

Nicotine Addiction, Alcohol Use Disorder and Bipolar Disorder

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Abstract. Bipolar affective disorder has a wide range of effects on human health and is extremely harmful, and the mortality rate of patients continues to grow. Meanwhile, most people, especially those with mental illness, tend to numb themselves by smoking and drinking. Unfortunately, tobacco and alcohol abuse are also extremely harmful to human health, moreover, the cost of living will be increased due to addiction of these things. At the same time, the unconscious mind after using alcohol and tobacco has also brought great uneasiness to society, thus leading to increased burden on individuals and society. This review discusses the genetics, comorbidity, and treatment of nicotine dependence, alcohol use disorder, and bipolar disorder, and finds that the severity of bipolar disorder patients is positively correlated with the severity of alcohol use disorder and nicotine dependence. Both patients with bipolar disorder and alcohol use disorder exhibit mutations in the BDNF gene, and an age peak in bipolar disorder coincides with a peak in nicotine dependence. In the end, it is believed that the interaction between comorbidities may become a breakthrough in the diagnosis or treatment of bipolar disorder in the future, and the easy-to-observe alcohol and nicotine intake can be used to assist in judging the current state of patients.

Keywords: Bipolar disorder, nicotine addiction, alcohol use disorder.

1. Introduction

Bipolar disorder is one of the top ten causes of disability globally, affecting more than 1% of the world's population, rising to 4% if bipolar spectrum disorder is defined more broadly. Bipolar disorder increases mortality, especially suicide. Among people with bipolar disorder, 10% die by suicide. The biological basis of bipolar disorder is unknown, but what is certain is that bipolar disorder is highly heritable, largely due to a few common gene mutations with small effects. Several risk genes and gene networks for BD have been identified. However, its treatment is still unsatisfactory. All current treatments for BD have limited efficacy, and drug treatment may cause serious adverse reactions to patients [1].

Alcohol is a major cause of disease worldwide, and the delirium associated with drinking also adds a risk factor to society. Alcohol use disorders cost at least \$249 billion annually in the United States. It is often said that "drinking hurts the body", people with alcohol use disorders have been demonstrated with physical or mental damage caused by drinking, such as: gastrointestinal diseases, coronary heart disease, diabetes, gout etc., and even memory loss, emotional instability and other problems. Nicotine use disorder is another major cause of disease.

It is not difficult to find in life that patients with bipolar disorder are often accompanied by a lot of alcohol use and tobacco use. In recent years, the co-morbid phenomenon of bipolar disorder has also been gradually studied. The inner connection between alcohol use disorder, nicotine dependence and bipolar disorder is the key to their treatment. This review summarizes the symptoms and harms of bipolar disorder, alcohol use disorder and nicotine dependence, explores whether they are genetically related, and the comorbidity caused by the three and the existing treatment methods.

2. Bipolar Disorder

Bipolar disorder is a chronic condition characterized by recurrent episodes of elevated mood and depression [2]. It encompasses bipolar I, II disorder (BD-I, II), cyclothymic disorder, other specified bipolar and related disorders, as well as unspecified bipolar or related disorders [3]. Accurate diagnosis of bipolar disorder is difficult in clinical practice because depressive symptoms are often

more common and longer-lasting than elation, which makes the patient look more like unipolar depression [2]. It is one of the top ten causes of disability in the world, and its incidence peaks are at the age of 15-24 and 45-54 and affects more than 1% of the world's population [2,3]. Although it has been associated with high levels of creativity, it causes cognitive and functional impairment in most patients. Cognitive and functional impairments contribute to mortality, especially suicide, with more than 6% of people dying by suicide within 20 years of a bipolar disorder diagnosis. The risk of natural death also increases with disease, most commonly cardiovascular disease [4].

3. Alcohol Use Disorders

Alcohol is a major cause of disease worldwide and a preventable category of major cause with a highly prevalence and co-morbid [5,6]. The 12-month prevalence rate of alcohol use disorders was 13.9%, and the lifetime prevalence rate was 29.1% [6]. Nearly one-third of American adults have suffered from alcohol use disorder, about 88,000 people die from it every year, and the loss of alcohol use disorder in the United States is at least 249 billion US dollars every year. It is the fifth leading cause of premature death and disability [5]. Alcohol use disorder often co-occurs with psychiatric disorders, such as anxiety and mood disorders. The co-occurrence of these diseases is more serious than either disease alone, with a worse prognosis and even a higher risk of suicidal behavior [7]. There was a significant correlation between bipolar I disorder and 12-month and lifetime AUD [6]. About 25%-50% of people with bipolar disorder also suffer from alcohol use disorder [8]. Patients with BD-AUD co-morbidity have more severe neurocognitive deficits than those with a single disease [9]. It is not clear why people with bipolar disorder are more prone to addiction, but alcoholism and dependence undoubtedly have huge costs, while greatly reducing the patient's ability to work [10]. This places a huge financial burden on patients from different economic backgrounds.

