

## **What Causes Schizophrenia?**

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Schizophrenia is a mental disorder affecting an estimated one half to one percent of the global population. Contradictory to popular belief, schizophrenia does not deal with multiple personalities. Rather, the disorder can cause hallucinations, paranoia or bizarre delusions and disorganized thought or speech pattern. People with schizophrenia often have other mental disorders (Sim et al. 2006). Thus schizophrenia can result in socially paralysing an individual. Treatment and prevention of the disorder are important steps in helping millions of people.

One vital point in the process of developing a treatment and prevention strategy for schizophrenia is identifying the cause or causes of the disorder. Over the years, as research into schizophrenia has progressed, the understanding of schizophrenia has improved. Scientists have been able to pinpoint possible causes in the environment and the genetics of individuals that have schizophrenia, for example. These advancements in turn have allowed for the making of clearer models of how schizophrenia develops in individuals. The aim of this essay is to clarify the current viewpoint on what causes schizophrenia. The development of causation models will be discussed in addition to going into detail on possible environmental and biological causal factors of schizophrenia.

## Causation Models

During the many years of research on the causes of schizophrenia, several different models have been proposed. The range of models has been suggested to be due to the addressing different aspects of the disease, or possibly diseases, we call schizophrenia (Keshavan et al. 2008). Another factor in the range of models is variety of ways in which schizophrenia manifests (Peralta and Cuesta 2000).

Several etiological models have been able to account for many features of schizophrenia. For example, in 1995, Olney and Faber suggested that NDMA receptor hypofunction may be able to explain many symptoms of schizophrenia, both psychological and biological (cited in Keshavan et al. 2008). Although the theory seems to have several consistencies with the genetic causalities thought to be related to schizophrenia, for instance, no definitive evidence has been found to prove the model correct (ibid.). Another model put forth by Crow in 1995 suggests that a "desynchrony of hemispheric development due to gene(s) involved in evolution of language" would explain several aspects of schizophrenia (Keshavan et al. 2008, p.101). Yet another proposed model suggests that stress may be the causal trigger in individuals (Corcoran et al. 2003). However, this model would not fully

explain why some individuals are prone to schizophrenia while others are not.

Furthermore, it has been suggested that a clear model for the causes of schizophrenia cannot be put forth, because the assumption of schizophrenia being one single disease may be incorrect (Keshavan et al. 2008). This proposal could certainly hold some validity and account for the broad range of manifestations in patients diagnosed with schizophrenia. In addition, it has been proposed that "as long as we are not able to disentangle the heterogeneity question at the clinical level, it is not likely that heterogeneity at the etiological and pathophysiological levels can be resolved" (Peralta and Cuesta 2000, p.253). That is, until we can see the symptoms of schizophrenia clearly, it is much harder to find a proper causal model to the disease.

Modern models of the causes of schizophrenia include the biopsychosocial model and the stress-diathesis model. The biopsychosocial model tries to achieve a unification of the biological causes with the psychological and social causes that may lead to schizophrenia (Harris 2010). The causes can also be categorized by whether they are predisposing factors, triggering factors, or factors that keep the disorder continuing (ibid.). Thus a table of categories can be created that can help in organizing the variety of causes of schizophrenia. On the other hand, the stress-diathesis model relates

stressors in the environment to the innate predisposition of individuals to become schizophrenic (Jones and Fernyhough 2007). Although the models differ, they agree on the fact that schizophrenia is a complex disorder with many possible causes that can predispose individuals to it or trigger it in them.

### Genetic Causes

Research shows that a combination of genetic vulnerability and environmental factors can lead to schizophrenia (Harrison and Owen 2003), and that the genetic problems leading to this disease are caused by different factors and different genes (Owen et al. 2005). However, the heritability of schizophrenia has been hard to estimate because of the difficulty of separating genetic and environmental causes (O'Donovan et al. 2003). Research made on twins has found a high level of heritability, and suggested that gene factors are the main cause of the disease (ibid.). The theory of genetic causation also argues that schizophrenia is an illness of complex inheritance; subsequently, research has focused on finding the group of genes that may cause this mental disorder (Owen et al. 2005). It was estimated that a group of fourteen genes may be causal, but recent research shows that the suggested group of genes is not associated with

schizophrenia (Sanders et al. 2008).

In some patients, schizophrenia may be caused by deletions or duplications of DNA sequences in genes that are responsible for neuronal signalization or brain development (Walsh et al. 2008). This leads to neural processes that may cause psychotic disorders such as schizophrenia. For example, a structural abnormality of the brain, such as differences of the volume of grey matter in some areas of the brain, leads to reduction in the amount of neurons, which can cause psychotic syndromes (Hoffman and McGlashan 2001). Research shows that such abnormality can be present from the birth of the subject, or it may develop later because of causes other than gene vulnerability (ibid.).

Other research shows that the problem may be in the neural network and will affect the functioning of the brain. Using brain imaging technologies, it has been observed that abnormal connection between different gene networks is something common for schizophrenic patients (Broyd et al. 2009). Such observations show that there is a rivalry between different neural networks that may lead to the deactivation of one of them and thus disrupt the function of some area of the brain. This explains most of the symptoms related to schizophrenia, such as memory loss, attention disorder, social cognition and problems with executive functions (ibid.).

