoms, and the drugs being prescribed to treat it. This helps to reinforce the need for excellent adherence and should be done in addition to any of these adherence techniques(30).

1. MONOGENIC THEORY

According to this view, schizophrenia is a particular genetic disease caused by a single recessive, dominant, or intermediate gene. It is further hypothesised that schizophrenia is caused by an unidentified metabolic mistake that is characteristic of the genotype(32).

2. TWO GENE THEORY

The two gene theory, according to which each gene is unique, inherited separately, and has a mutant counterpart, has been put forth. These two genes, along with their counterparts, can result in a child who is intellectually retarded or autistic, or in a normal or creative person(32).

3. POLYGENIC THEORY

This theory is predicated on the idea that several genes situated at various chromosome locations may exhibit similar expression patterns and cumulative effects. People are more likely to exhibit symptoms of schizophrenia if they have an excess of these genes(32).

THE MAIN NEUROCHEMICAL THEORIES ARE

- DOPAMINE THEORY
- GLUTAMATE THEORY
- TRANSMETHYLATION

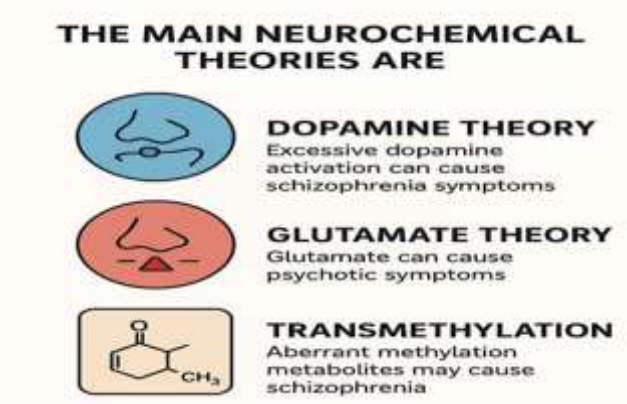

Fig.2. Neurochemical theories

DOPAMINE THEORY

Carlsson was the one who suggested this. The behavioural condition associated with schizophrenia can be caused by excessive dopamine activation. Strong D2 receptor antagonists, such as apomorphere and bromocriptine, can make schizophrenia symptoms worse. There have been reports of higher dopamine concentrations in the left hemisphere's amygdale and greater dopamine receptor density in the caudate nucleus, putamen, and nucleus accumbens. Imaging studies provide the strongest evidence for elevated dopamine release in individuals with schizophrenia(33).

GLUTAMATE THEORY

Glutamate is another transmitter that has been connected to the pathophysiology of schizophrenia. Glutamate NMDA receptor antagonists, like phencyclidine and dizocilpine, cause psychotic symptoms in people, including hallucinations and thought disorders. Postmortem brains of schizophrenia patients have also been found to have lower glutamate concentrations and glutamate receptor densities(34).

TRANSMETHYLATION

The methylated chemical compound mesclaine, a hallucinogen, shares a chemical bond with both dopamine and adrenaline. Osmond proposed the formation of aberrant methylation metabolites in the brain as a potential cause of schizophrenia's psychiatric symptoms. A methylated compound was found in the urine of some people with schizophrenia, which seemed to lend some support to this notion(35).

Dopaminergic receptor and dopaminergic neuron.

There are two main receptor type.

D1 – which increases adenyl cyclare activity.

D2 – which medicate main presynaptic and post synaptic inhibitory action of dopamine.

D3 and D4 receptors belong to the same group as D2. The antipsychotic drug probably owes their therapeutic effect mainly to blockade of D2 receptors.

As previously mentioned, approximately 80% of D2 receptors must be blocked for antipsychotic effects to occur. Several techniques can be used to measure antagonistic activity at D2 receptors in experimental antigens. For example, in vitro, by preventing radioactive D2 antagonists from binding to brain membrane fragments, amphetamine-induced stereotypic behaviour or apomorpheine-induced turning behaviour can be inhibited in animals with unilateral strial lesions. Phenothiazeries, thioxanthenes, and butyrophenones are the primary groupings that exhibit the same preference for D2 receptors over D1 receptors. While clozapine is largely nonselective between D1 and D2 that has a high affinity for D4, some of the more recent drugs are extremely selective for D2 receptors(36).

It has been discovered that all antipsychotic medications first speed up dopamine synthesis in areas with dopaminergic nerve terminals. An increase in tyrosme hydroxylase activity and a rise in the levels of homoranillic acid, DOPAC, and other dopamine metabolites are indicators of this. Simultaneously, electrical activity recording has demonstrated that these medications first boost the activity of dopaminergic neurones in the substantia nigra and ventral tegmentum of the midbrain. While the unintended motor impact caused by antipsychotic medications is thought to be caused by effects on the former, the latter is thought to correlate with antipsychotic effects. Therefore, dozapine, an unusual medicine that has no motor

effects, only affects the ventral segmental neurones, while haloperidol, a conventional drug with undesirable motor effects, works on both sides of dopamine neurones(36).

