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The Current Research Status and Progress of Bipolar Disorder

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Abstract: Bipolar disorder is a common but serious mental illness with extremely high mortality and a high suicide rate. It has variable symptoms of both depression and mania and can separate into three types of sub-types---bipolar disorder type I, bipolar disorder type II and Rapid cycling bipolar disorder. So far, scientists and medical researchers had got a lot of success in the field of bipolar disorder. Therefore, this paper proposes to conclude the recent research to discuss the status and progress of bipolar disorder, which mainly discusses the history of bipolar disorder, symptoms, treatments, and possible etiology; this paper will discuss them from the view of genetic and environmental. Besides, this paper specifically focuses on the recent innovative discovery of genetic etiology and genetic model treatment methods.

Keywords: Bipolar disorder, treatments, symptoms, etiology

1. Introduction

Mantel disorders, nowadays, have already become an important topic that should be focused on by the world. With the rapid development of the economy and society, the accelerated pace of life, and the increasing pressure caused by competition, the types, characteristics, and prevalence of mental illnesses are also changing. For instance, bipolar disorders. As known as one of the most complex clinical manifestations of mental illness, it has a high rate of suicide risk, even higher than the rate of risk to suicide of depression patients. According to the research made by Jann, the suicide rate of patients who suffer from bipolar disorder is higher than that of patients who suffer from any other general mental illness [1]. Patients with bipolar disorder have an average annual suicide rate of 0.4%, which is nearly 20 times more than the suicide rate of the general population in the United States. In the epidemiological watershed database, the lifetime suicide attempt rate of patients with bipolar disorder is 29.2%, almost twice that of depression (15.9%). To save these patients, recently, researchers and medical workers have recently made much progress on the possible methods to overcome bipolar disorder by researching bipolar disorder behavior and the possible factors of becoming bipolar disorder. With the help of this discovery, the rate of bipolar disorders returning healthy tends to increase. Therefore, here is a review of the recent research progress on bipolar disorder.

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2. Definition and the History of Bipolar Disorder

Bipolar disorder is a common mental disorder featured by both mania and depression episodes, its first onset can occur at any age. Bipolar disorder is a long-standing disease that dates back to the 4th century BC. The materialistic ancients once classified depression and manic disorder as two separate diseases. It was not until the 19th and 20th centuries that they came up with the concept of bipolar disorder and classified patients with recurrent symptoms of depression and mania as bipolar disorder. Most recently, according to several authoritative academic research papers made by Muneer, bipolar disorder has been redefined as a continuous phenotype, ranging from mild depression and transient hypomania to a long cycle of persistent depression or a psychiatric characteristic characterized by mania [2]. According to Carvalho et.al, bipolar disorder generally manifests as two symptoms: severe depression and manic depression, which can be further subdivided into bipolar type I disorder and bipolar type II disorder [3]. Patients with recurrent symptoms of mania or depression but no opposite symptoms were classified as a single affective disorder. The incidence of bipolar disorder is almost the same in women and men, and it shows a strong familial genetic pattern [3]. From the research paper done by Dols & Beekman, it also seems to be confirmed that Patients with bipolar disorder have a high probability of relapse after the age of 60 [4].

