The Dopamine Hypothesis and the Multiple phases of Schizophrenia: A Misdiagnosis that leads to Mistreatment.

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Abstract

The clinical and parametric analysis of schizophrenia show a multifaceted symptom phase in which many other major categories of mental disorders can be diagnosed. This is leads to the complicated nature of schizophrenia both in its diagnosis and interventions. Even with the claims of high-tech diagnostic processes, advanced low side-effect antipsychotic drugs, and research in this area, high rate misdiagnosis and under-treatment of schizophrenic patients, especially in developing nations, are very high. The major categories of schizophrenia that distinguishes it from other mental disorders, are psychotic features, which have been linked to neurocircuitry, genetic vulnerability, and environmental exposures. Yet vulnerability theories have implicated psychodynamic processes, cognitive abilities, personality trait, interpersonal and family upbringing as precipitating and escalating factors of schizophrenia. However, due to its ravaging effects in visuospatial, visuoperceptual and visuoconstruction abilities, neuropsychologists, as well as psychiatrists, are in continuous controversial debate as what may constitute the actual etiology of schizophrenia. Even though with monozygotic twins and the experiment with amphetamine, chlorpromazine, and phenothiazines, have unequivocally depicted schizophrenia as a genetically transmitted mental disorder, yet obvious difference in symptom expressions, especially with cognitive degeneration, have led researchers to the study of dopamine receptor genes, which they believe could hold the key to the multifaceted nature of schizophrenia. The search is centered on the dopamine hypothesis. The analysis of this claim, to which this paper is interest in, will centre around Dopaminergic pathways, which are neural pathways in the brain that transmit the neurotransmitter dopamine from one region of the brain to another.

Keywords: Heredity, Genetics, Schizophrenia, Biochemical theory, Vulnerability theory, dopamine receptor gene, dopaminergic pathways.

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Introduction

The strong genetic component of dopamine hypothesis has spilt neurobiologists into two camps, “lumpers” and “splitters” (Hedaya, 1996). The lumpers believe that the symptoms manifested by schizophrenic patients may be the result of underlying abnormality, defect, or deficit in integrative functioning in the central nervous system. Wexler (1991) remarked that the basic problem in the schizophrenics is their inability to handle complex tasks. The reason he presented was that, when a schizophrenic patient is presented with almost any task that activates a group of cortical neurons, there is a failure of those neurons to recruit, activate, connect, or link to additional cortical brain regions for effective coordination (Weinberger, 1994). Such linkage helps the individual to get ready for the next response. The lumpers did not emphasize the heritability of these defect, rather they maintained that the low frontal cortex dopamine secretion is hamper at the base of abnormal neural linkage. On the other side of the camp, the splitters think of schizophrenia as having unfortunate inheritance of three semi-independent genes. These genetic defects would then cause a cluster of symptoms, and each of these genes would be responsible for the separate symptom domains of schizophrenia Kendle, 1994).

Judging from the diversities in research opinion, an absolute acceptance of the dopamine hypothesis will be foggy, especially, its habitability position. It is important, therefore, to investigate and ascertain whether the dopamine receptor genes really carry heritable trait capable of replicating themselves in offspring. Even if they do, we must know also whether the affected chromosome-genes have the propensity disrupt mechanism of the neurotransmitters. Furthermore, we must look into the claims of the three schools of researchers will verify whether their claims are scientifically attainable and sustainable. First the Splitters, strict believe that schizophrenia runs in families. Second the Lumppers, believe that the irregularity or disruption of the neurochemical transmission might damage the neural pathways thereby resulting to poor reception of messages intended for their zones. The third is the ecovulnerability theorists. Contrary to the dopamine hypothesis, the environmental vulnerability theory maintains that psychological, genetic, and ecological factors are responsible for the etiology of schizophrenia. It is the aim of this paper highlight the real position of dopamine hypothesis and able to draw line between accidents in biogenetic codification and heritability of schizophrenic episodes.