4. Nicotine use of behavioral addictions

Nicotine addiction is an extremely complex process involving biological, psychological, behavioral and cultural factors [11]. Stress has led to an increase in smoking, with more than 1 billion people smoking worldwide. But without a dramatic increase in the number of quitters, at least half will die prematurely from smoking-related complications [12]. For humans, if nicotine in tobacco can bring stimulation and pleasure, and can reduce stress and anxiety has not been confined [11,13]. Psychiatric disorders often co-occur with nicotine use behavioral addiction. A peak onset of bipolar disorder occurs between the ages of 15 and 24, and once a teen starts smoking, he or she is more likely than an adult to become addicted [2]. It has been hypothesized that smoking in people with mental illness reduces symptoms: There is evidence that nicotine improves cognitive function and reduces psychotic symptoms. If a nicotine-addicted smoker is deprived of nicotine, nicotine withdrawal occurs [14]. Smokers may experience symptoms of irritability, depression, irritability, anxiety, hunger, increased eating, insomnia, and difficulty getting along with family and friends [13]. Smokers' concentration and cognitive abilities are also impaired. This deficit can be reversed if the smoker is brought back to smoking or taking nicotine. However, other scientists think that the tobacco industry paid for the study's funding. He made the suggestion that psychiatric disorders and smoking have an interaction. Early-onset smoking may also increase a person's risk of developing schizophrenia, anxiety, and depression. The researchers concluded that if people self-administered nicotine to relieve acute neuropsychiatric symptoms, nicotine would not have a sustained effect [13].

5. Heredity

5.1. Bipolar Disorder and Genetics

Although studies of twins have shown that BD is highly heritable (approximately 80%), the risk of developing a variety of symptoms and neurological abnormalities in children increases when one

parent is affected [15]. However, it is still difficult to identify risk genes through linkage and candidate gene association studies. However, recent GWAS97 quiz sequencing identified candidate genes for BD, results consistent with twin family and familial studies [15, 16].

Loss-of-function mutations in bipolar patients encompass many genes that are rarely mutated in the normal population, as a result of a search for novel mutations in 79 families with BD. Carriers of de novo mutations had a lower age of onset, which also corresponds to a peak age group for the onset of bipolar disorder: 15-24 years old. Bipolar I disorder in bipolar disorder is a typical representative. The de novo mutation rate of bipolar I disorder was higher than that of the control group, and the calcium-binding protein was abundant and dense, reflecting the effect of de novo mutation [16].

5.2. Alcohol use disorder and genetics

Genetic factors are thought to contribute to the development of AUD, and quantitative genetic studies have shown that the heritability of AUD is about 50% [17,18]. Alcohol addiction is also considered to contain complex genetic factors. These include neurobiological vulnerability, polygenicity, phenotypic replication, and genetic heterogeneity at the level of gene-environment interactions. Therefore, the identification of genes associated with alcoholism susceptibility holds significant importance as these genetic products play a crucial role in the metabolism of alcohol in humans (alcohol-metabolizing enzymes) and have implications for clinical interventions [17].

5.3. Nicotine use disorder and genetics

Twin studies have shown high heritability (50%) for the prevalence of smoking and the ability to quit (nicotine dependence). Twin studies have even demonstrated that the nature of the specific symptoms experienced by smokers remains hereditary even after they stop smoking [19]. Researchers have sequenced a large number of genes in an attempt to identify the genes responsible for nicotine addiction. However, genetic sequencing studies remain problematic due to the complexity of environmental factors and the fact that nicotine use disorder may not be affected by only one gene [20].

6. Comorbidity

6.1. Bipolar Disorder and alcohol use disorder

In the experiment of Janiri et.al, a study of 69 patients with both bipolar disorder and AUD and 63 patients with both bipolar disorder and PSU. (The screening conditions for the patients participating in the experiment are the patients are all aged between 18 and 65 years old, are BD class I or II patients assessed by SCID-I/P, and have no other additional diagnoses) [21]. BD patients without SUD were more often bipolar I disorder than BD patients with AUD, that is, more often manifested as mania. In addition, the onset of BD patients without SUD was earlier than that of BD patients with AUD.