ANTIPSYCHOTIC DRUGS USED IN SCHIZOPHRENIA:

Category	Drugs
Typical antipsychotics	Chlorpromazine Loxapine Penfluridol Fluphenazine Trifluperidol Triflupromazine Haloperidol Thioridazine Trifluoperazine Pimozide Zuclopenthixol Prochlorperazine Flupenthixol
Atypical antipsychotics	Clozapine Olanzapine Risperidone Ziprasidone Quetiapine
Deport preparations	Fluphenazine decanoate Haloperidol decanoate Flupenthixol decanoate Zuclopenthixol decanoate Penfluridol Pimozide

MECANISM OF ACTION OF ANTIPSYCHOTIC DRUGS

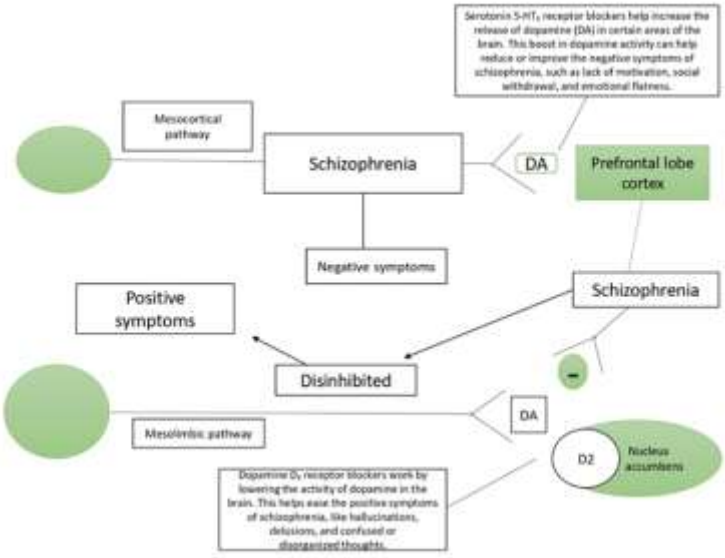

Fig.3.MOA of Antipsychotic Drugs

As shown in the above (fig.3), the mechanism of action of antipsychotic drugs in schizophrenia involves modulation of dopamine activity in specific brain pathways. The diagram demonstrates how antipsychotics primarily target dopamine D2 receptors in the mesolimbic pathway, which results in a reduction of dopamine activity. This decrease alleviates the positive symptoms of schizophrenia, such as hallucinations, delusions, and confused thinking, which are depicted in the pathway leading from "Schizophrenia" to "Positive symptoms" through "Disinhibited" and finally to the "Nucleus accumbens" where D2 receptors are blocked. The negative symptoms of schizophrenia, including a lack of motivation, emotional withdrawal, and social flatness, are related to reduced dopamine activity in the mesocortical pathway and the prefrontal cortex. The diagram illustrates that serotonin 5-HT2 receptor antagonists (found in newer antipsychotic medications) help boost dopamine release in certain brain areas like the

prefrontal cortex. This increase in dopamine helps improve the negative symptoms of schizophrenia, as highlighted by the connection between “DA” (dopamine) and “Prefrontal lobe cortex” and the explanatory text above the figure. the efficacy of antipsychotics depends on their receptor targets. Typical antipsychotics mainly block D2 receptors and are most effective at managing positive symptoms, but they also cause extrapyramidal side effects due to dopamine blockade in motor pathways such as the extrapyramidal system. In contrast, atypical antipsychotics also block serotonin 5-HT2 receptors, which confers added benefits for negative symptoms and generally results in fewer extrapyramidal side effects. Among the atypical agents, clozapine is well known for its efficacy in treatment-resistant schizophrenia, and its dual-action profile (rapid D2 dissociation and 5-HT2A antagonism) is reflected in the diagram and supported by clinical evidence. The blocking of D2 receptors leads to antipsychotic action in the mesolimbic pathway while serotonin antagonism in the prefrontal cortex improves negative symptoms. This dual mechanism, with the balance between dopamine and serotonin modulation, explains the profile of both typical and atypical antipsychotics as reflected in modern pharmacology. The diagram accurately captures these relationships and the information you provided aligns well with these current scientific concepts(37).

DRUG SIDE EFFECTS

Like almost all medications, antipsychotics have both positive and negative side effects. In the initial stages of medication therapy, patients may have adverse effects such fatigue, agitation, tremor, muscle spasms, dry mouth, or blurred vision. Most symptoms are treatable by reducing the dosage or managed with additional drugs. The adverse effects and responsiveness to therapy of different antipsychotic medications vary from patient to patient. A patient might respond better to one medication than another(38).

The long-term adverse effects of antipsychotic medications can be a far more significant issue. Involuntary movements that mostly affect the mouth, lips, and tongue, but can also occasionally affect the trunk or other body parts including the arms and legs, are the hallmark of tardive dyskinesia (TD). Although TD can develop in individuals who have been treated with the earlier, "typical" antipsychotic medications for shorter periods of time, it happens in approximately 15 to 20 percent of people who have been receiving these medications for several years. Most of the time, TD patients have minimal symptoms and may not even be aware of their motions(39).

All antipsychotic drugs created recently seem to have a far lower chance of causing TD than the more established, conventional antipsychotics. However, the risk is not zero, and they may cause their own negative consequences, such weight gain. Furthermore, if administered at excessive dosage, the newer drugs might cause issues like social disengagement and symptoms like Parkinson's disease, a movement disorder. A lot of current research is focused on the best ways to treat schizophrenia with the newer antipsychotics, which represent a major advancement in treatment(39).

