Mechanism and Treatment of Anxiety Disorders

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Abstract. Anxiety disorder is a disease that has a high incidence and has long plagued people's lives. In academia, there are roughly three types of factors that can lead to anxiety disorders, namely cognitive factors, genetic factors, and environmental factors. This article will discuss anxiety disorders from these three aspects and summarize the current research status and list relevant important research.

1 Introduction

Anxiety disorder is a common mental illness, almost everyone has heard of anxiety disorder, but in fact, few people know whether they have an anxiety disorder or pay attention to its harm. A shocking statistic shows that there is about one anxiety disorder in every 20 people in the world, over 40 million adult patients in the U. S [1]. Anxiety is a natural response to stress that may be useful under some circumstances. It can alert us of impending dangers and assist us in planning and paying attention. Anxiety disorders are marked by intense fear or anxiety, as opposed to natural feelings of nervousness or anxiety. Anxiety disorders are the most common psychiatric illnesses, afflicting about one-third of all people at some time in their lives [1].

There are many types of anxiety disorders, and they are usually classified by what makes them happen. At present, the pathogenesis of anxiety disorder is unclear. Some people think it is caused by genetic factors, some people think it is caused by environmental factors, and some people think it is caused by cognitive factors. Common types of anxiety disorders are Generalized anxiety disorder, Specific phobias, Panic disorder, Agoraphobia, Social anxiety disorder, post-traumatic stress disorder, Separation anxiety disorder, Obsessive-compulsive disorder, Selective mutism.

This article will expand from these three aspects and provide some treatment options based on these factors.

2 The Influence of Cognition on Anxiety Disorders

On the cognitive level, some scholars believe that anxiety is a false perception of the world. Many spiritual practitioners achieve inner peace by correcting their misconceptions. In some religions, meditation is a means of self-cultivation.

"Cultivation of mindfulness, the nonjudgmental awareness of experiences in the present moment, produces beneficial effects on well-being and ameliorates psychiatric and stress-related symptoms" [2].

2.1 Research of Mindfulness Therapy

Mindfulness is effective because it is an effective way of relaxation. Negative emotions such as anxiety and fear usually do not co-exist with relaxation.

Many scholars have a strong interest in the research of mindfulness meditation and have done many studies on the negative effects of mindfulness meditation on anxiety in different situations.

a) ninety-three people with DSM-IV-diagnosed GAD were randomly assigned to either an 8-week community MBSR intervention or an attention modulation, Stress Management Education (SME). The Hamilton Anxiety Scale (HAM-A, key outcome measure), the Clinical Global Impression of Severity and Improvement (CGI-S and CGI-I), and the Beck Anxiety Inventory were used to assess anxiety symptoms. Anxiety and depression were compared during pre- and post-treatment Trier Social Stress Tests to determine stress reactivity (TSST). According to an intention-to-treat study that included participants who finished at least one session of the MBSR or SME sessions, the treatments were found to have been equally effective, although they did not quite have the same magnitude of difference. MBSR, on the other hand, was linked to a slightly lower level of distress as assessed by the CGI-S, CGI-I, and BAI (all Ps0.05). To the TSST challenge, participants recorded a significant rise in both depression and self-relatedness (statistically significant) stress and decrease in anxiety (P = 0.05) and clinical anxiety (P = 0.004), as well as a significant increase in

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optimistic comments (statistically significant) stress reduction in results [3].

b) These students especially those who are behind their peers in academic achievement and have significantly more stress at school and less desirable social skills with learning difficulties may need support. Previous health literature suggests that yoga and calming training will help reduce anxiety and improve social skills. A pre-post-no-control framework was used in this pilot study to explore the effectiveness, attitudes toward, and outcomes of a 5-week mindfulness mediation intervention provided to 34 adolescents with LD. Positive views toward the initiative were reflected predominantly in post-intervention survey responses. Both result outcomes demonstrated substantial progress, with program members showing reduced state and trait distress, increased social skills, and better academic achievement. The conclusions are compatible with a cognitive-interference model of learning disorder, which shows that mindfulness meditation can lower anxiety and foster social and academic abilities, or school, competence [4].

