

SCHIZOPHRENIA

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GLOSSARY

Anti-Psychotics: A group of medications known to reduce many symptoms of schizophrenia.

Behavioral Genetics: The study of the extent to which individual differences in behavior are attributable to genetic makeup, as opposed to environmental factors.

Dopamine: A catecholamine neurotransmitter located throughout the brain, particularly the substantia nigra and basal ganglia.

Frontal Lobes: The portion of each cerebral hemisphere that is anterior to the central sulcus and above the lateral fissure, and is active in reasoning, planning, and other higher mental processes.

Ventricles: Large cavities in the brain that are continuous with the central canal of the spinal cord and filled with cerebrospinal fluid.

Schizophrenia is a psychotic disorder characterized by disturbances in thought, emotion, and behavior. This article will discuss the symptoms, etiology, treatment, and other pertinent information concerning this mental illness.

I. DESCRIPTION AND CLASSIFICATION

Schizophrenia is a serious mental illness that afflicts about 1% of the population at some point in their lifetime. In the current Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), it is described as an illness that involves psychotic symptoms and significant interpersonal or occupational dysfunction that has persisted for a period of at least 6 months. The term 'psychotic' is used to refer to symptoms that indicate an impairment in the patient's ability to comprehend reality. This includes beliefs that have no basis in reality and that are not susceptible to corrective feedback (delusions), and sensory perceptions that have no identifiable external source (hallucinations). In addition to hallucinations and delusions, the

DSM lists three other key symptoms of schizophrenia: “disorganized speech,” “disorganized or catatonic behavior,” and “negative symptoms.”

A. Symptoms

1. Delusions

Delusions are the primary example of abnormal thought content in schizophrenia. Delusional beliefs conflict with reality and are tenaciously held, despite evidence to the contrary. There are several types of delusions. *Delusions of control* entail the belief one is being manipulated by an external force, often a powerful individual or organization (e.g., the FBI) that has malevolent intent. The term *delusions of grandeur* refer to the patients’ beliefs that they are especially important and have unique qualities or powers (e.g., the capacity to personally influence weather conditions). In contrast, some patients express the conviction that they are victims of persecution or an organized plot, and these beliefs are referred to as *delusions of persecution*. Examples of more specific delusions include *thought broadcasting*, the patient’s belief that his or her thoughts are transmitted so that others know them, and *thought withdrawal*, the belief that an external force has stolen one’s thoughts.

2. Hallucinations

Hallucinations are among the most subjectively distressing symptoms experienced by schizophrenia patients. These perceptual distortions vary among patients, and can be auditory, visual, olfactory, gustatory, or tactile. But the majority of hallucinations are auditory in nature, and typically involve voices. Examples

include the patient hearing someone threatening or chastising them, a voice repeating the patient's own thoughts, two or more voices arguing, and voices commenting. The second most common form of hallucination is visual. Visual hallucinations often entail the perception of distortions in the physical environment, especially the faces and bodies of other people.

Other perceptual distortions that are commonly reported by schizophrenia patients include feeling as if parts of the body are distorted in size or shape, feeling as if an object is closer or farther away than it actually is, feeling numbness, tingling, or burning, being hypersensitive to sensory stimuli, and perceiving objects as flat and colorless. In addition to these distinctive perceptual abnormalities, persons suffering from schizophrenia often report difficulties focusing their attention or sustaining concentration on a task.

It is important to note that in order for an unsubstantiated belief or sensory experience to qualify as a delusion or hallucination, the individual must be convinced of its reality. Thus, for example, if a patient reports hearing something that sounds like voices when alone, but adds that he or she is certain that this is a *misinterpretation* of a sound, such as the wind blowing leaves, this would not constitute an auditory hallucination.

3. Disorganized Speech

The DSM uses the term *disorganized speech* to refer to abnormalities in the form or content of the individual's verbalizations. It is assumed that these abnormalities reflect underlying distortions in the patient's thought processes. Thus

the term “thought disorder” is frequently used by researchers and practitioners to refer to the disorganized speech that often occurs in schizophrenia.

Problems in the form of speech are reflected in abnormalities in the organization and coherent expression of ideas to others. One common abnormality of form, *incoherent speech*, is characterized by seemingly unrelated images or fragments of thoughts that are incomprehensible to the listener. The term *loose association* refers to the tendency to abruptly shift from one topic that has no apparent association with the previous topic. In general, the overall content of loosely associated speech may be easier to comprehend than is incoherent speech. In *perseverative speech*, words, ideas, or both are continuously repeated, as if the patient is unable to shift to another idea. *Clang associations* involve the utterance of rhyming words that follow each other (e.g., “a right, bright kite”). Patients choose words for their similarity in sound rather than their syntax, often producing a string of rhyming words.