SUBSTANCE ABUSE

Substance abuse is a common concern of the family and friends of people with schizophrenia. Some drug abusers may exhibit symptoms that are like those of schizophrenia, therefore people with schizophrenia may be mistaken for those who are "high on drugs." People with schizophrenia frequently abuse alcohol and/or drugs, and they may have particularly negative reactions to certain

drugs, even though many academics do not think substance abuse causes schizophrenia. The effectiveness of treatment for schizophrenia may be diminished by substance usage. Patients with schizophrenia may experience significant issues when using stimulants (such amphetamines, cocaine, PCP, or marijuana). The use of such medications causes some people's schizophrenia symptoms to worsen. Patients who abuse substances are also less likely to adhere to the treatment regimens that their physicians offer(40).

Schizophrenia and Nicotine: Nicotine dependency from smoking is the most prevalent type of substance use disorder among individuals with schizophrenia. About three times as many people with schizophrenia smoke than the general population in the United States, which has a smoking prevalence of 25 to 30 percent. Smoking and schizophrenia have a complicated relationship, according to research. Smoking has been shown to affect the way antipsychotic medications work, even though patients with schizophrenia may smoke to self-medicate their symptoms. Smokers with schizophrenia require greater dosages of antipsychotic medicine, according to several studies. People with schizophrenia may find it particularly difficult to quit smoking since the symptoms of nicotine withdrawal can temporarily exacerbate their schizophrenia symptoms. Nonetheless, nicotine replacement techniques may be useful in smoking cessation programs. Physicians should closely monitor medication dose and reaction when smoking is initiated or discontinued by individuals with schizophrenia(41).

Psychosocial Treatments for Schizophrenia

Hallucinations, delusions, and incoherence are among the psychotic symptoms of schizophrenia that antipsychotic drugs are good at treating. However, they are not always successful in treating the behavioural symptoms of the condition. Even in cases where psychotic symptoms are mostly absent, many individuals with schizophrenia nonetheless have remarkable difficulties with self-care, motivation, communication, and establishing and maintaining relationships with others. Furthermore, because they frequently experience schizophrenia during the critical years that define a person's career (e.g., ages 18 to 35), people with schizophrenia are less likely to complete the training required for a skilled employment. As a result, many persons with schizophrenia struggle not only with their thoughts and feelings but also with their social and professional skills and experience(42).

The psychological, social, and occupational issues that psychosocial treatments may be most helpful with include these ones. While psychosocial techniques may be helpful for patients with less severe symptoms or for patients whose psychotic symptoms are under control, they are not very helpful for acutely psychotic patients (those who are out of touch with reality or who exhibit vivid hallucinations or delusions). There are many different types of psychosocial therapy for individuals with schizophrenia, and the most of them concentrate on enhancing their social functioning, whether at home, at work, or in the community. Here are descriptions of a few of these methods. Regretfully, different types of treatment are not always readily available in one location(43).

REHABILITATION

Rehabilitation for people with schizophrenia encompasses a broad range of non-medical approaches. The goal of rehabilitation programs is to assist patients and former patients in overcoming obstacles in these areas by emphasising social and vocational training. Programs may cover social skills training,

problem-solving and money management techniques, job training, vocational counselling, and public transit use. These methods are crucial to the success of community-centered treatment for schizophrenia because they give patients the tools, they need to live fulfil lives outside of the safe haven of a mental health facility(44).

INDIVIDUAL PSYCHOTHERAPY

A patient and a mental health practitioner, such as a psychiatrist, psychologist, psychiatric social worker, or nurse, have regularly planned conversations during individual psychotherapy. The topics of the sessions could be past or present issues, relationships, thoughts, feelings, or experiences. By discussing their reality with someone and sharing experiences with a qualified empath. People with schizophrenia can benefit from a wide variety of non-medical rehabilitation techniques. Rehabilitation programs emphasise social and vocational training to help patients and former patients overcome barriers in these areas. Programs may include instruction in social skills, money management and problem-solving strategies, job training, career advice, and using public transportation. Because they provide patients with the necessary resources, these techniques are essential to the success of community-centered therapy for schizophrenia(45).

Outside of it, people with schizophrenia could progressively learn more about their issues and themselves. They can also learn to distinguish between the distorted and the real. According to recent research, outpatients with schizophrenia may benefit from cognitive-behavioral therapies that teach coping and problem-solving techniques, as well as supportive, reality-oriented individual psychotherapy. Psychotherapy is most beneficial after pharmacological treatment has alleviated a patient's psychotic symptoms, but it cannot replace antipsychotic medication(45).

How to Support Someone Living with Schizophrenia

Patients with schizophrenia and other mental diseases, as well as their families, can benefit from the knowledge and support offered by active family, peer, and advocacy support organisations. This document concludes with a list of some of these organisations(46).

Schizophrenia sufferers may require assistance from family members or community members in a variety of circumstances. Schizophrenia patients frequently refuse treatment because they think that their hallucinations or delusions are real and that they don't need mental health care. It may occasionally be necessary for friends or family to actively assist in getting them seen and assessed by a professional. Any attempt to provide treatment is impacted by the civil rights issue. Families and community organisations may be frustrated in their attempts to ensure that a seriously mentally ill person receives the necessary assistance, as laws protecting patients from forced commitment have become increasingly stringent. These rules differ from state to state, but in general, police can help get someone who has a mental illness that makes them hazardous to others or themselves an emergency psychiatric evaluation and, if needed, hospitalisation. In certain locations, if a person refuses to voluntarily seek treatment, workers from a nearby community mental health centre may assess their disease at home(46).

