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Research

Neurobiological Correlates of Schizophrenia and Implications for Psychotherapy

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Abstract:
The nature of schizophrenia makes it a complex mental disorder that is associated with severe problems in perception, emotion, behaviour and cognition. The neurological causes of this disorder were clarified with the help of recent decades in terms of molecular genetics, neurochemistry, neuroimaging. In conjunction with impairments in the functionality of corporal connections within the fronto-temporal and fronto-limbic loops, structural changes in the brain, such as the depletion of gray mass in the prefrontal premises and hippocampus, are often found. Neurochemical researches point to the problem that positive and negative symptomatology are both caused by the malfunction of the dopaminergic, glutamatergic, and GABAergic systems. Moreover, recent evidence also highlights the importance of oxidative stress and neuroinflammation as well as abnormal synaptic pruning in neurodevelopment as pathological processes. These discoveries will have an enormous effect on psychotherapy, which gradually incorporates neurobiological theories to achieve more accurate treatment. Cognitive remediation therapy, metacognitive training, and neurofeedback are some of the treatments used to improve functional recovery based on brain plasticity and cognitive deficits knowledge. Given the way neurobiology and psychosocial determinants interact, customized treatment preconditioned by the neurophysiological and experience aspects of the schizophrenic condition can be developed. Such a combined approach to the issue supports a better long-term recovery and the creation of a universal treatment plan as it relates clinical practice to the brain research.

Keywords: Schizophrenia, Neurobiology, Dopaminergic Dysregulation, Cognitive Remediation, Neuroplasticity, Psychotherapy Integration, Brain Connectivity, Synaptic Pruning

1. Introduction to Schizophrenia

Schizophrenia is a serious and complicated mental disease that is associated with problems in the perception of reality, the emotional regulation and cognitive processing. Schizophrenia is not a unitary and homogeneous condition, but instead is a continuum of similar disorders, which have converging biology and clinical features. The disorder is the most frequent manifestation of which is observed in late adolescence or early adulthood, the period of development when all matters are social, cognitive, and psychological maturation. It can develop insidiously with insignificant behavioral and cognitive abnormalities and eventually develop into more severe symptoms, or can manifest suddenly with acute psychotic symptoms.

In the past, schizophrenia has been conceptualized to have undergone significant changes in psychiatric studies. Initial therapies with early explanatory theory were provided by Emil Kraepelin who called it dementia praecox and he more stressed a gradual decline in mental capacities. Subsequently, the term schizophrenia came into being by Eugen Bleuler to emphasize a breakdown of the normal way of integrating thoughts, emotion and action. The modern view incorporates clinical findings in conjunction with neuroscientific developments whereby the issue of schizophrenia is viewed as both a neuroscientific and psychiatric problem.

Traditionally, the symptomatology of schizophrenia is divided into three areas. Positive symptoms encompass existence of aberrant experiences such as delusions, hallucinations and disorganised speech or behavior. Negative symptoms are associated with and indicate lowered or lack of normal functioning, including show of reduced emotional expression, lack of social interaction, and lack of drive or motivation. Cognitive symptoms are impairments in attention, memory and executive functioning. Such cognitive impairments usually lead to the functional disability which is long term. The interplay between these domains of symptoms may be different across people and may change with treatment, environmental stressors and psychosocial conditions.

Albeit there is relatively low prevalence of schizophrenia, having an influence on 0.3-0.7% of the world population, it causes major individual and social costs. The condition often interferes with the education achievement, working life, and human interaction. Furthermore, social stigma is still one of the most essential obstacles to early diagnosis and treatment that may lead to a delay in the seeking of help and further social isolation. Perceptions and interpretations of mental illness might also be influenced by cultural beliefs, which in turn may influence the person to seek treatment services.

Research evidence has in this and previous several decades presented a steadily increasing evidence that schizophrenia is correlated with quantifiable neurochemical and brain structural alterations. Neuroimaging has often found changes in the prefrontal cortex, the hippocampus, and the temporal lobes which are parts of the brain involved in memory, reasoning, and regulation of emotions. Involvement in symptoms The neurotransmitter systems that include dolphin system, glutamate, and gamma-aminobutyric acid (GABA) have been dysregulated. It is also becoming increasingly clear that schizophrenia can be viewed as a neurodevelopmental condition, which develops as a result of a combination of inborn disability and environmental risk factors. Such risk factors could be prenatal infections, obstetric complications and early in life psychosocial stress.

Interventions are based on the complexity of the disorder. Antipsychotic drugs continue to be the major drug therapy, especially in the treatment of positive symptoms. The low success in correcting negative and cognitive symptoms has however resulted in the creation of complementary forms of therapeutic interventions. Psychosocial interventions (cognitive remediation, social skills training, and supported employment) aim at providing people with improved functional recovery. Also, it has been found that family psychoeducational programs, through enhancing the social environment of the patient, through understanding and support, reduced the rate of relapses. There is a particular effectiveness of early intervention programs that combine pharmacological treatment, psychotherapy with support of the community when they are developed in the first episode of psychosis.

With all these improvements, there are serious challenges still. Availability of evidence-based mental health care is still not equitable especially in low-resource situations where trained experts and crucial medications could be restricted. Despite the well-resourced healthcare systems, the gaps in treatment also persist among the individuals who have a complex presentation or co-occurring disorders. These gaps can only be met through synergies in healthcare policy, population education and long-term investments into mental health infrastructure.

Schizophrenia needs to be understood with both the accuracy of science but also with the understanding of the experience of the sufferers. The disorder is characterized by its neurobiology and the clinical signs as well as the personal and social reality of the people and the families. The key issue to researchers and clinicians is to fill the gap between scientific finding and personalized and caring care.

Further progress in both research and therapy has the potential to make schizophrenia no longer a devastating condition but a disease where the recovery and a better quality of life are achievable.

1.1 Historical Overview and Clinical Features

The conceptualization of schizophrenia has evolved considerably over the past two centuries, reflecting advances in psychiatric theory, diagnostic systems, and scientific research. Although descriptions of psychosis-like states can be traced to ancient medical traditions—including references in the writings of Hippocrates, the Egyptian *Ebers Papyrus*, and sections of the *Atharvaveda*—the modern scientific understanding of schizophrenia began to develop during the late nineteenth century (Porter, 2002; Tandon et al., 2013).

A pivotal figure in this development was **Emil Kraepelin**, who introduced the term *dementia praecox* in the 1890s to describe a group of mental disorders characterized by early onset and progressive deterioration in cognitive and emotional functioning (Kraepelin, 1919). Kraepelin distinguished dementia praecox from manic–depressive illness based on differences in course and prognosis, emphasizing its chronic nature and comparatively poor outcomes. His systematic review of hospital case records identified key clinical features such as social withdrawal, emotional blunting, delusions, and hallucinations. Kraepelin's classification laid the foundation for modern psychiatric nosology and strongly influenced subsequent research on psychotic disorders (Jablensky, 2010).

In the early twentieth century, **Eugen Bleuler** challenged Kraepelin's assumption that the disorder inevitably involved progressive deterioration. In 1911, Bleuler introduced the term *schizophrenia*, derived from the Greek words *schizo* (split) and *phren* (mind), to emphasize the fragmentation of mental processes rather than early-onset dementia (Bleuler, 1950). Bleuler proposed that the core disturbance involved disruptions in the integration of thought, emotion, and volition. He further differentiated between *primary symptoms*, which included fundamental disturbances in associations, affectivity, and ambivalence, and *secondary symptoms*, such as hallucinations and delusions. This conceptual framework shaped psychiatric understanding of schizophrenia for several decades.

During the mid-twentieth century, the definition of schizophrenia broadened considerably, resulting in substantial variability in diagnosis across countries. Cross-national research, particularly the U.S.–U.K. Cross-National Project, demonstrated significant differences in diagnostic rates and interpretations of symptoms between clinicians in different regions (Cooper et al., 1972). These discrepancies highlighted the need for standardized diagnostic criteria. In response, structured classification systems—including the **Diagnostic and Statistical Manual of Mental Disorders (DSM)** and the **International Classification of Diseases (ICD)**—introduced explicit diagnostic thresholds and duration criteria, significantly improving diagnostic reliability and comparability across clinical settings (American Psychiatric Association, 2022; World Health Organization, 2019).

Clinically, schizophrenia is characterized by a constellation of symptoms commonly categorized into **positive**, **negative**, and **cognitive** domains (Tandon et al., 2009). Positive symptoms refer to the presence of abnormal experiences, such as delusions, hallucinations, and disorganized speech or behavior. Delusions may take persecutory, grandiose, or bizarre forms, while hallucinations are most frequently auditory, often involving voices commenting on or conversing about the individual. Disorganized speech may manifest as abrupt topic shifts, incoherent associations, or illogical reasoning, and behavioral disturbances may include agitation or socially inappropriate actions.

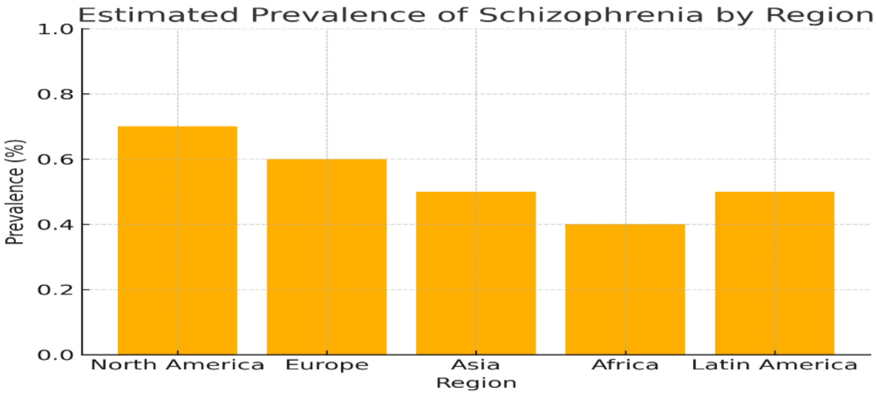
Negative symptoms represent a reduction or absence of typical emotional and behavioral functioning. Common manifestations include diminished facial expressiveness, monotonic speech, social withdrawal, and **avolition**, or reduced motivation. Although these symptoms often receive less clinical attention than positive symptoms, research indicates that they contribute substantially to long-term functional impairment and reduced quality of life (Kirkpatrick et al., 2006).

Increasingly, cognitive impairments are recognized as a central component of schizophrenia. Deficits in working memory, attention, and executive functioning can interfere with everyday tasks such as managing finances, maintaining employment, or adhering to medication schedules (Green et al., 2004). Importantly, these cognitive difficulties may emerge prior to the onset of overt psychotic symptoms, suggesting their potential role in early identification and intervention strategies.

The clinical presentation of schizophrenia also varies across individuals and cultural contexts. Cultural beliefs and social environments can influence both symptom expression and interpretation. For example, auditory hallucinations are reported more frequently in Western populations, whereas individuals in some non-Western settings may report a greater prevalence of visual hallucinations (Luhrmann et al., 2015). Similarly, the content of delusions often reflects culturally specific themes; accusations of witchcraft may appear in rural communities, whereas concerns about technological surveillance may be more common in highly urbanized societies.