Schizophrenia is a severe psychopathology and psychotic disorder (Rosenzeig et al., 1999) that affects more than 50 million people worldwide (Mann, 1996, Berquier & Ashton, 1999). Schizophrenia comes in varieties of forms, symptoms, and severity that ranges from distorted and bizarre thought processes to psychomotor abnormality. Owing to its total and devastating impairment or breakdown in normal human functions, and the number of the world’s population affected, researchers are confronted with multiple questions about the nature of schizophrenia. Judging from the sporadic and total loss of cognitive and motor controls, recurrence, and many a time, the incurable episodic nature of schizophrenia, many researchers have come up with notion that this ailment is genetic.
Nevertheless, “no single gene has yet been identified for any psychiatric condition” (Hedaya, 1996, p. 39) has been isolated. Notwithstanding this limitation, both neuroscientists and psychiatry researchers have continued to fuel the notion that heritability is a prime factor in the etiology of schizophrenia (McGuffin, 1995).

The most explicit studies made toward the heritability theory are through the families of schizophrenia, especially with monozygotic (MZ) twins and the dizygotic (DZ) twins. For example, Kendler (1983), vehemently believed that genes account for approximately 60-70% of the variance in transmission of schizophrenia. His claims, however, are based on his variety of studies on more than 800 MZ and 1000 DZ twin. In these studies, it was discovered that paranoid and schizotypal personality disorders were higher in relatives of schizophrenics (Kendler, 1995: kety et al. 1994).

Apparently, we may not hold firm to the accuracy of these studies if they are not entirely based on the presupposition that a gene that directs the production of the dopamine receptor (D2) is associated with schizophrenic episodes (Crowe, 1995, Nathan & Gorman, 1998). The reason is that, since heredity involves the deoxyribonucleic acid (DNA) mapping, there should be a chronological connotation that vividly demonstrates that the so call ruptured or damaged D2, is as a result of DNA cloning from the parents. The DNA mapping or cloning effects, at this juncture, must not be confused with chromosomal developmental abnormality due to poor prenatal development. In 1987, however, researchers believed that they have finally found a gene responsible for major psychiatry disorders (schizophrenia). Chromosome 11 was identified. It was subsequently believed that this chromosome holds the genetic mapping that directs the production dopamine receptor (D2) (Carpenter, 1993). Dopamine receptor is found in abundance in the mesocortical and mesolimbic tracts. This tract has clinical importance in depression, mania, and schizophrenia, it is not surprising however, that this D2 is link with genes that are responsible for transmitting schizophrenia to offspring.
Our concern in this regard is, would it be scientifically possible that children of schizophrenia can inherit the defective chromosome 11 that subsequently recycle itself in family history? If this is true, how can we reconcile the ecological vulnerability (ecovulnerability) theory that upholds predisposition (episode implied, but not absolute) rather destined (episode is absolute) to the schizophrenic states? Ecologically, psychologists as well as biologists believe that environmental events can actually turn some genes related to memory, emotion, learning on or off within seconds (Hedaya, 1996). Can we then conclude that during mutation, environmental factors disrupt or distort the normal developmental process, thereby resulting to a defective chromosome? A resolution of these thought-provoking questions are at the center of this paper. First let us to understand what genetic transfer or heritability means.

**Mesocorticolimbic Projection**

1) mesolimbic pathway

The mesolimbic pathway transmits dopamine from the ventral tegmental area (VTA) to the limbic system via the nucleus accumbens. The VTA is located in the midbrain, and the nucleus accumbens is in the ventral striatum. The "meso" prefix in the word "mesolimbic" refers to the midbrain, or "middle brain", since "meso" means "middle" in Greek. This pathway is part of the mesocorticolimbic projection.

schizophrenia, ADHD, addiction

2. mesocortical pathway

The mesocortical pathway transmits dopamine from the VTA to the frontal cortex. The "meso" prefix in "mesocortical" refers to the VTA, which is located in the midbrain, and "cortical" refers to the cortex. This pathway is part of the mesocorticolimbic projection.

