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Review Article

NEUROTRANSMITTER AND BRAIN PARTS INVOLVED IN SCHIZOPHRENIA

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ABSTRACT

Schizophrenia (SCZ) is a major debilitating, complex, and costly illness that strikes 1% of the world's population. It is characterized by three general types of symptoms: Atypical symptoms (aggressiveness, agitation, delusions, hallucinations), depressive symptoms (alogia, avolition, anhedonia, apathy), and cognitive symptoms (impaired attention, learning, memory). The etiology of SCZ has still not been fully understood. Alteration in various neurochemical systems such as dopamine, serotonin, norepinephrine, gamma-aminobutyric acid, and glutamate are involved in the pathophysiology of SCZ. The lack of understanding regarding the exact pathogenic process may be the likely a reason for the non-availability of effective treatment, which can prevent onset and progression of the SCZ. The tools of modern neuroscience, drawing from neuroanatomy, neurophysiology, brain imaging, and psychopharmacology, promise to provide a host of new insights into the etiology and treatment of SCZ. In this review, we will discuss the role of the various neurotransmitter concerned and brain parts exaggerated in the SCZ.

Keywords: Schizophrenia, Memory, Cognitive dysfunction, Dopamine, Glutamate.

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INTRODUCTION

Schizophrenia (SCZ) is categorized by a spectrum of symptoms that characteristically consist of chaotic thinking, societal withdrawal, hallucinations (both acoustic and optical), delusions of persecution (suspicion), and peculiar manners. These symptoms are sometimes considered as "positive" (such as hallucinations) and "negative" (such as communal departure and lethargy). SCZ is a common and devastating disease which is categorized by chronic psychotic symptoms and psychosocial destruction [1]. An understanding of the pathophysiology of SCZ will be important to the invention of an anticipatory method and healing intervention. Rapidly advancing research into SCZ includes diverse etiological hypothesis and offers instructions for prospect investigate and treatments [2]. SCZ is a constant and distressing neuropsychiatric disorder affecting 1% of the world population. It is associated with disturbances in social performance and has high suicidal rates leading to personal and family suffering. In psychiatric disorders, improper alterations in cortical circuitry and synaptic transmission in the developing brain occurs due to primary alterations in the activity of these molecules, which could then translate into the neural dysfunction [3].

The onset of the disease occurs mainly in late adolescence and adulthood. There is certain evidence, which signifying the susceptible genes and environmental risk factors associated with the SCZ and how these interactions between them self-leading to the progression of disease. All these evidence have supported the fact that there are deficits during neurodevelopment that is the main root cause of the pathophysiology of the disease [4,5]. The risk factors operate synergistically with both neurodevelopment and glutamate-associated signaling [6]. The characteristic feature of the disease is intense and long-lasting impairments mainly in language, memory, and cognition, as well as the brain regions, subserving these domains are affected structurally and functionally [7]. It imposes an excessively large financial load in terms of hospitalization, chronic treatment, psychotherapy, and lost efficiency [8]. Males are more vulnerable to SCZ rather than females which start from mid to late adolescence through early adulthood [9]. During the premorbid stage of the disease, minor physical anomalies and subtle motor, societal, or cognitive impairments are often observed. However, these differences commonly fail to place persons outside the regular range of performance. Attenuated positive symptoms, mood symptoms, cognitive symptoms, societal withdrawal, or obsessive activities may arise in the prodromal stage [10,11]. It is a remarkable challenge for the scientific community represented by SCZ, which produces the human suffering, family tragedies, and financial burden [9]. Even though some insights into the etiology of SCZ have been developed, an indulgent of the disease on the molecular level remains indescribable. Thus, essential avenues characterized by neuroanatomy, neurophysiology, brain imaging, and psychopharmacology during modern investigation [10].

CLINICAL FEATURES OF SCZ

SCZ is a destructive ill health that strikes at some of the highly developed functions of the human brain. Psychotic or "positive" symptoms (aggressiveness, agitation, delusions, and hallucinations), deficit or "negative" symptoms (alogia, avolition, anhedonia, and apathy), and cognitive dysfunction (impaired attention, learning, and memory) are three main categories of symptoms. The psychotic symptoms of SCZ are a feature of many brain diseases but are often the most disturbing and noticeable symptom to others. Hallucinations, delusions, and thought disorder are three main categories included in psychotic symptoms. The rigorous disturbances in social relations, enthusiasm, expression of affect, ability to understanding enjoyment, and natural tongue considered under the negative symptoms [12,13]. Elite functions such as concentration, memory, and general cerebral performance are affected by cognitive disfigurement in SCZ. The psychotic symptoms have an episodic pattern, but the negative and cognitive symptoms are more persistent and chronic and when active is usually the impetus for hospitalization [14,15].