4. Disorganized or Catatonic behavior

The overt behavioral symptoms of schizophrenia fall in two general areas: motor functions and interpersonal behavior. Motor abnormalities, including mannerisms, stereotyped movements and unusual posture, are common among schizophrenia patients. As with other symptoms of the psychosis, the manifestation of motor abnormalities varies among individuals. Some common signs include bizarre facial expressions, such as repeated grimacing or staring, and repeated peculiar gestures that often involve complex behavioral sequences. Schizophrenia patients sometimes mimic the behavior of others, known as echopraxia, or repeat

their own movements, known as stereotyped behaviors. Although a subgroup of patients demonstrate heightened levels of activity, including motoric excitement, (e.g., agitation or flailing of the limbs), others suffer from a reduction of movement. At the latter extreme, some exhibit *catatonic immobility* and assume unusual postures that are maintained for extended periods of time. Some may also demonstrate *waxy flexibility*, a condition in which patients do not resist being placed into strange positions that they maintain. Catatonia has decreased dramatically in recent decades, so that they are now rare. Several researchers have attributed this decline to the introduction of antipsychotic medication (described below).

In the domain of interpersonal interactions, schizophrenia patients frequently demonstrate behaviors that are perceived as bizarre or inappropriate by others. For example, it is not uncommon for patients to use socially unacceptable language and unusual tones of voice, or to show overly dependent or intrusive behavior. Another common symptom, *inappropriate affect*, involves unusual emotional reactions to events and experiences. For example, patients may laugh at a sad or somber occasion, or be enraged by insignificant events. Finally, many patients manifest increasingly poor hygiene as their illness progresses. Their appearance may also be marked by disheveled clothing or inappropriate clothing, such as gloves and coats in the summer.

5. Negative Symptoms

The symptoms of schizophrenia can be classified into the general categories of “positive” and “negative.” Positive symptoms involve behavioral excesses, and

most of the symptoms described above fall in to this category (e.g., delusions, hallucinations, and bizarre behaviors). In contrast, negative symptoms involve behavioral deficits. Examples include *flat affect* (blunted expressions of emotion), *apathy*, and *social withdrawal*. In the domain of verbal expression, schizophrenia patients who manifest a very low rate of verbal output are described as showing *poverty of speech*. Patients whose speech is normal in quantity, but lacks meaning, suffer from *poverty of content*. Recently, some researchers have suggested that positive and negative symptoms may be due to different neural mechanisms.

It is important to mention that a reduction in overt displays of emotion does not necessarily imply that patients have less intense subjective emotional experiences than the average person. In fact, recent research findings indicate that blunted emotional expressions can coexist with intense subjective feelings of emotion.

B. Variability among patients in symptoms

According to the DSM-IV, patients must show two or more of the above five symptoms in order to meet diagnostic criteria for schizophrenia. Thus, none of these symptoms is *required* for the diagnosis. Further, the following four criteria must also be met: 1) the patient shows marked deterioration in occupational, interpersonal, or domestic functioning, 2) the patient manifests continuous signs of symptoms or dysfunction for at least 6 months; 3) the patient does *not* manifest predominant signs of mood disturbance (e.g., depression or mania); and 4) the symptoms are not due to substance abuse or a primary medical condition.

Because the diagnostic criteria for schizophrenia are relatively broad, with no one essential symptom, there is a great deal of variability among patients in their symptom profiles. It has therefore been proposed that schizophrenia is a heterogeneous disorder with multiple causes. It is also the case, however, that patients must show a marked and persistent impairment in order to meet diagnostic criteria for schizophrenia. Thus, those who meet criteria for the diagnosis are significantly impaired in everyday functioning. As described below, for many individuals who are diagnosed with schizophrenia, independent functioning is never achieved.