The historical trajectory of schizophrenia research—from Kraepelin's detailed clinical case studies to contemporary neuroimaging investigations—illustrates the dynamic relationship between clinical observation and scientific inquiry. Situating current diagnostic frameworks within this historical context not only improves diagnostic precision but also supports the development of culturally sensitive and evidence-based approaches to treatment and care

1.2 Diagnostic Criteria and Epidemiology



Contemporary systems of diagnosis for schizophrenia result from a long history of studies aimed at enhancing the reliability and cross-cultural applicability of diagnosis. Two classification systems have been extensively used in clinical practice and research the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR) and the International Classification of Diseases, Eleventh Revision (ICD-11) (American Psychiatric Association [APA], 2022; World Health Organization [WHO], 2019). Both systems provide standardised criteria to make for consistent diagnosis, irrespective of the clinical and cultural context.

According to the DSM-5-TR, the criteria for a schizophrenia diagnosis is there must be a minimum of two core symptoms during a significant amount of time in a one month period; there has to be continuous evidence that the signs of disturbance exist; and it has to occur for at least half a year (APA, 2022). The symptoms of diagnosis include:

A. Delusions
B. Hallucinations
C. Disorganized speech
D. Grossly disorganized catatonic behavior

Negative symptoms (i.e. decreased expression of emotions or avolition)

At least one of the symptoms should be delusions, hallucinations or disorganized speech. In addition to these clinical features, the disorder must cause significant impairment in the functioning of a person's social, occupational, or self-care activities (APA, 2022). The ICD-11 offers largely similar criteria but focuses on more widespread symptom areas, namely positive, negative, cognitive, and psychomotor disturbances, and also lets clinicians rate the severity of symptoms on a continuum (WHO, 2019).

Historically, some symptoms were considered to be especially characteristic of schizophrenia. For example: Kurt Schneider formulated a list of "first-rank symptoms," including some of the following: hearing voices that comment on one's behavior or the perception that your thoughts are being inserted into your mind (Schneider, 1959). These symptoms, while very distinctive, modern diagnostic systems warn against using them solely as some symptoms are experienced and interpreted differently in different cultural situations. Cultural frameworks can greatly influence the perception of the psychotic experiences. For instance, auditory hallucinations in highly industrialized societies in the Western world may be seen as technological surveillance, whereas similar phenomena in some rural African communities may be explained in the framework of spiritual or religious belief systems (Luhrmann et al., 2015).

From an epidemiological point of view, schizophrenia occurs in around 0.3% to 0.7% of the worldwide population, which represents millions of people around the world (McGrath et al., 2008; WHO, 2019). Although the disorder occurs worldwide and there are relatively consistent rates of both incidence and prevalence across cultures and geographic locations, it may be that low-resource settings have lower prevalence rates due to underdiagnosis and poorer mental health reporting systems.

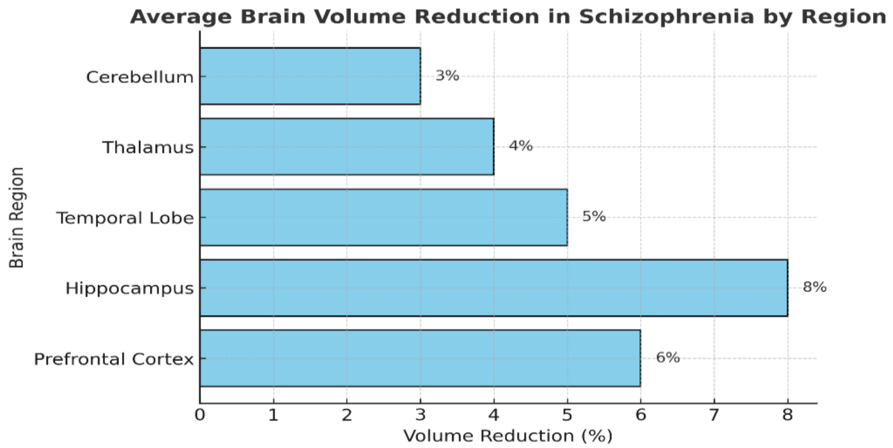
The age of onset is usually different in both sexes. Males on the other hand tend to develop schizophrenia earlier and threshold between 18-25 years of age while females experience onset later and threshold at 25-35 years (Abel et al., 2010). Early onset often is linked to more severe symptomatology and functional outcomes, which may be due to the fact that the disorder interferes with critical time periods of development pertaining to education, employment, and social relationships.

Genetic vulnerability plays an important role in the development of schizophrenia. People with a first-degree relative with the disorder have an estimated 10% lifetime risk (compared with the general population, where the estimated risk is 1%) (Gottesman, 1991). However, the role of genetic susceptibility cannot completely explain the appearance of the illness. Environmental and developmental factors, including prenatal infections, obstetric problems, living in an urban setting, or exposure to early life trauma along with genetic predispositions (e.g., genes) interact with environmental factors (i.e., situations, conditions, or locations) that lead to the onset and course of the disorder (e.g., Development strove for consumption) (Howes & Murray, 2014).

The comprehension of both diagnostic criteria as well as epidemiological patterns is vital for the currently development of effectual global mental wellbeing strategies. Reliable diagnostic frameworks are important to help with early identification and intervention and epidemiological data help shape policy decisions, evaluation of resources, and implementation of culturally sensitive treatment approaches. Together, they add up to better and more equitable access to mental health care and achieve better outcomes for people affected by schizophrenia anywhere in the world.

2. Structural Brain Abnormalities

Advances in neuroimaging techniques, especially magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI), have led to significant evidence conflicting with structural abnormalities of the brain of schizophrenic. These technologies have enabled researchers to study brain morphology and white matter connectivity in vivo and identify consistent neuroanatomical changes in people with the disorder. Such findings have helped reinforce the notion that schizophrenia is first and foremost associated with a brain-based aspect with biological correlates rather than exclusively a psychosocial condition (Shenton et al., 2001; van Erp et al., 2018).



One of the most consistent structural changes that has been reported is decreased gray matter volumes in the prefrontal cortex, and especially in the dorsolateral prefrontal cortex (DLPFC). This region is thought to play an important role in executive functions, like working memory, decision making and impulse control. Functional MRI (fMRI) studies have found that in people with schizophrenia there are decreased activations within the DLPFC that are accompanied by observed deficits in problem-solving and executive functioning (Barch & Ceaser, 2012; Weinberger et al., 1986).

Another well-established neuroanatomical finding is that of reduction in the hippocampus volume. A structure involved in the consolidation of memories and spatial navigation, the hippocampus is often seen to be measurably atrophic in people with schizophrenia. Meta-analytic studies indicate that the hippocampal volume may be decreased by about 5% - 8% relative to healthy controls (Heckers & Konradi, 2010; van Erp et al., 2016). These alterations of the structure are thought by researchers to underlie problems with episodic memory, and may also contribute to the formation of distorted or fragmented memories that may support certain delusions.

Structural abnormalities have also been found in the temporal lobes especially in a region called the superior temporal gyrus, which has been associated with auditory perception and language processing. Changes in this area have been correlated to the presence of auditory hallucinations that is one of the most characteristic symptoms of schizophrenia. Neuroimaging research studies estimating a disruption in temporal lobe structure and integration might affect the way the auditory information is being processed, which may lead to the perception of internally generated thoughts as external voices (Allen et al., 2008; Shenton et al., 2001).

The thalamus, or central relay for sensory and motor substance, likewise generally shows slight decreases in volume in people experiencing from schizoaffective illness. As the thalamus has an important role in filtering and integrating sensory information, structural abnormalities in this area may contribute to sensory gating deficits which are often also seen in the disorder. These deficits may cause a challenge of sorting out relevant information as opposed to irrelevant inputs in the environment, which may lead to sensory overload or misinterpretation of sensory experiences (Andreasen et al., 1994; Pergola et al., 2015).

In addition, growing attention has also been focused on the cerebellum, a structurally traditional structure of the brain that is involved in motor coordination. The various contemporary researches suggest that cerebellum also plays a role in higher-order cognitive processes and emotional regulation. Abnormalities in the structure of cerebellar and its connections have been suggested as part of a larger disruption of neural circuitry in schizophrenia especially at the cortico-cerebellar-thalamic-cortical circuit underlying coordinated cognitive functioning (Andreasen & Pierson, 2008).

Importantly, structural abnormalities in the brain in schizophrenia are not the same in all people. Variability in neuroanatomical findings may reflect variability in the genetic vulnerability to the illness, environmental exposures, duration of illness, and history of treatment. Longitudinal neuroimaging studies have shown that some structural changes are potentially progressive over time (e.g., grey matter volume changes), while others will be rather static. These patterns indicate that both neurodevelopmental and neurodegenerative may play a role in pathophysiology of the disorder (Insel, 2010; Vita et al., 2012).

Ongoing research focuses on finding reliable neuroimaging biomarkers that may help in the early diagnosis of diseases, monitor disease progression and determine a personalized treatment approach. Mapping the structural alterations in the brain not only provides a better understanding of the biological basis of schizophrenia but also helps bridge the gap between the neurobiological and clinical approach to guide either pharmacological and psychosocial approach.

2.1 Gray Matter Reduction and Regional Atrophy

One of the most consistent neuroanatomical findings in schizophrenia is reduction of gray matter (there). This phenomenon is defined as the occurrence of measurable declines in the size of neuronal cell bodies, branching of dendritic components and synaptic density in certain brain areas. Advances in neuroimaging - specifically structural magnetic resonance imaging (MRI), structural mapping of the brain and voxel-based morphometry (VBM) - have allowed researchers to identify both general and region-specific patterns of gray matter loss in individuals with schizophrenia (Ashburner & Friston, 2000; Shenton et al., 2001; van Erp et al., 2018).

Brain Region	Average Volume Reduction (%)	Associated Functional Deficits
Prefrontal Cortex	6.5	Impaired decision-making, working memory, and executive control
Hippocampus	8.2	Memory loss, spatial disorientation, and distorted recall
Temporal Lobe	5.1	Auditory hallucinations, language processing deficits
Anterior Cingulate Cortex	4.8	Emotion regulation difficulties, impaired attention control
Parietal Lobe	3.9	Reduced spatial awareness, difficulty with sensory integration

One of the most affected in this respect is the prefrontal cortex, where structural studies have revealed volume decreases of around 6 - 7% compared to healthy control groups (Glahn et al., 2008). The prefrontal cortex is part of executive functioning which include planning, working memory, cognitive flexibility and goal directed behavior. Degeneration in this part of the brain is thus highly correlated with deficits in higher order thinking processes. Clinically, people with severe loss of prefrontal gray matter can have problems organizing daily activities, adapting to changing circumstances, or solving complex problems (Barch & Ceaser, 2012).

Another area that is consistently involved in schizophrenia is the hippocampus, an area crucial for memory consolidation and attainment of spatial orientation. Neuroimaging studies have shown reduction of the hippocampus of up to 8% among people with schizophrenia compared to healthy people (Heckers & Konradi, 2010; van Erp et al., 2016). Degeneration in this region has been regarded as being associated with disorders in episodic memory and contextual processing. In clinical situations, people with severe atrophy in the hippocampus may show an inability to accurately remember the sequence of events or mis-attribute responsibility for the sequence of experiences, which may contribute to distorted perceptions of reality and the invention of delusions.