During the first 5-10 years, both positive symptoms such as delusions, hallucinations, negative symptoms like impaired cognition, decision, sensation and deterioration of the substantial functions such as work, interpersonal relationships as usually occurs after the onset of full syndrome. Fuzzy disturbances in the form and content of thought, observation, cognition, feeling, sense of self, desire, social relationships, and psychomotor behavior which further defines SCZ characteristically [16].

- Symptoms of a acute episode may include the following: Being out of touch with actuality; hallucinations (particularly hearing voices); delusions (fixed false beliefs); ideas of influence (performance embarrassed by external influences); detached thought processes (wobbly relations); ambivalence (differing in belief); flat, improper, or labile influence: Autism (solitary and secretly directed opinion); lack of support, lack of sympathy, and orally or bodily violence: Impaired self-cured skill; and distressed sleep and hunger [13].
- The patient usually has remaining character (e.g., nervousness, suspiciousness, lack of desire, lack of enthusiasm, poor insight, impaired judgment, societal extraction, complexity in wisdom from understanding, and poor personality skills), after the acute psychotic episode [12]. The various clinical features of SCZ are summarized in Fig. 1 [12].

Neurotransmitter hypothesis of SCZ

There are a number of theories of SCZ, dominated for many years by neuropharmacology, that implicate aberrant neurotransmission systems, in particular, aberrant dopaminergic, serotoninergic, and glutamatergic systems. It is unclear; however, to what extent any neurochemical findings reflect primary rather than secondary pathology, compensatory mechanisms, or environmental influences [15,23,24]. Certain studies have suggested that dysregulation of dopaminergic, gamma-aminobutyric acid (GABA), glutamatergic neurotransmission, and their interactions are involved in the pathophysiology of SCZ [25-27]. Neurotransmitters and the pathogenesis of SCZ are summarized in Table 1.

Dopaminergic hypothesis

Psychoses may result from hyper- or hypoactivity of dopaminergic processes in specific brain regions. This may comprise the presence of a dopamine (DA) receptor defect. The dopaminergic hypothesis of SCZ considers that an improper dopaminergic transmission at the dopamine D2 receptor in the mesolimbic and prefrontal brain regions is responsible for schizophrenic symptoms mainly positive [24]. In spite of having several limitations until now, this hypothesis remains the prominent neurochemical theory. There is certain evidence such as dopamine presynaptic storage dysfunction, abnormal vascular transport, release, reuptake, and metabolic abnormality in the mesolimbic dopamine system, which suggests the involvement of presynaptic dopaminergic abnormality in the illness. Dysregulation and hyperresponsiveness of presynaptic dopamine neurons further induce oxidative stress which may lead to long-lasting consequences. As a result, dopamine activity may be decreased in the neocortex, responsible partially for negative symptoms such as emotional or cognitive impairment [11].

GABAergic inhibitory input that arises from the ventral pallidum is considered to be the most potent input to the dopaminergic neurons. Dopaminergic projections that are linked to SCZ which involved in the mesocortical system. This system arises in the ventral tegmental area (VTA) and projects to numerous cortical areas including mainly the prefrontal cortex, anterior cingulate cortex (ACC), and the temporal lobes. Abnormality in dopaminergic signaling, as well as the mesolimbic and nigrostriatal projections, is likely to be involved in SCZ [28].

The dopamine levels are found to be enhanced in the substantia nigra and the striatum of the basal ganglia, the levels found to be decreased in the cortex of schizophrenic patients. In neuroleptic-naive patients, changes in dopamine synthesis, storage, and release results in an overactive striatal dopaminergic system [29]. The high striatal dopamine function has been strongly linked to motor dysfunction and psychotic symptoms [30]. The D1 and D2 dopamine receptor abnormality, likely thought to be responsible for some of the abnormal behavioral and motor symptoms seen in SCZ [31].