C. Subtypes of schizophrenia

The DSM lists five subtypes of schizophrenia. In schizophrenia of the *Paranoid type*, delusional concerns about persecution and preoccupation with threat dominate the clinical presentation, although delusions of grandeur are also often present. *Disorganized* schizophrenia involves extremely incoherent speech and behavior, as well as blunted or inappropriate affect. In *catatonic* schizophrenia, the clinical picture is dominated by abnormalities in movement, such as those described above. Patients classified as having *undifferentiated* schizophrenia do not meet criteria for any of the previous subtypes. Finally, the diagnosis of *residual* schizophrenia is applied to patients who have had at least one episode of schizophrenia, and who continue to show functional impairment, but who do not currently manifest any positive symptoms.

II. HISTORY

During the late 1800's and early 1900's, Emil Kraepelin and Eugen Bleuler provided the first conceptualizations of schizophrenia. Kraepelin defined "dementia praecox," the original term for schizophrenia, as an endogenous psychosis characterized by intellectual deterioration (dementia) and early onset (praecox). Kraepelin included negativism, hallucinations, delusions, stereotyped behaviors, attentional difficulties, and emotional dysfunction as major symptoms of the disorder. Kraepelin's work focused on description and phenomenology, leaving subsequent researchers to investigate the cause(s) of the disorder.

In contrast to Kraepelin, Eugen Bleuler, a Swiss psychiatrist, proposed a broader view of dementia praecox, with a more theoretical emphasis. Bleuler contested two of Kraepelin's defining assumptions: specifically, that the psychosis was typically characterized by early onset and intellectual deterioration. Bleuler attempted to identify an underlying commonality among the diverse variations of what Kraepelin referred to as "dementia praecox" and concluded that all patients suffered from a "breaking of associative threads," causing a disharmony among communicative and thought processes. He believed this abnormality accounted for the problems of thought, emotional expression, decision making, and social interaction associated with schizophrenia. Guided by the defining principle of disharmonious mental structures, Bleuler renamed the disorder "schizophrenia," directly translating to "split mind."

In the early to mid 1900's, American psychiatrists continued to utilize a broad definition of schizophrenia. The distinction between process and reactive schizophrenia was considered important, however, because it was assumed to distinguish between cases characterized by gradual deterioration (process), and cases that were precipitated by acute stress (reactive).

During this time, some clinicians and researchers viewed specific diagnostic criteria for the major mental illnesses (schizophrenia, bipolar disorder, major depression) as artificial and discretionary, and used flexible and inconsistent standards for diagnoses. Studies that compared the rates of disorder across nations revealed that schizophrenia was diagnosed at a much higher rate in the U.S. than in Great Britain and some other countries. This national difference was found to be due to the use of broader criteria for diagnosing schizophrenia in the United States. Many patients who were diagnosed as having depression or bipolar disorder in Britain were diagnosed with schizophrenia in the U.S. Because subsequent revisions in the DSM have included more restrictive criteria for schizophrenia, U.S. diagnostic rates are now comparable with other countries.

In addition to a more restrictive definition of schizophrenia, subsequent editions of the DSM have included additional diagnostic categories that involve similar symptoms. Thus the range of 'schizophrenia-spectrum disorders' continued to broaden with the description of variants of schizophrenia such as "schizoaffective disorder," which is characterized by a mix of affective and psychotic symptoms. The diagnostic category of "schizophreniform disorder" was also added. This diagnosis

is given when the patient shows the typical symptoms of schizophrenia, but does not meet the criterion of 6 months of continuous illness.

III. DEMOGRAPHIC CHARACTERISTICS OF SCHIZOPHRENIA

Estimates of the prevalence of schizophrenia range around 1% of the population. Although there is evidence of cross-national differences in the rate of schizophrenia, the differences are not very large (i. e., 1-2% difference). It is, in fact, striking that the rate of occurrence is so consistent across cultures.

The modal age at onset of schizophrenia is in early adulthood, usually before 25 years of age. Thus most patients have not had the opportunity to marry or establish a stable work history prior to the onset of the illness. As a result of this, and the often chronic nature of the illness, many patients never attain financial independence.

It is relatively rare for preadolescent children to receive a diagnosis of schizophrenia. Similarly, it is rare for individuals beyond the age of 40 to experience a first episode of the illness.

A. Sex Differences

Although it has traditionally been assumed that there is no sex difference in the rate of schizophrenia, some recent research findings indicate that a somewhat larger proportion of males than females meet the DSM-IV criteria for the disorder. Nonetheless, the overall rates do not differ dramatically for men and women. It is

well established, however, that women are more likely to have a later onset of illness, as well as a better prognosis. Women also show a higher level of interpersonal and occupational functioning during the period prior to illness onset. The reasons for this sex difference are not known, but it has been proposed by several theorists that the female sex hormone, estrogen, may be involved in attenuating the severity of the illness.