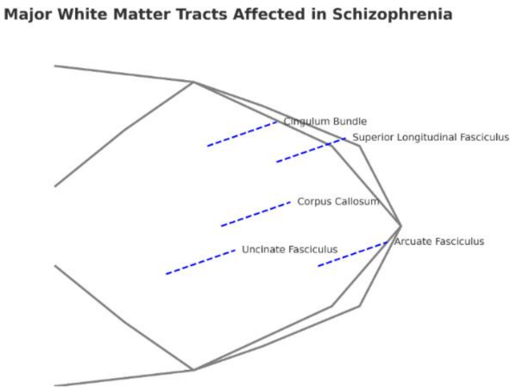
Structural abnormalities are also apparent in the temporal lobes of the brain, especially in the superior temporal gyrus, a brain region that is involved in the perception of sounds and the processing of language. Decreases of gray matter volume in this region have been highly correlated with auditory hallucinations, one of the definitive symptoms of schizophrenia (Allen et al., 2008; Shenton et al., 2001). Additionally, diminished gray matter volume in an important region of the anterior cingulate cortex involved in emotional regulation, attention, and motivational processes has been associated with negative symptoms such as reduced emotional expression and reduced motivation (Fornito et al., 2009).

Longitudinal studies of neuroimaging have suggested that gray matter loss may be especially evident at early stages of the disorder. Evidence shows that decreases in gray matter volume can continue during the first few years after illness onset, this is especially true in people who do not get early treatment (Vita et al., 2012). These findings are supportive of the importance of early intervention strategies in that the early treatment may help slow or mitigate progressive structural changes. Furthermore, the extent of gray matter atrophy varies among individuals and may be determined by many different variables, such as genetic susceptibility, illness duration, exposure to environmental stresses and the prolonged use of anti-psychotic medications (Insel, 2010; van Haren et al., 2011).

Identification and quantitation of patterns of gray matter attenuation has important prognostic and therapeutic implications. By relating abnormalities in regional brain structure to specific defects of function, it will be possible for clinicians and researchers to improve the tailoring of therapeutic approaches, such as cognitive remediation and rehabilitation programs designed to target regions of cognitive dysfunction most vulnerable to regional cell atrophy. In this way, neuroimaging results help to achieve a more accurate understanding of schizophrenia and to develop individual treatment strategies.

2.2 White Matter Integrity and Connectivity Deficits

While structural studies examining schizophrenia have been focused on gray matter abnormalities, there is a growing literature implicating disruptions in white matter in the understanding of the neurobiology of schizophrenia. White matter is the myelin coated axonal fibres that link various regions of distributed brain tissues thus enables a good communication between neural networks. Disturbances in these connections can hinder the coordination of the cognitive, emotional and sensory processes, which may contribute to the dissociality of thinking, emotional dyscontrol and perceptual disturbances that characterize schizophrenia (Kubicki et al., 2007; Peters et al., 2010).



Advances in the diffusion tensor imaging (DTI) have led to the possibility of investigating white matter microstructure in vivo. A major metric to which values for DTI are related is fractional anisotropy (FA), which indicates the extent of directional diffusion of water molecules along axon fibers. Higher FA values usually correspond to intact and well-organized white matter tracts whereas lower FA values are associated with reduced structural connectivity, reflecting compromised structural connectivity due to demyelination, axonal damage and/or altered fiber organization (Basser & Pierpaoli, 1996). Numerous studies have reported on the decrease in FA of several white matter connecting pathways in people with schizophrenia, which suggests widespread disruptions in neural connectivity (Ellison-Wright & Bullmore, 2009).

One of the structures typically involved is the corpus callosum, which is the largest white matter tract within the brain and is responsible for transfer between the left and right interior hemispheres. Decreased FA in the corpus callosum has been linked to difficulties in integration of perceptual, cognitive and emotional information across hemispheres (Arnone et al., 2008). Clinically, types of such disruptions could play a part in discrepancies between verbal and nonverbal responses or conflicts between combining emotional experiences with cognitive interpretations.

Another significant pathway is the arcuate fasciculus as well which encompasses Broca's area and Wernicke's area which are involved in language production and language comprehension. Structural abnormalities in this tract such as reduced FA have been associated with disruptions in language processing and are possibly involved in the causation of symptoms such as disorganized speech and auditory hallucinations, which are considered hallmark features of schizophrenia (Catani & Mesulam, 2008; Geoffroy et al. 2014).

Similarly, this connection between frontal cortex cortical regions and the limbic system as a white matter bundle, the cingulum, is often associated with loss of structural integrity in schizophrenia. Because this pathway plays an essential role in emotional regulation, attention and cognitive control functioning, there is a possibility that the cingulum's disruption contributes to impaired functioning in affective processing and attention.Because of the critical role of this pathway in emotional regulation and attention and cognitive control functioning, it may be that there is at least some contribution of cingulum disruption to impaired functioning in affective processing and attention.

Another form of neuroimaging feature that is commonly detected in schizophrenia is the presence of white matter hyperintensities, which are usually identified in T2-weighted MRI scans. These hyperintense regions are represented by brighter areas and may be correlated with underlying pathological process including demyelination, gliosis, and/or small vessel injury. Studies have found that white matter hyperintensities occur more often in a schizophrenia population than in a healthy population and are correlated to reduced cognitive function and an earlier development of symptoms (DeLisi et al., 2006).

Also, disruptions of the uncinate fasciculus, which connects the frontal lobes with anterior temporal regions have been reported. Reduced FA in this

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pathway has been associated with deficits in emotional processing and reality monitoring processes which are implicated in the development of delusional beliefs (Phillips et al., 2009). Similarly, abnormalities in the superior longitudinal fasciculus (a major association pathway which is involved in working memory and executive control) have been linked to deficits in cognitive functioning commonly found in schizophrenia (Karlsgodt et al., 2008).

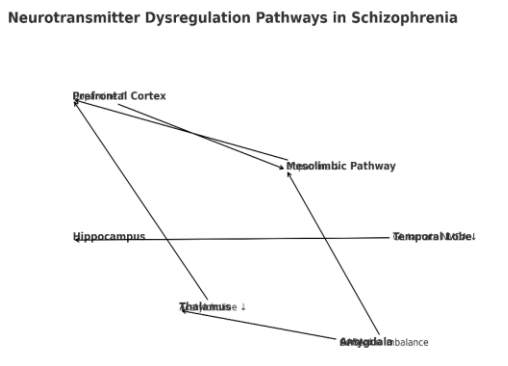
These abnormalities in white matter are likely to reflect a combination of any neurodevelopmental abnormalities and the progressive pathological changes that occur throughout the course of the illness. Evidence from studies of individuals at clinical high risk of psychosis suggest that losses in fractional anisotropy may be evident even before full psychotic symptoms manifest, and thus they may prove useful as early biomarkers of vulnerability (Karlsgodt et al., 2009). Consequently, the identification of changes in the integrity of the white matter may provide support for strategies to detect cases of schizophrenia at an early stage and to identify interventions to prevent or reduce the progression of schizophrenia.

3. Neurochemical and Neurotransmitter Dysregulation

Schizophrenia is generally known as a disorder of complex disturbances in the neurochemical and neurotransmitter structure of the brain. Although sometimes these terms are used interchangeably, there are differences between these processes, yet they're related to one another. Neurochemical dysregulation is a general term that refers to imbalance of a variety of brain chemicals such as hormones, peptides, and ionic signaling molecules. In contrast, neurotransmitter dysregulation is more focused on the issues associated with chemical messengers responsible for passing messages from neuron to neuron across synapses. Together, these disturbances are involved in the cognitive, emotional and perceptual abnormalities which characterise schizophrenia (Howes & Kapur, 2009; Stahl, 2013).

Neurotransmitter	**Role in Brain**	**Dysfunction in Schizophrenia**
Dopamine	Motivation, reward, attention	Hyperactivity in mesolimbic pathway (positive symptoms), hypoactivity in prefrontal cortex (negative symptoms)
Glutamate	Learning, memory, synaptic plasticity	NMDA receptor hypofunction linked to cognitive and negative symptoms
GABA	Inhibitory control, emotion regulation	Reduced GABAergic signaling contributes to disinhibition and sensory overload
Serotonin	Mood, appetite, cognition	Imbalance may modulate symptoms or affect treatment response
Acetylcholine	Attention, learning, sensory processing	Deficits linked to attention and sensory integration issues

Historically, the most powerful analytic scheme has been the dopamine hypothesis of schizophrenia. According to this model, the so-called symptom emergence is central in the development of symptoms, and this is mediated by a dysregulation of the dopaminergic pathways. Hyperactivity of dopaminergic transmission in the mesolimbic is believed to play a role in the production of positive symptoms (hallucinations, delusions). In contrast, decreased dopaminergic activity in the mesocortical pathway, with a significant impact of this reduced activity in the prefrontal cortex, has been associated with negative symptoms and cognitive impairment, including decreased motivation, impaired working memory and executive dysfunction (Howes & Kapur, 2009; Grace, 2016). Clinically, this dual imbalance may present as people who may show reinforcing psychotic symptoms at the same time that they have difficulty planning or organising everyday activities.



More recent models of neurobiology have gone beyond dopamine to include other neurotransmitter systems. One of the most prominent is glutamate, an excitatory neurotransmitter that is mostly found in the central nervous system. The glutamate hypothesis of schizophrenia proposes that a decrease in the activity of N-methyl-D-aspartate (NMDA) receptors is involved in cognitive deficits and negative symptoms seen in schizophrenia (Coyle, 2012). Evidence in favour of this hypothesis comes from pharmacological studies showing that the administration of substances that block the actions of the N-methyl D-Aspartate (NDA; also known as the N-methyl-D-Aspartate receptor) neurotransmitter, that is ketamine and phencyclidine (PCP), can provoke transient schizophrenia-like symptoms, including hallucinations and disorganization of thinking, in healthy people (Javitt & Zukin, 1991).

Another important system of neurotransmitters implicated in Schizophrenia is the gamma-aminobutyric acid (GABA), which is the primary inhibitory neurotransmitter in the brain. GABAergic interneurons are integral to control the cortical circuitry and put excitatory and inhibitory neural activity into balance. A number of studies have shown that people with schizophrenia tend to have lower overall functioning of their gamma-aminobutyric acid system, especially in the prefrontal cortex. This disruption can result in a decreased ability of inhibitory control over the neural networks, and may lead to sensory overload and disorganization in cognition, as well as problems with the ability to filter irrelevant information (Lewis et al., 2005).

Additional neurotransmitter systems have also been involved in the pathophysiology of schizophrenia. For instance, serotonin has been implicated in regulating both modulating the symptoms and responding to treatment. Many second-generation antipsychotic medications exert their effect in part by serotonin (serotonin, 5-HT2A) receptor antagonism, which may influence dopamine release, and improve both positive and negative symptoms (Meltzer, 2013). Similarly, disturbance of acetylcholine especially in the cholinergic system related to functions involved in attention and memory has been linked to cognitive impairments common in schizophrenia (Sarter et al., 2009).

The increased appreciation of the multiple mode of neurotransmitter abnormalities emphasizes the multifactorial neurochemical basis of schizophrenia. Dopaminergic dysregulation may be a primary contributor to psychotic symptoms such as hallucinations and delusions whereas glutamatergic and gamma-aminobutyric acid (GABA) signaling may contribute to deficits in cognitive, learning, and emotional regulation. This integrated perspective demonstrates the complexity of the disorder and promote the evolution of more often including ways of treatment.

Understanding the avenue of the system of these neurochemicals is crucial not only to the development of focused pharmacological therapies, but emerging treatments and models such as neuromodulation treatments and cognitive re-entry therapies. By helping to clarify both the way the systems that use neurotransmitters interact with the larger networks in the brain, researchers and clinicians may be better able to understand and design interventions calculated to provide a better balance, not just between managing the symptoms but between better functional outcomes for the individuals with schizophrenia.

