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Schizophrenia, a Health Disorder

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Abstract

Schizophrenia is a chronic, disabling mental health disorder that affect about 1 per cent of the world population. It includes delusions, hallucinations, disorganized speech or behavior, and impaired cognitive ability. Schizophrenia implicate severe levels of anxiety, poorer psychosocial function and lesser levels of hope for the future. Most of these symptoms center on neurotransmitters, including dopamine, serotonin, and glutamate. The cause of the disorder remains unknown, but has been primarily associated with dopamine dysfunction, and treatments have been developed that target the dopamine pathway in the central nervous system with both positive and negative symptoms of schizophrenia, the most common functional psychotic disorder.

Accumulating evidence shows that the core pathophysiology of schizophrenia may involve dysfunction in dopaminergic, glutamatergic, serotoninergic, and gamma-aminobutyric acid (GABA) signaling, adding cognitive and social dysfunction. The first-generation antipsychotic medication and widely utilized since it was only antipsychotic medicine available at time for treatment of schizophrenia. Antipsychotics of second-generation atypical antipsychotics are sometimes also specified as generation antipsychotics.

Many studies indicate that either dopamine D2 receptors or interneuron NMDA receptors are related to the cause of the disorder, a syndrome associated with the microdeletion of chromosome 22q11. Approximately 30% of children displaying this microdeletion develop a form of schizophrenia that clinically and neurocognitively cannot be distinguished from the idiopathic disorder. Current advancements in categorization, etiology, and treatment of schizophrenia, implicate some inferences from literature about future advancements in schizophrenia therapies.

Keywords: Schizophrenia, Dopamine, Dopamine D2

INTRODUCTION

Schizophrenia is the most common mental condition. Kraepelin in 1896 coined term “dementia praecox,” which was later renamed to “schizophrenia” by Bleuler in 1911. Disturbances in thinking, perception, and mood are symptoms of this illness (Insel,.2010). The symptoms lead to the classification into three basic groups: 1) auditory hallucinations, 2) passivity experience, and 3) delusional thought. Schizophrenia patients hear hallucinating “voices” that may offer running commentary on their actions or direct them to perform certain activities. Some people hear voices that are rude or offensive.

Four dopaminergic pathways have been identified. Substantia nigra is the start of nigrostriatal pathway. Low dopamine levels in this pathway are considered to cause motor symptoms through affecting extrapyramidal system. In presence of excess dopamine mesolimbic pathway, which extends from ventral tegmental area (VTA) to limbic regions, they may have role in positive symptoms of schizophrenia.