B. Social Class differences

Compared with the general population averages, schizophrenia patients tend to have significantly lower incomes and educational levels. Poor urban inner city districts, inhabited by the lowest socioeconomic class, contain the largest proportion of schizophrenia patients. There is a sharp contrast between the rates of schizophrenia in the lowest socioeconomic class as compared with all other levels, including the next higher. Findings from various cultures suggest that rates of schizophrenia are almost two times higher in the lowest social class group compared with the next lowest.

These social class differences appear to be a partial consequence of the debilitating nature of the illness. The *social-drift theory* suggests that during the development of schizophrenia, people drift into poverty. When the incomes and educational levels of the parents of patients are compared with those of the general population, the differences are not as striking.

There is, nonetheless, evidence that patients do come from families where the incomes and educational backgrounds of the parents are slightly below the average.

These findings have led researchers to conclude that there may be a causal link between social class and risk for the illness. The *sociogenic hypothesis* posits that situational factors associated with low social class, such as degrading treatment from society, low levels of education, and few opportunities for achievement and reward, produce stress that contributes to the risk for schizophrenia.

IV. LIFE FUNCTIONING AND PROGNOSIS

Prior to the introduction of antipsychotic medications in 1950, the majority of patients spent most of their lives in institutional settings. There was little in the way of programs for rehabilitation. But contemporary, multifaceted treatment approaches have made it possible for most patients to live in community settings.

Of course, during active episodes of the illness, schizophrenia patients are usually seriously functionally impaired. They are typically unable to work or maintain a social network, and often require hospitalization. Even when in remission, some patients find it challenging to hold a job or to be self-sufficient. This is partially due to residual symptoms, as well as the interruptions in educational attainment and occupational progress that result from the illness. But there are many patients who are able to lead productive lives, hold stable jobs, and raise families. With the development of greater community awareness of mental illness, some of the stigmas that kept patients from pursuing work or an education has diminished.

A. Long-term course

For about one third of patients, the illness is chronic and is characterized by episodes of severe symptoms with intermittent periods during which the symptoms subside, but do not disappear. For others, there are multiple episodes with periods of substantial symptom remission. About one third of those who receive the diagnosis eventually show a partial or complete recovery after one or two episodes.

Several factors have been shown to be linked with a more favorable prognosis for schizophrenia. The provision of early treatment seems to be important, in that the shorter the duration between the onset of the patients' symptoms and the first prescribed medication, the better the clinical outcome. Another indicator of better prognosis is a high level of occupational and interpersonal functioning in the premorbid period. Also, as noted earlier, females and patients who have a later onset of symptoms have a better long-term outcome.

B. Premorbid Characteristics of Schizophrenia

Some of the difficulties experienced by individuals with schizophrenia can be observed before the onset of the clinical symptoms. Deficits in social skills, concentration, emotional expression, motivation, and occupational or academic performance often precede the first clinical symptoms. This period of gradual decline in functioning before the first illness episode is referred to as the "prodromal" phase.

However, there are often more subtle signs of dysfunction long before the onset of the prodromal period. Controlled studies using archival data sources, such as medical and school records or childhood home-movies, indicate that subtle differences are discernible as early as infancy in some patients. Individuals who

succumb to schizophrenia in adulthood sometimes have abnormal motor development and show deficits in emotional expression and interpersonal relationships in early childhood. Cognitive impairment and difficult temperament have also been observed. During middle childhood and adolescence, researchers have found evidence of neurological abnormality, poor emotional control, social immaturity, and academic performance deficits. During adolescence, some exhibit behavioral disturbances and cognitive abnormalities that resemble the clinical symptoms of schizophrenia.

V. ETIOLOGY: THEORIES AND RESEARCH FINDINGS

The causes of schizophrenia are unknown, but it is now widely accepted by both researchers and clinicians that schizophrenia is biologically influenced. This is in striking contrast to the early and mid 1900s, when many subscribed to the theory that faulty parenting, especially cold and rejecting mothering, caused schizophrenia in offspring.

A. Brain Abnormalities in schizophrenia

There are several sources of evidence for the assumption that schizophrenia involves an abnormality in brain function. First, studies of schizophrenia patients have revealed a variety of behavioral signs of central nervous system impairment, including motor and cognitive dysfunctions. Second, when the brains of patients are examined with *in vivo* imaging techniques, such as Magnetic Resonance Imaging

(MRI), many show abnormalities in brain structure. Similarly, post-mortem studies of brain tissue have revealed irregularities in nerve cell formation and interconnections.

