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Comprehensive Insights into Schizophrenia Causes Treatments and Prevention

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Abstract: With the significant improvement in material life in recent years, people now focus more on the status and well-being of spiritual life. The discovery and diagnosis of schizophrenia, a severe mental disorder, thus came into the attention. Current studies have centered on the causes and associations, which are often combined with the symptoms of schizophrenia. As a consequence, scientists developed various treatments. Some scholars suggested control and prevention methods, but many of them remained uninformative and unimplemented on account of real factors. The study combines most of the available information and gives a general overview of schizophrenia as an influential mental disorder. The mechanism of certain genes or alleles inherited from ancestors or unpleasant grown-up environments that can affect the risk of getting schizophrenia is analyzed. Treatment approaches referring to pharmacologic, psychotherapeutic, and other commonly mentioned ones are included. Some prevention techniques that correlate with health literacy, governance participation and parental environment are advocated. The meaning of this review lies in proposing a summarized thesis for schizophrenia, investigating present methods and indicating the inadequacies. In consideration of the shortcomings in medical care and public health system, it is expected that future research can inquire into innovative treatments and public prevention strategies.

Keywords: Schizophrenia, Antipsychotics, Systematic review

1. Introduction

Schizophrenia is a mental disorder that affects approximately 24 million people worldwide or 0.7% to 1% of the world population [1]. Onset occurs more frequently among adolescents and young adults and happens earlier among men than women [1]. It is relatively uncommon compared to other mental disorders; yet, it is a severe mental health problem. It is considered one of the top 25 causes of disability globally [1]. People with schizophrenia are 2-3 times more likely to experience earlier death than the general population due to physical ailments, and often suffer stigma, discrimination, and violations of human rights throughout their lives [1]. It is often associated with several psychoses including hallucinations, delusions, or disordered speech, thinking, and behaviors [1]. Its diagnosis is created on the basis of positive, negative and disorganized symptoms. These symptoms usually lead to patients' mental and physical disabilities and threaten their personal, familial, and social well-being.

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Current studies have indicated no single cause of schizophrenia. It is believed that genetic information is one of the main causes [2]. Environmental and psychosocial factors, such as growth environment and childhood experiences, can also impact one's risk for psychosis or schizophrenia [3]. Cognitive dysfunctions are thought to be associated with onset of schizophrenia [4]. The usage of antipsychotic drugs is the main treatment for schizophrenia. Nonetheless, they are only temporary solutions due to their inefficacy in treating most of the symptoms, instability in successfully treating psychosis, and the numerous negative side effects [2]. Scientists are searching for refined psychotherapy approaches, but they still face many clinical challenges.

In current days, only about 15% of people who undergo psychosis can recover from schizophrenia [1]. The majority of people experiencing schizophrenia are unable to receive professional mental help. Less than one-third of the patient population are able to receive mental care, despite that over half of people diagnosed with mental health problems in hospitals show psychosis symptoms [1]. Mental hospitals are not offering enough mental care, and the communities are not providing enough resources for patients to acquire help. Consequently, improving effectiveness of treatments and therapies, and increasing access to professional and stable mental care for people with schizophrenia remain a particularly important problem.

This review aims to give an overview of schizophrenia, focusing on how it is caused, diagnosed, and associated with, treatment options, and guidelines for probable solutions of prevention, with the purpose of gaining general population information about the mental disorder. Researchers in the field are seeking a more accurate diagnosis of schizophrenia, as well as an alternative approach to a more effective and less harmful treatment. By summarizing current studies and potential lines of inquiry, this research might inspire future scholars to overcome the medical challenge.

2. Causes, associations, and diagnosis of schizophrenia

2.1. Genetic factors

Existing researchers have regarded rare copy number variants are the main risk of causing schizophrenia [2]. People with schizophrenia usually have a significantly higher amount of rare copy number variants than controls. Genome-wide association Studies (GWAS) have also identified the relationship between common variation and schizophrenia [2]. After it recognized a single gene named ZNF804A as the risk gene, significant evidence have shown that in total of 287 associated alleles with 5 X-linked alleles are found to be related or causing schizophrenia from 76,755 subjects with schizophrenia and another 243,649 controls according to the genome-wide standard [2]. Genetic covariation between schizophrenia and three magnetic resonance imaging metrics (surface area, cortical thickness, neurite density index) is significant, which indicates that the nature of schizophrenia correlates to several neurobiological mechanisms as well as genetic factors [5].