c) Mental wellbeing issues and quality of life are also being recognized as high-stress challenges for police officers. More and sustained studies indicate that mindfulness programs are effective in reducing tension. there were three assessment points at the beginning (baseline, post, and 6-month follow-up) and a single data point at the end. QoL, depressive, and/anxious signs are examined here. Mechanisms of transition and MBHPS were examined. there was observed to be significantly correlated with QoL, though not to the organization; stress and anxiety, as well as non-organ measures, were moderately correlated. According to the data from a between-group, enhancements in the MBHP have demonstrated as well as post-intervention (from 0.41 to 0.74) and at the 6-month follow-up (from 0.51 to 0.50) concerning non-organized religiosity change, 0 A shift in self-compassion affects the general well-being (which includes the relationships of others) in all realms and facet subdomains of well-being. the relationship between the post-intervention mental well-being facet level of group improvement and spirituality on overall QoL health was lessened. The use of MBHP to increase QoL and symptoms of depression and anxiety in Brazilian officers is both feasible and efficient [4].

Although cognitive behavior therapy has been shown to be successful in the treatment of generalized anxiety disorder (GAD), many people do have residual symptoms [5].

3 The Influence of Genes on Anxiety Disorders

In the following sections, we will focus on the influence of genes on anxiety disorders, including their pathogenesis and evidence, and in the following sections, we will propose some therapeutic approaches.

3.1 Different Genes Cause Anxiety Disorders

SLC6A4

Genes that control the production of the serotonin transporter protein may be involved in the development of anxiety. The specific mechanism is that the 5-HT transporter is affected by mutations in the polymorphic region of the SLC6A4 gene, which reduces the transcription efficiency of 5-HTT producing mRNA, thus reducing the uptake of 5-HT by lymphoblast cells. And 5-HT has an inhibitory effect on anxiety, so it will eventually lead to the production of anxiety [6]. They performed a meta-analysis of association analyses and found a significant association between 5-HTTLPR and NEO neuroticism and no significant association between 5-HTTLPR and TCI/TPQ harm avoidance. According to Ming et al. [7], the polymorphism region of the SLC6A4 gene, 5-HTTLPR, increases the risk of depression if people carrying the L allele are exposed to a negative environment. However, according to statistics, the frequency of 5-HTTLPR genotype SS in patients with GAD is significantly higher than that of other genotypes [8], which may be related to ethnic differences [7]. Ming et al. report further explaining their findings that the frequency of the L allele in the SLC6A4 genome is significantly lower than that of the S allele in Asian populations, especially Chinese and Japanese, but that the L allele is higher than that of the S allele in Caucasians and African Americans. And the effect of 5-HTTLPR on serotonin uptake inhibitors is different in Caucasians and Asians according to the results of the meta-analysis [7], 5-HTTLPR carrying the S allele has been shown to have latent anxiety traits [9]. Gottschalk found in his study that people with S allele scored significantly higher in the Maudsley Personality survey than those with the L allele, and in the meta-analysis of anxiety disorders, NEO Personality.

The increased neuroticism score of Inventory showed a strong correlation with the S allele. Both points suggest that the presence of the S allele is strongly associated with anxiety [9].

MAOA

Monoamine oxidase A (MAOA) gene is also one of the factors leading to anxiety. According to the study of the association between the MAOA gene and GAD, the MAOA gene may be related to the production of anxiety. It is related to the T941G single nucleotide polymorphism of the MAOA gene. Specifically, people with GAD have a higher frequency of the 941T allele than healthy [10]. Secondly, the researchers believe that the longer allele, polymorphism, and higher activity of UVNTR in the MAOA gene of individuals may also cause anxiety disorder, because people with the above characteristics usually have higher GAD scores in generalized anxiety for Childhood Anxiety and Related Emotional Disorders (SCARED) [9]. This is consistent with the research of Reif et al. According to a study by Reif et al [11], who conducted the Standardized Behavioral Avoidance Test (BAT) on 283 patients with anxiety, most of them had accelerated heart rate and showed anxiety symptoms. They believe that the pathogenesis of the MAOA gene may be related to the decrease of norepinephrine levels.