One method of examining the integrity of brain function is through the administration of neuropsychological tests. Research on the neuropsychological performance of schizophrenia patients were first conducted in the 1950s and continues to the present time. Theoretically, individual neuropsychological tests measure the functioning of specific regions of the brain. An early finding in this area was that schizophrenia patients were the one psychiatric group whose performance on neuropsychological tests was indistinguishable from people with known brain damage. The findings suggested a generalized cerebral dysfunction in schizophrenia. Patients show the most consistent deficits on tests of attention and memory, indicating dysfunction of the frontal and temporal lobes and the hippocampus. Further evidence of dysfunction in these brain regions is derived from poor performance on tests of executive functions: the ability to formulate, maintain, and adapt appropriate responses to the environment.

Brain-imaging studies of schizophrenia have yielded results that mirror those obtained from neuropsychological research. Some relatively consistent findings are that the brains of schizophrenia patients have abnormal frontal lobes and enlarged ventricles. Enlarged ventricles suggest decreased brain mass, particularly in the limbic region, which is intimately involved in emotional processing. Further, more ventricular size correlates with negative symptoms, performance deficits on

neuropsychological tests, poor response to medication, and poor premorbid adjustment. These associations between ventricular enlargement and both premorbid and postmorbid characteristics suggest that the brain abnormalities are long-standing, perhaps congenital.

In addition to brain *structure*, investigators have examined biological indices of brain *function* in schizophrenia. Functional brain imaging studies, using procedures such as positron emission tomography (PET) and measurement of regional cerebral blood flow, reveal that schizophrenia patients have decreased levels of blood flow to the frontal lobes, especially while performing cognitive tasks.

Researchers are now pursuing the question of what causes the brain abnormalities observed in schizophrenia. Although we do not yet have any definitive answers, investigators have made continuous progress in identifying factors that are associated with risk for the disorder.

B. Biochemical Factors

The structural brain abnormalities that have been observed in schizophrenia support the assumption that it is a disorder of the central nervous system. But it has also been shown that similar structural abnormalities (i. e., ventricular enlargement and volume reductions) are present in other disorders, both neurological and psychiatric. It is therefore assumed that specific abnormalities in brain biochemistry may play a role in schizophrenia.

The functioning of the central nervous system is dependent upon a host of chemicals that serves as the ‘messenger substances’ among neurons. These

chemicals or ‘neurotransmitters’ have been the subject of intensive investigation. Among the various neurotransmitters that have been implicated in the neuropathophysiology of schizophrenia, one is called “dopamine.” Dopamine has been viewed as a likely candidate for two main reasons; 1) drugs that act to enhance the release or activity of dopamine can produce psychotic symptoms, and 2) drugs that have been established to have antipsychotic properties (i.e., reduce psychotic symptoms) reduce the activity of dopamine in the brain. Current theories of the role of dopamine in schizophrenia have focused on dopamine receptors. There is evidence that there may be an abnormality in the number or sensitivity of certain dopamine receptors in the brains of schizophrenia patients. To date, however, this evidence remains inconclusive.

Several other neurotransmitters have also been hypothesized to play a role in schizophrenia. Current theories that are under investigation include a malfunction of the receptors for a neurotransmitter called glutamate, and an abnormality in the balance between dopamine and serotonin (another neurotransmitter which, like dopamine, is a catecholamine). As research findings on the biochemical aspects of schizophrenia accumulate, it increasingly appears that the illness may involve multiple neurotransmitters, with different biochemical profiles for different patients.

C. Genetics

A convincing body of research supports the notion of a genetic predisposition to schizophrenia. Behavioral genetic studies of families, twins, and adopted offspring

of schizophrenia patients indicate that an inherited vulnerability is involved in at least some cases of the disorder.

There is an elevated risk of schizophrenia for individuals with a biological relative who suffer from the disorder, and the risk rates increase as a function of the genetic closeness of the relationship. For example, it has been estimated that children of schizophrenia patients have a 9% to 15% likelihood of developing the illness; siblings of patients have an 8% to 14% likelihood; and cousins have a 2% to 6% likelihood of being diagnosed with schizophrenia. Given the general population rate of approximately 1%, relatives of patients are at statistically increased risk. It must be noted, however, that relatives share common experiences as well as common genes. Therefore, examinations of the prevalence of schizophrenia in the relatives of patients cannot elucidate the relative contributions of environmental and genetic factors.