3.1 Dopaminergic and Glutamatergic Pathways

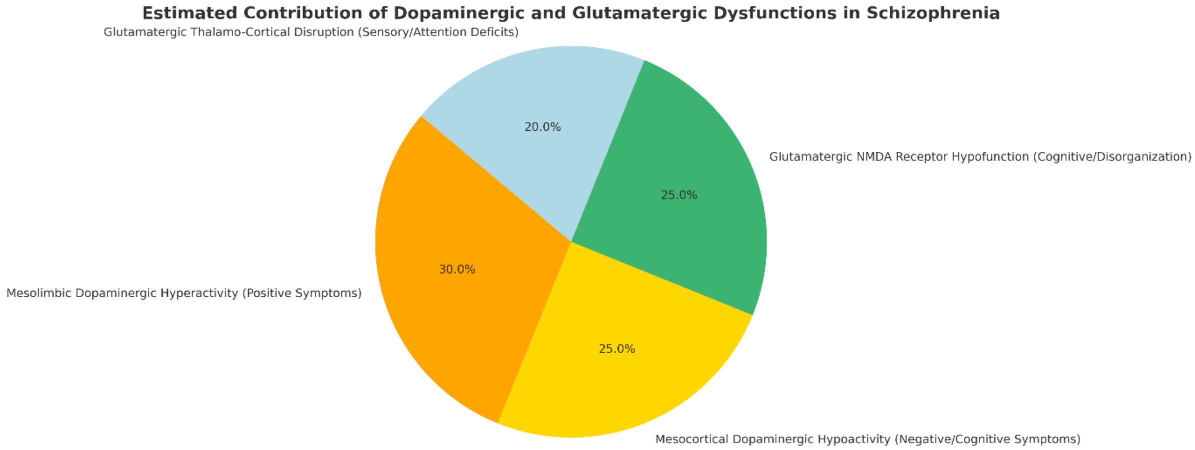
The neurobiological understanding of schizophrenia has been focused on problems in two major neurotransmitter systems for many years; these are dopamine and glutamate. These systems are highly interactive there within the neural circuits that control perception emotion cognition and behavior. Contemporary models of schizophrenia increasingly focus on the fact that both dopaminergic and glutamatergic signaling abnormalities contribute to the range of diverse symptoms of the disorder (Howes et al., 2017; Stahl, 2013).

Historically, the dopamine hypothesis of schizophrenia was the first major neurochemical hypothesis of schizophrenia. This model is primarily concerned with 2 dopaminergic pathways, the mesolimbic and the mesocortical systems. Hyperactivity of dopamine transmission in the mesolimbic pathway that extends from the ventral tegmental area (VTA) to the nucleus accumbens has been strongly linked with positive symptom development, which includes hallucinations and delusions (Howes & Kapur, 2009). Elevated dopamine signaling in limbic structures may result in abnormal attributing of the importance of internal thoughts and/or external stimuli as causative of experiences such as hearing voices or developing persecutory beliefs.

The mesocortical pathway, which leaves the ventral tegmental and projects to prefrontal cortex, is often associated with a decreased dopaminergic activity in people with schizophrenia. Hypoactivity in this pathway has been associated with negative symptoms, such as social withdrawal and flattened affect, as well as cognitive impairment, such as working memory deficits as well as deficits in attention and executive functioning (Grace, 2016). These neurochemical imbalances help to explain how people with schizophrenia sometimes have quite severe psychotic symptoms and at the same time struggle with social interaction and activity in the long-run.

Pathway	**Primary Role**	**Dysfunction in Schizophrenia**
Mesolimbic Dopamine	Emotion, reward processing	Hyperactivity leads to positive symptoms (e.g., hallucinations, delusions)
Mesocortical Dopamine	Cognition, executive function	Hypoactivity causes cognitive and negative symptoms (e.g., anhedonia, avolition)
Glutamatergic Cortico-Striatal	Motor planning, cognitive integration	NMDA receptor hypofunction contributes to thought disorganization
Glutamatergic Thalamo-Cortical	Sensory relay, attention	Disrupted relay of sensory signals; linked to attention deficits and perceptual distortions

In addition to dopamine, much attention has recently been focused on the system modulated by glutamate, which has a critical role in synaptic plasticity, learning, and memory. The glutamate theory of schizophrenia therefore states that the dysfunction of N-methyl-D-aspartate (NMDA) receptors, in particular in the prefrontal cortex and hippocampus, plays an important role in the cognitive deficits as well as the negative symptoms of the disorder (Coyle, 2012). Evidence to support this hypothesis is from experimental studies that have shown that potential medications for schizophrenia known as the N-methyl-D-aspartate (NMDA) receptor antagonists, such as ketamine and phencyclidine (PCP), can cause temporary states in healthy individuals in which schizophrenia-like symptoms such as hallucinations, disorganized thinking, and cognitive impairment can be seen (Javitt & Zukin, 1991).



Two glutamatergic circuits seem to be especially involved in schizophrenia, the thalamo-cortical pathway and the cortico-striatal pathway. These circuits have been found to be critical for sensory processing, information integration and cognitive control. The disturbance in the signalling of the NM receptors in these pathways may cause perception abnormalities and the inability to differentiate internally generated thoughts and external stimuli (Anticevic et al., 2015). Such disturbances could be involved in the characteristic symptoms of schizophrenia such as disorganized thinking and perceptual distortions.

Recent studies have focused more on the interaction of the glutamatergic and dopaminergic systems. For instance, decreased activity of the NMDAs on inhibitory interneurons could result in an underinhibition of dopamine neurons, which results in increased dopamine activity in mesolimbic circuits (Grace, 2016). This interaction implicates abnormalities of dopeamine in schizophrenia as possibly being a consequence of some of the effects alcohol has on glutamatergic function to some extent, and highlights the interconnectedness of neurotransmitter systems in schizophrenia.

However, understanding the motility between dopamine and glutamate is important to treatment development While the traditional antipsychotic medications are mostly directed to the DA receptors, novel approaches to therapy focus on addressing multiple neurotransmitter systems simultaneously. Such approaches involve pharmacological agents that are aimed at increasing glutamatergic signaling or provide better balance within neural circuits, which could provide better outcomes for people with schizophrenia (Howes et al., 2017).

3.2 GABAergic Dysfunction and Excitatory-Inhibitory Imbalance

An important neurobiologic mechanism that is implicated in schizophrenia is an imbalance between the excitatory and inhibitory neural signaling within the brain. Normal cognitive and perceptual functioning depends on the concerted action of the glutamatergic neurons that provide excitatory input, and inhibitory control by the inhibitory neurons that release the neurotransmitter, glucocorticoids. This equilibrium is necessary for synaptic stability, regulation of neural oscillations and is necessary for a co-ordinated cognitive processing. In terms of schizophrenia, it has been shown that there is growing evidence of a disturbance in the signaling of gamma-aminobutyric acid (GABA) involved in an imbalance of excitation and inhibition, causing disorganisation of neural communication and altered mental states (Lewis et al., 2005; Uhlhaas & Singer, 2010).

Country/ Region	Reported GABA Reduction (%) in Prefrontal Cortex	Prevalence of E/I Imbalance Findings in Studies (%)	GABA Interneuron Density Reduction (%)
USA	15.2	78	18
Germany	13.9	74	16.5
Japan	14.5	69	17.2
India	12.7	65	15.3
Brazil	13.3	67	16
South Korea	14	71	17
Australia	13.8	73	16.4

GABA is the major inhibitory neurotransmitter in the central nervous system and defects in functioning of the neurotransmitter has been observed in several areas of the brain in people with schizophrenia. One of the best studied areas is the so-called prefrontal cortex, which plays a central role in what are called executive functions, like planning and attention and working memory. Postmortem and neurophysiological studies have found a decrease in parvalbumin-expressing, interneurons of the gamma-aminobutyric acid (GABA) system of the prefrontal cortex of patients with schizophrenia (Lewis et al., 2012). These interneurons contribute in a significant way to generating Gamma oscillations, a rhythmic pattern of neuronal activity that synchronizes the activity of neurons when a person is performing a cognitive task. Disruption of gamma oscillatory activity has been linked to an impairment of working memory and integration of cognitive functions of thought that may be clinically presented as disorganised thought processes and fragmented speech (Uhlhaas & Singer, 2010).

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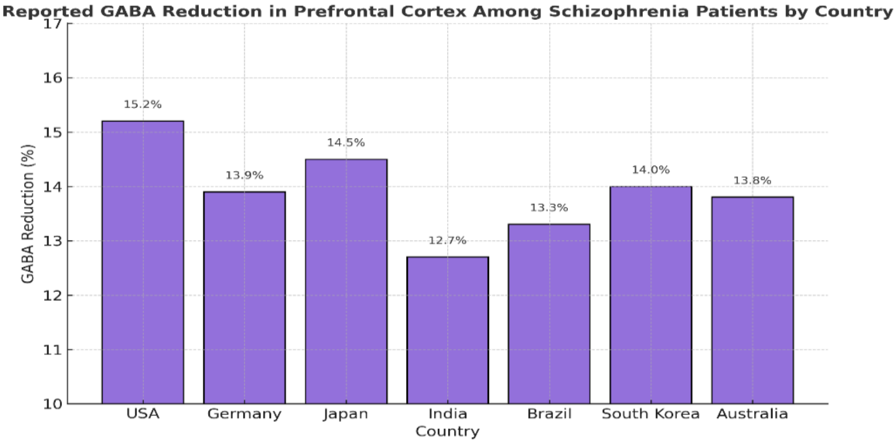


GABAergic dysfunction has also been identified in the hippocampus that is central in the formation of memory and processing of context. Reduced inhibitory control within hippocampus circuits can result in hyperexcitability which can perturb the encoding and recalling of memories. Such disturbances may be responsible for the generation of distorted/intrusive memories, which may affect perceptual misinterpretations, or contribute to explaining the development of psychotic symptoms in an indirect way (Heckers & Konradi, 2010).

Similarly, abnormalities with regard to the signaling of the neurotransmitter gamma amino-acid (GABA) within the brain region called the amygdala has been implicated as playing a role in emotional dysregulation observed in patients with schizophrenia. Altered inhibitory regulation across the circuits of the amygdala may be a part of inappropriate emotional response or reduced emotional expression, both hallmarks features of the disorder (Benes & Berretta, 2001).

Another relevant area in which inhibitory function is disrupted is in the thalamus which acts as a major relay station for sensory information. GABAergic inhibition in thalamic circuitries contribute to a process known as 'sensory gating' that is important for the brain to filter and to prioritize sensory stimuli that are constantly received. Deficits of thalamic inhibition may affect this 'filtering mechanism' and disruptions may lead to the overflow of sensation or perception, such as hypersensitivity between the senses towards the environment or auditory hallucinations (Andreasen, 1997).

The complexity of this dysfunction is further increased by the interaction of the systems of neurotransmitters gamma amino acids (GAB) which are influenced by glutamates. One of the mechanisms which posited is through the hypofunction of the novel N-methyl D-aspartate receptors (commonly found in schizophrenia). Reduced activity at the neurotransmitter receptor (NMDA) on inhibitory interneurons may result in suppression of inhibitory neurotransmitter signaling (GABA) and thus disinhibition of excitatory glutamatergic signaling pathways which may result in local neural circuitry destabilisation (Coyle, 2012). This disruption can contribute to excitatory activity, and can contribute to the greater youth and dissociation of neural network associated 4 the individuals with schizophrenia.

