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Symptoms of Bipolar Disorder and Its Distinction with Other Disorder

Xiang Fei

Shanghai Starriver Bilingual School, Shanghai, China

100987@yzpc.edu.cn

Abstract. Bipolar disorder (BD) is a severe mental disorder and had high prevalence among the world. The overall lifetime prevalence of BP-I, BP-II and subBP are 0.6%, 0.4% and 1.4%, respectively. This article will discuss symptoms, genetic traits, hereditary patterns and treating procedure of BD. Also, differences between BD and other mental disorders and differences between sub types of bipolar disorder will be discussed in this article. For bipolar disorder patients, they will experience manic episode and depressive episode alternatively, with interphase between the two episodes. Differences in etiological agents between BD and other mental disorder lied in difference in expression of allele and environmental factors, such as childhood trauma or stressful environment. Improvement in understanding of the etiological factors and symptoms of the disease could help researchers and psychiatrists to diagnose and treat the patients.

Keywords: bipolar disorder, comorbidity, subtypes, genetic traits

1. Introduction

Bipolar disorder (BD)is characterized by alternatively appearance of manic episode and depressive episode. Episode of symptoms may last for weeks, months, or years.

During manic episode, patients will experience increase in self-perception, fell hopeful and euphoric. They will also be more easily to be irritated, perfrom hostile act, feel unstable and uneasy. They will feel hard to focus attention and have poor judgement, and are more likely to have unpractical goals. Patients will have less sleeping time and have increased sexual desire. Somatization symptom of Bipolar disorder patient include dehydration and lost in weight due to over excitement. Patients will have mydriasis, increase in heart rate, and hyperfunction in sympathetic nerves [1].

During depressive episode, patients will have pessimistic thought, feel despair, and will be deprived of sense of value. They will lose interest for daily activity and be deprived of the sense of joy. They will experience change in appetite and gain or lose weight.

If a bipolar disorder patient doesn't get therapy in time, BD may cause impair of relationship within and outside of family, overdose of alcohol or drug, and poor performance in school or workplace [2].

In the 1970s and 1980s, epidemiological surveys in western developed countries showed that the lifetime prevalence of bipolar disorder was 3.0-3.4%, and in the 1990s, it increased to 5.5-7.8%. Googwin report that bipolar type I obstacles (history of diagnostic criteria of manic or mixed episode) had a lifetime prevalence of 1%, lifelong prevalence of BD I and BD II together was 3%. BD I, II and cyclothemic disorder together has a life time prevalence of 4 %. It was found found that if the whole spectrum of bipolar disorders is considered, the prevalence of bipolar disorder may be between 2.6%

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and 7.8%. Recently, an epidemiological study in the United States showed that the lifetime prevalence rates of bipolar type I, type II and sub threshold bipolar disorder were 1.0%, 1.1% and 2.4%, respectively; and the 12-month prevalence rates were 0.6%, 0.8% and 1.4%, respectively.

According to the World Health Organization's (WHO) Global Burden of Disease (GDB) study, the disease burden of bipolar disorder is estimated to be the 11th highest among all categories of disease burden and the second highest among mental disorders (after depression). Dilsaver reported that the economic cost of bipolar disorder in the United States in 2009 was $15.10 billion (direct losses of $3.07 billion, indirect losses of $12.03 billion) [3].

The following paragraphs will talk about two subtypes of Bipolar Disorder, BD I and BD II, and how to discern the differences in symptoms and pathogenesis between the two subtypes.

2. Prodrome

Surveys have been done to determine the prodrome of BD, so that it will be possible for future prevention of deterioration of disorder. Multiple surveys traced subjects with high risk of getting bipolar disorder (patients with unipolar depressive disorder, relative of BD patients, etc) to study possible prodrome of BD.

A community survey showed that people who develop bipolar disorder were more likely to be sensitive in preschool age, more likely to be anxious and worry, experience lower mood, have lower energy and decreased sleep. Results from survey in hospital demonstrated that new onset BD was mostly preceded by a period of episode of depression. Also, subthreshold manic symptom also predicted BD syndrome. Results from a research showed that subthreshold manic episode, major depressive disorder, disruptive behavior disorder, anxiety, depression, sleep difficulties could be precursor of bipolar disorder [4].

3. Comorbidity

Bipolar disorder is usually comorbid with other disease more than 60 % of bipolar patients has comorbid diagnosis. BD patients are more easily to have anxiety disorder, ADHD, substance use disorder. The rate of anxiety disorder and substance use disorder was higher among BD patients, and vice versa. Also, panic disorder and OCD (obsessive control disorder) were more common in BD patients than in depression patients. BD patients were also related with borderline personality disorder, and eating disorder. BD patients with eating disorder usually gain weights.