Some investigators have studied the development of adopted children whose biological mothers had schizophrenia. This approach has the potential to provide more conclusive information than family studies. The results of these investigations show that when biological offspring of schizophrenic mothers are reared from infancy in adoptive homes they are more likely to develop schizophrenia than are adopted children from healthy mothers. Further, these children also exhibit a higher rate of other adjustment problems when compared with controls. Studies of this type have clearly illustrated that vulnerability to schizophrenia can be inherited.

Research on twins examines differences in concordance rates between identical (monozygotic or MZ) and fraternal (dizygotic or DZ) twins. Twin studies rely on the fact that MZ twins essentially share 100% of their genes. Thus, environmental influences account for any behavioral differences between MZ twins. In contrast, DZ twins are no more genetically similar than regular siblings. DZ twins do, however, share more similar environmental factors than do non-twin siblings. To date, the results of twin studies have consistently shown that MZ twins are significantly more likely to be concordant for schizophrenia than are DZ twins.

At the same time, it is important to note that in at least 50% of the cases in which one member of an MZ twin pair has schizophrenia, the other does not. Such “discordant” pairs have been the subject of a recent, comprehensive investigation in the United States. Among the most important findings from this research project are those from the MRI scans conducted on the twins. The ill twins in the pairs showed significantly more brain abnormalities than the healthy twins. Most notable were reductions in the volume of certain brain regions, especially the hippocampus, and increases in the size of the ventricles. These results clearly indicate the importance of environmental factors in the etiology of schizophrenia.

D. Obstetrical complications

As is the case with many other disorders that involve brain dysfunction, there is evidence that schizophrenia is associated with exposure to prenatal and delivery complications. Obstetrical complications (OCs) are defined as physical deviations from the normal course of events during pregnancy, labor, or the neonatal period.

Estimates of OCs in schizophrenics have been as high as 67%, significantly higher than the rate of OCs found in normal controls.

Among the prenatal factors that have been found to be associated with increased risk for schizophrenia are prenatal maternal nutritional deficiency, viral infection, bleeding, and toxemia. Complications of delivery that can result in hypoxia have also been linked with heightened risk for the disorder. Hypoxia, a deficiency in the amount of oxygen available to the fetus, can affect the development of various parts of the brain. Some researchers argue that hypoxia results in hippocampal damage, thus contributing to vulnerability for schizophrenia. Low birth weight, a neonatal complication, is another potential early factor contributing to schizophrenia. There is evidence that low birth weight is related to increased ventricular size, which is a common characteristic of schizophrenia patients.

The findings on prenatal complications support the notion that fetal brain development may be disrupted in individuals who later manifest schizophrenia. A central question raised by these findings concerns the nature of the etiologic role of OCs. Some hypothesize that OCs produce the neural predisposition to schizophrenia, while others posit that OCs exacerbate, or ‘interact’ with, an existing genetic predisposition.

Findings from prospective, high-risk research projects lend support to the hypothesis that OCs interact with genetic vulnerabilities in the etiology of schizophrenia. High-risk studies involve the repeated assessment of children of schizophrenia patients, based on the expectation that a larger percentage of these

children will eventually develop the illness than individuals in the general population. The high-risk method offers some advantages when compared with retrospective studies of the precursors of schizophrenia. One advantage is that it allows for the direct assessment of subjects in the premorbid period, as well as the selection and study of variables that are thought to have prognostic relevance. Further, because a significant portion of the data collection takes place during the premorbid period, this reduces confounds that often occur in the study of diagnosed patients (e.g., medication and institutionalization).

Studies using the high-risk method have shown an interactive effect of genetic risk and exposure to OCs in predicting adult psychiatric outcome. In other words, the correlation between OCs and adult psychiatric symptoms was greater for offspring of schizophrenia parents than for children of healthy parents. The same pattern was apparent for the relation between OCs and adult brain morphology, suggesting that pre- and peri-natal factors contribute to brain abnormalities.

E. Viral Infection

As noted above, prenatal exposure to maternal viral infection has also been linked with schizophrenia. Specifically, the rate of schizophrenia is increased for cohorts who were in the second trimester during flu epidemics. Another source of evidence for the viral hypothesis is the finding that the births of schizophrenia patients do not seem to be randomly distributed throughout the course of the year. Instead, the births of schizophrenia patients occur more frequently in winter months.