It has important implications for the development of treatments to get a hold of the mechanism of the excitatory-inhibitory imbalance in schizophrenia. In addition to traditional treatment strategies, which depend on dopaminergic agents, novel takes approaches of treatment are being developed that look to restore the stability to the neural network by either augmenting the function of the gamma-aminobutyric acid, or by modulating the function of the glutamatergic system. Examples of such approaches include use of pharmacological agents targeting the Gamma receptors and neuromodulatory interventions including restoration of synchronized neural oscillations with the goal of improving cognitive functioning and decreasing the patient's negative symptoms (Lewis et al., 2012; Uhlhaas and Singer, 2015).

4. Neurodevelopmental and Genetic Factors

Schizophrenia is known to be a complex neurodevelopmental disorder that is caused by a combination of both genetic vulnerability and life longer environmental exposures. Contemporary research has conceptualized the disorder as an outcome of complex interactions involving many genes and developmental factors affecting the maturing process of the brain. This integrated neurodevelopmental version of genetics is providing important information about the early origins, heterogeneity, and long-term course of schizophrenia (Insel, 2010; Rapoport et al., 2012).

The neurodevelopmental theory of schizophrenia suggests that abnormalities in brain development which may start during the prenatal or perinatal period can cause subtle abnormalities in the neural connectivity and cognitive functioning. These early changes can be clinically ascertained as having minimal impact in childhood but as they manifest themselves during the key developmental periods of brain maturation, especially in adolescence, when there is extensive synaptic pruning, cortical reorganization, and refinement of neural networks in key brain regions, such as the prefrontal cortex (Rapoport et al., 2012; Weinberger, 1987). Disturbances in these development processes may make a person vulnerable to the development of psychotic symptoms during late adolescence or early adulthood.

From a genetic perspective, schizophrenia is among the most inherited psychiatric disorders, having a heritability score of around 70% to 80% (Hilker et al. 2018, Sullivan et al. 2003). Large effort genome-wide associations genomic wide association studies (GWAS) has describe the differences between these populations and identify hundreds of genetic loci with increased risk of schizophrenia. Many of these genes have been implicated in the processes of neurodevelopment, such as synaptic formation, neurons moving from one location to another in the brain, and the regulation of neurotransmitters. Notable candidate genes include DISC1 (Disrupted in Schizophrenia 1), COMT (catechol-O-methyltransferase) and NRG1 (neuregulin 1) that are involved in synaptic plasticity, dopaminergic signaling and cortical development (Harrison & Weinberger, 2005; Schizophrenia Working Group of the Psychiatric Genomics Consortium, 2014). Importantly, a number of these genetic pathways overlap with other genetic pathways involved in other forms of neurodevelopmental conditions, such as autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD), suggesting commonality of biological mechanisms in psychiatric disorders (Cross-Disorder Group of the Psychiatric Genomics Consortium, 2013).

The interplay of genetic vulnerability and the elements in the environment is key to the development of schizophrenia. Environmental exposures occurring at a critical time of development, that interact with genetic tendencies, can make development more likely to be sick. Examples include prenatal infections, obstetric complications, perinatal hypoxia, as well as maternal malnutrition (Brown & Derkits, 2010; Cannon et al., 2002). These environmental "hits" may affect gene expression and neural development and these effects may increase the effects of the underlying genetic risk. For example, epidemiological research has proven that maternal infection with the influenza virus during pregnancy is linked to a risk of developing schizophrenia in a future child, especially in those with a higher polygenic risk profile (Brown & Derkits, 2010).

Neuroimaging evaluations have provided additional evidence for the neurodevelopmental model by detecting abnormalities in structure and function of the brain in persons at genetic or clinical high risk for schizophrenia, even before the onset of psychotic chemicals. These findings include enlarged lateral ventricles, low gray matter volume in the prefrontal cortex, and atypical white matter connection (Pantelis et al., 2003). Such abnormalities imply that the changes in the brain that occur with schizophrenia develop slowly over time and do not occur suddenly in adulthood.

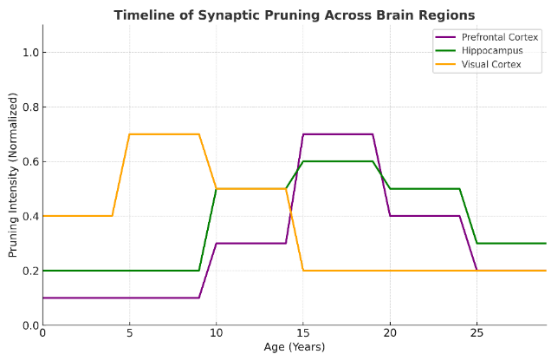
The understanding that schizophrenia is a disease caused by the interacting effects of genetics and development has huge implications for prevention and early intervention. Identifying people at higher risk (with help from genetic screening, family history and cognitive or behavioral assessment) may enable clinicians to implement preventative strategies early on. These may include psychoeducation, cognitive training, lifestyle interventions, and possibly more specific pharmacological approaches in an attempt to decrease the likelihood and/or severity of future psychotic episodes (Fusar-Poli et al., 2013).

Overall, conceptualizing the etiology of schizophrenia within a neurodevelopmental and genetic model promotes a broader and more integrated approach to mental health care, and a more preventive strategy. By understanding that the disorder develops on a continuum of development that is affected by both biological vulnerability and environmental exposures, researchers and clinicians can pay attention to identifying risk earlier and implementing intervention before the illness is fully established.

4.1 Synaptic Pruning and Developmental Timing

Synaptic pruning is a basic but crucial process of the neurodevelopment process in which the brain removes weaker or useless synaptic connections and retains stronger and more efficient neuronal connections. This process helps in increasing the efficiency of the neural circuits as well as helps with maturing cognitive and emotional functioning. Synaptic pruning occurs throughout development but is especially prominent during adolescence/early adulthood, a developmental time period that corresponds with the age-of-onset of schizophrenia in the typical adult. Consequently, abnormalities in synaptic pruning have been suggested as a fundamental process that bridges from neurodevelopmental processes to the development of psychotic symptoms. (Feinberg, 1982; Rapoport et al., 2012).

Under normal developmental conditions, synaptic pruning leads to refinement of neural circuits that are involved in executive functioning, emotional regulation and social cognition. However, in people with a genetic predisposition to schizophrenia, the processes of pruning can take place too much or too early, causing loss of important synaptic connections. This phenomenon seems to be especially true for areas in the prefrontal cortex and the hippocampus which are crucial for higher-order cognitive functions like working memory, decision making or context memory formation (Sekar et al., 2016; Thompson et al., 2001). Disruption in these neural circuits could be clinically manifested as problems in thought organization, interpretation of social cues or ability to have a coherent goal-directed behavior during late adolescence or early adulthood.



Recent genetic research has given rise to some important information regarding the biological systems underlying abnormal synaptic pruning. One notable discovery is regarding the complement component 4 (C4) gene that is a part of the immune-related complement system involved in tagging synapses to be eliminated in the brain during development. Variants that are linked to up-regulation of C4 expression have been associated with an increased risk for schizophrenia. Experimental evidence shows that increased C4 activity may promote excessive synaptic pruning in adolescence, which may account for the low levels of synaptic density observed in people with the disorder (Sekar et al., 2016). These findings support the idea that the causes of schizophrenia may originate in the waning, rather than in degenerative processes that occur later in life.

The study of synaptic pruning has also helped with the understanding of differences between different neurodevelopmental disorders. For example, schizophrenia and autism spectrum disorder (ASD) seem to be examples of opposite dissections of synaptic pruning. While schizophrenia is commonly linked with excessive pruning and a lack of synapses, in ASD this has been shown to be due to inadequate pruning, with a higher level of local connectivity in some brain regions (Tang et al., 2014). These opposite patterns are a boy-Monique-Dogs in the genetics of the material that produces different types of neuropsychiatric outcomes, pointing to the range of neurodevelopmental conditions that are influenced by the genetic and environmental factors.

The timing of developmental processes is also important to the vulnerability to schizophrenia. Adolescence is a sensitive period of time when there is much cortical change called remodeling of the cortex, especially in the prefrontal cortex. It is at this stage that environmental stressors such as chronic stress, substance use or inflammatory processes can interact with the genetic predispositions to disrupt the normal pruning that is part of synaptic maturation (Paus et al 2008). Such gene-environment interactions may make it more likely to develop psychotic symptoms during transition to adulthood.

An understanding of the role of synaptic pruning, and the role that developmental timing plays, has important implications in the early detection and prevention of interven potentials. The identification of people at increased risk during the teenage years may allow the introduction of strategies to protect neural development. These approaches may involve stress reduction intervention programs and/or cognitive training programs, as well as pharmacological and/or neuroprotective treatments aimed at stabilizing the neural circuitry and potentially delaying or preventing the onset of psychosis (Fusar-Poli et al., 2013). As the molecular processes of abnormal synaptic pruning become better defined, such information presents the potential for targeting and developmentally appropriate prevention and treatment responses for schizophrenia.

4.2 Heritability and Candidate Gene Studies

Schizophrenia is well-known to be one of the most inheritable psychiatric disorders, and a large body of evidence now comes from family, twin and adoption studies that show the risk of disease is significantly influenced by genetics. While environmental and developmental factors are also factors in susceptibility, the estimated genetic influence on the overall liability to schizophrenia is about 70%-80% (Hilker et al., 2018; Sullivan et al., 2003). This considerable heritability has led to much research that is aimed at identifying specific genes and molecular pathways involved in the pathophysiology of the disorder.

Twin studies have led to some of the strongest evidence for the genetic basis of schizophrenia. Research on monozygotic of two twins (identical twins) and dizygotic twins (fraternal twins) allows to demonstrate a markedly higher rate of concordance for genetically identical individuals. For example, if one identical twin is ill and has schizophrenia the risk that the other twin will also develop the condition is estimated to be about 40% to 50%, in comparison to a lifetime risk of 1% in the general population (Cardno & Gottesman, 2000; Sullivan et al., 2003.

In addition to heritability studies, candidate gene studies attempts have been made to find specific genes associated with schizophrenia. These investigations have been concentrated mainly on the genes that are associated with neurodevelopment, neurotransmission and synaptic plasticity. One of the most studied genes is the gene that is located on the chromosome, named DISC1 (Disrupted in Schizophrenia 1) and was first discovered by a chromosomal translocation, which was found in a large Scottish family where several family members suffered from schizophrenia and other related psychiatric disorders (St. Clair et al., 1990). DISC1 is critically involved in neuronal migration, synapse formation and the cortex development, which are tightly associated with the neurodevelopmental defects seen in schizophrenia (Brandon & Sawa, 2011).

Another candidate gene that has been well studied is the gene COMT (catechol-O-methyltransferase), which regulates dopamine metabolism in the prefrontal cortex of the brain. The gene harbor a functional polymorphism, the Val158Met that affects the functional metrics of the enzymes, including dopamine degradation. The Val variant is linked with greater enzymatic activity and accelerated break-down of dopamine which may also lead to a reduced amount of dopaminergic signaling in the prefrontal cortex. This difference has been correlated with differences in working memory and executive functioning, cognitive areas often indexed that are impaired in people with schizophrenia (Meyer-Lindenberg et al., 2006). Furthermore, those individuals with the Val allele may be more vulnerable to cognitive impairments related to stress and psychotic symptoms especially during adolescence when dopaminergic systems undergo great developmental changes.