The function of dopamine in the mesolimbic and mesocortical pathways of the brain has been given particular attention in research on the causes of schizophrenia. Based on drug experiments, the "dopamine hypothesis of schizophrenia" proposes that a malfunction in this area causes the disorder's symptoms (Seeman et al. 2005). Evidence includes findings that genes coding for mechanisms involved in dopamine function may be more prevalent in schizophrenics (Arguello and Gogos 2008). However, later research suggests that excessive dopamine function not be the sole cause of schizophrenia symptoms. In particular, low levels of glutamate, another neurotransmitter, have been found to produce similar effects (Lahti et al. 2001).

### Drug Use

Strong evidence indicates that use of certain drugs can act as a trigger for either the onset or relapse of schizophrenia in some people. Cannabis has been linked to schizophrenia most frequently; other suspected triggers include amphetamines and hallucinogens. The relationship between schizophrenia and drug use, however, has been found to be complex. A clear causal connection between substance use and disorder has thus not been established yet.

Most evidence for a link between drug use and schizophrenia has been found in research on the effects of cannabis. Studies suggest that the drug significantly increases the risk of developing schizophrenia, but found that it is neither a sufficient nor a necessary factor in developing the disorder (Arsenault, Cannon, Witton, & Murray, 2004). Rather, it is assumed that it is only one of a complex combination of factors causing the disorder (ibid.). According to a review of studies conducted by Arsenault et al (ibid.), cannabis doubles the risk of developing schizophrenia on the individual level, and could, a causal relationship assumed, account for 8% percent of cases in the overall population.

Besides cannabis, hallucinogens and stimulant drugs such as amphetamines have been linked to causing schizophrenia. Amphetamines may worsen schizophrenia symptoms, since the drug triggers the release of dopamine (Laruelle et al. 1996). Heavy use of hallucinogens as also been found to sometimes trigger schizophrenia (Mueser et al. 1990). However, both amphetamines and hallucinogenic drugs, like cannabis, have been found to be neither sufficient nor necessary factors in explaining the disorder's development. Nevertheless, when a predisposition exists, these drugs may trigger the onset or relapse of schizophrenia (Laruelle et al. 1996).

## Social environmental causes

Childhood experiences of social adversity, abuse and urbanicity have been credited with contributing to schizophrenia. Adversities, evidence suggests, may alter dopamine neurotransmission in a process termed "sensitization"; and may lead to cognitive biases. Krabbendam and van Os (2005) suggest a gene-environment interaction. Based on observed within-city variation of the effects of urbanicity, and an independent association of experiences of urban living and social isolation, they propose that the degree of "social capital" impacts children's development.

Studies suggest that higher number of adverse social factors such as socio-economic disadvantage and social exclusion present in childhood correlates with an increased risk of developing schizophrenia in later life (Wicks et al. 2005; Mueser et al. 2004). Significantly, personal or recent family history of migration, which is linked to socially adverse factors such as racial discrimination, family dysfunction, unemployment and poor housing conditions, has been found a considerable risk factor (Cantor-Graae and Selten 2005; Selten et al. 2007). More specifically, childhood experiences of abuse and trauma have been found to be linked with an increased risk of developing schizophrenia in later life (Janssen et al. 2004; MacMillan et

al. 2001; Read et al. 2001; Schenkel et al. 2005). Recent findings indicate a causal relationship exhibiting a dose-effect (Read et al. 2005).

Living in an urban area has repeatedly been found to be a strong risk factor in developing schizophrenia, even after controlling for other factors such as drug use or migration (van Os 2004). The chance of being diagnosed with the disorder has been found to increase with the number of years spent living in urban environments in childhood and adolescence; as well as with the degree of urbanicity (Pedersen and Mortensen 2001). In Sweden, people living in the most urbanized areas were found to have a 68%-77% increased risk of developing psychosis, a proportion of which is thought to be schizophrenia (Sundquist et al. 2004). These findings suggest that constant, cumulative, or repeated exposures during upbringing to factors occurring more frequently in urban environments may cause schizophrenia (Pedersen and Mortensen 2001).

### Conclusion

Current research suggests that schizophrenia is a disorder caused by a complex set of interrelated factors. Genetic predispositions, environmental influences, and drugs such as cannabis

have been examined in search for what causes schizophrenia. However, unification of individual findings remains difficult, also because the diagnosis is based on symptom profiles, write Marcotte et al. (2001): "Current research into schizophrenia has remained highly fragmented, much like the clinical presentation of the disease itself."

Further research seems necessary in order to understand the neural processes related to schizophrenia. Seeman (2010) proposes that "all roads to schizophrenia lead to dopamine supersensitivity"; however, there are reasonable doubts about the omnibus claim of the dopamine theory of schizophrenia (Lahti et al. 2001). In fact, neural correlates do not provide sufficient criteria to diagnose schizophrenia (Manji et al. 2003). For the moment, what exactly causes schizophrenia remains a question that cannot yet be answered.

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