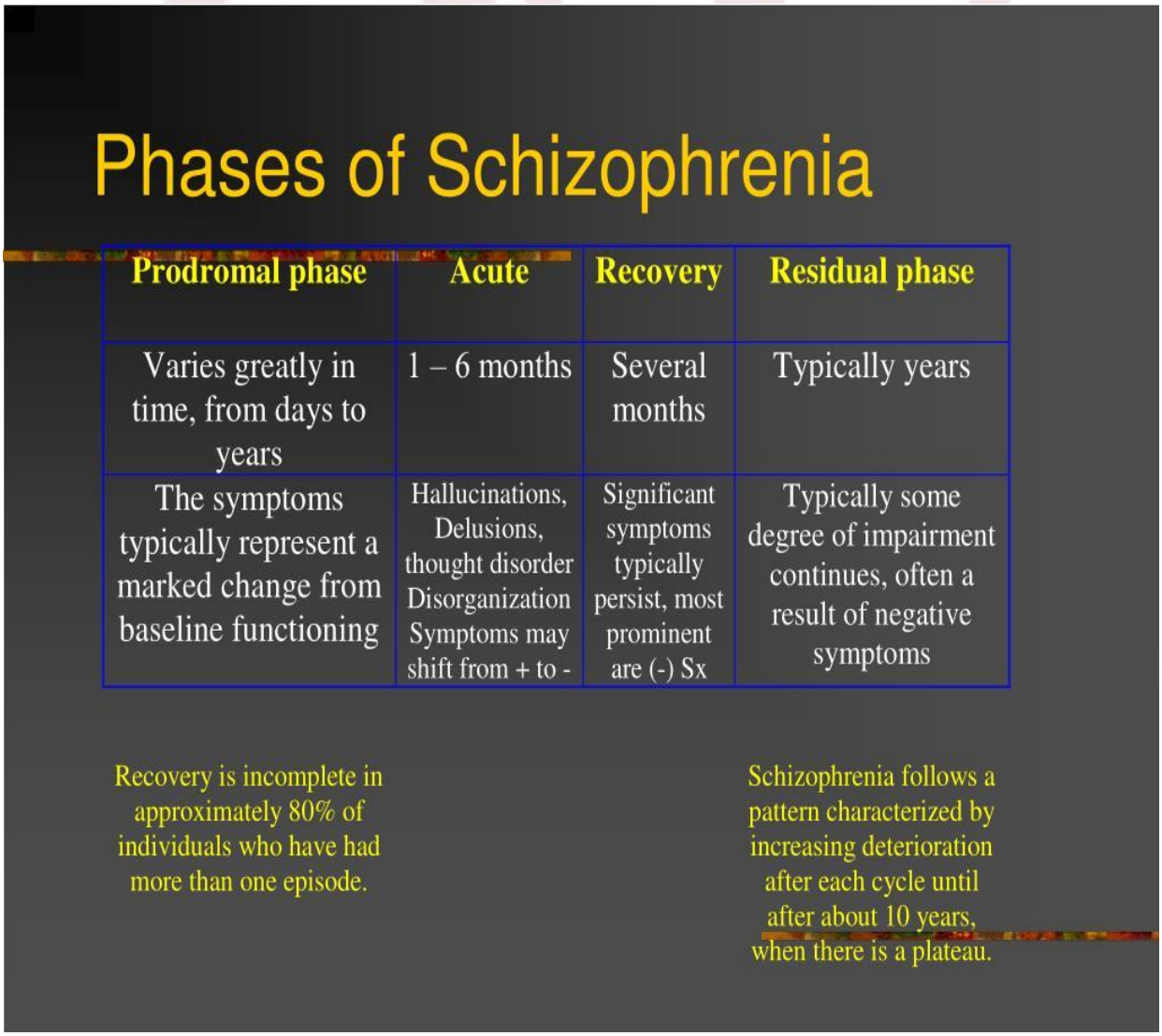

Table 1: Summarizes the different phases of schizophrenia.

Schizophrenia implicates severe levels of anxiety with greater levels of hallucinations, poorer psychosocial function and lesser levels of hope for the future (Lysaker & Salyers, 2007). A cluster analysis was established to distinguish three groups with varying levels of anxiety: severe, moderate and subclinical.

The hypotheses is that the participants in the severe anxiety group would have greater levels of symptoms, poorest psychosocial function, lesser hope and a higher incidence of trauma reports than either the subclinical or moderate anxiety groups.

1	Delusions- strange beliefs and ideas which are resistant to rational/logical dispute or contradiction from others.
2	Hallucinations - typically auditory, or less frequently, visual.
3	Disorganized Speech- incoherence, irrational content.
4	Disorganized or Catatonic behavior- repetitive, senseless movements, or adopting a pose which may be maintained for hours. The individual may be resistant to efforts to move them into a different posture, or will assume a new posture they are placed in.
5	Negative symptoms- flat affect, amotivation, anergia, failure to maintain hygiene.

Table 2

The first six items in the negative symptom scale (Fatigue, Loss of interest, Loss of sexual interest, Slowed speech, Slowed body movements, and Depressed appearance) were included in a depression factor.

The last five items (Inappropriate affect, Blunted affect, Loose associations, Poverty of content, and Incoherence) were included in a schizophrenic factor. Flat affect, poverty of speech, and psychomotor retardation were included as negative symptoms, and delusions, hallucinations, and florid thought disorder were included as positive symptoms.

Schizophrenia could be divided into two major syndromes referred to as type 1 and type 2.

Type 1: Schizophrenia was characterized by prominent positive symptoms, normal brain structure, relatively good response to treatment, and an underlying neurochemical mechanism that was probably dopaminergic.

Type 2: Schizophrenia was characterized by prominent negative symptoms, structural brain abnormalities seen on computed tomographic (CT) scan, impaired cognitive function, and poor response to treatment (Andreassen et al., 1990).

ETIOLOGY

Scientists known for long time that schizophrenia may run in families. The sickness affects less than 1% of general population, but 10% of those who have first-degree relatives with conditions, such as parents, brothers, or sisters, are affected. Many environmental variables, such as virus infection or starvation prior to delivery, complications during birth, and other unidentified psychological variables, may also have role. Another prevalent cause of schizophrenia is an increase in dopamine levels in most persons diagnosed with schizophrenia, however it is yet unknown how everyone diagnosed with schizophrenia has too much dopamine.