schizophrenia, ADHD, addiction

3. Nigrostriatal pathway

The nigrostriatal pathway transmits dopamine from the substantia nigra pars compacta (SNc) to the dorsal striatum (specifically, the caudate nucleus and putamen). This pathway is associated with motor control. schizophrenia, ADHD, addiction

Parkinson's disease, chorea

4. Tuberoinfundibular pathway

The tuberoinfundibular pathway transmits dopamine from the hypothalamus (arcuate nucleus aka "infundibular nucleus") to the pituitary gland. This pathway influences the secretion of certain hormones, including prolactin. "Infundibular" in the word "tuberoinfundibular" refers to the cup or infundibulum, out of which the pituitary gland develops.

5. Hyperprolactinaemia
1) Methods of Accounting for Heredity and Genetics.

Behavioral geneticists, in their efforts to study human heredity and genetics, typically yield to statistical estimate of the proportion of the total variance in a trait that is attributable to genetic variation within a group. With this method, the definition of heritability will rotate around the statistical estimate of the proportion of the total variance in some trait within a group that is attributable to genetic differences among individuals within the group (Tavris & Wade, 1997). Even though heredity and genetic are connected, it must be understood also that the two do not mean the same thing. In order to explain the difference, we will discuss this topic under the following concepts: a) Biochemical b) Ecological Vulnerability (ecovulnerability), and c) Genetic analysis of dopamine receptor gene.

a) Biochemical Concept of Human heritability

The genetic traits in each individual are located on chromosomes, which consist of strands of deoxyribonucleic acid (DNA). During intercourse, each couple deposits 23 chromosomes from the male sperm and the female ovum cells. The unity of this mating results to one fertilized egg with a total number of 46 chromosomes. Except for one pair of the chromosomes, which usually determines a person’s anatomical sex characterization (the YX male and the XX for female), others, called genomes, are responsible for the expression of a particular trait or character in the individual person. The DNA houses thousands of genes that content the specifications and characteristics of each couple. The major function of the DNA is to transfer genetic characters, by way of coded instruction, from parents to the embryos. The genes, therefore, are the basic units of heredity. Within each gene, the sequence of four molecules, called bases, constitute a basic chemical code that helps determine the synthesis of a particular protein by specifying the sequence of amino acids.

Research experiences have shown that the transfer of genetic characters from parent to offspring does not always follow a mathematical or logical sequence as to say 1+1= 2 or that this couple is tall therefore their offspring will be tall. This is because most human traits, even such seemingly straightforward thing like height, and eye color, depend on more than one gene pair. This situation makes it very complicated to track down the genetic factors responsible for any behavioral character in offspring. One method, which is being used to search for genes associated with mental disorders, involves doing Linkage studies. These studies take advantage of the tendency of some genes lying close together on a chromosome to be inherited together across the generations. The researchers started out by looking for markers, DNA segments vary considerably among individuals and those locations on the chromosomes are already known. They then look for patterns for inheritance of these markers in large families in which a particular condition is common.

If a marker tends to exist in individuals who have the condition and not in those who don’t, then the variant of the gene involved in the condition is apt to be located nearby on
the chromosome, and the research have some idea where to search for it. This method of linkage studies, for example, was used to locate the gene that causes Huntington’s disease. This break through in the neurogenetics stirred up an added conviction among neuropsychologists that there could possible neurological explanation for the causes of schizophrenia. Although in the case of Huntington’s disease (the neurological disorder said to have killed Woody Guthrie), only one gene was responsible, yet search took a decade of painstaking work. Consider then schizophrenia that has several genes involved.