Some researchers have suggested that postnatal viral infection may also be relevant to schizophrenia, and that the illness may be due to a long-acting virus. This hypothesis claims that “slow viruses,” which are active over a long period of time, interact with a genetic predisposition to produce schizophrenia. Various findings are cited in support of this hypothesis. Some researchers have identified a viral infection in fatal catatonia, a disorder characterized by schizophrenia-like symptoms, suggesting that a similar viral infection may be found for schizophrenia. Other researchers have found signs of viral activity in the cerebral spinal fluid of patients with schizophrenia.

F. Diathesis-Stress Model

The “diathesis-stress” model has dominated theorizing about the etiology of schizophrenia for several decades. This model assumes that certain individuals inherit or acquire a vulnerability to schizophrenia (the diathesis), and that the behavioral expression of this vulnerability is determined or triggered by environmental stressors. Although ‘stress’ was originally conceptualized as psychosocial in origin, contemporary versions of this model broaden the definition of stress to include prenatal and postnatal insults to the central nervous system. Thus the diathesis, combined with exposure to environmental stressors, can produce schizophrenia.

Exposure to stress within the context of the family has been the focus of attention by researchers in the field. Families in which there is a schizophrenic patient show more conflict and abnormalities in communication than do other

families. However, it has also been shown that there is greater conflict and more abnormalities of communication in families in which any member has a severe debilitating illness. Thus, family communication styles are unlikely to play a unique causal role in schizophrenia.

There is good evidence, however, that exposure to high levels of criticism from family members can increase the likelihood of relapse in schizophrenia patients. The number of critical comments, expressions of hostility, and emotional over-involvement compose a construct referred to as Expressed Emotion (EE). Recovering schizophrenia patients in families high in EE are much more likely to have a relapse as compared with patients in families low in EE. There is also evidence from studies of the adopted offspring of schizophrenia patients suggesting that familial stress can hasten the onset of symptoms.

VI. TREATMENT AND THERAPY

Prior to the turn of the century, our knowledge of the nature and causes of mental disorders was limited. Individuals with psychiatric symptoms, particularly psychotic symptoms, were typically viewed by others with disdain or amusement. But social trends and advances in medical knowledge converged to produce greater sympathy for those with mental illness. This led, especially during the early part of the century, to the construction of public and private hospitals devoted to the care of the mentally ill.

Today, most schizophrenia patients experience at least one period of inpatient treatment. This is usually precipitated by the first psychotic episode. During this initial hospitalization, an extensive assessment is usually conducted in order to determine the most appropriate diagnosis. Treatment is then initiated in order to reduce symptoms and stabilize patients so that they can return to the community as soon as possible.

In the past, periods of hospitalization were longer in duration than they are today. This is due, in part, to the availability of better medical treatments, as described below. Another factor that has contributed to shorter hospital stays is the deinstitutionalization movement. Initially spurred by concerns that too many of the mentally ill were becoming ‘institutionalized’ and losing their ability to function in the community, financial support for state psychiatric hospitals was gradually cut. But community support services and transitional living arrangements were not readily available to many patients. As a result, former psychiatric inpatients now constitute a substantial proportion of the homeless found in U.S. cities.

A. Antipsychotic Medication

Introduced in the 1950’s, antipsychotic medication has since become the most effective and widely used treatment for schizophrenia. Belonging to the class of drugs known as “major tranquilizers,” antipsychotics decrease many symptoms of schizophrenia, especially positive symptoms. But they are not as effective in reducing the negative symptoms. Further, some patients show no response to antipsychotic drugs.

Chlorpromazine (Thorazine) was the first antipsychotic commonly used to treat schizophrenia. Chlorpromazine reduces hallucinations, delusions, and thought disorder, and engenders more calm, manageable, and socially appropriate behavior. As mentioned, all currently used antipsychotic drugs block dopamine neurotransmission. Thus it has been assumed that their efficacy is due to their capacity to reduce the overactivation of dopamine pathways in the brain.