People with certain alleles, such as complement component 4 (C4) gene that is essential for immune system, potentially have higher risk of exposure to schizophrenia than some other mental disorders. Inherited alleles contribute to about 60-80% of population variance in susceptibility to schizophrenia [2]. Moreover, people with overlapping common risk alleles to mental disorders are more likely to be infected due to biological pleiotropy [2]. Yet, genomic data today are insufficient to explain such great differences.

2.2. Childhood experiences and growth environment

Childhood experiences, particularly the negative ones, may lead to long-term consequences and ultimately contribute to the risk for schizophrenia by influencing one's physical and mental health conditions [3]. Child maltreatment including direct abuse such as physical and sexual abuse, and cold violence such as emotional abuse and neglect are continuous threats to humans' well-being. Physical

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abuse leads to direct injuries to children, who are very unlikely to have access to regular medical care [3]. On the other hand, emotional and sexual abuse mainly lead to poor mental states, which often cause anxiety disorders and depression and increase suicidal rates among patients [3]. Although different cultures give alternative definitions to the degrees of abuse, there is a consensus that environmental disruption factors during child growth like family poverty and unhealthy parent-to-child relationships are associated with abuse and thus with possible causes of schizophrenia [3].

There is a systematic review in 2012 that gives a hypothetical estimation that childhood adversities are the causes of schizophrenia for over 33% of the patient population [3]. Among them, 39% are self-reported with physical abuse, 34% with emotional abuse, and 26% with sexual abuse [3]. Besides the relationship between childhood maltreatment and diagnosis of schizophrenia, it is considered that the probability of establishing treatment-resistant schizophrenia after diagnosis would rise along with the history of child abuse [3].

2.3. Cognitive dysfunctions

Cognitive dysfunctions are one of the core features associated with schizophrenia. It is defined by the impairment of intellectual abilities, such as perception, reasoning, and remembering. People with schizophrenia do not only have lower cognitive levels compared to healthy controls, but they also face worse cognitive dysfunction problems than people with affective disorders. Over 98% of people with schizophrenia experience cognitive dysfunction, and they often suffer a broader range of impairment, especially for those who do not take antipsychotic drugs [4]. Research found people with schizophrenia have a much higher rate of cognitive impairment compared to other common mental disorders, such as bipolar disorder [4]. Their other aspects of cognitive process (processing speed, verbal and working memory) regarded as associated with poor functionality and insight reported even greater cognitive impairment [4].

Evidence has shown about 5% of variance in susceptibility to schizophrenia is likely due to the shared common risk alleles that cause schizophrenia and affect cognition abilities; however, the association with schizophrenia genetic liability and poorer than average or decreasing cognition ability trend still wait to be proven [2]. Factors like functionality, duration of untreated psychosis, traumatic childhood experiences, age of patients, and hostile behaviors may also contribute to cognitive impairment [4].

2.4. Early symptoms and diagnosis

Psychotic symptoms, mainly consisting of hallucinations, delusions, disordered speech, thinking and behavior, are the best known symptoms of schizophrenia [1]. Those include positive, negative and disorganized symptoms separately. Among all the symptoms, negative symptoms are the most prevalent and clinically significant and occur earlier than other kinds of symptoms [6]. They include extremely restricted or nonexistent emotion expression, loss of pleasure and desire, memory and function impairment, and social withdrawal [7]. On the other hand, positive symptoms consist of hallucinations, imaginary voices that discourse with the patient, and paranoid delusions [7]. Lastly, patients' disordered thoughts, speeches and behaviors are the disorganized symptoms [7]. All symptoms cause harm to patients and their families, as they often lead to many long-term problems and will need long-term treatments.

The diagnosis of schizophrenia falls within the criteria of the latest edition of the Diagnostic and Statistical Manual of Mental Illnesses (DSM-5) or the International Classification of Diseases 11th Revision (ICD-11) [8]. They both require some expressions of negative symptoms, while DSM-5 further requires at least 6 months duration of the symptoms, and ICD-11 only requires one month duration time [8]. Medical diagnosis with psychiatric history and inspection of mental state act as

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supplements to diagnosis [9]. Among the patient population, most of the cases are diagnosed with early-onset schizophrenia (EOS) that occurs during middle to late adolescence before age 18 (0.7%-1% in the whole population) [8]. Only a few childhood-onset schizophrenia (COS) happen before age 13 (0.0025%) [8]. Clinicians should be careful in identifying and diagnosing schizophrenia, since many psychotic-like symptoms reported are not psychotic disorders. Once psychotic disorders like schizophrenia are diagnosed, the causes of disorders along with specific treatments are yet to be determined.