Sometimes, the only people who are aware of the peculiar behaviour or thoughts that a person with schizophrenia has exhibited are their family members or other close relatives. Family members or friends should ask to talk with the person evaluating the patient because people might not

provide such information during an evaluation. This way, all pertinent information can be considered(47).

It's also critical to make sure a person with schizophrenia receives ongoing care after being sent to the hospital. Psychotic symptoms frequently recur when a patient stops taking their meds or attending follow-up appointments. Recovery can be positively impacted by supporting the patient over the course of treatment and encouraging them to continue. Some persons with schizophrenia become so insane and chaotic that they are unable to take care of their basic requirements, like clothing, food, and shelter, if they are not treated. People who suffer from serious mental diseases like schizophrenia sometimes wind up on the streets or in prisons, where they hardly ever get the kind of care they require(47).

When persons with schizophrenia make odd or obviously untrue remarks, those who are close to them frequently don't know how to react. The strange hallucinations or ideas appear to be quite real to the person suffering from schizophrenia; they are not only "imaginary fantasies." While accepting that things may appear differently to the patient, family members or friends might express their disagreement with the patient's conclusions or that they do not share their perspective, rather than "going along with" their delusions(48).

Those who know the individual with schizophrenia well may also find it helpful to document the kinds of symptoms that have manifested, the drugs (including dosage) that have been taken, and the outcomes of different therapies. Family members may be better able to recognise the signs in the future if they are aware of what has previously been present. Even better and sooner than the patients themselves, families may be able to spot some "early warning signs" of possible relapses, like increasing withdrawal or altered sleep habits. As a result, psychotic episodes can be identified early and treated to avoid a full-blown relapse. Additionally, the family can assist those treating the patient in locating the optimal course of therapy more rapidly if they are aware of which medications have previously produced problematic side effects, and which have helped(48).

Apart from actively seeking assistance, family, friends, and peer groups can offer support and motivate the individual with schizophrenia to restore their talents. Setting realistic goals is crucial since a patient who feels under pressure and/or frequently chastised by others is likely to experience stress, which can exacerbate symptoms. People with schizophrenia need to be aware of when they are doing things correctly, just like everyone else. Long-term, a constructive approach might be more beneficial than a critical one. This advice is applicable to all those who meet the individual(47).

WHAT IS THE PROGNOSIS FOR SCHIZOPHRENIA?

Over the past 25 years, the prognosis for individuals with schizophrenia has improved. Even though there is now no completely successful treatment, it is crucial to keep in mind that many patients recover enough to enjoy fulfilling, independent lives. We should be able to assist more patients in achieving positive results as we gain more knowledge about the causes and therapies of schizophrenia(49).

Numerous outcomes are possible, according to studies that have tracked individuals with schizophrenia over extended periods of time, from the first episode until old life. Certain characteristics, such as a history of normal social, academic, and occupational adjustment before to

sickness, are typically linked to improved outcomes when studying large groups of individuals. However, the existing level of information makes it impossible to forecast long-term outcomes with enough accuracy(49).

Given the intricacy of schizophrenia, study is necessary to answer the main problems regarding this condition, including its cause or causes, prevention, and therapy. People who claim to know "the cure" or "the cause" of schizophrenia should be avoided by the general population. Such assertions have the potential to create irrational expectations that, if not met, result in even more disappointment. Even though there has been progress in understanding and treating schizophrenia, more research is desperately needed. From molecular genetics to extensive population epidemiology studies, NIMH, the principal Federal agency for mental disorder research, carries out and funds a wide range of mental illness research. It is believed that this extensive scientific endeavour, which includes fundamental brain investigations, will keep shedding light on concepts and mechanisms crucial to comprehending the origins of schizophrenia and creating more potent therapies(49).

TYPES OF SCHIZOPHRENIA AND DIAGNOSTIC CRITERIA

The International Statistical Classification of Disease and Related Health Problems, 10th division (ICD-10) WHO, Geneva, 199244, divides schizophrenia into the following categories: residual, post-syndromic and other schizophrenia, hebephrenic, catatonic, differentialized, paranoid, and schizophrenia unspecified. Misconceptions over the legitimacy of the diagnostic process45 have resulted from the history of schizophrenia diagnosis being misinterpreted. The diagnosis of typical cases of schizophrenia has been a source of worldwide disagreement among diagnosticians for the majority of the twentieth century(50).