More recently, advances in genome-wide association studies (GWAs) have helped increase the understanding of the genetics of schizophrenia through identification of many risk loci throughout the genome. Large scale collaborative studies have identified more than 100 genetic loci that are linked to higher risk of schizophrenia, many of which are involved in synaptic signaling, immune regulation, and calcium channel functioning (Schizophrenia Working Group of the Psychiatric Genomics Consortium, 2014). Among these, two genes, ZNF804A and CACNA1C, have been the topic of interest due to their connections with their neuronal connection and calcium signaling pathways. Notably, some of these genetic variants have also been linked to bipolar disorder and other psychiatric conditions, among others, suggesting that there may be some common biological mechanisms that underlying multiple mental health disorders (Cross-Disorder Group of the Psychiatric Genomics Consortium, 2013). Importantly the presence of genetic risk factors does not lead inevitably to the person developing schizophrenia. Many people with high genetic risk do not develop this disorder, demonstrating the role of protective influences of environment, resilience mechanisms and developmental context on disorder development. This understanding re-emphasizes the idea that schizophrenia is caused by a complex interaction between genetic susceptibility and environmental factors as opposed to individual gene mutations. Overall, the studies involving heritability and candidate genes highlight the heterogeneity of schizophrenia from a biological perspective. Rather than representing a singular disease entity, schizophrenia appears to be caused by a diversity of genetic pathways and molecular mechanisms that converge and converge in the same circuits within neurons that underlie cognition, perception and emotional regulation. Continued investigation of these genetic mechanisms may lead to the earlier detection of individuals, predict risk, and contribute to developing personalised therapeutic strategies based on the biology of the specific pathways detected to be important in the individual.

5. Implications for Psychotherapy

Advances in neurobiological understanding of schizophrenia are of great significance for psychotherapeutic practice. Contemporary treatment approaches have begun to recognize prominently that effective treatment of schizophrenia involves intervention not only for the psychotic symptoms but also for the cognitive deficits, emotional dysregulation, trauma-related experiences and social functioning. As a result, psychotherapy is now considered a key element of a biopsychosocial model of treatment, in addition to pharmacological treatments, and aiding in longer-term recovery (Mueser & McGurk, 2004; van Os & Kapur, 2009).

Though, cognitive behavioral therapy (CBT) remains one of the most widely studied psychotherapeutic interventions for schizophrenia, the approach to treatment has broadened to encompass a number of specialized treatment modalities. For example, trauma-focused therapy has received growing attention because there is increasing evidence that persons with schizophrenia have histories of childhood adversity, abuse, or neglect. Exposure to trauma experienced in early life has been linked to the increased susceptibility to psychosis, and works that focus on trauma may be helpful in lowering emotional burden and strengthening coping mechanisms (Read et al., 2005).

Similarly, family-based interventions have a significant role for schizophrenia treatment. Family psychoeducation programs try to equip caregivers with the knowledge about the disorder, communication strategies and problem-solving skills that contribute to recovery. Research has shown that such interventions may decrease relapse rates and enhance medication adherence as well as reduce stress for caregivers that can strengthen supportive social environments [Pharoah et al., 2010].

These different approaches to therapy have a common basis in neurobiologically informed therapy. By understanding how schizophrenia impacts specific brain circuits, including those that help us work memory, regulate our emotions and identify threats, clinicians are able to target psychotherapeutic interventions to best assist individuals experiencing with the unique cognitive and emotional problems that affect them. In this regard, psychotherapy is more than supportive counseling; rather it serves as a specific intervention that provokes neural adaptation, social functioning, and long-term rehabilitation (Wykes & Reeder, 2005).

Psychotherapy Modality	**Primary Target Domains**	**Clinical Example/Outcome**
Cognitive Remediation Therapy (CRT)	Attention, memory, executive function	Improves verbal working memory for organizing daily tasks
Cognitive Behavioral Therapy for Psychosis (CBTp)	Delusions, hallucinations, reality testing	Helps reinterpret paranoid thoughts and reduce anxiety
Metacognitive Training (MCT)	Cognitive biases, self-reflection, insight	Reduces overconfidence in delusional interpretations
Trauma-Focused Therapy	PTSD symptoms, emotional regulation, trust building	Supports emotional processing in patients with abuse histories
Family Intervention Therapy	Communication, family stress reduction, relapse prevention	Decreases caregiver burden and improves patient stability
Social Skills Training (SST)	Social interaction, assertiveness, daily life integration	Enhances role-play skills and reintegration into community life

As the conceptualization of schizophrenia integrates more insights from the field of neurobiology and developmental neuroscience, treatment strategies are likely to change as well. Modern therapeutic models focus less on symptom reduction and more on focusing more on functional recovery such as improving cognition, daily functioning, and social participation (Mueser & McGurk, 2004). One example is Cognitive Remediation Therapy (CRT) which is designed to address the cognitive deficits that are commonly associated with schizophrenia such as impairments in attention, memory, and executive functioning. CRT usually entails the structured exercises and strategy-based training that seeks to strengthen cognitive processes that underlie everyday functioning (Wykes et al., 2011).

Another important intervention is Cognitive Behavioral Therapy for psychosis (CBTp). Unlike traditional CBT, CBTp is specially tailored to target psychotic experiences as well as delusions and hallucinations. Through exploring current issues collaboratively and with guiding questions, a therapist supports an individual to scrutinize the available evidence for upsetting beliefs and possible alternative interpretations. While CBTp will not necessarily get rid of psychotic experiences, it can significantly decrease the distress and functional impairment that is associated with psychotic experiences (Morrison et al., 2014).

A complementary approach to therapy is using Metacognitive Training (MCT), which is focused on recognizing and changing cognitive biases that are adding to the persistence of psychotic symptoms. Individuals who have schizophrenia often make cognitive distortions such as leaping to conclusions, attributional distortions, or overconfidence in false beliefs. Procedures that involve the patient in thinking about these cognitions, as well as developing more flexible cognitive strategies, are the focus of MCT interventions and can result in a reduction of paranoia, anxiety and social misunderstandings (Moritz & Woodward, 2007).

Taken together, these therapeutic approaches illustrate how therapy for cognitive rehabilitation and for psychosocial rehabilitation in schizophrenia can be used to support each other. Integrating insights from neurobiology along with the proven methods of psychological treatment, clinicians can craft an individualized treatment strategy that will strengthen the person's cognitive capacities, enhance their ability to control their emotions and help them reintegrate into their social and occupational roles. This changing tide of perceptions makes the importance of psychotherapy as a component of comprehensive schizophrenia care begin to shift to a fluid and scientific approach.

5.1 Cognitive Remediation and Metacognitive Approaches

Cognitive deficits are a key characteristic of schizophrenia and they are sometimes more debilitating thanCopyright positive features of the syndrome such as hallucinations and delusions. Impairments of attention, memory, speed at which cognitive tasks are completed, and executive functioning have a significant impact on daily activities and independence and life quality for people with the disorder (Green, 1996; Green et al., 2004). This cognitive difficulties are highly related to worse social and occupational outcome, thus there is a need for interventions that directly address the area of cognitive functioning. As a consequence of these changes, cognitive remediation and metacognitive therapies are now an essential part of the modern psychotherapeutic practice in schizophrenia.

Cognitive Remediation Therapy (CRT) is focused on improving specific forms and types of thinking - using cognitive exercises and learning-based modalities. In contrast to traditional psychotherapy, the emphasis is placed on working memory and attention and executive functioning skills and problem solving skills rather than a strong focus on emotional insight and interpersonal processes (Wykes et al., 2011). CRT represents an inclusion of computer-guided activities, therapist-guided cognitive activities and simulation of real life situations that stimulate the patient to practice cognitive strategies within a meaningful environment.

For example, people with problems in remembering appointments or daily activities may be allowed to do exercises that will improve their verbal memory, planning skills, and sequence skills. Through repetition and forming strategies, patients will be able to gradually increase their time management skills and organizational skills. Often these improvements are what result in heightened self-efficacy and functional independence in order for individuals to successfully complete their everyday responsibilities (Medalia & Choi, 2009).

Feature	Cognitive Remediation	Metacognitive Approaches
Primary Focus	Improve specific cognitive skills (e.g., memory, attention)	Increase awareness of oneâ€™s own thinking and beliefs
Cognitive Domains Targeted	Working memory, attention, executive functioning	Self-reflection, cognitive bias awareness, social cognition
Method of Delivery	Computer-assisted tasks or therapist-led modules	Group sessions or one-on-one guided reflection
Example Techniques	Memory recall games, sequencing tasks, cognitive drills	Reality-testing exercises, belief re-evaluation, social inference
Typical Outcomes	Improved attention, task organization, planning skills	Greater insight, reduced delusional conviction, improved social interactions
Best Used For	Enhancing functional performance (e.g., job, daily tasks)	Challenging dysfunctional beliefs and improving insight
Clinical Example	Patient improves scheduling and follow-through at work	Patient questions paranoid interpretations of others behaviour

Cognitive remediation programs often go outside of the clinical setting and are a part of psychosocial rehabilitation and vocational training programs. Supported employment models often include cognitive remediation, in an effort to improve working functioning and job maintenance in persons with schizophrenia. Research has shown the intervention of combining cognitive remediation and vocational rehabilitation to be quite effective in helping sufferers improve outcomes in employment over common treatment approaches (McGurk et al., 2007).

Complementing cognitive remediation are metacognitive strategies or those focused on cognitive skills such as making people more aware and in control of their thought processes. Metacognition is the ability to reflect about the beliefs one has, assess the bias of one's thought and know about the mental state of other people. In the case of schizophrenia, it might be that differences in metacognitive capacity are involved in social misunderstanding, delusional interpretations and persistent paranoid thinking (Lysaker et al., 2013).

One intervention that has been widely studied as a potential tool is Metacognitive Training (MCT) that tackles cognitive biases that are typically seen in psychosis. MCT is frequently offered in groups and encourages individuals to gain awareness of thinking patterns that may include: Jumping to conclusions, attributional biases as well as overconfidence in incorrect beliefs (Moritz & Woodward, 2007). Through an active processes of discussion and participatory exercises participants learn to test the evidence behind how they interpret something and will also learn about alternative interpretations. For example, an individual with a neutral social interactions modality in the form of hostile may be guided to explore other possible interpretation of the situation in such a manner that reduces anxiety and interpersonal conflict.

These interventions belong to a larger category of cognitive, metacognitive and affective therapies, which recognize the interrelated relationship between cognition, processing emotion and self-reflection. This integrated view is particularly relevant in a population characterized by schizophrenia in which emotional awareness and insight on the presence of illness is often limited (Lysaker et al., 2013).

When these cognitive and metacognitive interventions are used consistently they can drastically improve recovery outcomes. By improving cognitive functions by increasing the capacity to think reflectively and correcting the way one thinks these therapies help individuals to regain their autonomy, build resilience and lessen the chances of relapse. Importantly, such interventions are complementary to pharmacological treatment by addressing cognitive and social abilities which are required for competent decisions, interpersonal interactions and long-term goals achievement.

5.2 Neurofeedback and Brain Stimulation Techniques

Recent advances in neuroscience have contributed to the evolution of neurofeedback and brain stimulation techniques without invasive electrodes as new tools in the rehabilitation of people with schizophrenia. These approaches involve direct manipulation of abnormal neural activity related to such symptoms as cognitive disorganization, emotional blunting and impaired self-awareness. By specifically targeting dysregulated neural circuits, neurofeedback and brain stimulation technologies are an important area of intersection between neuroscience and psychotherapy approaches in providing novel approaches for improving cognitive and emotional functioning (Keshavan et al., 2011; Slotema et al., 2010).