The highly active and the highly expressed MAOA gene might have led to an increased amount of catecholamine degradation, which would have resulted in a decreased level of norepinephrine delivered by synapse from locus coeruleus. Second, they suggest that the overexpressed MAOA gene may contribute to anxiety disorders by reducing the use of serotonin (5-HT), similar to the effect of the SLC6A4.

BDNF

The BDNF gene also plays a role in the development of anxiety. This was mainly manifested in the BDNF polymorphism BDNF Val66Met. First, polymorphism in the BDNF Val66Met gene was found. The injury avoidance (TCI) subscale scores of patients with anxiety disorders were higher than those of healthy subjects. The frequency of the BDNF 66Met gene is higher in patients with a generalized anxiety disorder than in healthy people [4]. The researchers tested its effect by inserting the allele BDNF MET/MET into mice and found that mice carrying the gene showed anxiety symptoms similar to those seen in humans during adolescence. BDNF Val 66 Met polymorphism is also associated with GAD by blocking BDNF processing, release, and transmission. BDNF is a neurotrophic protein. Its presence can improve synaptic plasticity and the survival rate of neurons, and BDNF is recognized to counteract the negative effects of stress hormones on hippocampal volume [12]. In anxiety disorders, the BDNF gene polymorphism BDNF Val66Met blocks the synthesis and release of BDNF and reduces the activity of BDNF, which will affect the normal function and volume of the hippocampus, leading to people more prone to anxiety disorders. In addition, the BDNF Val66Met polymorphism was more common in Asians and some Caucasians [13].

3.2 Drug treatment

Fluoxetine

Fluoxetine is an effective treatment for anxiety disorders caused by the BDNF gene polymorphism BDNF VAL66MET. According to Ronald S. Deman, Ph.D., who administered Fluoxetine to mice, mice with BDNF Met polymorphism at P21 to 42 were given Fluoxetine, compared with control mice. The prefrontal cortex and hippocampus of the mice showed normal 5-HT fibers, while the density of the uninjected 5-HT fibers decreased. But the drug's effect lasted only up to P42, and after day 42, the fiber density of the genetically defective BDNF Met/Met mice remained the same, while the fiber density of normal BDNF VAL/VAL mice continued to increase to reduce anxiety. The researchers hypothesized that the drug would only work for people with anxiety disorders in adolescence [14].

Table1. The body changes of mice treated with Fluoxetine in different periods

	Physiological changes in mice	The effect of the drug during this period
P21 — 42(Mouse puberty)	The 5-HT fiber density of the diseased mice remained almost unchanged after treatment, while that of the untreated mice decreased.	The medicine works.
After P42(Adult mouse)	The density of 5-HT fiber remained the same in the diseased mice, but continued to increase in the healthy mice	The medicine didn't work.

4 Environmental Factors Associated with Anxiety Disorder

4.1 Mental Factors Affected by Living Range

4.1.1 Factors in Living Range

Even though there is less knowledge about which psychological processes are involved and how they may moderate disease risk like trait anxiety disorder. The sound, noise, and air quality in daily life are believed some reasons causing anxiety disorder. Most researchers believe that the effect on exposure to sound and air quality is something negative or unwanted. Long time exposure to the noise can induce hearing impairment, even if the noise is lower than the threshold of inducing that, there is still a concern. Björk et al. experimented with high exposure to traffic noise and NO_x levels showing a positive association with ratings of annoyance from total traffic noise, sounds from neighbors, sound from ventilation, exhaust fumes from traffic, sounds from other installations and vibrations from traffic (ORs between 1.37 and 2.14).

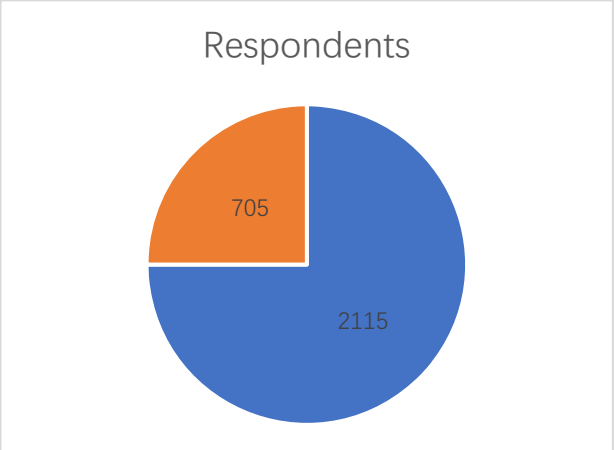

Figure 1. Normal respondents are represented by orange and Self-reported asthma and the rest constituted gender-matched referents are represented by blue.

