Schizophrenia is a complex brain disorder characterised by disruptions to thinking and emotions, and a distorted perception of reality. It usually begins in late adolescence or early adulthood. While some people with schizophrenia may experience only a few brief episodes, for most, it is a chronic condition. People with schizophrenia have a high risk of suicide.

**Symptoms: positive, negative and cognitive**

Symptoms of schizophrenia can vary but are often described in terms of positive, negative and cognitive. Not all individuals affected by schizophrenia have all these symptoms highlighting the complex and varied nature of this disorder. Moreover, some symptoms may appear only for short periods or ‘episodes’.

*Positive symptoms* include hallucinations, delusions, disordered thoughts and speech typically regarded as manifestations of ‘psychosis’. Positive symptoms generally respond well to medication. *Negative symptoms* include social withdrawal, ‘blunted emotion’ or flat expressions, inability to experience pleasure, lack of desire to form relationships, and lack of motivation. Negative symptoms respond less to medication. *Cognitive symptoms* involve difficulties in working and long-term memory, attention, executive functioning (such as inhibiting inappropriate responses), speed of processing and lack of insight.

**Causes**

A combination of genetic and environmental factors plays a role in the development of schizophrenia.

*Genetic factors*

Growing evidence suggests there are strong genetic factors that contribute to schizophrenia. Studies on twins have shown that the concordance rate in schizophrenia is higher in identical twins (40-60%) than in fraternal twins (10-20%), suggesting a genetic disposition (Gottesman and Shields, 1982). There is an increased risk for developing schizophrenia if an individual has a first-degree relative with the disease. It is accepted that many genes are involved in schizophrenia, and evidence is emerging that the genetic architecture of schizophrenia involves both common and rare risk variation (Singh et al., 2014). Many possible gene candidates have been proposed, including specific copy number variations and mutations in many synaptic genes; genes that are essential for the normal formation and function of synapses, the site of communication sites between brain cells. There is also a large overlap in the genetics of schizophrenia with other mental disorders including bipolar disorder, autism spectrum disorders, intellectual disability and epilepsy.
highlighting the complex nature and overlapping symptoms that are often observed across these disorders.

**Environmental factors**

Environmental factors associated with the development of schizophrenia include the living environment, drug use and prenatal stressors (Brown, 2011). Factors such as childhood trauma, separation from one’s family and being bullied or abused increases the risk of psychosis. Other factors that play an important role include social isolation, family dysfunction, unemployment, and poor housing conditions. A large proportion of individuals suffering from schizophrenia also use drugs or alcohol excessively. For example, amphetamine and cocaine can result in psychosis that presents very similarly to schizophrenia. People with schizophrenia use nicotine at much greater rates and cannabis use can also potentially be a contributing factor in schizophrenia. Factors such as hypoxia and infection, or stress and malnutrition in the mother during fetal development have also been suggested to potentially increase the risk of schizophrenia later in life.

**Mechanisms**

A number of attempts have been made to explain the link between altered brain function and schizophrenia. Functional magnetic resonance imaging (fMRI) and other brain imaging technologies like PET (positron emission tomography) allow for the study of differences in brain activity in people diagnosed with schizophrenia. These techniques allow the identification of areas in the brain that are more or less active compared to healthy controls. Schizophrenia is associated with subtle differences in brain structures (Canu et al., 2014), found in 40 to 50% of cases, and in brain chemistry during acute psychotic states. Studies using neuropsychological tests and brain imaging technologies such as fMRI and PET to examine functional differences in brain activity have shown differences most commonly occur in the frontal lobes, hippocampus and temporal lobes. Reductions in brain volume have been reported in areas of the frontal cortex and temporal lobes. These differences have been linked to the cognitive symptoms often associated with schizophrenia (discussed above).

Early attention was paid to the function of dopamine in the mesolimbic pathway of the brain (Lau et al., 2013). This focus largely resulted from the accidental finding that phenothiazine drugs, which block dopamine function, could reduce psychotic symptoms. It is also supported by the fact that amphetamines, which trigger the release of dopamine, may exacerbate the psychotic symptoms in schizophrenia. The influential dopamine hypothesis of schizophrenia proposed that excessive activation of D2 receptors was the cause of the positive symptoms. Although postulated for about 20 years based on the D2 blockade effect common to all antipsychotics, it was not until the mid-1990s that imaging studies provided supporting evidence. The dopamine hypothesis is now thought to be simplistic, and it is accepted

Interest has also focused on the neurotransmitter glutamate and the reduced function of the NMDA glutamate receptor in schizophrenia, largely because of the decreased levels of glutamate receptors found in the postmortem brains of those diagnosed with schizophrenia, and the discovery that glutamate-blocking drugs such
as phencyclidine and ketamine can mimic the symptoms and cognitive problems associated with the condition (Laruelle, 2014). Reduced glutamate function is linked to poor performance on tests requiring frontal lobe and hippocampal function, and glutamate can affect dopamine function, both of which have been implicated in schizophrenia. Therefore, alterations involving the glutamate pathways have been suggested to have an important mediating and potentially causal role of in this disorder.

**Current treatments**

The most common treatment option for schizophrenia is antipsychotic medication, which primarily suppresses dopamine receptor activity in the brain (Correll and Kane, 2014). Effective antipsychotic medications enable many people with schizophrenia to lead full and productive lives. While antipsychotic drugs help stabilise some symptoms, they do not cure the disease and are frequently associated with side effects. Most people need to stay on medication to prevent relapse. The lack of treatment options that address the positive, negative and cognitive symptoms in schizophrenia highlight the strong need for further research into this complex disorder.

**References**