The difficulties in claiming “absolute” genetic heritability of schizophrenia from patients are the complication human genome. Even though science has figured why individuals have characteristic resemblances with their parents, yet it is obvious that “each of us, with the exception of identical twins, is a unique genetic mosaic, one that never existed before and never will again” (Tavris & Wade, 1997, p.88). To explain this genetic uniqueness of the individual person Tavris and Wade maintain that chromosomal replication, division (mitosis and meiosis), and mutation drastically and spontaneously alter genetic codification. The result is that children who share very thing with their biological parent can be quit unlike their parents-in purely genetic terms (1997). Can the same theory apply to the heritability of schizophrenia?

b) Ecological Vulnerability theory

The supporters of the vulnerability theory are on the midway between the biological etiology (lumpers), genetic etiology (Splitter), and behavioral etiology. They seem to acknowledge the neurophysiological and genetic presence in the causes of schizophrenic episode. But they reject the view of schizophrenia as a persistent, progressive chronic disorder leading to complete deterioration of personality. They believed that the heritability of the schizophrenic traits does not automatically result to the episode (state), but makes the individual more vulnerable than the person without the genetic traits. The vulnerable individuals who are not subjected to high magnitude stresses and strains or who had learned to adjust properly to situations, may experience any episode even though their parents suffered the episode. They further hold that the persistent chronic episode found in majority of the suffers is chiefly as a result of iatrogenic (wrong treatment method and hospitalization) and ecogenic (due to noxious and improvising environment) circumstances rather than of the natural consequence of the disorder itself. We must remember that the iatrogenic and ecogenic effect on the individual may start immediately after conception. This is why Hedaya maintains that the environment and genes share each other and each can actually influence the other at any given time (1996). Danie Freedman replicated the idea when he stated that schizophrenia and other major disorders involve a variety of environmental stressors acting on genetic or other biological vulnerability (1975).

The vulnerability theorists have proposed number of models for the explanation of the causes and persistent nature of schizophrenia. These models range from molecular-biological model (psychogenetic model) to a field-theory model (influenced by ecological factors). They are based on the phenomenological concept that the actual etiology of
schizophrenia is concomitant and interwoven in such a way that the network of human neurobiogenetics and ecology are in interplay.

![Diagram of Scientific Model of Etiology of Schizophrenia](image)

**SCIENTIFIC MODEL OF ETIOLOGY OF SCHIZOPHRENIA** as presented by Joseph Zubin.

The above diagram projects the basic concept that no one element is solely responsible for the causes of schizophrenia. Rather genetic trait, developmental abnormality, internal environmental status, and neurophysiological implications intermingle to cause schizophrenia. The progenitors of genetic models believe that what an individual inherits from parents is **predisposition** to “episode” rather than a “trait”. (Zubin, 1975). On body is born with schizophrenic trait, not even the monozygotic twins, but one can inherit defective genes which puts the individual at the edge. It means therefore that such person is not destined to suffer the ailment if every other condition is put under control.

If a child had a schizophrenic genetic trait, prenatal complications, nutritional problem, and lagged maturational development (Gottesman, Aston, and Moldin, 1999), he or her stands a greater chance of becoming schizophrenia than the same sibling who had normal development processes (Kety et al., 1994). Since monozygotic twins share equally on these areas of human development, their affectability should be counted as developmental factor rather than inheritability (Thapar A. Holmes et al., 1999). Researchers also indicate a higher risk of schizophrenia for individual born with cerebral injury but with no known history of schizophrenia in their families.

The internal environment model has been the most controversial concept for the etiology of schizophrenia. It has stimulated the search for biochemical abnormalities in
The topic will be treated in detail on the session. However the quest to study schizophrenia to the network of the central nervous system (CNS) started as far back as 1940s. More than ever, the research has shifted to the metabolic actions of the synaptic mechanisms which recognizes the presence and the possibilities of chemical imbalances in metabolic processes, hormonal distributions and drugs and their affects in the psychological function they mediate (Kety, et al, 1994). Kety and his colleagues believe that the psychological processes which are mediated through biochemical reactions of the synapses control the individual’s power of perception, cognition, attention, motivation, mood, and other emotional and mental states. The impairment of synaptic metabolism may affect the emotional ability of individuals, which can be complicated by other factors, like iatrogenic factor and ecology.

c) Genetic analysis of dopamine receptor gene

While family, twin, and adoption studies suggest that genetic factors play a major role in the etiology of schizophrenia, the mode of genetic this genetic transmission remains clouded and uncertain. Researchers have maintained that the complex traits of schizophrenia are probably represented by more than one locus in human genome. Many investigators have based their findings in many factors which focus on the DNA, gene mapping technique, the dopaminergic system.