BD could comorbid with substance use disorder. Alcohol was the most common substance for substance use disorder; 33 percent of the sample had substance use disorder for alcohol in life time. Substance for substance use disorder also included marijuana (16%), stimulant (9%), cocaine (9%), sedative (8%) and halllucinogen (6%) [5].

In addition, the prevalence of various somatic diseases, including endocrine, cardiovascular, respiratory, digestive, and urinary diseases, is higher in patients with BD than in the general population. People with bipolar disorder are twice as likely to die from cardiovascular disease as the general population, and obesity and excess weight may also be risk factors. Mackinrit et al. summarized the results of several studies and found that 31 to 35 percent of people with bipolar disorder were overweight and 25 to 34 percent were obese [5].

4. Genetic traits

BDNF (Brain derived neurotrophic factor) gene was considered to be important in development of bipolar disorder. Earlier research of 5 HT monoamine neurotransmitter showed that abnormality in metabolism of this neuron transmitter would result in Bipolar disorder. BDNF would stimulate 5 HT neurons development in brain. It has been proven that BDNF was involved in processes related to symptom of depressive disorder since experimental results have shown that animals in depressive states showed short term or long-term repression of BDNF in hippocampus region.

Besides BDNF, GRIN1 gene was also considered to be crucial and affected Bipolar Disorder. Liu et al. used SNP browser to detect two SNP positions in BDNF gene and GRIN1 gene. The experiment

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chose rs7103411 and rs6265 for BNDF gene and rs2301363 and hcv1840191 for GRIN1 gene. The result was that for genotype, there was statistically significant difference between two SNP position of GRIN1 gene or the control group and the experiment group, and there was no statistically significant difference between two SNP position of BDNF gene and for the control group and the experiment group. For difference in allele frequency, there was statistically significant difference between hcv1840191 SNP position for control group and for experimental group, and there was no significant difference between rs2301363 SNP position for control group and the experiment group. There was no significant difference between allele frequency of control group and experimental group.
these two SNPSThe locus and exon 2 of GRIN1 gene form a haplotype, in the remnant to be transmitted as a genetic unit in groups even though they are both Located on introns, but still indirectly indicating GRIN1 variation in BP may play an important role in the pathogenesis of the disease [6].

5. Two sub types of bipolar disorder

Among bipolar disorders, the DSM (Diagnostic and Statistical Manual of Mental Disorders) further classifies bipolar disorder into these subtypes: Bipolar Disorder Type I, Bipolar Disorder Type II, Cyclothymic Disorder. There are also related BD disorders caused by substance or drug use.

Patients who got BD I have a complete history of manic onset. Onset of manic episode should last for one week, and must cause harm. Patients might need to stay in hospital for therapy because of their unsafe behavior during manic episode. Their symptoms were usually related to depression disorder.

Patients with BD II disorder usually had at least once onset of hypomanic episode and don't have severe episode of manic symptom. BD II required onset of major depressive disorder. Patients with BD type II disorder did not have delusion or illusion, and the harm caused by BD II patient are also less severe.

It has long been thought that patients with BD I and BD II have different neurological dysfunctions. Although both subtypes have deficits in working memory, fluency, and interference control, patients with BD I were thought to have more impaired brain function. In recent studies by Dittmann et. al, study results showed that there were no differences in neurocognitive function between type I and type II bipolar patients. The test included 57 samples BP I, 42 samples BP II and 84 samples in the control group. The test was administered to measure multiple skills including learning, retention, recognition, color word, colors, color name, design flow, and more. There were no significant differences between bipolar I and bipolar II patients.
In previous studies, results showed that BD I patients had significantly lower metabolite level. Also, results in H-MRS showed that patients with BD showed frontal-temporal dysconnectivity. For BD I, cortical thinning was observed. BDI was also distinct for auditory processing deficit, a symptom that was related to left hemisphere superior temporal cortices [7].