Schizophrenia is more challenging to diagnose since its symptoms can occasionally resemble those of other serious mental disorders, such bipolar disorder or even depression47. Schizophrenia, like many other mental illnesses, is diagnosed based on the behaviour of the individual being evaluated. To be diagnosed with the illness, a person must fulfil several diagnostic requirements. This is dependent on whether specific signs and symptoms are present and how long they last. Standardised diagnostic criteria, systematic interviews, and psychiatric rating scales are among the tools used to diagnose schizophrenia. The diagnostic and statistical handbook of mental disorders (DSM-IV), fourth edition, American Psychiatric Association, and the ICD-10 diagnostic criteria issued by the World Health Organisation are the two primary diagnostic criteria that offer distinctive signs and symptoms of schizophrenia and its subtypes. Present state examination (PSE), composite international diagnostic interview (CIDI) schedule for affective disorders and schizophrenia (SADS), diagnostic interview schedule (DIS), and comprehensive assessment of symptoms and history (CASH) are examples of structured interviews that are intended to give a thorough basis of information about past psychopathology and functioning that is pertinent to the diagnosis, prognosis, and overall severity for the symptomatologic assessment of the psychiatric illness. Rating scales are usually employed to monitor changes in clinical status over time, whereas structured interviews and diagnostic criteria are utilised to diagnose patients with a variety of symptoms. The original rating system, the Brief Psychiatric Rating system (BPRS), can rate symptoms such as psychic anxiety, low mood, distorted thinking, emotional withdrawal, blunted

affect, and conceptual disorganisation. The TLC scale was developed to evaluate formal thought disorder in people with schizophrenia(50).

CLINICAL FEATURES

Disturbances in thought and verbal behaviour, perception, mood, motor behaviour, and interpersonal relationships are hallmarks of schizophrenia. None of the following clinical characteristics are pathogomonic on their own; the diagnosis is wholly clinical. The clinical features include disorders of speech and thought (autistic thinking, loosening of associations, thought blocking, neologisms, mutism, poverty of speech, preservation, variegation, delusions, and ambivalence), disorders of perception (visual and auditory hallucinations), disorders of affect (apathy, emotional blunting, and anhedonia), disorders of motor behaviour (either increase or decrease in psychomotor activity), and negative symptoms such as alogia, affective flattening, inattentiveness, anhedonia, and avolition-apathy. Because they are not found in healthy people, delusions, hallucinations, and thought disorders are referred to as positive symptoms(51).

NEUROCHEMICAL BASIS FOR SCHIZOPHRENIA

Deficiency in monomine oxidase (MAO) activity, impairment of noradrenergic function (NA), impairment of neuroactive pepdide systems, impairment of gamma-amino butyric acid (GABA) system function, impairment of serotonergic function, and excitatory amino acid systems have been the main focal points of the neurochemical basis for schizophrenia research. Chronic schizophrenics decreased peripheral MAO activity has been the most often reported biochemical finding in schizophrenia. 22 patients with schizophrenia had their cerebrospinal fluid (CSF) examined for platelet MAO activity and amine metabolites, and the results showed a low MAO activity. In seven areas of the postmortem brains of 39 schizophrenia patients and 44 control participants, Owen et al. found a decrease in MAO activity. Stein et al. hypothesised that the absence of goal-directed behaviour seen in schizophrenics might be explained by a degradation of the cortical noradrenergic system. By revealing a marked decrease in dopamine beta hydroxylase (DBH) activity in postmodern brain samples from schizophrenia patients, they support this theory. Hartmann et al. expanded on Stein and Wise's theory by speculating that an imbalance between dopamine and NA may contribute to the pathophysiology of schizophrenia and that a decrease in cortical DBH activity may result in an elevated concentration of NA in the cortical region(52).

However, there isn't much proof that schizophrenia patients have a central noradrenergic deficiency. There was no discernible difference in DBH activity between controls and schizophrenics in any of the six brain regions that Cross et al. evaluated from 12 control and 12 schizophrenics. The use of peripheral bodily fluids and tissues, such as lymphocytes and plasma serum, to evaluate central noadrenergic function in schizophrenia has been attempted multiple times. Overall, the findings have been conflicting and frequently of questionable significance in regulating noradrenergic function(53).

Numerous studies have examined the potential for changed levels, aberrant brain opioid metabolism, and the involvement of neuropeptides in schizophrenia. According to Swedish researchers Terenius et al., people with schizophrenia have higher levels of endogenous opioid peptide in their cerebrospinal fluid. In their study of schizophrenia, Lindstorm et al. found that the CSF

percentage of the neuropeptide was higher in four out of six patients with acute schizophrenia and two out of nine patients with chronic schizophrenia. However, Naber et al. used a radioreceptor test to demonstrate a substantial decrease in CSF opioid activity in male schizophrenia patients. It has also proven challenging to clinically support the idea that schizophrenia may be linked to opioid system activity. The results of giving beta endorphins to people with schizophrenia have been equivocal. By measuring the activity of glutamate decarboxylase (GAD), an enzyme that catalyses the decarboxylation of glutamate from GABA and serves as a marker for GABA-ergic neurones, Roberts hypothesised that the loss of GABA in schizophrenia could be easily confirmed(54).

Bird et al. later discovered a substantial decrease in GAD activity in schizophrenics' protmorten barin samples. Examination of the CSF levels of 87 people, 29 normal control subjects, 11 patients with schizophrenia, 26 patients with depression, 6 patients with mania, and 15 patients with anorexia nervosa revealed reduced GABA levels. Cross and colleagues, however, discovered that the levels of GABA in the brain areas of control and schizophrenia patients were comparable. A substantial decrease in GABA agonists, such as baclofen, is not supported by pharmacological evidence, and muscimol does not lessen symptoms(54).