The method that they operated was a trait anxiety scale in a cross-sectional public health survey with 2,856 respondents. Of these, 705 had self-reported asthma and the rest constituted gender-matched referents. They used the psychic trait anxiety scale from the Swedish

universities Scales of Personality (SSP) and the health survey from 2004 annoyance scores was dichotomized as follows: 1 = not aware, 2 = aware, but it does not annoy me, 3 = not especially annoyed, 4 = fairly annoyed, 5 = very annoyed, 6 = extremely annoyed. The result shows the traffic noise and the sound from neighbors are two conditions that have the highest and second-highest score, each scored 2.17 (Mean), 1.00 (Standard deviation) and 2.02 (Mean), 1.02 (Standard deviation) respectively, which takes place of 8% of the participants [15]. The experiment performed a positive association between anxiety and noise. However, some participants might exaggerate the score. Therefore, a more accurate procedure is need. For example, a procedure like to exam the physiology of the brain before the noise condition is added and compare with the after the noise condition added can modify the accuracy of the exam.

4.1.2 Common Influence of Environmental Factors in Gender Difference

The anxiety condition or disorder exhibits a high level of a lifetime or life-events comorbidity. Many experiments have suggested the anxiety disorder is the product of environmental factors and genetic influence. The neuroplasticity of the brain demonstrates the traits that can be explained by both genetic information and environmental factors, but in this section, we mainly focus on the environmental factors. In 2005, Hettema, Prescott, Myers, Neale, & Kendler presented an experiment to explain the comorbidity of anxiety disorder by analyzing the structure of the underlying genetic and environmental risk factors. This experiment was carried by mailed questionnaire between the first and the second wave, the group was divided into MM (Male-male pairs) and FF (Female-female pairs). The first wave concluded 2156 participants and the second wave concluded 1999 participants and the zygosity of each person. They found the pattern of genetic and environmental risk factors does not differ significantly between men and women, from the comparison of model 2(Akaike information criterion is −43111.21) and model 2(Akaike information criterion is −43111.21). Moreover, there is a small role of a shared environmental influence which is a single common factor that accounted for less than 12% of the total variance for any disorder [16]. The experiment primarily targets the gender influence in anxiety disorder and the association of genetic and environmental conditions. From the comorbid result, the effect on the environment does not take a considerable proportion to represent the importance of non-genetic influence. The purpose of this experiment is just to present there is no significate difference effect of the cause-anxiety factor between males and females.

4.2 Lifestyle

4.2.1 The Relationship between Alcohol and Anxiety Disorder

People's styles form people's minds, behaviors, personalities, physical conditions, and brain conditions (feelings). Many alcohol-dependent individuals show aggressive and abusive behaviors in their families, but it is unclear whether these anxiety conditions are independent psychiatric disorders or temporary syndromes likely to disappear on their own. Schuckit & Hesselbrock tested the relationship between alcohol dependence and anxiety. They evaluated 6 reports since 1975, and they are 1) lifelong anxiety disorders are unusually prevalent among alcohol-dependent individuals, 2) children of alcoholics are more likely to develop anxiety disorders than comparison populations, 3) anxiety syndromes are likely to disappear with abstinence, 4) the rate of alcohol dependence among subjects with lifelong anxiety disorders is higher than normal, 5) there is the familial crossover between alcohol dependence and anxiety disorders, and 6) alcoholism is often preceded by anxiety disorders in groups from the general population studied prospectively. They found in many of those reports, there is not a piece of convincing evidence to prove the close relationship between lifelong anxiety disorders and alcohol dependence. Further, studies of children of alcoholics and individuals from the general population do not indicate a high rate of anxiety disorders preceding alcohol dependence. Those studies were published before the discovery of alcoholism. The population with alcoholism that can be passed by genesis at a higher risk of anxiety disorder, but it does not indicate the effect on alcohol for a general population [17]. Although, this critical paper disproves the relationship between alcohol, however, anxiety disorder might be comorbidly affected by other variables. This section is just to suggest an idea that the complexness of genetic and environmental factors is very rigid to determine, it is still uncertain to conclude that what particular environmental factors can affect anxiety disorder.