All genetic variations originate from a change in DNA sequence called mutation. A large number of agents in our environment are known to cause mutations which include ionizing radiation and many other different chemical reactions. However, mutations can occur spontaneously during the process of DNA replication. The differing DNA sequences of a gene are called “alleles”. If an individual has the same alleles on both members of a chromosomes pair (from both parents), he or she is said to be a homozygote. Difference in alleles of DNA sequence, however, means that the individual is heterozygote. It is known that many of the different physical characteristics, such as height, color of skin and eyes, are determined by genetic variations. Some of the genetic variations are inconsequential while others cause diseases.

A number of laboratory techniques have been employed to determine gene variation that cause schizophrenia. For example, protein electrophoresis, which recognizes differences in proteins on the basis of their electrical charges, has been used to determine amino acid variation in human beings. This method has been rejected because it cannot detect all the variations in the amino acid sequences.

A new deoxyribonucleic acid (DNA) based research method, which, detects the amino acid variations at DNA level has been recognized by many genetic. This technique, known as Restriction Fragment Length Polymorphism (RFLP), is developed from the availability of large number of bacterial enzymes which cleave or cut DNA at the specific recognized sites known as restriction or recognized sites (Asherson, P. Curran, S., McGuffin, P., 1999)

Using this technique, many studies have been made of the schizophrenic-gene replication. Bruce Bower reported investigation of more than 100 families that suggest a
gene located on the chromosome 13, which contributes to at least some cases of schizophrenia that usually appear in younger ages (1998). A specific sequence on chromosome 8 also shows signs of boosting susceptibility to schizophrenia for some people who possess the signature sequence on chromosome 13 (Bower, 1998). The genetic epidemiologist, Ann Pulver, maintains that what’s exciting is that we have the first evidence to support the theory that different sets of genes can create a susceptibility to schizophrenia. Earlier efforts to locate susceptibility of schizophrenia have had mixed results. Some evidence indicates that an unidentified gene on chromosome 6 contributes to the disorganized thinking, delusions, and hallucination typical of this mental ailment.

In order to support their views, researchers have used the DNA blood samples of those diagnosed with schizophrenia and their members of their extended families. The studies maintained that a genetic link to the chromosome 13 and 8 areas was found in the both individuals diagnosed with schizophrenia and their families. A genetic link only to chromosome 13 characterized the families in which several members had mood disorder, as well as hallucination and delusion. In a similar research, Sevilla Detera-Wadleigh of the National Institute of Mental Health in Bethesda, believed to have found the same chromosome 13 sequence often in family members of individuals diagnosed with bipolar disorder, or manic depression. This finding argues that if heritability is composed of DNA trait, therefore, the gene on chromosome 13 can be inheritability and can increase the likelihood of schizophrenia in offspring of those suffering the ailment. This finding has been challenged because of its lack of precession and limited assess to other areas of great importance in determining heritability.

Molecular biologists have resort to the technique called “gene mapping technique” to study genes-chromosome interplay and heritability. These techniques are used widely in the study of CNS structure and function. The methods permit investigation of different proteins, step by step, from gene transcription to the post-transcriptional processes. They are being applied also in the investigation of enzymes responsible for the synthesis of neurotransmitters and receptor.