3. Treatments

3.1. Drugs

Information on pharmacological treatment and drug usage of schizophrenia remains less due to the conflicting information of randomized-controlled trials (RCT) and clinical guidance [10]. Many public health regulatory institutions, for instance the US Food and Drugs Administration (FDA) and European Medicines Agency (EMA), also set restrictions on the publicity of RCT results [10]. Thus, the utilization of drugs for schizophrenia still poses challenges for current clinicians.

Presently there are two first-generation antipsychotics (FGA) drugs approved by FDA, which are haloperidol and molindone respectively, and eight second-generation antipsychotics (SGA) drugs approved by FDA or EMA, which include aripiprazole, paliperidone, clozapine, risperidone, quetiapine, lurasidone, olanzapine and amisulpride [10]. By specifically looking at outcomes of each drug containing Acceptability, Efficacy, Tolerability, Motor side effects, Metabolic side effects, Hyperprolactinemia, Cognition, Functional outcome/Disability, Suicidal behavior, Mortality, Services use and admissions and Cost-effectiveness and economic outcomes, most clinical guidelines for schizophrenia suggest SGAs over FGAs [10]. Among them, aripiprazole, lurasidone and olanzapine are the most effective and safe to use, though other drugs are not prohibited as well [10].

Up to now, despite the limitations on drug use and the risk of adverse effects, all antipsychotic drugs that are approved by at least one of the public health regulatory authorities were found to be more effective than placebo and psychological mediation [10]. The type of antipsychotic used, dosage, period of medication, together with patients' own expectations and priorities are what clinicians need to consider when selecting the best medical option for each individual. Pharmacological methods continue to be the main treatment for schizophrenia, yet investigations on newly developed drugs and solutions to previous side effects remain to be tested and improved in future trials.

3.2. Psychotherapy

Due to the risk of negative side effects and the hardships of selecting the correct type of drugs, many people prefer using psychotherapy as another treatment for schizophrenia. Thus, psychological and psychotherapeutic approaches related to the pathology of schizophrenia are still the main tendency of the therapeutic method [11]. Psychotherapy is based on the understanding of patients' thoughts and experiences [12]. The foremost point for therapists is to accurately interpret their languages, which is often inaccessible [12]. Strategies, for instance, creating a warm and welcoming therapeutic environment, organizing plans and scheduling activities, encouraging patients step by step to engage in social activities, as well as practicing body-oriented and art-related therapies, were recommended to overcome the barrier [12].

It is factually proven that cognitive and behavioral psychotherapy specifically combined with use of antipsychotic drugs leads to declination of symptoms of schizophrenia [11]. Moreover, psychotherapeutic methods are plausibly more effective for particular symptoms, such as auditory hallucinations or problematically recognizing facial or emotional expressions [11]. In spite of the application of psychotherapy, it has its limitations as a result of utilization of some overly traditional

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strategies [11]. Many authorities in the field are working to investigate novel treatments that resolve such problems.

3.3. Novel treatments

There is still a pressing need for new treatments for schizophrenia, especially those that can effectively treat negative symptoms [6]. Some treatments aim at investigating the effect of increasing N-methyl-d-aspartate (NMDA) and decreasing synaptic glutamate levels, as researchers have found that glutamatergic abnormalities are related to schizophrenia [6]. Scientists now pay great attention to the invention of augmented NMDA-dependent transmission; however, their progress does not go smoothly, as they face challenges of failing to show a data disparity over placebo or applying it to all patient populations [6].

Other than the most promising NMDA-related method, novel trends of treatment also consist of nicotinic acetylcholine receptors (nAChRs) and muscarinic acetylcholine receptors (mAChRs), which are believed to be helpful in improving patients' positive and cognitive symptoms [6]. Yet not all types of such receptors work for schizophrenia, just as results with α7-nAChR had shown no evidence in successfully treating symptoms of the disorder [6]. At present there is not much information on the advancement of developing novel treatments, but the new attempts might give future scholars possible research orientations.

4. Prevention

4.1. Health literacy

Health Literacy, or the accessibility from societies given to individuals to get and utilize basic health information and knowledge, has a great impact on patients' engagement in disorder detection and treatment as well [13]. Low HL is often related to poor health outcomes in physical illnesses [13]. Although the association of HL and most mental disorders are undiscovered and thus unknown, the risks of low HL were concerned potentially leading to negative effects on people with schizophrenia, as symptoms of schizophrenia co-occur with metabolic incidences such as diabetes, obesity and cardiovascular diseases [13].

