Xournals

Academic Journal of Modern Applied Sciences

ISSN UA | Volume 01 | Issue 01 | January-2019

Role of Genetic and Environment in the Development of Disorder: Schizophrenia

Kavit S. Mehta[1]

Available online at: www.xournals.com

Received 3rd September 2018 | Revised 6th October 2018 | Accepted 8th December 2018

Abstract:

Human population have one of most common, devastating and least understood neuropsychiatric illness that is schizophrenia. This disorder is generated by the action of genetic and environmental effects. Genome-wide association studies (GWAS) shows the result that more than 100 loci has been identified which have high risk of schizophrenia. Monozygotic twins have a high risk of this disorder as compare to the dizygotic disorder. Different models has been developed to find the relation between genetic and schizophrenia. In the same way, Environmental is also a factor that give their impact in the generation of schizophrenia. In environmental factors, parental, perinatal, season birth and so on may be the cause of schizophrenia. But it is found that individually genes or individually environment is not responsible for the development of disorder. The gene as well as environment both are necessary to produce the disorder. This paper represents the role of genetic and environment in the development of schizophrenia disorder.

Keywords: *Schizophrenia, Genetics, Perinatal, Monozygotic*

Authors:

1. *Mehsana Urban Institute of Sciences, Ganpat University, Ganpat vidyanagar, Gujarat, INDIA*

Introduction

A debilitating disorder that occurs approximately 0.5 to 1% within any given population. Complex genetic, environmental and psychological etiologies come under the pathophysiology of schizophrenia. A multi-factorial sickness 'Schizophrenia' is described by a genetic factor (great hereditary) and biological threat issues including societal pressure and cannabis habit. It is caused by the mutual act of various genes that have minor result and various environmental factors due to which mental disorder developed. It is considered as 'Two-Hit Hypothesis' of schizophrenia that assumes that both inherited and ecological threat issues aggressively because of the advancement of the sickness. Genetic interacts with the environment when the expression of one's genetic tendency depends on the environment in which he/she is living or the effects of environment on a trait are differed according to the genome of an individual.

Nowadays, mental disorders are recognized as a disease that affects human populations around the world. In most common and important disorders, hereditary features play an essential part. The most severe psychiatric disorders of adults are functional psychoses that are separated into two chief analytic groups: schizophrenia and bipolar disorder. Schizophrenia is a syndrome that occurs equally in male and female at risk 1%. Schizophrenia is characterized by psychotic features like delusions and hallucinations.

Genetic epidemiology of Schizophrenia

A group of pathologies from which schizophrenia belongs is called as multifaceted hereditary illnesses. It means many genes are involved in each disorder with each gene that has a small effect on the phenotype. The mechanisms of genetic in the production of schizophrenia have been explained by many theories. One hypothesis in which schizophrenia has a standardized pathogenic genotype with pleiotropic influences. Example of pleiotropy is Marfan's syndrome that is a connective tissue ailment with 12 recognizable abnormalities. 88% of patients are affected by the most common of this disorder and only 12% of patients have the least common disorder. A variety of symptoms may be present in an individual with schizophrenia. The great numbers of evidence show that most of the matters involving schizophrenia are caused by a common gene. Particularly, single gene models are not able to define the ancestral arrangements of sickness precisely. Families or twins; multiple factor polygenic representations can explain such data in the better way.

Genetic Transmission Model for Schizophrenia

It is well recognized that the insanity and such other human diseases and features move from generation to generation. Some authors/ researchers described that schizophrenia is inherited characteristic because of the family combination of the illness or its slighter alternatives. The schizophrenic monogenic model was very attractive because of the various reasons such as plainness, a faith of determining a conforming, meek pathophysiological contrivance and fit into theoretic possibilities like dominant, recessive and with fluctuating penetrance. But it is not followed now these days because it does not fit adequately into the observed data and the idea of one specific gene or few specific genes required for etiological not satisfactory for the development of schizophrenia. For example in 1962, Meehl used monogenic necessary gene in which polygenic factors were used to modify the action. Holzman in 1989 gave latent trait model in which dominant gene as a concealed attribute, a hypothesized neural discrepancy with hypothetically pleiotropic expressions like as schizotypy, eye-movement disorder or schizophrenia. Then, Risch and Bardon in 1984 discussed an assorted ideal in which a particular gene in the blend with some oligogenes and the genetic substrate is formed with the polygenic multifactorial background. All these representations have been applied to suit the environment that have a erratic ratio of achievement to the accessible epidemiological statistics of schizophrenia.

