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Pathogenetic and Therapeutic Insights of Depression

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Abstract: Depression has become one of the major diseases that endanger public health and safety. With the march of society, people have become more aware of the dangers of depression, and scientists have made extensive research on depression. Now scientists have put forward some hypotheses recognized widely by the academic world about the pathogenesis of depression, while the exact pathogenesis of depression remains to be studied. Although some clinical treatments for depression have been explored, effective therapies to completely cure depression haven't been found. This thesis mainly concludes the progress of previous research on the symptoms, pathogenesis, diagnosis and treatments of depression, and gives a detailed and full introduction of depression. I hope that this paper can provide a multi-faceted knowledge for people who want to understand and do research on depression, and give a reference to future research on depression.

Keywords: depression; pathogenesis; treatment; diagnosis

1. Introduction

Depression is an important disease prevailing in society. Statistics from the World Health Organization (WTO) show that more than 300 million people are now afflicted with depression. What's worse, depression can lead to suicide, and about 800,000 people die by suicide every day [1]. In the United States, depression exerts a large impact on 20% Americans [2]. However, effective therapy for the mechanism of depression is not very clear currently. Therefore, research on depression will enable people to have a knowledge of its essential pathogenesis, so as to find more science-based and efficient therapies.

Depression can manifest itself in various forms, mainly including persistent low mood, loneliness, trouble with thinking, pessimism and disappointment, etc. [3]. According to the previous research, the causes of depression can come down to the following: genetic factors, biological and chemical elements, and acquired factors, etc. The causes of depression vary from person to person. Therefore, different depressed patients should be treated in different ways. Currently, effective treatments for depression mainly include medication, psychological interventions and exercise therapy, among which medication has significant side effects. It may affect people's memory and cognition, and is generally used when patients are diagnosed with severe depression. While the psychological intervention features short effectiveness, a high risk of recurrence and different people respond differently to this treatment. Exercise therapy is an emerging and effective treatment and research have shown that exercises can stimulate the brain to release dopamine, so as to buffer negative emotions [4].

This paper mainly reviews and summarizes the research progress of the causes, symptoms, treatments of depression, aiming to give a reference to clinical treatment for and research on depression.

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2. Symptoms of Depression

The symptoms of depression are diverse and pose significant challenges to a patient's work and daily life. The symptoms can be single or multiple bouts and are generally categorized as the following: mood changes, slow thinking, declined volitional activities, cognitive impairment, and changes in somatic symptoms.

2.1. Mood Changes

The major manifestations of depression are prolonged low mood and the loss of pleasure. And the latter is defined as a loss of the ability to pursue, experience or learn happiness [5], mainly including the loss of anticipatory joy in decreased motivation to engage in activities, the loss of consumption joy in enjoying the pleasure of the activity itself, and the loss of decision joy of making optimal choices [5,6]. Some patients may also show pessimism, lowered self-evaluation and even feelings of helplessness and self-blame. Because they are pessimistic for a long time and it's hard to arouse their interest, everything seems boring to them. Therefore, depression can seriously affect the patient's normal life.

2.2. Slow Thinking

Depression is also shown in the form of slow thinking, retarded reactions and decreased associative ability, etc. Some patients with depression will obviously slow down their speech with deep voices when communicating with others, and they cannot communicate effectively. Besides, there is a noticeable decline in the time used to respond when they deal with work-related affairs.

2.3. Declined Volitional Activities

Depression also features decreased volitional activities, such as social avoidance, alienation from families and friends, refusal to have contact with others, hiding in corners by themselves, being completely bedridden, being numb and passive and having no desire for physical needs. While the most severe symptom is committing suicide, which makes depression a serious disease that significantly endangers human society. According to the statistics from the WHO, depression will become the second largest disease burden in the world by 2020, and the No.1 killer of human psychology in the 21st century [7]. Statistics demonstrate that 15% of the depressed patients worldwide will eventually choose to commit suicide, which costs the United States about $20 billion every year [8].

2.4. Cognitive Impairment

With the march of research on MDD (Major Depressive Disorder) in recent years, more and more people have come to realize that cognitive impairment plays a decisive role in the pathogenesis of MDD, and is a core primary symptom of MDD. The main symptoms of cognitive impairment include the inability to concentrate, worsening learning ability, declining memory, slow thinking, worsening reasoning and problem-solving skills, and poor abstract associative skills [9]. For students who spend considerable time in thinking and memorizing, MDD will prevent them from concentrating in classes, significantly decline their memory of knowledge points, and easily impair their abstract associative skills.

2.5. Changes in Somatic Symptoms

The effects of depression on somatic symptoms shouldn't be underestimated, which include tiredness, pain in body parts, insomnia, and loss of appetite. For example, in experiments on the rodent, when placed under constant pressure, rats showed not only flagging interest in sugar water (i.e. reduced appetite), but also a reduced kinetic performance in swimming tests [10]. The same holds true for people.

It is worth mentioning that we cannot diagnose whether patients suffer from depression by their symptoms alone because some diseases produce the same symptoms as depression. For example, patients with autism also show symptoms such as communication difficulties, social avoidance, alienation from families and friends, and pessimism. Diagnosing from symptoms alone can easily lead to the misdiagnosis, which not only cannot treat patients, but also may result in more severe conditions.

3. The Pathogenesis of Depression

The pathogenesis of depression is still unclear. No any experiment or research has shown that depression is caused by some single factor alone, or that there is only one pathogenesis of depression. In fact, multiple factors will lead to depression and the pathogenesis varies. After people's unremitting research on depression, scientists have come to a conclusion that the causes of depression mainly include genetic factors, the influence of neurotransmitter, psychological factors and immune changes induced by stress, etc.