3. Symptoms of Bipolar Disorder

According to the words of Culpepper, bipolar disorder serves as a chronic paroxysmal disorder, usually initially appears in early life but may also occur in childhood or old age [5]. Its characteristic is recurrent manic or depressive symptoms. Bipolar disorder can mainly be separated into two subtypes: bipolar I and bipolar II. The characteristic of Type I bipolar disorder is a comprehensive manic episode, with a more severe degree of damage than the mild manic episode of Type II bipolar disorder. Depression is the main symptom of bipolar disorder in most patients, and compared to manic symptoms, depression may become a great burden in terms of duration and impact. These symptoms usually have a serious weakening effect on the patient's functional mechanisms, work or learning abilities, and living standards and greatly increase the suicide rate, especially during depressive episodes with or without mixed characteristics. According to the research done by Alda & Hajek et.al, the most common symptoms of bipolar disorder are periodic emotional disorders, manifested as depressive and manic episodes in type I bipolar disorder and depressive and hypomanic episodes in type II bipolar disorder [6]. From the research done by Jann, it can be seen that the main difference between these two types is the severity of manic symptoms [1]. According to research, complete mania can lead to severe functional impairments, including psychiatric attacks. To the statements of Paykel & Abbott et.al [7], although milder forms such as type II bipolar disorder and cyclic affective disorder have been fully recognized, there is limited research on the subliminal symptoms between major episodes. Among them, the signs of mania are high emotions, swelling or irritability, increased oriented activities, and impaired joy-searching behavior and ability to judge. Patients with mania often experience decreased sleep demand, excessive excitement, and unrestricted thinking; Lack of pleasure and low mood are the main characteristics of depression. Depression patients often experience decreased social skills, lack of energy and motivation, sleep and appetite disorders, distracted attention, and impaired memory. In addition, patients with the symptoms of mania and depression all have hallucinatory psychiatric symptoms during the onset of symptoms. Besides, bipolar disorder can result in important situations of intentional self-harm and suicide and is associated with depression and mixed states. The lifetime prevalence of self-harm among patients is about 30%, and it may be as high as 50% in secondary depression. In addition, among all bipolar disorder patients, especially male patients, a higher risk of violent and nonviolent criminal behavior has been found. Its triggers may be mixed states, rapid cycling, alcohol and drug abuse, early abuse

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experiences, etc. What's more, in the essay of Hirschfeld & Bowden, et.al, DSM-IV-TR (1) defined that rapid cycling bipolar disorder refers to the emerge of four or above mood disturbances within a single year that meets criteria for a major depressive, mixed, manic, or hypomanic episode [8]. Bipolar disorder includes a series of diagnostic sublevels mainly divided based on the degree of emotional elevation during acute episodes. In the research of Yatham & Kennedy et.al, according to DSM-V, bipolar disorder(I) is set at the extreme level because of the presence of threshold manic episodes [9]. Characterized by increased self-esteem, reduced sleep demand, speech pressure, restless thoughts, distraction, psychomotor arousal, and dangerous behaviors that lead to serious consequences. On the other hand, the characteristic of cycling bipolar disorder is the presence of subthreshold symptoms of chronic hypomania and depression. Bipolar disorder (II) is defined between two situations, with mild manic episodes similar in nature to manic episodes, its symptoms can be clearly obvious and observed, patients with this state of bipolar disorder may also experience threshold depression episodes.

4. Possible Etiology of Bipolar Disorder

Since this mental illness has extremely complex clinical reactions and symptoms, the accurate etiology of which has not yet been confirmed. However, From Frías, et.al, scientists have discovered some possible orientations, and they divided into environmental factors, genetic factors, and neurology [10].

4.1. Environmental Etiology

The scientists found that the environmental factors are worth researching deeply. Scientists have found that environmental factors are worth further research. It was confirmed that some of the environmental factors can affect on brain development processes. According to Aldinger & Schulze, and Muneer, infection, mothers smoking during pregnancy, delivery complications, climate, childhood trauma, life experiences, and social impacts can be the environmental factor that raises the risk of becoming a bipolar disorder or having stronger clinical symptoms [2,11]. Especially the patients who experienced childhood trauma seemed to have a higher possibility of becoming bipolar disorder, according to the word of Etain & Henry et.al [12]. According to the research done by Aldinger and colleagues, nearly 50% of the bipolar disorders that they interviewed can confirm that they had the experience of childhood trauma [11]. From the literature, it can be seen that positive or negative life events and goal achievement are more likely to lead to bipolar disorder. The pain of bereavement is believed to trigger mania, while personal illnesses are more likely to lead to depression. In addition, the occurrence of work-related events such as entrepreneurial failures and company bankruptcies often leads to mania. Besides, people with fewer social relationships, such as family, friends, and colleagues, have a higher risk of developing the disease, and patients with lower social support rates have a higher recurrence rate. Researchers have drawn the following conclusions by investigating patients' pre-illness life experiences and childhood experiences, as well as interviewing their family members to elucidate their behavior after the illness.