6. Genetic difference between two bipolar disorder sub-types

Numerous researches have examined the monoaminergic system to better understand the genetic variations among the various bipolar disorder subtypes. BD II was connected with DRD2/ANKK1 TaqIA A1/A1, although Alzheimer's disease was unrelated. Additionally, ALDH2*1/1, which was connected to BD II but unrelated to Alzheimer's disease, would interact with DRD2/ANKK1 TaqIA A1/A1. It has been demonstrated that the DRD3 Ser9Gly Gly/Gly genotype increases the risk of BDII illness. In order to predict bipolar disorder subtypes, I and II, DRD3 Ser9Gly was used. It interacted with the temperament scale for novelty seekers. Patients carrying more DRD Gly + will have greater novelty sensing scores. For the risk of developing BDII disease, COMT Val/Val interacted with MTHFR T+, and COMT val/Met was associated with BD II risk. BDII was connected to ADH1B*1. It also has to do with alcohol dependence. The overall and impulsivity WURS (Wender Utah Rating Scale) scores in the BDII were related to the SLC6A4 5-HTTLPR l + genotype. Three SNPs were linked to BDII.

The paragraph that follows discusses BD I-related genes. ALDH2*1 is linked to a higher chance of developing BDI illness (OR = 4.48, 95% CI 1.76-11.40, p = 0.002). For the risk of BDI disease,

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ALDH2*1 interacted with 5-HT2A -1438A/G. Between HC and BDI, there was an excess of ALDH2*1. BDI and BDII illness risk is related with SLC6A4 5-HTTLPR S +. Manic-psychotic BDI patients had a higher probability of developing SZ than other BD I or BD II patients [8].

7. Hereditary

50% of bipolar patients have at least one parent with affective disorder. A child with a parent with bipolar disorder has a 25% chance of having an affective disorder. If both parents have bipolar disorder, the risk increases to 50 to 75 percent. The twin survey showed that the co-occurrence rate of bipolar disorder between monozygotic twins was 65.1%, while that between dizygotic twins was 14.0%. It was estimated that the heritability of bipolar disorder was about 80% in monozygotic twins. Studies on foster children showed that children of sick parents in normal family Settings still had a high incidence of emotional disorders, and the prevalence was close to that of non-foster children, about 26% [9].

8. Compare and contrast between bipolar disorder and other diseases

8.1. Depression

Bipolar disorder and major depressive disorder had different prevalence rates. The overall prevalence of bipolar disorder was 4.5 percent, compared to 16.2 percent for major depressive disorder. Bipolar disorder was signaled by symptoms of alternation of manic episode and depressive episode, which was easily to be misdiagnosed with major depressive disorder. There was significant consequence of misdiagnosis with bipolar disorder students with major depressive disorder patients. Drugs treating bipolar disorder showed no effect when applied on major depressive disorder patients, and drugs for major depressive disorder patients (antidepressants), including paroxetine, imipramine, sertraline didn't function as mood stabilizers in treatment of bipolar depression [10].

Among major depressive disorder patients, bipolar disorder patient shows common traits that were more frequent in sample of major depressive disorder patients than in the population. After taking antidepressant, bipolar disorder patients have a higher possibility of entering manic phase. They were also more likely to have history of treatment resistant depression.

Researchers noted that possible indicators of bipolar disorder patients in a study to distinguish them from depressed patients included seasonality, many past episodes, a history of psychiatric hospitalization, mixed states, mood reactivity, a history of treatment-resistant depression, starting antidepressants, and a history of suicide attempts.

There were also screening tools for bipolar disorder and depression. For the bipolar scales, there were mood disorder questionnaires and hypomania / mania symptom checklists, all of which were self-assessment scales. For depression, there were Patient Health Questionnaire, Beck Depression Inventory-II, Inventory of Depressive Symptomology, and Quick Inventory of Depressive symptomology, Hamilton Depression Rating Scale, and Montgomery-Asberg Depression Rating Scale. Based on the result of this questionnaire, the patients were able to realize the extent to which a bipolar disorder or a depressive disorder developed.

8.2. Schizophrenia

Both schizophrenia and bipolar disorder had multiple etiological risk factors, and had similar prodrome, such as longtime of functional lesion before the first time of acute attack of the disease. Schizophrenia and cyclothymic disorder showed similar abnormality in brain morphology. An increase in frontal cortex and temporal lobe's ventricle to room ratio, and decrease in gray matter and region of hippocampus and amygdala would decrease.

Patients of schizophrenia would show Hallucinations, delusions, speech disorders and behavior disorders or catatonia; they will have insipid emotion and social withdrawn. Patients of schizophrenia would have depressive, intense and anxious mental state. Their memory function and learning ability would be impaired.

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One difference between schizophrenia and bipolar disorder was that psychopathic trait would show effect in schizophrenia patients when patients when patient were in emotional attack phase. In comparison, in Bipolar disorder patients, psychopathic traits would appear only when patients were in emotional attack periods, including manic phase and depressive phase.