Unfortunately, the benefits of standard antipsychotic drugs are often mitigated by unpleasant side effects. Minor side effects include sensitivity to light, dryness of mouth, and drowsiness. The more severe effects are psychomotor dysfunction, skin discoloration, visual impairment, and tardive dyskinesia (an involuntary movement disorder that sometimes appears after prolonged use of antipsychotics). It is unfortunate that tardive dyskinesia is sometimes irreversible when patients are withdrawn from neuroleptics. Many of these physical signs are known to be caused by chronic blockade of dopamine pathways. Although additional medications can serve to counter some of the negative effects of antipsychotics, schizophrenia patients often resist taking neuroleptics because of an aversion to the side effects.

Within the past decade some new, 'atypical' antipsychotic drugs have been introduced. It was hoped that these drugs would be effective in treating patients who had not responded to standard antipsychotics. Also, researchers hoped to identify medications that had fewer side-effects. Clozapine, released in 1990, seems to reduce negative symptoms more effectively than typical antipsychotic drugs.

Clozapine not only offers hope for patients who are nonresponsive to other medications, but also has fewer annoying side effects than ‘typical’ antipsychotics. However, clozapine can produce one rare, but potentially fatal side effect; agranulocytosis, a blood disorder. Consequently, patients who are on this medication must be monitored on a regular basis. It is fortunate that several other new antipsychotic medications have recently become available, and some of these have no known serious side effects.

It appears that it is important to begin pharmacological treatment of schizophrenia as soon as possible after the symptoms are recognized. The longer patients go without treatment of illness episodes, the worse the long-term prognosis. Medication also has the benefit of lowering the rate of mortality, particularly suicide, among schizophrenia patients.

Patients who are treated with anti-psychotic medication generally require maintenance of the medication in order to obtain continued relief from symptoms. Termination of antipsychotics often results in a relapse of symptoms. The associated long- and short-term side effects of antipsychotics, especially the neuroleptics, endanger patients who continue drug consumption for extended periods of time. In light of the negative effects of extended drug use, researchers have investigated the effects of drug withdrawal. A subgroup of patients who are withdrawn from drug treatment do not experience relapse. One goal of future research is to identify the factors that predict relapse following withdrawal from medication.

It is not surprising that depression is common among schizophrenia patients. Given the debilitating and potentially chronic nature of the illness, some patients have recurring bouts of depression and hopelessness. As noted, there is a heightened risk of suicide among schizophrenia patients. As a result, antidepressant medications are frequently prescribed as an adjunctive treatment.

B. Psychological Treatment

Clinicians have used various forms of psychological therapy in an effort to treat schizophrenia patients. Early attempts to provide therapy for schizophrenia patients relied on insight-oriented or psychodynamic techniques. The chief goal was to foster introspection and self-understanding in patients. Research findings provided no support for the efficacy of these therapies in the treatment of schizophrenia.

It has been shown, however, that supportive therapy can be a useful adjunct to medication in the treatment of patients. Similarly, psychoeducational approaches that emphasize the provision of information about symptoms and their management have proven effective in reducing relapse. Among the most beneficial forms of psychological treatment is behavioral therapy. Some psychiatric hospitals have established programs in which patients earn credits or 'tokens' for appropriate behavior and then redeem these items for privileges or tangible rewards. These programs can increase punctuality, hygiene, and other socially acceptable behaviors in patients.

In recent years family therapy has become a standard component of the treatment of schizophrenia. These family therapy sessions are psychoeducational in

nature, and are intended to provide the family with support, information about schizophrenia, and constructive guidance in dealing with the illness in a family member. In this way, family members become a part of the treatment process and learn new ways to help their loved one cope with schizophrenia.

Another critical component of effective treatment is the provision of rehabilitative services. These services often take the form of structured residential settings, independent life-skills training, and vocational programs. These services play a major role in helping the patient recover from illness.

VII. SUMMARY

It is now firmly established that schizophrenia is due to an abnormality of brain function that, in most cases, has its origin in early brain insults, inherited vulnerabilities, or both. But the identification of the causal agents and specific neural substrates responsible for schizophrenia must await the findings of future research. There is reason to be optimistic about future research progress. We have available new technologies for examining brain structure and function. In addition, dramatic advances in neuroscience have expanded our understanding of the brain and the impact of brain abnormalities on behavior. We are likely to witness great strides in our understanding of the causes of all mental illnesses within the coming decade.

It is hoped that advances will also be made in the treatment of schizophrenia. New drugs are being developed at a rapid pace, so more effective medications are

likely to result. Advocacy efforts on the part of patients and their families have resulted in improvements in the services available to patients. But further expansion of services is greatly needed to provide patients with the structured living situations and work environments they need to make the transition into independent community living.

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