4.2. Genetic Etiology

To stand on the other side, many scientists also considered that there might be some genetic etiology [13,14,15]. According to the data given by Culpepper, family history can provide available information for diagnosing bipolar disorder [5]. Statistics show that 80% -90% of patients with bipolar disorder describe their family members as having historical records of mental disorder, containing but not limited to depression and bipolar disorder. The later generation of patients with bipolar disorder has been confirmed to have a high risk of becoming a bipolar disorder, ranging from

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5% to 15%.To analyze the research paper done by Kerner deeply, bipolar disorder can result from some genetic factors for instance, the chromosome mutation, according to his words [15]. He started his research by studying the gene molecules and chromosomes of bipolar disorders. After his research, he found that there is an undeniable connection between mutations in certain specific molecules and bipolar disorders. Wherein, according to Kerner, the SNP rs1 in gene CACNA1006737C is the most replicated and studied common genomic variant associated with bipolar disorder to date [15]. The A allele is considered a possible factor for bipolar disorder, and mutations in it greatly increase people's chances of developing bipolar disorder. Inside the brain, the mutation of CACNA1C can result in a rare human Mendelian disease called Timothy syndrome by participating in axonal guidance and synaptic transmission. Instead of this, other genetic factors such as the mutation of ODZ4, the mutation of NCAN, Prader-Willi syndrome, chromosome 15q13.3 deletion syndrome, and chromosome 10q26 deletion syndrome have been proven to have a strong connection with bipolar disorder. Kerner accurately describes the behavior of the patients who suffer from bipolar disorder that results from these genetic mutations as children with Prader-Willi syndrome are considered to have severe emotional disorders, accompanied by irritability, aggressive bursts, frequent emotional fluctuations, and compulsive behavior as well [15]. Kerner considered that these genetic mutations have a possibility above 50% to recurrence, and they also have a considerable rate of influence on the offspring of the patient. To illustrate, use the Prader-Willi syndrome as an example. This syndrome is confirmed to result from an imbalance between maternal and paternal genetic material on chromosome 15q11 due to partial deletions on the paternal chromosome. The mutation gene will be passed on through the generations. Hence, their later generation will have the risk of being influenced by these genetic mutations, which can result in bipolar disorder.

5. Treatment of Bipolar Disorder

Bipolar disorder, as a mental disorder with a long history, has been explored by researchers in the following types of treatment methods. Due to the complex clinical response dynamic chronic, and fluctuating nature of bipolar disorder patients, the treatment process is very challenging. According to the research of Hirschfeld & Bowden et.al, until now, the recovery of bipolar disorder is still a difficult task to achieve. Whereas effective treatment can reduce mobility and mortality [8].

5.1. The Medical Treatment of Bipolar Disorder

Bipolar disorder is generally treated in three stages, which are manic, depressive, and preventive, with the main treatment method being medication. Among them, drugs with lithium salt as the main chemical component are more common and effective drugs in the treatment of bipolar disorder because lithium salts play a very important role in inhibiting and resisting mania during the treatment of manic patients. As early as the 20th century, before the discovery of the anti-manic effect of lithium salts, some early European scientists utilized the hypnotic properties of some barbiturates to treat patients with mental illness and mania. The drugs suppressed manic effects by inducing patients to enter deep and prolonged sleep states. One of the important reasons why lithium has been introduced into drug therapy and played an important role is the rise of Sir Alfred B. Garrod's theory of "uric acid quality" and the discovery by a Western surgeon, Alexander Ure, of the dissolution experiment of lithium carbonate. At that time, lithium became an indispensable raw material for the treatment of kidney stones, rheumatism, and gout and was widely used. According to the research findings of Fountoulakis & Vieta et.al, individual patients are expected to experience adverse events during lithium therapy [16]. In general, it is neurological, endocrine (usually involving the thyroid), cardiovascular, renal, gastrointestinal, hematological, and dermatological manifestations, as well as lithium poisoning. According to the research done by Hajek & Alda et.al, several predictive factors