Multi-factorial Polygenic Models

Schizophrenia results as the threat of sickness is enlarged between the families of concerned folks due to genes rather than environments. The risk of schizophrenia is high in children and siblings compared to the parents. The studies of research show the result that monozygotic concordances criteria are at high risk (41-65%) compared to dizygotic concordances (0-28%). Hereditary epidemiology clears that the mode of spread is complicated. There are many factors which are still unknown that include sickness threat is discussed by every point, number of vulnerability spot, the degree of hereditary heterogeneity and the degree of interface amongst the spot. Improved twin and

adoption studies became very important for the determination of family bundling and concordance percentages for schizophrenia in the 1960s. The etiology of illness has a strong genetic component that contributes to challenge the psycho-analytical assumption of schizophrenic relationship which claims that schizophrenogenic nurturing is an adequate reason for the development of schizophrenia. The twin studies have the basic intuition which are these as follows:

- Monozygotic twins (share 100% genes) and dizygotic twins (share 50% genes) also share the environment in which they are growing.
- Genetic similarity results in the form of high concordance rates in monozygotic (MZ) and Dizygotic (DZ) twins.

Many studies have been done on twin theory in monozygotic twin have a high risk of schizophrenia compared to a dizygotic twin. A meta-analysis of twin studies is done that estimates the liability of genetic to schizophrenia at 81% while environmental influences that are shared by twin have only 11%. According to studies, unaffected monozygotic twins also carry a silent vulnerability genes for schizophrenia. While, in offspring of discordant dizygotic twins, affected dizygotic twins have a higher risk rather than children of an unaffected dizygotic twin.

In adoption studies, it is documented that adopted kids of mothers adopt schizophrenia spectrum disorders more frequently than their control adoptees. A cross-fostering study stated that the kids of well-built and healthy parents adopted by a family where one parent has schizophrenia disorder do not have an effect on the children. The children of schizophrenic mothers have the same threat of growing sickness if they are adopted by another parent that does not have any history of illness.

Molecular genetic

In molecular genetic research, the Human Genome Project has been instrumented for schizophrenia. It was an international study project in which the sequence of the human genome that has 3 billion base pairs was determined and mapped the genes. In the early 1980s, according to the researchers DNA availability would disclose the biological causes of disorder joined with the twin and adoption studies.

The 'linkage analysis' was the first DNA based method that had the aim to discover the genome regions in a sample of influenced, stretched or nuclear families and sibling pairs without the specific allelic variant. The degree of co-segregation of genetic markers and predetermined phenotypic traits like schizophrenia spectrum analysis is examined by which linkage between the sickness and genomic loci was estimated. This linkage examination is based on the genetic marker opinion which is positioned physically on the same chromosome incline to get inherited together as they remain allied at the time of meiosis. A number of linkage trainings regarding the schizophrenia disorder were showed but constructive results showed difficulty to replicate in subsequent studies. In short term, a meta-analysis was considered as many chromosomal regions can have schizophrenia vulnerability loci. It is a well-known fact that loci do not converse any risk by own but may encourage the variance in this. These results make clear that linkage design power was very weak for addressing the genomic loci with minor impacts; the sample size that was required to perceive the linkage was basically impossible. Hence, there is a requirement of other DNA-based methods to point out the genes that are indulged in the etiology of schizophrenia.

Another phenomenon in molecular genetic study for schizophrenia is 'candidate gene' methodology that uses a case-control design and discover if vulnerability genes get connected with the sickness. In comparison to linkage analysis, candidate gene methodology are able to detect genes with small effect alleles provided that the sample size is appropriate. Due to their position and functionality, candidate genes have been selected. More than 1000 candidate genes have been verified, although the identification of some genes with small effect alleles, the candidate gene studies results were disappointed. There are some candidate genes such as DISC1, DTNBP1, NRG1, and COMT. These candidate genes' pathogenic engagement in schizophrenic disorder remains questioned. Significant discoveries were absent because of many reasons complications in duplicating positive results, insufficient arithmetical power and restricted knowledge of genes as the involvement in the field of the pathophysiology of schizophrenia.

Environmental Factors in Schizophrenia

The ancient and powerful belief that place and time do not affect the incidence of schizophrenia has been

failed by the productive stage for the study of the epidemiology of schizophrenia. The outcomes of epidemiology indicate the specific circumstances in which schizophrenia risk is increased. These circumstances are numerous obstetric complications, urban birth and residence, famines, migrant status and seasonal changes. Other than these, advanced paternal age, cerebral hypoxia and other severe pregnancy and perinatal complications are also environmental risk factors. Overall, the landscape of ecological threats is fruitful and grow quickly that point out to many threat features act early at the time of development. Those individual effects that are biologically catastrophic such as famines caused by environmental risks are small. Between environmental risk factors and schizophrenic, specific pathophysiological connections remain largely tentative. Finally, the risk for schizophrenia is increased by the additional environmental factors. The understanding of gene-environment interactions is very important for disclosing the biology of schizophrenia.