Compare to schizophrenia patients, bipolar disorder patients had a higher probability of having mood disorder (38.2 % v.s. 18.0 %), had higher promorbid adjustment ability, higher social baseline ability, higher baseline cognitive flexibility, higher baseline manic symptom and less baseline negative symptom [11].

9. Treatment

Lithium salt was commonly used to treat bipolar disorder. It could reduce duration, frequency, and order of severity of onset of disorder, and reduce the danger of the sub symptoms which showed effect between period of onset of the disease. Although death rate of bipolar disorder patients was generally twice to three times more than the population, patients who have received 6 months of lithium salt treatment have the same death rate with the population.

A comparison was made between BD patients who ended lithium salt treatment in a short period of time (within 2 weeks) with patients who ended treatment gradually (between 2 weeks to 4 weeks). The former group were more likely to show symptoms again within 5 years (94%) when compared to the latter (53.5%). These two groups had the same possibility to show depressive symptom after five years. However, patients who ended treatment within 2 weeks were significantly more likely to show manic symptom when compared to the latter. (91 % compared to 33%)

Lithium salt had unfavourable effect on treating symptoms related to manic period. Expression of manic period included cyclothymic symptom, restless mania and mixed state. For these symptoms, using valproic acid and carbamazepine could be a better choice. An experiment conducted by Galabrese found that 54 percent of manic patients and 87 percent of mixed state patients showed observable curative effect to valproic acid.

Clozapine was used to treat manic symptoms. According to report by McEloy, 14 patients who showed resistance to treatment or couldn't tolerate other medical treatment accepted treatment of clozapine. Patients who received treatments more than 6 weeks showed improvement in their symptoms. Patients who continue to take clozapine was never hospitalized. Because clozapine could be harmful for causing deficiency of granulocyte, clozapine was only appropriate to be used to treat BD when patients could not accept other way of treatment.

Another way to replace lithium sat treatment was to use electroconvulsive treatment. Electroconvulsive treatment was effective when treating patients with severe manic symptom, pregnant patients, and patients with tendency to murder or commit suicide. In an experiment conducted by Black et al, 78 percent of patients who accept ECT treatment had their symptoms improved. For lithium salt treatment, 62 percent of patients who received lithium salt treatment showed improvement in treatment. Manic patients had fast reaction to ECT treatment, so, there was no need to increase frequency of treatment or to prolong the duration of the treatment [12].

10. Current difficulties

Treatment of BD by using lithium salt has its limitation. If lithium salt was taken when the patient was pregnant, deficiency might appear on the new born infant. For female patients who used lithium salt during the first three months of pregnancy, the probability for infant to get Ebstein malformation was 1/8000, which was approximately 2.5 times more than the probability of getting this malformation than in the population.

For bipolar disorder, patients who took lithium salts were 28 times more possible to show cyclothymic disorder than the population. For patients who stopped lithium salt treatment, the possibility for them to show symptom of cyclothymic disorder was 50%.

Lithium salt treatment had a 33 percent possibility of failure in prevention of the disorder. Also, it had side effects such as increase in body weight, increase in need of sleep [12].

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Treatment of Bipolar disorder using antidepressant was effective in treating symptoms during depressive period; however, it might also cause manic symptom. It was also difficult to differentiate Bipolar disorder with attention deficiency hyperactivity disorder. ADHD patients could be classified into three types [13].

11. Conclusion

Diagnosing of bipolar disorder has still been hard in recent years since BD usually had comorbidity with other mental disorder. Major depressive disorder, anxiety disorder and ADHD have high probability to be comorbidity with BD. In this article, it was concluded that the one key difference between BD and other diseases lied in the pattern of allele. For example, patients of BD and patients with other disorder will show different single nucleotide polymorphism (SNP) pattern.

Also, bipolar disorder had two subtypes, BD I and BD II. These two sub types of bipolar disorder have different symptoms and require different treatment. It has been found that there have been few differences in gene between these two sub types, but they a difference in Monoaminergic system was found between BD I and BD II. In addition, difference in behavior pattern of BD I patients and BD II patients were also found.

The most commonly used treatment for Bipolar disorder was lithium salt, while other treatment, including substance treatment and behavior treatment, can also be effective in treating Bipolar Disorder.

The current difficulty in diagnosing and treating bipolar disorder is that the diagnostic scale for bipolar disorder is still indistinct; in addition, the most common treatment has multiple drawbacks which could threaten patient's heath condition.

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