Recent studies have not yet identified the direct consequences of HL on severity of schizophrenia, but they indicated its significant relations with factors that could impact people's health attitudes and their quality of life to a great extent, including their abilities on self-health management, self-efficacy and physical performances [14]. Hence, they circumstantially proved that HL levels can ameliorate the conditions of being mentally ill and having schizophrenia.

4.2. Governance Intervention

Government approaches to public health policy can positively affect mental health programs and thus people with schizophrenia. Global governance in concept of health refers to encouraging equal access to health systems through the application of policies and practices, as defined by the World Health Organization [15]. The main concept of governance in case of health systems is to establish several tasks and functions that provide professional health services and protect population's rights to health in order to improve the whole medical health system [15]. The health governance in field of mental health remained underexplored; yet it can be confirmed that current societies require a scope that is restricted, observable, consistent and able to popularize [15].

Several papers have defined governance of mental health as evidence-based, patient-focused process of authoritative decision-making [15]. It does not only require government intervention, but also includes civil organizations, community and social leaders, researchers, networks of support, and

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non-profit organizations [15]. However, only very few countries have adopted the systems to a limited extent [15]. Relative to its low prevalence, governance of mental health has made a good model for development and applications of mental health policies [15]. More attention is still needed on this topic for later studies.

4.3. Parental Environment

Relationships between parents and children might be an intergenerational factor that impacts the mental health of both sides. Impulsivity, a factor that leads to potential risk of negative effects on brain and cognition, mental disorders and psychiatric problems, is known for being affected by both genetic and environmental elements [16]. It is defined by lack of planning, persistence, sensation, and positive and negative urgency [16]. Even though schizophrenia is not a mental disorder mainly controlled by impulsivity, it is likely for patients with schizophrenia to report more than average impulsive behaviors, have higher rates of substance use, and have impairments in brain and cognitive functions that relate to impulsivity [17]. The linkage between parental environment and people's impulsivity especially in youth has been detected, although the intermedium remained underreported.

Studies are trying to determine the role of parental and family conflict, an important concept in parental environment and youth development, in the associations between parental mental health and children's impulsivity [16]. From a large national Adolescent Brain Cognitive Development (ABCD) study, it is suggested that bad conditions of parental mental health set difficulties in parent-to-child relationships, and might address family conflicts that are to the disadvantage of children's well-being [16]. In response, family-based interventions such as family therapy can be effective ways to reduce conflict, adolescent impulsivity, and thus risks of schizophrenia [16]. More research aimed at effects of interventions in parental environment on youth impulsivity and its relationship with mental disorders like schizophrenia can still be done, and similar results are expected in future studies.

5. Conclusion

The study has given a brief overview of schizophrenia, a mental disorder affecting 24 million people globally that relates to symptoms including hallucinogens, delusions, disorganized speeches, ideas and behaviors. Given that, there might be multiple causes of schizophrenia, genetic inheritance and psychosocial environments are believed to be the main causes of disorder, whereas cognitive impairments are also considered linked to disease onset. Most common treatments today contain the uses of antipsychotic drugs and psychotherapies, yet there are limitations to both approaches. Thereupon, scientists now are working on novel methods relating to NMDA. On the public health approach, methods to prevent spread of schizophrenia such as increasing health literacy on population level, using governance intervention, and establishing better parental or familial environments are suggested. Due to resistance to implementation in real-life situations, most of them are not taken seriously.

There is no review paper that summarizes the research status and shortcomings of schizophrenia. Thus, this review not only includes the generalization of common research progress on schizophrenia, but aims to give suggestions on possible directions for future treatment methods along with ways of prevention measures for psychiatrists, medical workers, and public health authorities. Research on schizophrenia remained understudied, underreported, and unvalued, whether it is the study of the disorder itself or the operation of methods of treatments and prevention. More attention on schizophrenia as well as people with schizophrenia is required. It is difficult to include all potential treatment methods and ways to prevent schizophrenia. Only the most common, most used techniques are covered. The review proposed limited but possible tendencies for future researchers. Future research can attempt to focus more on inventing novel treatments for schizophrenia other than the

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existing approaches on drugs and therapies. Despite the challenges, more prevention methods should be created and executed so that people with schizophrenia and other psychosis could have a stable way to professional help. As stated in this review, schizophrenia is a severe mental problem that deserves more attention from experts as well as the general public. A more comprehensive review of schizophrenia that consists of more effective approaches is waiting for in-depth research.

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