Neurofeedback, or electroencephalographic (EEG) biofeedback, is the process by which the brainwave activity is actually monitored in real time and given some immediate visual or auditory feedback to the individual who can then learn to control their brain waves. During neurofeedback training sessions, participants view representations of their brainwave patterns and are provided with instructions on how to alter brainwave patterns to more adaptive patterns. For example, individuals can learn to shed excessive theta or beta brainwaves that have been linked to poor attention and to promote more egalitarian brainwaves (Gruzelier, 2014).

In a determinant therapeutic environment the repeated neurofeedback data can enhance continuous stakeholder attention, impulse control and emotional regulation. For people with schizophrenia who suffer from the problems of distractibility or cognitive disorganization, such training may improve engagement in psychotherapy and daily activities. Although there is still relatively little neurofeedback research in schizophrenia, there are some promising results that indicate that it may help those affected improve cognitive functioning and self-regulation (Surmeli et al., 2012).

Neurofeedback has also been done in related neuropsychiatric conditions. For example, the Paediatric Autoimmune Blame for Organisms Syndrome or Paediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) has been shown to benefit OCD symptoms and emotional dysregulation with the use of Neurofeedback (Frank et al., 2018). Although PANDAS is distinct from schizophrenia in its etiology, there are many similarities between the conditions in terms of disruption of neural regulatory processes, and neurofeedback interventions share the same goal of increasing functional connectivity through the process of guided self-regulation.

Technique	Mechanism	Target Symptoms	Delivery Setting	Key Benefit
Neurofeedback	Real-time EEG-based brainwave training	Attention, impulsivity, emotional regulation	Clinic or supervised home setup	Enhances self-regulation and focus
Transcranial Magnetic Stimulation (TMS)	Magnetic pulses modulating cortical excitability	Negative symptoms, depression, cognitive slowing	Outpatient medical centers	Modulates prefrontal circuits non-invasively
Transcranial Direct Current Stimulation (tDCS)	Low-intensity electrical current applied to scalp	Working memory, verbal fluency, motivation	Clinical or remote with professional guidance	Boosts effects of cognitive remediation tasks

On top of the use of neurofeedback, techniques of non-invasive brain stimulation such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) have attracted growing interests in psychiatric treatment. These techniques use various methods of controlled magnetic or electrical current application to targeted areas of the brain in an attempt to control excitability and improve the neuroplasticity (Brunelin et al., 2012). TMS has already been approved for treatment-resistant depression and is currently being investigated as a potential treatment for schizophrenia, essentially, negative symptoms and cognitive deficits related to dysfunction in the prefrontal cortex (Slotema et al., 2010).

Similarly, tDCS is a form of electrical stimulation of low intensity derived via the use of electrodes placed on the scalp, to modulate cortical excitability. Research has suggested that sometimes combining tDCS and cognitive training will improve treatment outcomes. For example, patients receiving tDCS during completion of cognitive remediation exercises have shown greater improvements in verbal fluency, working memory and executive functioning compared to individuals receiving cognitive training alone (Mondino et al., 2016). These findings demonstrate the increasing integration of cognitive, metacognitive, and affective approaches to treatment of schizophrenia.

Technological innovations have also allowed for the creation of portable brain stimulation devices, which allow for some forms of implementation of these interventions in supervised locations such as in the home. Preliminary studies suggest that when used in conjunction with clinician-guided digital therapsy platforms, that these devices can promote enhanced treatment adheisment and accessibility - especially for those who are living in an underserved area or in a rural area (Palm et al., 2016).

Importantly, neurofeedback and brain stimulation techniques are not designed in any way to take the place of extant treatments. Instead, they are adjunctive types of interventions that complement pharmacological therapy and psychotherapy. By improving the neuroplasticity, these methods help the brain reorganize the neural networks and the enhancing adaptive cognitive and emotional processes. When used under the proper clinical supervision neurofeedback and non-invasive brain stimulations show great promise for specifying personalized, neurobiologically informed approaches to improving the long-term outcome of recovery in schizophrenia.

6. Integrated Neurobiological-Psychotherapeutic Models

Contemporary research enhances more acknowledgement the schizophrenia can not be understood by only biological or psychological parameters. Instead, the disorder is thought about most conceptually as the product of interacting neurobiological vulnerabilities and experiential influences, including developmental, environmental and psychosocial. This recognition has paved the way for the introduction of integrated models of neurobiological approaches and psychological interventions, an approach which combines knowledge from neuroscience and evidence-based psychology-based interventions for changing the biological and the experiential dimensions of the disorder (Insel, 2010; van Os & Kapur, 2009).

Traditional psychotherapeutic approaches--where maladaptive beliefs are re-interpreted by the therapeutic process, emotional responses are regulated, and interpersonal functioning is re-built such as cognitive behavioral therapy (CBT) and supportive psychotherapy--have been shown to be effective in helping individuals to process maladaptive beliefs, regulate emotional responses, and re-build interpersonal functioning. However, they can be less successful when they fail to consider the neurocognitive limitations associated with schizophrenia such as working memory and executive functioning and emotional processing (Mueser et al., 2013). On the contrary purely neurobiological models that focus on mechanism like dopaminergic dys regulation, the disrupted neural connectivity or abnormalities in the prefrontal limbic circuits may neglect the lived experiences, identity formation and personal narratives that affect patients recovery process (Keshavan et al., 2011).

Integrated models try to address this shortcoming by combining the psychotherapeutic strategies with the underlying neurobiological basis of dysfunction. One example is the use of cognitive remediation therapy (CRT) combined with metacognitive intervention using findings from neuropsychological and neuroimaging. In clinical practice individuals with marked working memory deficits or those individuals with decreased insight may be the first subject of detailed cognitive assessments in order to determine the presence of particular deficits in executive function. The target of cognitive remediation is cognitive domains that are particularly affected, which can then also be put into place to strengthen the affected cognitive domains. Subsequently, however, metacognitive interventions are introduced in order to train the patients to reflect on their thinking processes, and to aim to seek an evaluation of cognitive biases. Can mean knowing what circuits may be underactive or inefficient in the brain so that therapists can tailor their therapeutic goals and expectations accordingly and adapt them to the patient's cognitive capacity (Wykes and Reeder 2005; Lysaker et al. 2013)

Another example of the integrative practice would be trauma-informed psychotherapy of folks with schizophrenia. Research has found that patients with histories of early adversity often have neurobiological changes, such as reduced dorsolateral prefrontal cortex (hippocampal) volume and increased amygdala reactivity, with which are associated increased stress sensitivity and/or emotional dysregulation (Teicher & Samson, 2016). In such cases, cognitive behavioral interventions - which are specific to the trauma - may be adapted for cognitive and emotional vulnerabilities. Therapists may use simplified language, gradual pacing of therapeutic exposure and repetition of coping strategy reinforcement in order to prevent over stimulation of the stress response system as well as limitations in cognitive processing.

In addition to the use of psychotherapeutic adaptations, integration of monitoring physiological instruments to the therapeutic process has been made possible with technological innovations. For example, biofeedback systems can be used to measure things like Heart Rate Variability (HRV) in therapy sessions providing information on the autonomic stress responses of patients. These physiological signals can also be used to help guide therapeutic pacing so that clinicians can identify a time where emotional arousal levels get out of control and interventions with a goal of providing relaxation and/or grounding may be helpful (Lehrer & Gevirtz, 2014). Such approaches are relevant to illustrate in situ neurobiological information integration in psychotherapeutic decision making.

The development of neurobiological and adaptive models (which integrate neuroscience and psychological science for the study of psychotherapy) is part of a more general movement towards interdisciplinary models of mental health care (in which neuroscience, psychology and clinical psychiatry merge). By acknowledging the neurobiological basis of schizophrenia in addition to the psychological processes that affect people's experience, these models contribute to the spread of more individual-specific approaches to treatment. Ultimately, such integration enables clinicians to invoke a broad range of symptoms reduction, cognitive rehabilitation, emotional resilience and social reintegration in order for science and its application to the treatment of patients to come together.

6.1 Translating Neuroscience into Clinical Practice

Advances in neuroscience are broad-ranging and affecting the delivery of psychiatric care especially in regards to treating complex disorders such as schizophrenia. Historically, decisions were made in the diagnostics and treatment based on the behavioural observation and clinical symptoms. However, modern studies focus more on incorporating the findings of neurobiology with the practice of psychiatry in order to enhance the diagnostic accuracy and treatment outcomes. Translating discoveries from neuroscience into applications in the clinical setting is therefore required to close the bridge between neuroscience research and patient-centered care (Insel, 2010; Keshavan et al., 2011).

One key application in which neuroscience plays an important role in assessing clinical practice is that of neuropsychological profiling. Modern neuropsychological tests and computerized cognitive testing assess clinicians for impairments of specific areas of cognition such as executive functioning, working memory, and guiding attention. Neuroimaging techniques like functional magnetic resonance imaging (fMRI) have revealed that these deficits in these domains are frequently linked to some type of dysfunction in the dorsolateral prefrontal cortex which is responsible for cognitive control and goal-directed behavior (Barch & Ceaser, 2012). By identifying such deficits, clinicians can employ therapeutic strategies aimed at creating ways to compensate for the Cognitive Deficits. For instance, in individuals with prefrontal executive dysfunction, cognitive remediation techniques, structured routines, visual planning interventions and scaffolded task organization may be helpful to aid daily functioning (Wykes et al., 2011).

Neuroscience has also aided in the development of approaches of precision medicine in pharmacotherapy. Changes in the fields of neurogenetics and pharmacogenomics have allowed clinicians to explore genetic differences that affect a person's response to antipsychotic drugs. Variants in genes related to dopamine receptors, dopamine transporters and drug-metabolizing enzymes may influence both the efficacy of treatment and susceptibility to adverse effects (Arranz & de Leon, 2007). Pharmacogenetic testing can therefore help guide clinicians in choosing medications and our dosages that will have the fewest side effects and the greatest therapeutic benefit. This personalized approach is especially understandable for patients that sever adverse reaction to common antipsychotic regimens.

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Neuroscientific information is also changing the face of psychotherapeutic interventions. For example, studies of self-referential processing and neural network dysfunction in schizophrenia have led to an understanding of the development of metacognitive and narrative-based therapies. Functional neuroimaging studies have shown that CI may be associated with disruption in the default mode network (DMN) - a network engaged in self reflection and autobiographical thinking - among individuals with schizophrenia (Whitfield-Gabrieli & Ford, 2012). In response, therapeutic approaches are increasingly making use of guided self-reflection, narrative reconstruction and metacognitive exercises to help the patient re-create a sense of identity and personal meaning (Lysaker et al., 2013).

Another relevant clinical interest of neuroscience is early detection and intervention strategies. And adolescents or young adults who show subtle cognitive, emotional or social signs of change, such as a loss of emotional expression, decline in school performance or social withdrawal, may be given neurocognitive work-ups or electrophysiological screening, such as electroencephalography (EEG). Identifying individuals with high risk for psychosis enables the clinician to begin early interventions including cognitive training, family focusing therapy, psychosocial support and low dose pharmacological treatment for some (Fusar-Poli et al., 2013). Early intervention programs have been demonstrated to have beneficial long-term effects, and may help delay or prevent the development of full psychotic disorders.