Preconceptual risk factors for Schizophrenia

"Preconception" is one of the ecological threat issues that engage demographic or other parental aspects are recognizable preceding to conception. The prime example of a preconception risk factor is advanced paternal age. The mutation rate for base substitutions is much higher in men than in women because of a large number of cell divisions at the time of spermatogenesis. This mutation rate is increased with paternal age. A de nova mutations elucidation is offered for schizophrenia. Another reason for the risk of schizophrenia is a prolonged delay between pregnancies. A pointer of reproductive health and fitness may be calculated using a standard measure of reproduction function in both sex and can relate to the natural processes involves in the reproductive and genetic damage. In the addition, time to pregnancy is described as the reported length of time is taken to conceive an intended pregnancy may be the cause of schizophrenic risk in offspring. If the times of conception is more than 12 months, the risk of schizophrenia is increased. Schizophrenia may be caused by the parental reproductive health. The ecological subtleties like exposure to chemicals and smoking are collected in the body and affect the health and fertility. It is still not known that smoking and exposure to chemicals aid in to the development of schizophrenia directly or not. But these conditions give their effects on genetic material.

Prenatal Risk Factors for Schizophrenia

Maternal Infection

The development of schizophrenia is caused by the maternal acquaintance to infection during gestation. Research in the field of the infection that occurs in the mother during pregnancy affects the prenatal in the form of mental disorders. When viral pathogens exposed through the maternal placenta cause the disruption in normal fetal brain development resulting in abnormal neurodevelopment. In order to attain superior insight into the threat features of environment, schizophrenia investigators have pursued to relate this phenomenon to the specific early demonstration of disease in the studies of epidemiological, ecological and translation. The investigators have identified several maternally acquired infections which are the causes of schizophrenia. These infected viruses are herpes simplex virus type-2, genital and reproductive contaminations, polio, influenza, rubella and respiratory infections and protozoan parasite Toxoplasma gondii.

Perinatal Risk factors for schizophrenia

A serious risk for schizophrenia is developed by the brain trauma linked with obstetric complications. By the study of monozygotic twins for the schizophrenia, a significant correlation between an individual with increased lateral and third-ventricle size and history of obstetrical complications and extended delivery time was found by the researcher. They also detected a significant relationship between decreased left and right hippocampi size and a past of obstetrical difficulties.

The risk of schizophrenia is higher in the obstetrical complications compare to others. It has been studied that obstetric complications show the symptoms of schizophrenia at a younger age. Another study shows that there is no noteworthy difference between early-onset or very early-onset schizophrenia and a past record of obstetrical complications. One obstetric complication is Hypoxia or reduction of oxygen that relates with a diagnosis of schizophrenia later in life. During birth, hypoxia associated with greater structural abnormalities that affect both grey matter mass and cerebral spinal fluid levels in the brain of people with schizophrenia. This relationship is greater 2-3 times in the case of born pre-term and

small in gestational age. While another study stated that long-term exposure to intrauterine hypoxia is significant rather than the short-term hypoxia during birth. During childbirth, a lack of oxygen is related to the diagnosis of schizophrenia.

Cannabis

The psychotic symptoms are the symptoms of schizophrenia. These psychotic symptoms are increased with the use of cannabis. A person who is suffering from psychotic symptoms takes more cannabis to compare to the general population. According to the report of a meta-analysis, the risk of developing psychotic symptoms or psychotic disorders increase the use of cannabis. Some neuroimaging studies stated that in both gray and white matter linked with heavy cannabis, structural is changed that is used in both healthy subjects and FEP patients. While psychosis is developed early in cannabis users that can be explained by the differences in use patterns and age at that time it was used. In THE Dunedin birth cohort study, the person who starts to take cannabis at the age of 15 years or earlier has a great risk of schizophrenia at the age of 26 years than those who started at 18 years of age.

Review of Literature

Sobell, Mikesell, and McMurray (2002) in the development of schizophrenia, genetic contribution is a clear evidence. In spite of this, tested hypothesis and current methods have been failed in the identification of specific genetic factors due to which disorders occur. It is assumed that by the study in the field of neuroanatomy, functional neuroanatomy, neuropathology, neurochemistry, molecular neuroscience, neuropsychology, neurodevelopment, and molecular epidemiology, new clues can be developed about the pathophysiology and gene systems. With neurodevelopmental and neurodegenerative processes, Heterogeneity of genetic and etiologic factors is the expectation. Currently known, or yet to be identified as suspect candidate genes play a vital role in the development and progression of the disease, also in the medication response to therapy.

Leask (2004) in their study they concluded that awareness should be generated from a clinical perspective regarding the exposure. They found in their patient that genetic predisposition has a history in the development of schizophrenia or signs of illness prodrome. There is a need for more work before list any environmental influences can be confidently rejected or considered as casual that contribute to illness.