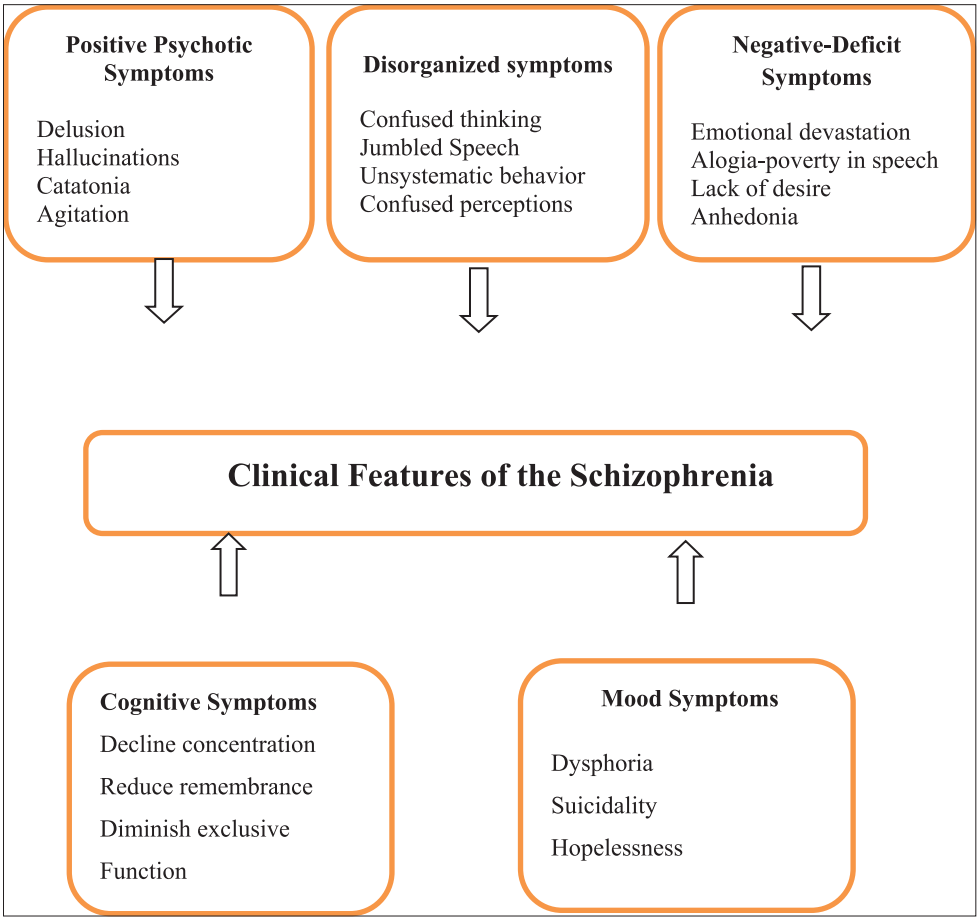

Fig. 1: Clinical features of schizophrenia

Table 1: Neurotransmitters and the pathogenesis of SCZ

Neurotransmitters	Action of NT	Brain part involved	Receptors	References
Dopamine	Increase/decrease	Mesolimbic (positive symptoms) and mesocortical (negative symptom)	D2 and D4	[17]
Serotonin	Increased	Prefrontal cortex (negative symptoms)	5-HT2A and 5-HT1A	[18,19]
Glutamate	Glutamate receptor binding changes	Prefrontal cortex, thalamus, and hippocampus	NMDA	[20,21]
GABA	Decrease	Limbic and prefrontal cortical	GABA A	[21,22]

GABA: Gamma-aminobutyric acid, NMDA: N-methyl-D-aspartate, SCZ: Schizophrenia

This hyperstimulation is thought to result from highly sensitive D2 receptors, antipsychotic drugs (amphetamine or methylphenidate) exacerbated psychotic symptoms in SCZ patients [32]. In the nigrostriatal projection, dopamine is produced and synthesized in the substantia nigra, in turn stimulating movement through D1 receptors. Dopamine by binding to the D2 receptors via the GABA neurons which inhibits the indirect pathway and suppresses movement [33].This indirect pathway begins with cortical excitation of the striatal neurons and excites the GABA neurons, discrete from those that are excited in the direct pathway. The neurons in the substantia nigra are projected and inhibit the motor-related functions of the thalamus. The balance between two conjugate pathways is needed for normal motor function [34]. There are four main dopamine pathways in the brain. The mesolimbic system concerned with the addiction, emotion, perception & pleasure and reward-seeking behaviors, cognition. The mesocortical pathway involved in attention, emotional behavior, learning, and memory. The nigrostriatal pathway implicated in movement and sensory stimuli and tubuloinfundibular pathway for the control of inhibition of the prolactin hormone secretions and functions of the hypothalamic–pituitary endocrine systems. The pathways of dopamine in brain and SCZ are summarized in the Fig. 2 [35].