Tryptophan, the precursor of 5-hyfroxy tryptamine (5-HT), has been shown to have a lower plasma content in acute schizophrenia patients. However, the usefulness of oral tryptophan dosages as a treatment to address this apparent deficiency has yielded conflicting findings. Joseph et al. conducted a direct investigation of central 5-HT metabolism in schizophrenia. They found no widespread alteration in 5-HT metabolism in the brains of schizophrenia patients after measuring the levels of 5-HT, 5-hydroxy indole acetic acid (5-HIAA), and their precursor tryptophan in three samples of post-mortem brain tissue from 15 schizophrenia patients and 23 controls. Schizophrenics with a family history of schizophrenia have greater amounts of homovanillic acid (HAV), the primary byproduct of dopamine metabolism, in their cerebrospinal fluid (CSF). Numerous studies have examined dopamine receptors in the brains of people with schizophrenia, and it is generally agreed upon that the basal ganglia have more D2 receptors. Higher D2 receptor densities were found in schizophrenic brains compared to 15 control brains in post-mortem dopamine receptor investigations(54).

Glutamate transmission anomalies have been found in several schizophrenia patients' postmortem examinations. Schizophrenic individuals, for instance, have changed glutamate concentrations, decreased cortial glutamate release, and increased cortical expression of N-methyl-D-aspartate (NMDA) receptor units and glutamate reuptake in the frontal cortex. However, lateralised alterations in glutamate absorption sites have also been found in the amygdala and other parts of the brain(52).

MANAGEMENT OF SCHIZOPHRENIA

Pharmacological intervention, electroconvulsive therapy (ECT), and psychosocial therapies such as psychoeducation, group and individual psychotherapy, family therapy, and psychosocial psychotherapy can all be used to treat schizophrenia. By applying electrodes to the scalp, a variable frequency electrical stimulation shock is administered to induce a seizure for therapeutic purposes. Its application in individuals with schizophrenia has fewer encouraging results. Patients who don't react well to antipsychotic medications may try ECT. Both during and after

ECT treatment, antipsychotic medicines should be given. Patients should first try antipsychotic drugs; if these don't work, ECT can be used to treat sick patients. ECT is therefore administered to those who have not responded to medication, resulting in a group that is comparatively resistant to treatment(55).

Most psychotherapies have not been proven to be effective in treating schizophrenia on their own. However, when used in conjunction with continuous pharmaceutical therapy, therapies aimed at enhancing family interactions can reduce the relapse rate in schizophrenia. Psychoeducation helps to build positive relationships between patients and their families by educating both the patient and the family about the nature of the illness, its progression, and its treatment. To address the issues that caused the disorder in the identified patient, family therapy aims to enhance family functioning, decrease conflict and distress among family members, and promote communication. The treatment involves some or all the family members. Individual psychotherapy is used to identify personal issues, improve interpersonal connections, significantly alter symptoms, or promote limited adaptations to certain issues, such as those related to physical or mental sickness or disability. Activity therapy, occupational therapy, and psychosocial rehabilitation services are examples of further psychosocial therapies(56).

PHARMACOLOGICAL INTERVENTION:

Before 1952, there was no widely used medication that effectively treated schizophrenia. In India, Sen and Bose had utilised reserpine (Rauwolfia serpentine extract) with varying degrees of efficacy. In the majority of cases of acute disturbance, electroconvulsive treatment (ECT) proved crucial in symptom reduction. Antidepressants, anxiety medications, and lithium have also been used to treat schizophrenia symptoms. These medications, however, have not shown themselves to be a successful substitute for antipsychotic treatment. The discovery of chlorpromazine, a phenothiazine, in the early 1950s may have been the most significant single development in the treatment of mental illness. Since their discovery by Delay and Deniker in 1952, antipsychotics have been the cornerstone of medication treatment for schizophrenia. Antipsychotic medications are primarily used therapeutically to treat schizophrenia and psychosis owing to a medical illness or mania by reducing hallucinations, delusions, agitation, and psychomotor excitation. The ability to occupy postsynaptic dopamine receptors in the brain is a common feature of all antipsychotic medications used to treat schizophrenia, despite their diverse modes of action. Typical antipsychotics, also known as dopamine antagonists, and atypical antipsychotics, sometimes known as serotonin dopamine antagonists, are two types of antipsychotic medications(57).

It appears that dopamine (DA) antagonists lessen psychotic symptoms by blocking dopamine-to-dopamine binding receptors. Chlorpromazine's capacity to block dopamine's receptors, particularly D2 receptor sites, may be explained by the structural similarity between the two neurotransmitters, as shown by X-ray crystallographic evidence. To explain the structural activity relationship (SAR) between the various antipsychotic medications and their capacity to block dopamine (DA) receptors in the brain, a thorough analysis of their x-ray structures has been conducted. Antipsychotics have been shown to inhibit DA receptors due to a structural complementarity between dopamine and specific parts of these medications. Often referred to as newer, novel, or more generally atypical antipsychotics, serotonin-dopamine antagonists

are effective against both positive and negative symptoms of schizophrenia and have fewer deleterious neurological effects than dopamine antagonists. They have different effects because of the antagonistic ratio between serotonin (5-hydroxy tryptamine, 5-HT2) and dopamine (D2)(58).