Environmental and social factors may also play a role in the development of schizophrenia, especially in individuals who are vulnerable to the disorder. Environmental stressors linked to schizophrenia include childhood trauma, minority ethnicity, residence in an urban area, and social isolation. In addition, social stressors, such as discrimination or economic adversity, predispose individuals toward delusional or paranoid thinking.

EPIDEMIOLOGY

Schizophrenia affects about one percent of world's population (between 0.6% and 1.9%). The rate of occurrence is around 1.5 per 10,000 persons. Men are diagnosed with schizophrenia at younger age than women, although women are more prevalent as they

become older. For men, typical age of onset is 18 to 25, while for women, it is 25 to 35.

DSM-III and its successors attempted to achieve a synthesis of these concepts. Nevertheless, heterogeneity in the clinical presentation of schizophrenia is certain, and heterogeneity in pathophysiology and etiology is likely. Although we can now define a particular construct of schizophrenia with reasonable agreement, the construct must be recognized as provisional and based on a need to achieve consensus about definitions rather than on an understanding of pathophysiology and etiology.

Diagnostic And Classification

Classification of Diseases-10 (ICD-10) and Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV). are two systems in question. They include paranoid schizophrenia, hebephrenic schizophrenia, catatonic schizophrenia, undifferentiated schizophrenia, residual schizophrenia, simple schizophrenia, and post-schizophrenic depression.

Diagnostic Statistical Manual of Mental Disorders-IV (DSM-IV) divides schizophrenia into four categories. DSM-IV diagnostic criteria differ somewhat from ICD-10 diagnostic criteria. Evidence and symptoms of schizophrenia must be present for “a major percentage of time over one-month period, with certain signs of condition continuing for at least six months”. On the other hand, ICD-10 criteria require symptoms to be present for at least one month. DSM-IV and ICD-10 classifications of schizophrenia subgroups are quite similar. It divides people into five subtypes: paranoid, disorganized, catatonic, undifferentiated, and residual.

Criterion Al is polythetic. Essentially, it requires any two out of five different symptoms. This list includes delusions, prominent hallucinations (defined on the basis of duration

rather than severity), several forms of formal thought disorder (incoherence or marked loosening of associations), catatonic behavior, and abnormalities in affect (either flat or grossly inappropriate).

Criterion A2 indicates that the diagnosis can be made on the basis of delusions alone if they are present in an "extreme" form.

Criterion A3 permits the diagnosis of schizophrenia to be made only in the presence of hallucinations if they are sufficiently severe. The "rate limiting" item in this instance is auditory hallucinations that are relatively persistent and non-affective in content or that involve one of two Schneiderian symptoms (voices commenting or voices conversing).

According the criteria DSM-5 (Diagnostic and Statistical Manuel of Mental Disorder), two or more symptoms allow the diagnostic of schizophrenia.

Schizophrenia spectrum and other psychotic disorders
Bipolar and related disorders
Depressive disorders
Anxiety disorders
Obsessive-compulsive and related disorders
Trauma- and stressor-related disorders
Dissociative disorders
Somatic symptom and related disorders
Feeding and eating disorders
Elimination disorders
Sleep-wake disorders
Sexual dysfunctions
Gender dysphoria
Disruptive, impulse-control, and conduct disorders
Substance-related and addictive disorders
Neurocognitive disorders
Personality disorders
Paraphilic disorders
Other mental disorders

Figure 3: DSM-5 diagnostic chapters (Regier et al., 2013): neurodevelopmental disorders:

ANTIPSYCHOTIC DRUGS USED TO TREAT SCHIZOPHRENIA

Chlorpromazine, first-generation antipsychotic medication developed in 1950 and widely utilized since it was the only antipsychotic medicine available at that time for treatment of schizophrenia. Potency of chlorpromazine will lessen severity of schizophrenia.

Other medicines of this family, including loxapine, fluphenazine, perphenazine, and haloperidol, were identified by modifying their structure and activity. However, they all have serious side effect, extrapyramidal symptoms. And it results, that most of these drugs are no longer in use.

Despite ongoing treatment improvements, life expectancy of patients with schizophrenia is lowered by 10 to 25 years when compared to that of healthy people. Management-related adverse events, inadequate treatment of associated medical disorders, and suicide have all been linked to higher mortality among people with schizophrenia.