The dopamine hypothesis of SCZ proposed that the positive symptoms of the illness arose as a consequence of the hyperactivity of the dopaminergic system, in the mesocortical and mesolimbic area of the brain whose origin lies in the VTA. The dopamine hypothesis has been made to reconcile by focusing on other neurotransmitters that may interact with dopamine in discrete cortical and subcortical neural circuits. Dopamine heteroreceptors have been suggested to regulate the release of glutamate in the striatum; this finding is an evidence for the hypothesis which suggests the involvement of abnormal levels of both glutamate and dopamine in the corticostriatal Pallidal thalamic circuit in the etiology of SCZ. Along with the dopamine-glutamate abnormality in the corticostriatal systems, the possible involvement of other subcortical regions has also accounted for schizophrenic symptoms. The important area of the brain involved in new memory formation, information processing, and generation of specimen-specific behaviors are hippocampus and entorhinal cortex. Morphological and cytoarchitecture abnormalities in these areas of the brain have been suggested for the positive symptoms of SCZ. Hippocampus and entorhinal cortex are innervated by the dopaminergic system, while glutamate is considered to be the predominant intrinsic excitatory neurotransmitter. Thus, the positive symptoms of the illness may be considered to be related to the hippocampus dopamine–glutamate system dysfunction [12].

Brain-derived neurotrophic factor (BDNF)

BDNF has been associated with the pathophysiology of SCZ. However, it is not clear whether alterations in BDNF observed in schizophrenic patients are a core part of disease neurobiology or a result of treatment. The neurotrophic factors, such as nerve growth factor, BDNF, neurotrophin-3 (NT-3), and neurotrophin-4/5 (NT4/5) support the development, differentiation, and survival of nerve cells during growth and are also involved in the maintenance and flexibility of adult neurons [36].

Dopamine (DA) has been strongly having a major role in the pathophysiology and management of SCZ. There are several studies, which show an interactions between BDNF and the DA system. In the cell cultures from embryonic rat and human ventral mesencephalon, BDNF reduces the loss of tyrosine hydroxylase and protects dopaminergic neurons from neurotoxic agents such as 6-hydroxydopamine and 1-methyl-4-phenylpyridinium [37]. It has been reported by several studies that there is a significant reduction in serum BDNF levels of chronic and medicated schizophrenic patients compared to healthy volunteers [38].

Serotoninergic system

Recent focus has been changed toward the involvement of serotonin (5-hydroxytryptamine, 5-HT) in the pathophysiology of SCZ [39]. Serotonin is an essential neurotransmitter synthesized from dietary tryptophan. The possible role of serotonin in SCZ was first recognized in the 1950's when serotonin was noticed to be similar to lysergic acid diethylamide (LSD). LSD competes for and occupies serotonin's receptor sites with very high potency, resulting in the development of psychosis-like symptoms. The hypothesis was supported by the fact that typical antipsychotics, when used in combination with a 5-HT2 antagonist such as ritanserin resulted in a considerable relief of patient's negative symptoms and motoric side effects. 5-HT2A receptor regulation appears essential for many of the features of the atypical antipsychotic drugs. All atypical antipsychotic drugs have been shown to have a favorable 5-HT2A/D2 affinity ratio *in vitro* and *in vivo*. The number of cortical 5-HT2A and 5-HT1A receptors is altered in schizophrenic brains [40]. 5-HT2C receptor antagonists are likely to produce weight gain and possibly seizures [18]. Certain polymorphisms of the 5-HT2A receptor gene are associated with SCZ; the trophic role of serotonin in neurodevelopment may be usurped in SCZ; 5-HT2A receptor-mediated activation of the prefrontal cortex may be impaired in some schizophrenics, and serotoninergic and dopaminergic systems are interdependent and may be simultaneously affected in SCZ [39]. Newer antipsychotic drugs are targeting serotonin receptors, and so the system is being studied for SCZ. Decreased in the cortical 5-HT2A receptor concentration and increased in the 5-HT1A receptor density have been reported in SCZ [41,42].