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for poor lithium response, including manic severity, anxiety and irritability, rapid cycling, and a bad family history of emotional disorders [6]. Therefore, in order to make up for this deficiency, medical workers use a tricyclic anticonvulsant compound called carbamazepine. Carbamazepine was initially developed by Japanese scientists for the treatment of depression and mania. In the early 1960s, its efficacy in epilepsy syndrome patients was confirmed in European countries. In research on carbamazepine, scientists found that the anti-manic effects of carbamazepine and lithium were comparable. Although carbamazepine has been used as a substitute for lithium in Europe or in combination in drug-resistant cases, and valproate is considered to have better side effects, interactions, toxicity, and teratogenicity in the field of epilepsy, they still have issues with patient drug tolerance, resistance to treatment, and poor treatment response. In order to address these issues, some new anti-epileptic drugs have been developed and produced, among which lamotrigine is a well-known treatment for bipolar disorder [17]. According to the experimental data mentioned in the López-Muñoz & Shen et.al's research, the lithium salt is superior to lamotrigine and placebo in preventing the manic phase in the drug therapy process for bipolar disorder, and lamotrigine is superior to lithium and placebo in preventing depressive phase [17]. Therefore, the combination of lamotrigine and lithium salt has become a new mainstream method for treating bipolar disorder. Many patients with bipolar disorder often complain about neurocognitive issues related to attention, attention, and memory. Fountoulakis found that lithium seems to have a negative impact on human neuro-cognitive issues, especially memory and psychomotor function [18]. In addition, lithium can also lead to long-term memory deficits, which may particularly affect language function. In the process of acute drug treatment for patients, some patients with special medical history may have side effects such as diabetes or obesity in the acute drug treatment, and excessive use of lithium drugs will lead to progressive renal insufficiency and the possibility of death. In addition, children and teenagers with bipolar disorder are particularly susceptible to the effects of drugs related to olanzapine on weight and metabolism [5].

5.2. Non-Adherence Effect

Based on the research done by Jawad & Watson et.al, the Medication non-adherence in bipolar disorders has become a big challenge in the way of medical treatment method: adherence refers to a range. Patients with complete compliance will exhibit taking all doses of medication at the prescribed frequency, and another extreme situation is complete non-compliance with regulations, which means not taking any prescription drugs [19]. The patients defined between these two situations have varying degrees of partial compliance or partial non-adherence, i.e., taking some but not all prescription drugs. The non-adherence effect will definitely influence the treatment. In an interview with 2000 psychiatrists from eight European countries, respondents estimated that 57% of bipolar disorder patients would not adhere to or partially adhere to treatment. The researchers do a lot of experiments to see what variables affect the non-adherence effect. According to their research, social population and socio-economic status do not seem to be the main determinants of compliance. On the contrary, an online survey shows that young patients are more likely to not persist in taking treatment drugs such as lithium salts, and the proportion of those who persist in taking lithium salts and anticonvulsant drugs will increase after the age of 41. Patients under 40 years old have the lowest compliance, but patients over 60 years old also have lower compliance. Therefore, the level of non-adherence seems to have a correlation with the age of patients. What's more, the understanding of patients' attitudes towards their own diseases and medications can also affect compliance, and those with less understanding of drugs and illnesses are more likely to not persist in taking medication. In addition, patients' criticisms of family attitudes and medication knowledge may also affect compliance: if patients have good social networks and family members who have a positive attitude towards treatment, their compliance will improve because they believe that clinical doctors and others such

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as family members determine their clinical outcomes. Psychological education is considered a good way to improve compliance, and if compliance is explicitly focused and included in behavioral interventions, it is more likely to improve compliance. The attitudes of family members and caregivers towards bipolar disorder and its treatment may have a significant impact on patient compliance. Therefore, considering some form of psychological education for important individuals in the patient's life may play a crucial role in the treatment process [19].

5.3. Psychosocial Interventions

By reviewing the research of Yatham & Kennedy et.al, new concepts are founded [9]. As a significant result, the disorder patients will have great feelings of stigma, and this will have a great possibility to influence the lives of themselves and their families. With the feeling of stigma, the patients may not be willing to talk about their illness with their families and even reject the treatment process in order to be aware of the feeling of stigma and being isolated from others. Stigma can be experienced and recognized by the patients during the communication process with others and the behavior of others.