DIFFERENT APPROACHES TO DRUG DEVELOPMENT:

Both positive and negative symptoms of schizophrenia can be brought on by phencyclidine (PCP), an antagonist of the glutamate receptor complex's NMDA subtype. A glutaminergic shortage in the pathophysiology of schizophrenia has been proposed as a result of this observation, raising the possibility that glutaminergic medications could be used to treat the disorder. In the pathogenesis of schizophrenia, disruptions of glutaminergic transmission mediated by NMDA receptors may be crucial. The polyamine spermidine and the glutamate and glycine have several binding sites on the NMDA receptor. Drug development is now focused on the glycine modulatory location. It has been proposed that glycine binding, which increases NMDA transmission, can lessen schizophrenia symptoms. Small-scale clinical trials have demonstrated the efficacy of a number of studies employing glycine site modulators, such as glycine, d-serine, and cyclomerize. However, the limited physiological responsiveness of NMDA neurotransmission poses a significant challenge to its increase(56).

ADVERSE EFFECTS OF ANTI-PSYCHOTICS

System affected	Adverse effects
Autonomic nervous system	Dry mouth, constipation, cycloplegia, mydriasis, urinary retention, postural hypotension, impaired ejaculation, ventricular fibrillation and impotence
Extrapyramidal systems	Pseudo parkinsonism, acute dystonia, akathisia, tardive dyskinesia, rabbit syndrome (peri-oral tremor) and neuroleptic malignant syndrome
Metabolic/Endocrinal side effects	Weight gain, galactorrhoea, gynaecomastia and hypothermia
Central nervous system Allergic side effects	Seizures, sedation and pseudo depression Cholestatic jaundice and agranulocytosis
Dermatological side effects	Contact dermatitis, photosensitivity reactions and hyper pigmentation

It has been observed that the presynaptic dopamine receptors in the prefrontal and cingulated corlex of the dopamine nerve terminals control dopamine release and neuronal activation in addition to inhibiting dopamine synthesis. The presynaptic receptor for dopamine release becomes extremely sensitive in neuroleptics. A promising strategy for lowering dopaminergic activity is the idea of a presynaptic dopamine receptor that tracks its release through feedback inhibition. This suggests that dopamine agonists at presynaptic receptors may be used clinically as treatment agents for schizophrenia. Presynaptic dopamine receptor antagonist aripiprazole has been shown to be beneficial for both positive and negative symptoms while having less adverse neurological effects. Clinical evidence for antischizophrenic effects associated with presynaptic receptor stimulation is far from definitive, though, and can range from a little improvement in certain patients to no effects at all. Small dosages of levodopa and large doses of bromocriptine have been used to treat schizophrenia, with varying degrees of success. Because they stimulate postsynaptic dopaminergic receptors, presynaptic DA receptor agonists may be effective in treating schizophrenia, but they may also raise the likelihood of psychotic episodes(57,58).

Since dopamine and cholecystokinin (CCK) coexist between mesolimbic and mesocortical dopaminergic neurones, changes in DA and/or CCK transmission in the central nervous system may be relevant to schizophrenia. This has raised awareness of CCK's potential involvement in schizophrenia. Schizophrenic individuals have a CCK deficit, according to multiple study lines, and giving CCK to them seems to have therapeutic benefits. CCKA and CCKB are the two varieties of CCK receptors that have been identified; CCKB is the form that is most prevalent in the brain. When given to redents, CCKB agonists produced behavioural effects that were comparable to those of antipsychotic medications. Rats' exploratory behaviour in the pre-exploration paradigm is reduced when exposed to CCK tetrapeptide, an agonist of the cCKB receptor, according to Mato et al. Early open research indicated antipsychotic activity after systemic administration of the CCK analogue caerulin, based on human studies of changed CCK levels in schizophrenia. Nevertheless, randomised, double-blind crossover experiments revealed no discernible impact from caerulin given consistently(58).

The manasavyadhi (mental diseases) that is most extensively discussed in Ayurveda is Unmade (schizophrenia). Several herbal medications have been used to treat unmade illnesses in ancient Ayurvedic texts. Here, a few of the clinical studies are reviewed. According to Fozedar, who treated 75 patients with schizophrenia using the indigenous medication Acorus calamus, 7 of them exhibited improvement of at least 75% and 9 of them showed improvement of at least 50%. Ramu et al. conducted a pilot study on 41 patients with chronic schizophrenia using brahmyadiyoga, an herbal compound made up of Centella asiatica, Acorus calamus, Rauwolfia serpentine, Saussurea lappa, Nymphoides macropermum, and Nardostachys jatamansi. Seven out of ten patients who finished the course reported improvement. In a pilot trial, Dash et al. assessed the clinical effectiveness of a compound formulation of five powerful medications—Convolvulus pluricaulis, Nardostachys jatamansi, Bacopa monnieri, Withania somnifera, and Acorus calamus—in patients with unmade disorders. Over the course of six weeks of treatment, the patients' grades of psychotic symptoms significantly improved, and the trial demonstrated the compound's efficacy in unmade. In 112 patients with schizophrenia, Kale utilised a natural chemical formulation called siledin; there were no significant negative effects and an improvement rate of 59.9%. Additional research is required to evaluate the relative effectiveness of different chemical formulations and individual medications. The neurotoxic side effects of modern medications, particularly movement abnormalities, are already well recognised. If herbal medications are shown to have no negative side effects, even after prolonged usage, this could lead to new developments in psychopharmacology(59).