Furthermore, Seaman et al (1994) studied the dopamine D4 receptor gene in a group of schizophrenia and control subjects. These studies are carried out in order to determine the frequency of the dopamine receptor gene variants in which serine or glycine substitutions have occurred. When administered with glycine substitutions, 23 out 183 control, representing 12.6% of the population, and three out 24 schizophrenia, representing 12.3% revealed a replacement of thiamine by guanine. The identical prevalence of this variant between two groups indicates that the variant is not associated with schizophrenia. This variant, however, was found only in black subjects, but none of the 147 Caucasians (113 controls and 34 schizophrenics) revealed this variant.

Concentrations of serine and glycine in the cerebrospinal fluid (CSF) and plasma have shown some evidence of the genetic control of these amino acid variations. cerebrospinal fluid levels of several amino acids showed a similar pattern in a twin sample (Hagenfeldt et al 1998). Devor and waziri (1993) reported significant genetic control of plasma
concentrations of serine and glycine in 28 nuclear families with 108 members. The authors suggested that the control of the plasma concentration was carried out via a single major gene locus and the glycine metabolizing enzymes, SHMT, was a likely candidate for this single gene locus.

2) Balancing the Dopamine hypothesis Debates

The dopamine hypothesis states that schizophrenia is caused by functional hyperactivity of the dopaminergic system in the brain. This hypothesis accounts for all the aberrations that occur in the synthesis, release, reuptake, and metabolism of dopamine, and changes in the dopamine receptors throughout the CNS. They will be discussed under the following sequence:

a). The Biological activities of Dopamine.
b) Chemical
   c) neurodevelopmental hypotheses
d) Neurodegenerative hypotheses

**Dopaminergic pathways**, sometimes called **dopaminergic projections**, are neural pathways in the brain that transmit the neurotransmitter dopamine from one region of the brain to another. Dopamine is one of the neurotransmitters. Neurotransmitters, on the other hand, are electrochemical substances released from pre-synaptic axonal terminals into the post-synaptic receptor (Crow, et al. 1979). The neurotransmitter that will occupy us here is the catecholamines that are released in form of epinephrine, norepinephrine, and dopamine (Friedhoff et al., 1977). The Calcium ion plays an important role in the release and responses of the transmitters. Irregularities in calcium ion may delay the arrival of action potential and the opening of the Ca+ + gates to allow the entry of the Ca+ + into the pre-synaptic terminal (Gomes, 1980). On the other side of the neurotransmitter is the receptors or post-synaptic terminal. They are the constituents of cells that have the ability to recognize a neurotransmitter, neuropeptide (Kety et al., 1994), hormones, and other chemical substances.

In neurons that localize dopamine (DA) as their transmitter, the biogenic amino synthertic pathways stored with Dopa decarboxylase, the enzyme that synthesizes DA. DA acts on two types of receptors, both of which are linked to adenylate cyclase- cAMP second messenger systems (Crowe, 1995). Investigators have identified several subtypes of DA receptors that are categorized as D1, D2, D3, D4, and D5. This categorization follows the order of their discovery (Rosenzenweig et al., 1999). With the exception of D1 and D5, all other DA receptors, D2, D3, and D4 share the same properties and are similar to each other. However, the stimulation of D1 receptors causes an increase in cAMP levels, whereas stimulation of D2 receptors decreases the cAMP (Nader et al., 1997). There are also autoreceptors on the presynaptic terminal, which are thought to exert an inhibitory feedback effect on the DA neuron. Dopaminergic synapses have been of great interest because of the evidence that antipsychotic drugs that are effective in alleviating the symptoms of schizophrenia have the common effect of interfering with transmission at dopaminergic synapse in the brain (Rosenzweig et al., 1999).
Recent research studies indicate that the primary mode of operation of antipsychotic drugs is to bind to, and block, the D2 receptors. In contrast to these blocking actions of antipsychotic drug, it is known that drugs that are DA agonists such as amphetamine, that enhance or mimic the actions of DA, can induce schizophrenia-like behavior. It has been tempting therefore to believe that schizophrenia is due to hyperactivity of DA neuron in the brain. But how this hyperactivity of the DA can be transmitter to generation of sibling is yet to be cleared (Schneider & Tarshis, 1987).