Glutamatergic system

Glutamate is the most abundant amino acid neurotransmitter in the mammalian brain. There are two types of glutamate receptors: Metabotropic and ionotropic receptors. The ionotropic receptors are subdivided into three subtypes and are the major focus in SCZ: N-methyl-D-aspartate (NMDA), quisqualate/gamma-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (amino-3-hydroxy-5-methyl-isoxazole-4-propionic acid [AMPA]), and kainate [43]. However, the NMDA receptor (NMDAR) is the most studied and relevant receptor subtype to understand the pathophysiology of SCZ. The NMDA receptor plays an important role in neurocognition and toxicity [44]. The NMDAR D-serine/glycine site on the NR1 subunit is not fully saturated at synapses in brain regions such as the prefrontal cortex, neocortex, hippocampus, thalamus, and brainstem slices, suggesting that agonists of the D-serine/glycine site are capable of regulating NMDAR-mediated neurotransmission [45]. Glycine is a major inhibitory neurotransmitter throughout the brain. The synapses are extensively reorganized during postnatal brain development up to young adulthood. NMDA receptor also plays a key role in the major changes of reorganization of glutamatergic synapses [46]. NR2A and NR2B subunits have dissimilar conductance and calcium permeability. NR2A and NR2B subunits are highly expressed

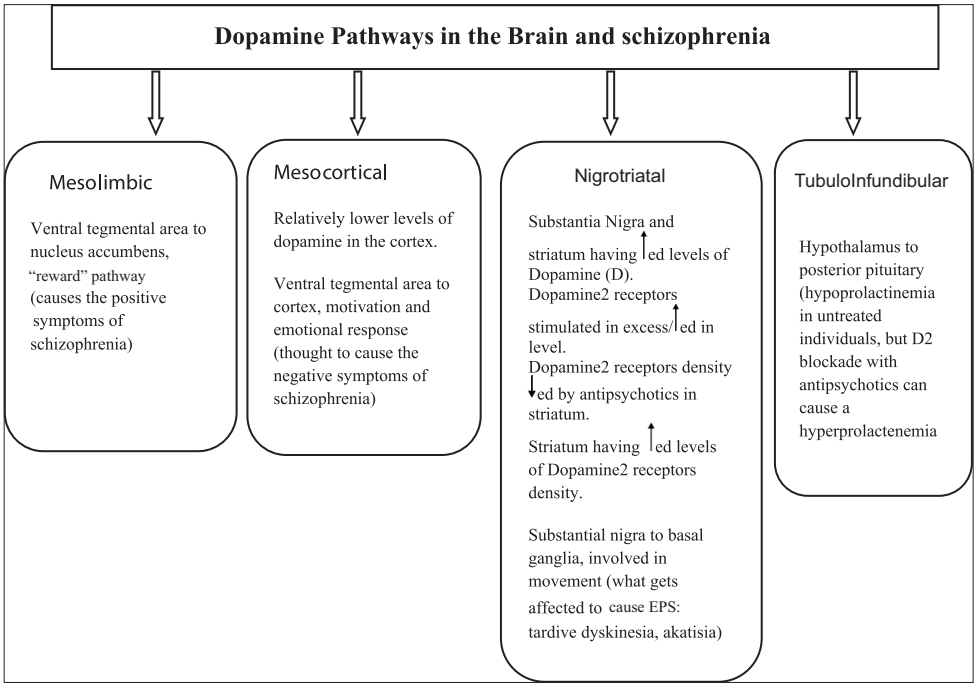

Fig. 2: Major pathways for the dopaminergic system in the brain and schizophrenia

in the forebrain corticolimbic regions and undergo a developmental shift: Switching progressively from richness in NR2B subunits in the early postnatal brain into richness in NR2A subunits during development [47]. A major role of this shift is to change the threshold for modifying synaptic power. Therefore, the ratio of NR2A/NR2B has a significant contribution in the development of cortical functions [48]. This developmental switch results in changes in brain plasticity and synaptic transmission [49]. One more important neurodevelopmental process is "synaptic pruning," in which synapses are reorganized into more competent configurations, including glutamatergic synapses. Much evidence suggests that hypofunction of NMDA receptor-mediated neurotransmission is a significant deficit in SCZ [50]. Effects on different symptom domains of SCZ such as negative symptoms, cognitive deficits, and quality of life, except neurotransmission, synaptic flexibility, memory, and cognition are also regulated by the NMDA receptor. Thus, reduction of NMDA receptor-mediated neurotransmission may result in loss of neuronal plasticity and cognitive deficits [51].