Ultimately, the combination of neuroscience and medicine is intended to involve the individualization of psychiatric care. By building a bridge between those neurobiological activities and the measured behavior/everyday functioning in human life, people in treatment science can tailor treatment plans that more precisely target the singular cognitive and emotional signature of each person. As technologies and genetic tools from neuroscience become increasingly accessible, the subordinate challenge will be implementation rather than discovery-and it will need mental health professionals who have both scientific literacy and clinical expertise. Through such interdisciplinary integration, neuroscience has a role to play in being able to provide more successful personalized and compassionate treatment approaches for individuals who are living with schizophrenia.

6.2 Personalized and Multimodal Treatment Strategies

In recent years, the focus of psychiatric care has been moving towards a promotion of personalized medicine, an approach that individualizes the strategy of treatment to meet the unique biological, psychological, and social backgrounds of each individual. This approach is especially applicable to schizophrenia, a disorder with obvious variability in the presentation of symptoms, course of the illness, and response to treatment. Personalized and multimodal treatment strategies attempt to account for this heterogeneity by combining multiple different treatment approaches into a custom care plan for each person in order to promote functional recovery (and long term stability) (Insel, 2010; Mueser & McGurk, 2004).

Personalized treatment commences with a thorough clinical evaluation, possibly consisting of structured diagnostic interviews, neuropsychological testing, functional evaluation and, where possible, genetic or neuroimaging evaluation. Such assessments provide clinicians the opportunity to recognize the specific cognitive, emotional and behavioural issues each patient faces. An example may be where an individual presents with marked impairment in cognitive symptoms as opposed to fairly moderate symptoms in positive symptoms so that cognitive remediation and psychosocial rehabilitation rather than aggressive pharmacological intervention may be more helpful. In such cases, the clinicians may focus mainly on cognitive interventions along with meticulous medication regimens to reduce adverse effects (Wykes et al., 2011).

Complementing personalized assessment is the use of multimodal treatment, which is the coordinated approach to pharmacological, psychological and social treatments within a unified treatment framework. Evidence-based care for schizophrenia is often a combination of antipsychotic medication and psychosocial therapy aimed at the person's cognitive deficits, the emotional distress, and the social functioning (Mueser et al, 2013). For example, a newly diagnosed young adult with schizophrenia may be given a treatment plan of antipsychotic pharmacotherapy, cognitive behavioral therapy for psychosis (CBTp), family psychoeducation, and vocational rehabilitation.

Each of these interventions addresses different areas of impairment and application of all of them can result in outcomes that may be greater than that obtained with any single intervention.

Importantly, not only the profiles of symptoms guide choosing an appropriate treatment, but preferences, personal strengths, and the environment of the sufferer also play a vital role. For instance, people with backgrounds of trauma may benefit from the addition of therapeutic approaches and interventions that are trauma-informed as well as emotional regulation and stress management. Conversely patients with someone having strong family involvement may benefit from structured family therapy programs (to improve communication, reduce interpersonal stress and reduce risk of relapse within the home environment) (Pharoah et al., 2010).

Emerging digital technologies are further providing more opportunities for treatment personalization. Smartphone-based monitoring systems and digital mental health platforms can measure daily statistics like sleeping patterns, mood shifts and social participation, for example. These kinds of tools enable clinicians to detect early warning signs of relapse and implement dynamic healing strategies (T намаа et al., 2018). In addition, novel interventions such as non-invasive brain stimulation techniques, including transcranial direct current stimulation (tDCS) may be combined with cognitive training in order to enhance neuroplasticity and improve cognitive outcomes in individuals with prefrontal cortical dysfunction (Brunelin et al., 2012).

Appropriateness of personalized and multimodal treatment strategies relies to a large degree on cooperation and flexibility. In this model, clinicians act as prescribers of treatment, but also coordinators of multi-disciplinary care, which is done with patients, families and rehabilitation specialists. Treatment plans are always adjusted along the way as the patient's needs change in the process of recovery. By breaking from the mold and introducing personalized and multimodal strategies to individuals with schizophrenia, they are enabled to play a larger role in their treatment and to define their own recovery as a complex and attainable process that is built upon scientific information as much as on compassion.

7. References

1. Arranz, M. J., & de Leon, J. (2007). Pharmacogenetics and pharmacogenomics of schizophrenia: A review of last decade of research. *Molecular Psychiatry, 12*(8), 707–747. https://doi.org/10.1038/sj.mp.4002009
2. Barch, D. M., & Ceaser, A. (2012). Cognition in schizophrenia: Core psychological and neural mechanisms. *Trends in Cognitive Sciences, 16*(1), 27–34. https://doi.org/10.1016/j.tics.2011.11.015
3. Brunelin, J., Mondino, M., Gassab, L., Haesebaert, F., Gaha, L., Suaud-Chagny, M. F., & Poulet, E. (2012). Examining transcranial direct-current stimulation (tDCS) as a treatment for hallucinations in schizophrenia. *American Journal of Psychiatry, 169*(7), 719–724. https://doi.org/10.1176/appi.ajp.2012.11071091
4. Fusar-Poli, P., Borgwardt, S., Bechdolf, A., Addington, J., Riecher-Rössler, A., Schultze-Lutter, F., et al. (2013). The psychosis high-risk state: A comprehensive state-of-the-art review. *JAMA Psychiatry, 70*(1), 107–120. https://doi.org/10.1001/jamapsychiatry.2013.269
5. Green, M. F. (1996). What are the functional consequences of neurocognitive deficits in schizophrenia? *American Journal of Psychiatry, 153*(3), 321–330. https://doi.org/10.1176/ajp.153.3.321
6. Green, M. F., Kern, R. S., Braff, D. L., & Mintz, J. (2004). Neurocognitive deficits and functional outcome in schizophrenia: Are we measuring the "right stuff"? *Schizophrenia Bulletin, 30*(2), 405–417. https://doi.org/10.1093/oxfordjournals.schbul.a007093
7. Gruzelier, J. H. (2014). EEG-neurofeedback for optimising performance. I: A review of cognitive and affective outcome in healthy participants. *Neuroscience & Biobehavioral Reviews, 44*, 124–141. https://doi.org/10.1016/j.neubiorev.2013.09.015

8. Insel, T. R. (2010). Rethinking schizophrenia. *Nature, 468*(7321), 187–193. https://doi.org/10.1038/nature09552
9. Keshavan, M. S., Nasrallah, H. A., & Tandon, R. (2011). Schizophrenia, "just the facts" 6. Moving ahead with the schizophrenia concept: From the elephant to the mouse. *Schizophrenia Research, 127*(1–3), 3–13. https://doi.org/10.1016/j.schres.2011.01.011
10. Lehrer, P., & Gevirtz, R. (2014). Heart rate variability biofeedback: How and why does it work? *Frontiers in Psychology, 5*, 756. https://doi.org/10.3389/fpsyg.2014.00756
11. Lysaker, P. H., Dimaggio, G., Buck, K. D., Callaway, S. S., Salvatore, G., Carcione, A., & Nicolò, G. (2013). Metacognition within narratives of schizophrenia: Associations with neurocognition and social functioning. *Schizophrenia Research, 144*(1–3), 122–127. https://doi.org/10.1016/j.schres.2012.12.006
12. McGurk, S. R., Twamley, E. W., Sitzer, D. I., McHugo, G. J., & Mueser, K. T. (2007). A meta-analysis of cognitive remediation in schizophrenia. *American Journal of Psychiatry, 164*(12), 1791–1802. https://doi.org/10.1176/appi.ajp.2007.07060906
13. Medalia, A., & Choi, J. (2009). Cognitive remediation in schizophrenia. *Neuropsychology Review, 19*(3), 353–364. https://doi.org/10.1007/s11065-009-9097-y
14. Mondino, M., Jardri, R., Suaud-Chagny, M. F., Saoud, M., Poulet, E., & Brunelin, J. (2016). Effects of fronto-temporal transcranial direct current stimulation on auditory hallucinations and cognitive function in schizophrenia. *Scientific Reports, 6*, 27618. https://doi.org/10.1038/srep27618
15. Moritz, S., & Woodward, T. S. (2007). Metacognitive training in schizophrenia: From basic research to knowledge translation and intervention. *Current Opinion in Psychiatry, 20*(6), 619–625. https://doi.org/10.1097/YCO.0b013e3282f0b8ed
16. Morrison, A. P., Turkington, D., Pyle, M., Spencer, H., Brabban, A., Dunn, G., et al. (2014). Cognitive therapy for people with schizophrenia spectrum disorders not taking antipsychotic drugs: A single-blind randomized controlled trial. *The Lancet, 383*(9926), 1395–1403. https://doi.org/10.1016/S0140-6736(13)62246-1
17. Mueser, K. T., & McGurk, S. R. (2004). Schizophrenia. *The Lancet, 363*(9426), 2063–2072. https://doi.org/10.1016/S0140-6736(04)16458-1
18. Mueser, K. T., Deavers, F., Penn, D. L., & Cassisi, J. (2013). Psychosocial treatments for schizophrenia. *Annual Review of Clinical Psychology, 9*, 465–497. https://doi.org/10.1146/annurev-clinpsy-050212-185620
19. Pharoah, F., Mari, J., Rathbone, J., & Wong, W. (2010). Family intervention for schizophrenia. *Cochrane Database of Systematic Reviews*, (12), CD000088. https://doi.org/10.1002/14651858.CD000088.pub3
20. Read, J., van Os, J., Morrison, A. P., & Ross, C. A. (2005). Childhood trauma, psychosis, and schizophrenia: A literature review with theoretical and clinical implications. *Acta Psychiatrica Scandinavica, 112*(5), 330–350. https://doi.org/10.1111/j.1600-0447.2005.00634.x
21. Slotema, C. W., Aleman, A., Daskalakis, Z. J., & Sommer, I. E. C. (2010). Meta-analysis of repetitive transcranial magnetic stimulation in the treatment of auditory verbal hallucinations. *Biological Psychiatry, 68*(2), 130–136. https://doi.org/10.1016/j.biopsych.2010.03.012
22. Surmeli, T., Ertem, A., Eralp, E., & Kos, I. H. (2012). Schizophrenia and the efficacy of qEEG-guided neurofeedback treatment: A clinical case series. *Clinical EEG and Neuroscience, 43*(2), 133–144.

https://doi.org/10.1177/1550059411429531

23. Torous, J., Bucci, S., Bell, I. H., Kessing, L. V., Faurholt-Jepsen, M., Whelan, P., et al. (2018). The growing field of digital psychiatry: Current evidence and the future of apps, social media, chatbots, and virtual reality. *World Psychiatry, 17*(3), 318–335. https://doi.org/10.1002/wps.20544
24. van Os, J., & Kapur, S. (2009). Schizophrenia. *The Lancet, 374*(9690), 635–645. https://doi.org/10.1016/S0140-6736(09)60995-8
25. Whitfield-Gabrieli, S., & Ford, J. M. (2012). Default mode network activity and connectivity in psychopathology. *Annual Review of Clinical Psychology, 8*, 49–76. https://doi.org/10.1146/annurev-clinpsy-032511-143049
26. Wykes, T., & Reeder, C. (2005). *Cognitive remediation therapy for schizophrenia: Theory and practice*. Routledge.
27. Wykes, T., Huddy, V., Cellard, C., McGurk, S. R., & Czobor, P. (2011). A meta-analysis of cognitive remediation for schizophrenia: Methodology and effect sizes. *American Journal of Psychiatry, 168*(5), 472–485. https://doi.org/10.1176/appi.ajp.2010.10060855

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