In the study of Grant et.al, it was shown that AUD was related to bipolar I disorder when sociodemographic characteristics and other irrelevant variables such as obstacles were controlled. Furthermore, any severe lifetime AUD was associated with PTSD and PTSD is also considered to be one of the most common comorbidities of BD (Table 1) [22].

Table 1. AUD, AOR (95% CI)

	Any	Mild	Moderate	Severe	Any	Mild	Moderate	Severe
BD-I	1.4 (1.08-1.78)	1.2 (0.84-1.81)	1.6 (1.06-2.55)	1.4 (1.03-1.90)	2.0 (1.59-2.44)	1.4 (1.01-1.83)	1.6 (1.13-2.30)	2.4 (1.84-3.11)
BD-II	1.3 (0.70-2.39)	1.4 (0.67-2.74)	1.0 (0.34-3.04)	1.4 (0.54-3.63)	1.2 (0.63-2.20)	0.8 (0.35-1.91)	1.0 (0.46-2.35)	1.4 (0.66-3.01)
Nicotine use disorder	2.5 (2.24-2.69)	2.0 (1.75-2.25)	2.7 (2.26-3.32)	3.6 (3.07-4.24)	3.2 (2.95-3.42)	2.2 (2.00-2.46)	3.0 (2.69-3.42)	4.3 (3.89-4.81)

6.2. Bipolar Disorder and nicotine use disorder

Also in the study by Stine Holmstul Glastad et.al, there was no relationship between the level of manic symptoms and the level of current nicotine use. But there are also studies showing that people with bipolar disorder have higher smoking rates than the general population. Smoking makes people with mental illness die 13-30 years earlier than the general population. Smoking is the single most identified risk factor hindering reductions in mortality among psychiatric patients. Smoking increases the incidence of psychosis in patients with bipolar disorder. Smoking makes people with bipolar disorder less successful in mania treatment. It also makes patients have an earlier age of first manic episode and a higher probability of lifetime suicide attempt.

7. Treatment

7.1. Alcohol use disorder

Among patients with 12-month AUD, only 7.7% actively sought treatment or assistance for their condition. Notably, a mere 4.5% of these individuals received support from esteemed 12-step groups, while a modest 3.6% sought professional help from healthcare practitioners. Additionally, a meager 2.0% opted for outpatient facilities as their treatment choice, and merely 1.8% turned to rehabilitation programs for assistance in combating AUD. Conversely, among those afflicted with lifelong AUD, a significantly higher proportion (19.8%) actively pursued treatment or aid for their enduring struggle.

They exhibited similar treatment rankings as the 12-month AUD patients. Rankings by severity were similar to those for treatment involvement. Overall, treatment-seeking rates ranged from mild to moderate to severe increases gradually. Although it is obvious from the above article that there is an inevitable connection between AUD and BD (the most typical example is the mutation in the BDNF gene), relevant data show that people will only Whether or not to seek treatment is a choice, and a large number of people with bipolar disorder do not experience relief from AUD treatment.

7.2. Nicotine use disorder

For nicotine use disorder, the most mainstream treatment option is to reduce the nicotine content in tobacco. Proponents of the idea argue that drastic reductions in nicotine levels in tobacco could ultimately disrupt the nicotine habit for large numbers of consumers and prevent new smokers from getting nicotine.

Although the society has provided a large number of adjuvant treatments for nicotine dependence, all of them have had little effect. In the United States, quitlines are free, convenient, and confidential, but in most states only 1% of smokers call them each year on average. The Internet, such as Twitter, and Facebook also provide smoking cessation treatment searches, but they only allow most young people to participate in smoking cessation treatment. There is little literature on smoking cessation options for people with bipolar disorder, even though most people with bipolar disorder are heavy smokers [14].

8. Conclusions

Although there is no clear experimental data showing a causal relationship between bipolar disorder, alcohol use disorder, and nicotine dependence, there is no doubt that there is a strong positive correlation between them. As mentioned above, mutations in the BDNF gene have been found in tests for both bipolar disorder and alcohol use disorder. At the same time, nicotine dependence is also more likely to occur during the peak stage of bipolar disorder. However, the existing treatment methods are limited. People do not have a highly popular treatment plan for a single bipolar disorder, alcohol use disorder and nicotine dependence, and it is even more difficult to treat their comorbidities. But perhaps, the commonality between comorbidities can be a breakthrough for researchers to study treatment options in the future. Alternatively, doctors can use easily observable

phenotype data such as alcohol use disorder and nicotine dependence to more accurately judge whether a patient has bipolar disorder.

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