The dopaminergic and glutamatergic system of the brain are interconnected, and thus, inhibition of one system will influence the functioning of the other system [52]. The NMDA receptor antagonist diminishes the corticofugal inhibition of subcortical dopamine neurons and hence enhances dopaminergic transmission [53]. It was concluded by PET studies that acute administration of NMDA-receptor antagonists increases dopamine release in the striatum and chronic administration elicits decreased dopamine release or hypoactivity in the prefrontal cortex [54]. AMPA and kainate receptors are non-NMDA glutamate receptors that get overactivated by NMDA receptor. Glutamate release as a response to NMDA receptor antagonists might in part be responsible for their behavioral effects. NMDA receptor hypofunction may alter synaptic connectivity leading to abnormality [35,55].

NMDA

Abnormality in the dopamine levels in schizophrenic brain remains highly pertinent to deficits in reward response, novelty detection, attention, and neuroplasticity [56,57]. Unusual dopamine signaling is a consequence of many other primary modulatory abnormalities, including NMDAR dysregulation [58]. Among relevant receptor systems, NMDARs have drawn maximum attention due to historical observations that the NMDAR antagonist phencyclidine produces a syndrome in healthy individuals which resembles SCZ. Electrophysiological findings provide additional support for a link between NMDA and GABA in SCZ, as reduced NMDAR depended on inhibitory drive results in the increased excitability that characterizes SCZ [59].

Acetylcholine

Neurotransmitter acetylcholine controls the activity of the cholinergic system in the central nervous system (CNS) and is important in many functions such as learning and memory [60]. Acetylcholine functions by activating two families of receptors, the nicotinic receptors which are ligand-gated ion channels and muscarinic receptors which a G-protein-coupled receptors [61]. There are five types of muscarinic (M1-M5) receptors and all are present in the human CNS but are expressed in a different way on CNS regions and different cells and capable of controling different CNS functions [62]. The belief that muscarinic receptors were involved in the pathophysiology of SCZ came from early clinical neuropsychopharmacological studies. It was the demonstration that in the caudate-putamen from patients with schizophrenia (3H) pirenzepine binding was less [63]. It was a good an effort in better understanding the role of muscarinic receptors in the pathophysiology of SCZ. The lower levels of (3H) pirenzepine binding were also reported in the cortex and hippocampus in schizophrenic patients. It is therefore significant that it is lower levels of muscarinic M1 receptor (CHRM1), that accounts for the decreased levels of (3H) pirenzepine binding in the cortex of patients with SCZ [64,65].

Cognitive and neurological abnormalities in SCZ

SCZ is associated with defective memory, attention, executive, and intellectual impairment [66,67]. Yet, a gracious literature has emphasized that dysfunction in basic motor function and control represents an extremely pertinent physiological pathway in the disease [68]. The motor dysfunction in SCZ is more direct, showing the impairments in basic motor processing and control. Medial orbitofrontal cortex and rostral part of the ACC (rACC) were responsible for emotional processing and decision-making, as well as playing an important role in social behavior and interaction. It was supported by the evidence that the brain regions such as the dorsal ACC, the basal ganglia, and the cerebellum, which are associated with memory and executive control are implicated in SCZ [69,70].

There are several evidences which indicate that the brain's limbic system is involved in SCZ. In addition, the dopaminergic mesolimbic tract (originates in the VTA of the midbrain and projecting to a number of limbic regions) is considered to play a most important role in the development of positive psychotic symptoms of SCZ. The neuroleptic drugs show improvement of the psychotic symptoms by blocking D2 receptors in the limbic structures [71]. There is a reduction in volume of limbic structures in SCZ and histological abnormalities are seen in medial temporal lobe structures, that is, the hippocampal formation, amygdala, and adjacent cortical areas [72]. The gray matter volume decreases in medial temporal lobe and an increase of the temporal horn of the lateral ventricles [73]. There is an increase and decrease in metabolic activity in the medial temporal lobe regions of schizophrenics [74]. The abnormalities include a decrease in area or whole volume of the hippocampus as well as in the number of hippocampal neurons, reduced neuronal size and density, and pyramidal cell disarray, the majority of cases consistent with hippocampal sclerosis [75]. The various brain parts and its features are shown in Fig. 3 [76].