4.3 Treatment

4.3.1 The Effectiveness of Pharmacotherapy and Phytotherapy on Anxiety Disorders

The current conceptualization of the etiology of anxiety disorders includes an interaction of psychosocial factors, e.g., childhood adversity, stress, or trauma, and a genetic vulnerability, which manifests in neurobiological and neuropsychological dysfunctions.

In 2017, Bandelow, B., S. Michaelis, and D. Wedekind combined most of the current studies to make some comprehensive treatments and categories of anxiety disorder. In a large European study, only 20.6% of participants with an anxiety disorder sought professional help. Of those participants who contacted health care services, 23.2% received no treatment at all, 19.6% received only psychological treatment, 30.8% received only drug treatment, and 26.5% were treated both with drugs and psychotherapy. Although, there are some licensed Pharmacological medicines, like selective serotonin reuptake inhibitors (SSRIs) and selective serotonin-norepinephrine reuptake inhibitors (SNRIs) to cope with anxiety disorders on DSM-5. However, these medicines always come with several adverse effects on

patients. Bandelow et al. listed all licensed drugs: Pregabalin, Tricyclic antidepressants, Buspirone, Benzodiazepines, and Moclobemide. Among those drugs that they have listed, Tricyclic antidepressants are a traditional antidepressant with a higher adverse event frequency than SSRIs and SNRIs, and it is usually used after SSRIs and SNRIs. Benzodiazepine is also widely used in the US. About 55% to 94% of patients with anxiety disorders are treated with 55% to 94% of patients with anxiety disorders. On the other hand, Benzodiazepine creates fatigue, dizziness, increased reaction time, impaired driving skills, and other adverse effects and impaired cognitive functions for anxiety disorder patients. Moreover, in a long-term study, dependency may occur in some patients. The resistance of most medicines commonly exists.

Bandelow and his colleagues performed some short-term studies that have been included in Bandelow, B., S. Michaelis, and D. Wedekind's paper for anxiety disorders and compared the pre-post effect size differences (before and after treatment) between medications and psychotherapies, which were based on 35.000 patients and the medications were associated with a significantly higher average pre-post effect size (Cohen's d=2.02) than psychotherapies (d=1.22; P<0.0001). Resulting in patients in psychotherapy have less illness than those recruited for medication trials. However, placebo groups also appeared some improvement, so Bandelow B and his colleagues suggested that placebo is also a way of psychotherapy [18]. Nevertheless, Bandelow, B., S. Michaelis, and D. Wedekind's paper collected other treatment options with some occasional improvement with different individuals, including exercise, hypnosis, autogenic training, and biofeedback or complementary medicine methods, but they are all lack basic methodological standards [19]. In the present day, doctors and scientists have found many treatments for anxiety disorder, but none of those that are effective have no adverse impacts on patients. researchers are still unfamiliar with the mechanism behind anxiety disorder. Even though Fluoxetine, SSRIs and SNRIs are commonly used effective medicines for anxiety disorder, researchers are still unfamiliar with the mechanism behind anxiety disorder, and those medicines also come with long-term non-effectiveness and adverse side-effects. For anxiety disorder, there is not a perfect solusion for it yet, but there is a chance to be improved by the combination of Pharmacotherapy and Phytotherapy.

5 Conclusion

Based on the above explanation, we can summarize the causes of anxiety disorders and some proven effective treatments.

The causes of anxiety disorders mainly include environmental factors and genetic factors. Environmental factors include the living environment, lifestyle and the influence of the environment on people of different genders, such as the intensity of noise, air quality, alcohol and so on. The gene level is related to the susceptibility genes of anxiety, these genes will reduce the brain's control level of anxiety through transcription, translation and other biochemical reactions, thus causing anxiety.

Nowadays, there are many ways to treat anxiety disorders, such as mindfulness meditation, MBSR, and medication such as fluoxetine, SSRIs and SNRIs.

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