Graae (2007) studied the social factor effects in the development of schizophrenia by taking the population of migrants in Europe. In this research, they concluded that the social factors exert their influence by which mechanism is unknown. They suggested that in the future investigation of social causation, the temporal relation between exposure to social defeat and social adversity, and the development of psychotic symptoms should be clarified.

Stilo, Forti, and Murray (2011) discussed the causal risk factors for schizophrenia. The gene-environment interactions highlight the development of schizophrenia. According to them, neither individual gene nor individually environment is responsible for the schizophrenia. The disorder is caused by the effect of both. A variety of approaches from medication and psychological interventions to this disorder are used in an attempt to prevent the onset of full-blown psychosis.

Sariaslan, Larsson, and Fazel (2016) proposed that the patients who are diagnosed with the psychotic disorder have a high risk of committing violent offenses because of the influence of genetic. In case of bi-polar, genetic influences increase the risk of violent crime by fifth times while genetic influence does not contribute to schizophrenia for increasing such risk. Future research should effort in integrating violence-related phenotypes into psychiatric genetic studies. And the identification of environmental predictors of violence in the patient groups.

Henriksen, Nordgaard, and Jansson (2017) studied pre-molecular and molecular genetic in which they concluded that a strong risk factor is formed by genetics for schizophrenia. The relationship between schizophrenia and more than 100 susceptibility loci (copy number variations (CNVs), and single nucleotide variants (SNVs)) indicated as a number of scores. It is also important to note that the thousands of common alleles give a small effect form a polygenic component of schizophrenia risk. In brief, the knowledge about the interaction of schizophrenia and genotype-environment is still unknown to a large extent.

Conclusion

'Schizophrenia' is a disorder that occurs rarely in population. But due to the generation of this disorder, a person may commit crime and harm to itself. This paper discussed the two factors which are responsible for the development of schizophrenia. Many studies have been conducted on this topic to find the main cause of it. Many researchers mentioned that genetic factor play a vital role in the development. As well as, environmental factors are also responsible for this disorder. Beside many studies results about genetic and environmental factors impact on the development, the main mechanism of the development is not understood. So, there is a need for more study to know the main mechanism of it by which the development of risk of schizophrenia can be reduced.

References:

Cantor-Graae, Elizabeth. "The Contribution of Social Factors to the Development of Schizophrenia: A Review of Recent Findings." The Canadian Journal of Psychiatry, vol. 52, no. 5, 2007, pp. 277–286.

Craddock, N. "The Genetics of Schizophrenia and Bipolar Disorder: Dissecting Psychosis." Journal of Medical Genetics, vol. 42, no. 3, Jan. 2005, pp. 193–204.

Gejman, Pablo V., et al. "The Role of Genetics in the Etiology of Schizophrenia." Psychiatric Clinics of North America, vol. 33, no. 1, 2010, pp. 35–66.

Henriksen, Mads G., et al. "Genetics of Schizophrenia: Overview of Methods, Findings and Limitations." Frontiers in Human Neuroscience, vol. 11, 2017.

Karl, Tim, and Jonathon C. Arnold. "Schizophrenia: a Consequence of Gene-Environment Interactions?" Frontiers in Behavioral Neuroscience, vol. 8, 2014.

Leask, Stuart J. "Environmental Influences in Schizophrenia: the Known and the Unknown." Advances in Psychiatric Treatment, vol. 10, no. 5, 2004, pp. 323–330.

Ohnuma, Tohru, and Heii Arai. "Pathophysiology of Patients with Schizophrenia: Genetic and Environmental Factors." Juntendo Medical Journal, vol. 63, no. 1, 2017, pp. 8–16.

Opler, Mark, et al. "Environmental Risk Factors and Schizophrenia." International Journal of Mental Health, vol. 42, ser. 1, 2013, pp. 23–32.

Sariaslan, A, et al. "Genetic and Environmental Determinants of Violence Risk in Psychotic Disorders: a Multivariate Quantitative Genetic Study of 1.8 Million Swedish Twins and Siblings." Molecular Psychiatry, vol. 21, no. 9, 2015, pp. 1251–1256.

Sobell, Janet L., et al. "Genetics and Etiopathophysiology of Schizophrenia." Mayo Clinic Proceedings, vol. 77, no. 10, 2002, pp. 1068–1082.

Stilo, Simona A, et al. "Environmental Risk Factors for Schizophrenia: Implications for Prevention." Neuropsychiatry, vol. 1, no. 5, 2011, pp. 457–466.

Tsuang, Ming T, et al. "Genes, Environment and Schizophrenia." British Journal of Psychiatry, vol. 178, 2001, pp. 18–24.