THE ALTERED REALITY OF INDIVIDUALS LIVING WITH SCHIZOPHRENIA

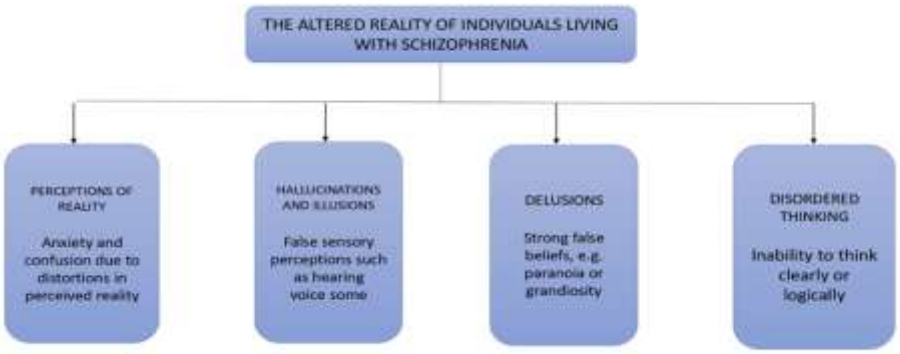

Fig.4. Distorted Reality in Schizophrenia

PERCEPTIONS OF REALITY

Individuals who suffer from schizophrenia may perceive the world very differently than those around them. People with schizophrenia may experience fear, anxiety, and confusion because of living in a reality that is warped by hallucinations and delusions.

People with schizophrenia may exhibit quite varied behaviours at different times, partly due to the odd reality they experience. They may appear aloof, disinterested, or distracted at times, and they may even sit still for hours on end without making any noise. At other times, they might be continuously on the go, looking alert, attentive, and wide-awake(60).

HALLUCINATIONS AND ILLUSIONS

Patients with schizophrenia, hallucinations and illusions are common perception abnormalities. Perceptions that don't have a proper cause are called hallucinations. While hallucinations can be auditory (sound), visual (sight), tactile (touch), gustatory (taste), or olfactory (smell), the most prevalent one in schizophrenia is hearing voices that other people do not hear. Voices can carry on a conversation, discuss the patient's activities, warn of potential dangers, or even give instructions. The opposite is true for illusions, which happen when a person interprets a sensory stimulus erroneously(61).

DELUSIONS

Delusions are erroneous personal ideas that cannot be supported by logic, contradicting data, or one's typical societal conceptions. Different topics can be found in delusions. Approximately one-third of individuals with schizophrenia suffer from paranoid-type symptoms, such as delusions of persecution, which are irrational and false ideas that they are being defrauded, harassed, poisoned, or the target of a conspiracy. These patients might think that they, a family member, or a loved one are the targets of this persecution. Additionally, schizophrenia can cause delusions of grandeur, where a person thinks they are a well-known or significant person. People with schizophrenia can often have quite strange delusions, such as thinking that their thoughts are being broadcast out loud to others, that someone on television is sending them unique messages, or that a neighbour is using magnetic waves to influence their behaviour(62).

DISORDERED THINKING

One of the most common effects of schizophrenia is the inability to "think straight." The person may tend to be easily distracted and unable to focus

their attention, and their thoughts may come and go quickly.

Schizophrenia patients might not be able to distinguish between things that are pertinent to a situation and those that are not. The individual's thoughts may become fractured and disorganised due to their inability to link them into logical patterns. This "thought disorder," which is characterised by a lack of logical continuity of thought, may make discourse extremely challenging and may even lead to social isolation. People are prone to feel uncomfortable and tend to leave someone alone if they are unable to understand what they are saying. Normal people can occasionally exhibit symptoms of schizophrenia in their thoughts, feelings, or behaviours(63).

NORMAL VERSUS ABNORMAL: -

Sometimes, normal people cannot be able to "think straight." For instance, they might have great anxiety when speaking in front of groups, which could cause them to get disoriented, lose their train of thought, and forget what they were about to say. Schizophrenia is not this. However, not all individuals with schizophrenia exhibit aberrant behaviour. In fact, even when they suffer from hallucinations or delusions, some individuals with the condition may seem entirely normal and responsible. Over time, a person's behaviour may shift; if medicine is removed, it may become strange; if proper treatment is received, it may revert to normal(64).

CONCLUSION

The treatment landscape for schizophrenia has significantly evolved, with current pharmacological strategic offering improved symptom management and reduced side effects compared to earlier generations of antipsychotics. Second-generation antipsychotics remain the cornerstone of treatment, emphasizing the importance of individualized therapy based on efficacy and tolerability. Despite these advancements, challenges such as treatment resistance and adverse effects persist, underscoring the need for more targeted approaches. Emerging therapies—including novel receptor modulators, immunotherapies, and personalized medicine-offer promising avenues for more effective and holistic care. Continued research into the neurobiological underpinnings of schizophrenia, coupled with innovation in pharmacological development, holds the potential to transform treatment paradigms and improve long-term outcomes for individuals living with this complex disorder.

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ABBREVIATION:

5-HT	5-Hydroxytryptamine (Serotonin)
ACh	Acetylcholine
ADRs	Adverse Drug Reactions
CBT	Cognitive Behavioural Therapy
CNS	Central Nervous System
DA	Dopamine
D2R	Dopamine D2 Receptor
FDA	Food and Drug Administration
GABA	Gamma-Aminobutyric Acid
GLUT	Glutamate
NMDA	N-Methyl-D-Aspartate
NIMH	National Institute of Mental Health
PET	Positron Emission Tomography
RCT	Randomized Controlled Trial

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