The molecular mechanism, activities, and metabolism of the dopaminergic synapses can be explained as follows: The synthesis of the enzymatic pathway starts with the action of tyrosine (Tyr). The Tyr catalyzed and converted to dihydroxyphenylalanine (DOPA). The DOPA is transported and stored within the neural network as dopamine (DA). Storage of DA is blocked and inhibited by the actions of reserpine (Res). DA is released by the actions of exocytosis. During the onward transmission from pre-synapses to receptors or post-synapses, the DA binds itself to D1 receptor, acting through stimulatory G protein (G2) to increase the level of CAMP, or binds with D2 receptor, acting through inhibitory G protein to lower levels of CAMP. Most of the antipsychotic medications/drugs, such as butyrophenones, block the action of the D2 receptor.

**Argument from D2 receptor**

Many eminent researchers have come to the gripping that the mere fact that the D2 receptors have bee identified as the cause of schizophrenia did not give the whole picture of the origin or etiology of this ailment. Keeping in mind that several factors can upset the chemical activities of the D2 receptors leading to the increase the camp, we are not yet satisfy that the D2 receptor gene can be inherited. On this topic we will try to know how much the individual can inherit from the defective D2 receptor genes. In medicine, for example, the type of diabetes in which the receptors do not recognize the presence of insulin has been linked to genetic trait, which is inheritable.

The introduction of both RFLPs and VNTRs, and PCR are geared toward the determination and accessibility of the genetic variation at DNA levels (Yang et al., 1993, Saha, et al., 1994, Sokoloff et al 1992). The linkage analysis makes it possible to determine the location of genes on chromosomes. Most of these techniques are used to determine the “association” levels between the two different alleles. And the term association in genetics refers to a statistical relationship between two traits, which may or may not be genetic or heritable. However, when two gene loci, one allele of a marker and other one of a disease gene, are located close to each other on the same chromosome, the two are transmitted together within the family (A.J. Publisher, 1998). All the dopamine receptors subtypes (D1-D5) have been cloned and each of the genes of the dopamine receptors have been found to have a number of mutations. The ongoing studies in this direction are to determine whether the occurrence of these mutations has something to do with the cause of schizophrenia. The results are still controversial in some areas, because most of the studies report no significant differences between the schizophrenic and
normal population with regard to the occurrence of dopamine receptor gene mutation (Sunahara et al 1991, Sobel et al., 1995).

Similarly, genes for enzymes tyrosine hydroxylase and COMT have been identified and localized (Rao et al 1994, Daniel et al 1996). Mutations in these genes do not appear to be associated with schizophrenia. It is of great interest to note that the recent effort to determine the genetics of schizophrenia have produced spectacular results from hundreds of family populations all over the world (Sedvall et al 1995, Sedvall and Farde, 1995). Several studies involved in this effort have agreed that a region on the short arm of chromosome 6 appears to be associated with schizophrenia. Although even this area of chromosome 6 is fairly large and contains about 700 genes, none of the dopamine receptor gene (1-5) have been known to occur in this region (Malmberg et al 1993).

Conclusion

That there is a genetic vulnerability to schizophrenia is not a controversy for variety of reasons. It has been shown that sibling schizophrenic patients have been an increased risk of the disorder only when they are biological siblings, not adopted. What this genetic vulnerability is, of course, is not known, as no single gene has been identified as a risk factor for schizophrenia. That the gene or genes involved interact with some environmental factor is clear since identical twins share the disorder only about 50% of the time. According to Schwartz and Africa (1988), individual has an 8% risk of schizophrenia if his or her sibling is schizophrenic, a 12% risk if one parent is affected, a 14% risk of sharing the disorder with a fraternal twin, a 38% risk if both parents are affected, and 47% risk when two individuals share the same exact genes.

In real life experience, these figures can vary extensively, giving the individual the course to think that the vulnerability theory rather than strict biological inheritability is more attainable than the notion that schizophrenia is inherited.

Reference


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