SCZ is a "thought disorder," and thinking has been conceptualized as an "active motor process." The basal ganglia are considered as cognitive and motor pattern generators [76]. It generates sequences of action which designs the future action. Schizophrenic patients with motor abnormalities predict deficits in memory, decision-making, and concentration [77]. The corticocerebellar inhibition of the motor cortex is important in the coordination of motor sequences, which has been suggested to be impaired in various findings. Thus, cerebellar organization influences the fidelity of perceptions, error detections, and quick modulation of coordination [78]. SCZ may impair these functions of cerebellum resulting in misinterpretation of incorrect sensory associations usually suppressed by the cerebellum, resulting in the repeatedly noted evidence of anomalous prophetic coding in the illness [79].

The basal ganglia play a role in sequencing the activation for fast actions by balancing movement and muscle activation [80]. Connections to the corticopontocerebellar system make the cerebellum which a main control area for voluntary motor control, enhances the structures relevance for SCZ [81]. The main output center of the cerebellum is the dentate nucleus, which links premotor, prefrontal, posterior parietal and primary motor cortex mainly through the thalamus. These areas of cortex sends back the projections for the processing through pons. These corticocerebellar loops link function of the cerebral cortex to the cerebellum and vice versa. The cerebellum is thought to act as a timer, updating and predicting body dynamics for fast movements based on sensory feedback, and this precision is assumed to have high temporal fidelity [82-84].