Therefore, the stigma has become a great barrier to the treatment process and an issue that needs to be solved. Although the medication treatment process of bipolar disorder is important and serves as the foundation of the treatment of patients, psychosocial interventions are also needed and have the possibility to be available and efficient. Generally, a number of methods are used in this process. For instance, provide psychological education to the disorders during the treatment process in order to prevent recurrence. Besides, interpersonal and social rhythm therapy, family-focused therapy, cognitive behavioral therapy, and peer interventions are considered to be useful during the process as well. Among them, support from family members, important friends, and partners that also disabled or other people who have important relationships with the disorders are confirmed to have the capacity to reduce self-stigma and isolation among patients and help increase treatment engagement [9].

Based on the papers of Swartz & Swanson [20], some effective psychotherapies have been invented for bipolar disorder treatment. For instance, CBT (Cognitive behavioral therapy) and CT (cognitive therapy) for bipolar disorder are based on a measuring schedule in the Beck Depression CT, which is an effective treatment method that can help individuals change and identify the correlation between maladaptive thoughts and emotions. By using mind recording, emotional diaries, and activity scheduling, patients learn to change their negative thoughts by themselves, eliminate distorted thoughts, and interrupt the cycle of mania and depression. As described by Lam and colleagues, CT for bipolar disorder has added additional psychological education modules, strategies for coping with prodromal symptoms, making sleep time more adjustable and active in daily life, and methods for treating long-term sequelae of the disease [20].

5.4. Genetic Model Treatment

According to Harrison & Cipriani et.al, some innovative models are created for future better experiments on bipolar disorder and the treatment of bipolar disorder [21]. For instance, the cellular model and mouse models are based on the genetic cells. By using the cellular model, the scientist can determine the effectiveness of treatment for bipolar disorder more easily during the process of observing the neuronal signals of patients, whether the calcium signaling function is abnormal, as well as whether there are changes in mitochondrial function, cell apoptosis, and circadian rhythm system. For the mouse model, one of the popular examples of the experiment using the mouse as the research object, the mouse with a mutated gene encoding CLOCK which was called the ClockΔ19 mouse, exhibiting behavioral characteristics of mania, specifically the process of hyperactivity during the day (or under light), less anxiety, and returning to normal behavior during the night. Learning the

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behavior of the mouse that has a mutated gene, just like the ClockΔ19 mouse, provides the scientist with suggestion that focusing on dopamine and circadian rhythms in bipolar disorder phenotypes, the treatment process may be support by the data after experiments.

6. Conclusion

In conclusion, bipolar disorder is a mental illness with extremely complex clinical responses and high suicide risk, and its etiology includes social psychology, living environment, biology, genetic inheritance, etc. Due to its complex symptoms, there are many barriers during the treatment process. The disorder patients face difficulties during their life, despise from the social, hurt their minds, and bring barriers to their living life: they are unable to find good work to support their lives, and they have trouble communicating with others, so they have few friends around them. They are looking forward to the understanding and help from their surrounding environment and society. Due to the possibility of bipolar disorder occurring in different age groups, adults in families are more responsible for concern about the mental state of the elderly and children. Nowadays, scientists have discovered useful treatment methods, including medical treatment, psychological treatment, and so on. In order to enable more patients with bipolar disorder to stay away from suicide and overcome the haze, more experimental research is needed in the future. Many bipolar disorder patients are stigmatized and discriminated against by the public due to their symptoms of madness. They not only bear the pain caused by illness but also bear the contempt of the public towards them. In order to protect them and improve their social environment, the scientists hope more and more people can focus on these patients and provide them with valuable support and assistance.

More research about treatments and the etiology needs to be done in the future since the population of bipolar disorders is getting greater. More psychological education and psychological relief are needed to be provided to the patients. Although lots of work has already been done in this field, the drawbacks, such as drug resistance, the non-adherence effect of patients, and potential side effects of the drugs, still have negative impacts on the treatment process. Therefore, more new and innovative models and new combinations of therapies can also be a possible orientation for scientists to study. People should also pay more frequent attention to their psychological and mental state and seek medical treatment as soon as they discover symptoms similar to bipolar disorder.

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