Genetic Approach

Schizophrenia is a highly polygenic disorder with a complex array of contributing symptoms Schizophrenia is a biological disorder with multifactorial mode of transmission. Non-genetic determinants play also important role. These genes include neuregulin (NRG-1, 8p12-21), dysbindin, (DTNBP1,6p22.3), G72 (13q34) / D-amino acid oxidase (DAAO,12q24), proline dehydrogenase (PRODH-2, 22q11.21), catechol-O-methyltransferase (COMT, 22q11.21), regulator of G protein signaling (RGS-4), 5HT2A and dopamine D3 receptor (DRD3). Applications of microarrays methods were able to locate positional candidate genes related to dopaminergic, seronergic and glutamatenergic neurotransmission. New genome scan project, seen in the light of previous scans, provide support for schizophrenia candidate region on chromosome 1q, 2q, 5q, 6p, 8p, 10p, 13q,15q and 22q.

A way forward is provided by the recent identification of several putative susceptibility genes (including neuregulin, dysbindin, COMT, DISC1, RGS4, GRM3, and G72). The evidence for these and other genes, along with what is known of their expression profiles and biological roles in brain and how these may be altered in schizophrenia is still a matter of discussion (Harrison & Weinberger, 2005).

A gene called PCDHA3 seems to be associated with schizophrenia. The PCHA3 variant blocks the normal proto-cadherin function. The gene is localized on chromosome 22. Molecular genetics of schizophrenia which focused on positional and functional candidate genes are postulated to be associated with schizophrenia. These findings include neuregulin (NRG-1, 8p12–21), dysbindin (DTNBP1,6p22.3), G72 (13q34) / D-amino acid oxidase (DAAO,12q24), proline dehydrogenase (PRODH-2, 22q11.21), catechol-O-methyltransferase (COMT, 22q11.21), regulator of G protein signaling (RGS-4), 5HT2A and dopamine D3 receptor (DRD3). Applications of microarrays methods were able to locate positional candidate genes related to dopaminergic, serotonergic and glutamatergic neurotransmission. New genome scan project provide support for schizophrenia candidate region on chromosome 1q, 2q, 5q, 6p, 8p, 10p, 13q,15q and 22q (Salleh 2004).

In preclinical studies genes, such as DISC1, NOS1, NOS1AP, GRM, Pdxdc1, or ZNF804A, have been implicated in the treatment target for the schizophrenia (Yang & Tsai, 2017). Susceptibility locus for schizophrenia seems to be also localized on chromosome 1 q22, chromosomes 5, 15q15, and chromosome 22.

CLINICAL PRESENTATION

The symptoms of schizophrenia are categorized as positive, negative, or cognitive. Each symptom is vitally

important as the clinician attempts to distinguish schizophrenia from other psychotic disorders, such as schizoaffective disorder, depressive disorder with psychotic features, and bipolar disorders.

Positive symptoms are the most easily identified and can be classified simply as "psychotic behaviors not seen in healthy people." Such symptoms include delusions, hallucinations, and abnormal motor behavior in varying degrees of severity.

Negative symptoms are more difficult to diagnose but they are associated with high morbidity as they disturb the patient's emotions and behavior. The most common negative symptoms are diminished emotional expression and avolition.

Cognitive symptoms are the newest classification in schizophrenia. These symptoms are nonspecific. Cognitive symptoms include disorganized speech, thought, and/or attention, ultimately impairing the individual's ability to communicate.

TREATMENT OPTIONS

Despite continued therapeutic advances, the life expectancy of patients with schizophrenia is reduced by approximately 10 to 25 years compared with that of healthy individuals. The increased mortality among patients with schizophrenia has been attributed to unhealthy lifestyles common among this population (i.e., lack of exercise, unhealthy diet, and excessive smoking and alcohol intake), treatment-related adverse events, the suboptimal treatment of concomitant physical illnesses, and suicide (Patel et al., 2014).

Pharmacotherapies (e.g. clozapine), psychotherapies, psychosocial therapies, natural therapies specific B vitamins (B6, 8, and 12) reduce psychiatric symptoms. Vitamin C, D, E, Omega 3 fatty acids, melatonin constitute treatment shown to be beneficial. Alternative therapies (meditation, yoga, herbal tea, music and art therapies, acupuncture, massage etc…) may also be used.

CONCLUSION

Schizophrenia is a complex disorder that requires prompt treatment at the first signs of a psychotic episode. The symptoms lead to the classification into three basic groups: 1) auditory hallucinations, 2) passivity experience, and 3) delusional thought. Clinicians must consider the potential for nonadherence and treatment-related adverse effects when developing a comprehensive treatment plan. It is hoped that future research will address gaps in treatment(s) and potentially bring a cure for schizophrenia.

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