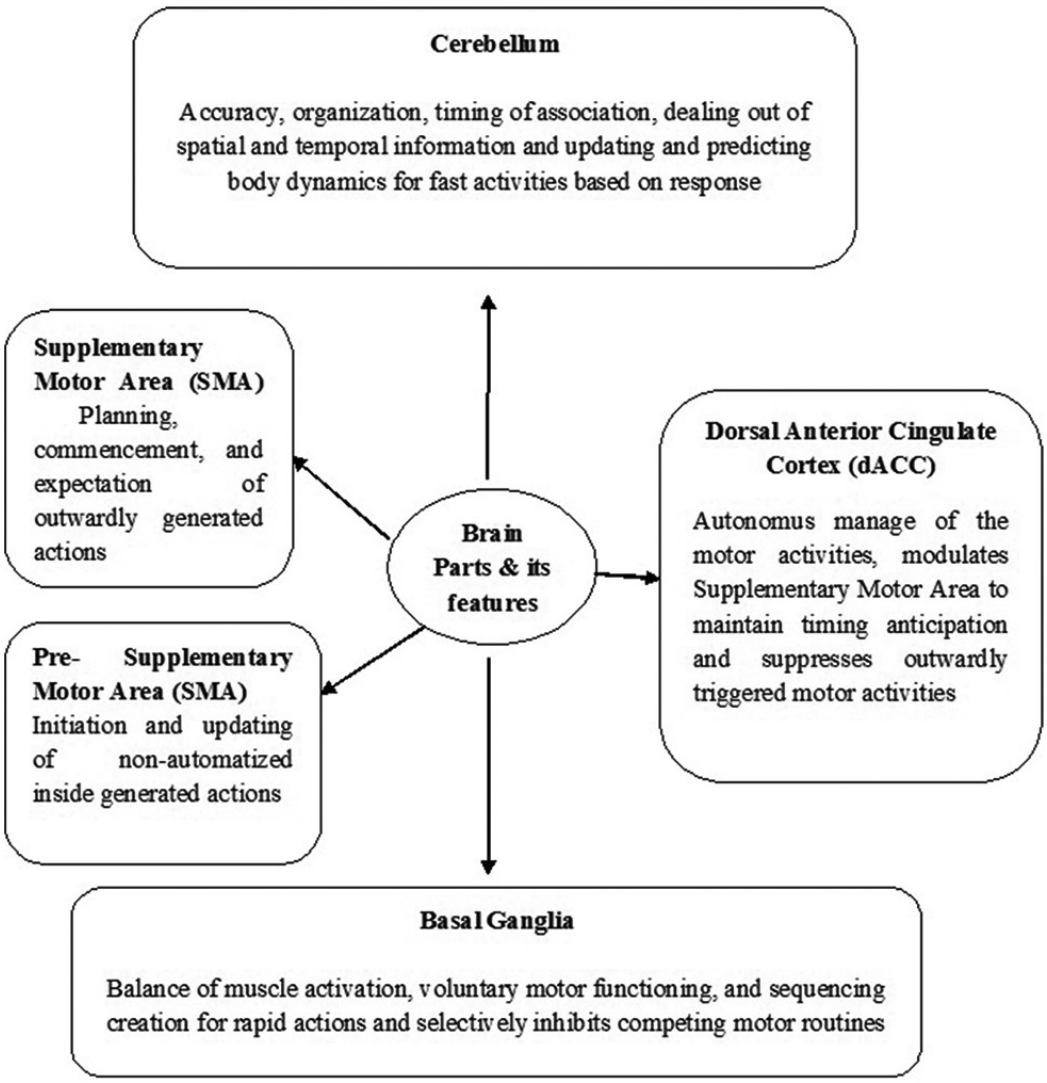

Fig. 3: Brain parts involved in schizophrenia

Table 2: Schizophrenic symptoms produced by different brain parts abnormality

S.No.	Brain part	Abnormality	Schizophrenic symptom	Reference
1.	mOFC and rostral part of the anterior cingulate cortex (rACC)	White matter abnormalities within connections between mOFC and rACC (reductions in fractional anisotropy)	Anhedonia-asociality and avolition-apathy	[90]
2.	Left superior and middle temporal gyri	Gray matter reductions	Auditory hallucinations	[91]
3	Ventricles and the basal nuclei	Larger than normal	Controlling and planning movements and cognition	[92]
4	Hippocampus and amygdale	Bilateral volume reduction	Thought disorder and negative symptoms	[93]
5	Thalamus	Volume reduction	Execution of function and sensory integration	[94]
6	Pre-frontal cortex	Altered functional connectivity, decreased gray matter (lower activation in response to goal-representation demands)	Suicidal behavior and impairment of executive functioning	[95-97]
7	Dorsolateral prefrontal cortex	Reduced GABA synthesis and disruption of the glycosylation process	Working memory dysfunction	[20]
8	Cerebellum	Abnormal morphology Purkinje cells have decreased size and density. Decreased functional connectivity with motor cortex	Role in voluntary motor control, balance, coordination, higher cognitive non-motor functions	[98,99]
9	Basal ganglia	Abnormal morphology of the striatum and globus pallidus	Motor function and higher level cognitive decision of voluntary movements are influenced	[100]
10	SMA (supplementary motor cortex)	Abnormal gray matter volume and decreased cortical thickness	Role in the externally generated movements	[101-103]
11	dACC (dorsal anterior cingulated/ midcingulated cortex	Reduction in gray matter volume and interneuron	Functional connections to the lateral prefrontal cortex, limbic structure, striatum, SMA	[102-104]

mOFC: Medial orbitofrontal cortex, rACC: Rostral part of the anterior cingulate cortex, GABA: Gamma-aminobutyric acid, dACC: Dorsal anterior cingulate cortex

Wide range of neurotransmitters' receptors (biogenic amines, amino acids, and neuropeptides) exists in the hippocampus, as well as other medial temporal cortical regions.

The prefrontal cortex is an area that is known to be concerned with executive functioning and it is well-known fact that these functions are impaired in SCZ [85]. Many studies also suggest the hyperactivity of hippocampus in SCZ [86]. The hippocampal formation is site of memory and learning. It has a major role in the medial temporal–diencephalic–basal forebrain system that mediates the compilation of short-term memory into long-term memory, thus it enables the attainment and preservation of novel information [87]. Schizophrenic patients show abnormal learning and memory performance related to verbal and visual material which is similar to temporal lobe epilepsy. SCZ is associated with hippocampal volume reduction, most of the neuroimaging studies had failed to express an association between long-term memory and hippocampal or temporal lobe volume reduction in schizophrenic patients indicating that non-hippocampal brain regions (e.g., cerebellum, thalamus, prefrontal, and parietal association cortex) play a major role in the cognitive deficits that characterize schizophrenia [88,89]. Schizophrenic symptoms produced by different brain parts abnormality are discussed in Table 2.

CONCLUSION

SCZ is a chronic heterogeneous syndrome of disorganized and bizarre thoughts, delusions, hallucinations, inappropriate affect, and impaired psychosocial functioning. SCZ is likely a neurodevelopment disorder that may also think to be affected by ongoing changes in the brain structure. The tools of modern neuroscience, drawing from neuroanatomy, neurophysiology, brain imaging, and psychopharmacology, promise to provide a host of new insights into the etiology and treatment of SCZ. The pathophysiology of brain regions known to be involved in motor function may help in understanding the disturbed cognitive functions in SCZ, given that thinking may be an active motor process. Nevertheless, a cure or at least better treatments are sorely needed, and a greater understanding of the neurobiology of SCZ is crucial to both destigmatizing the illness and advancing clinical care.

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