3.1. Genetic Factors

Research has shown that genetic factors exert a significant impact on depression. It is reported that the incidence rate of depression for family members of depressed patients is about 15 times higher than those of normal family, and the closer the relationship is, the higher the risk of having depression is. Previous studies have found that the 5-HT2a receptor gene T102C polymorphisms A2 alleles are relatively dominant in depressed patients [11,12].

3.2. The Influence of Neurotransmitter

Neurotransmitters are also one of the major factors that cause depression. As the neuroscience has developed, researchers began to study the relationship between the glutamatergic and dopaminergic transmitter systems and depression. The clinical observations have shown that there is a different metabolism of glutamatergic between depressed patients and normal individuals [13]. For depressed patients with extremely severe symptoms, a single dose of subanesthetic IV can produce an instant anti-depression effect, which shows that the modulation of glutamatergic neurotransmitter system for the brain can produce a temporary anti-depression effect [14]. However, in experiments where rats are stimulated chronically to depression, it is found that there is a sharp decline in the transmission of dopaminergic synapses of rats, and a decrease of dopamine in areas such as prefrontal lobe, striatum, and hippocampus, etc. [15,16].

3.3. Psychological Factors

Depression is a kind of psychological disorder. And in many cases, some psychological factors, such as prolonged low mood, anxiety or outside pressure tend to cause depression. In scientific experiments on rodents, depression phenotypes were induced when rats were placed in a constant stressful environment, such as flagging interest in sucrose and anxiety-like symptoms; besides, there is a reduced kinetic performance in swimming tests the rats were forced to take [10].

3.4. Immune Changes

The human body will produce certain immune changes in response to different pressure, and these changes may be exactly one of the causes of depression. Such special immune changes are characterized by reduced number and activity of natural killer cells (NK) and T cells, and the release of pro-inflammatory cytokine (TNF-α, IL-1 and IL-6, etc.). Such stimulative response will lead to an increase in the release of CRH, and activate the sympathetic nervous system and the HPA axis, so as to stimulate the release of hormone like cortisol, suppress the normal immune responses and eventually lead to depression [4].

Apart from several factors mentioned above, during the clinical research on some severe depressed patients, with the help of functional magnetic resonance imaging (FMRI), researchers found that patients with traumatic stress disorder showed a smaller or declining hippocampus volume [4]. At the same time, some researchers have found a relationship between exercise antidepressant and the theory of central nervous system degeneration, that is, appropriate exercise can lead to hippocampal neurogenesis and cause a increase in neurotrophic factors, so as to resist against depression. Conversely, depression will occur when the hippocampal neurogenesis and neurotrophic factors are inhibited [17].

4. Diagnosis and Treatment

4.1. Diagnosis of Depression

There are mainly three following ways to diagnose depression.

4.1.1. Executive Function Evaluation

Executive function mainly refers to the cognitive neural mechanism through which individuals are allowed to combine and perform the coordinated operation of higher cognitive processing in a flexible and optimal manner when they need to meet or attain a certain goal. Due to extremely impaired executive function, the depressed patients have poorer performance in both the digit symbol sub-test and the trail making test reflected in the Wechsler Adult Intelligence Scale (WAIS) [9].

4.1.2. Attention and Work Memory Assessment

For depressed patients, they will experience a sharp decline in memory and concentration. Therefore, the diagnosis of depression can be made by taking Stroop Color-Word Association Test, cognitive disorder questionnaire and Wechsler Memory Scale [18].

4.1.3. Computerized Cognitive Assessment Instrument

The assessment of cognition of depressed patients requires a combination of patient subjective questionnaires and neuropsychological tests. The THINC-integrated to THINC-it is an efficient and sensitive computerized tool which is easy to use, and it includes a patient subjective questionnaire and four neuropsychological experiments. The efficiency of the THINC-it for depressed patients has been fully evidenced, and such a instrument is especially applicable to patients suffering from constant cognitive impairment [18].

4.2. Treatment

For patients with depression, we should first ensure their life safety and increase the cure rate; meanwhile we should pay attention to their psychological health, regularly provide psychological counseling for them to reduce the self-harm and suicide rates; and eventually, we can improve their life quality, restore their social abilities. In addition, close attention should be paid to depressed patients so that they can maintain a good living status and prevent the recurrence of depression. At present, there are multiple clinical treatments for depression, while some of them are still unclear or slow to work. The frequently-adopted treatments for depression nowadays include medication, physical therapy and psychotherapy.

4.2.1. Medication

The most widely adopted treatment for depression is medication, and the main clinically well-established drugs for depression at current stage include: monoamine oxidase inhibitor (MAOI), tricyclic antidepressant (TCA), tetracyclic antidepressant, selective serotonin reuptake inhibitor (SSRI: fluoxetine, sertraline, paroxetine, fluvoxamine, etc.), norepinephrine reuptake inhibitor (NRI), 5-HT/NE reuptake inhibitor (SNRI: EFFEXOR

XR), Noradrenergic and specific serotonergic antidepressant (NaSSA: mirtazapine), etc. [7].

4.2.2. Physical Therapy

Physical therapy for depression mainly includes electro convulsive therapy (ECT) and repetitive transcranial magnetic stimulation (rTMS), and deep brain stimulation (DBS) [18]. The ECT is used more frequently in the early stage, which treats patients by discharging the brain and leading to a temporary loss of consciousness. Due to its high effectiveness, ECT now is the most used physical therapy for depression. rTSM is used for the treatment in which a magnetic field of a certain intensity is applied to the brain through the skull, so as to produce induced currents and excite neurons to varying degrees. rTMS is mainly used in treatment for adults with severe depression. The DBS is an invasive therapy, which implants electrodes into the patient's brain when the patient is awake. The deep brain tissue is stimulated by the pulse generator to alleviate the patient's symptoms. Compared with the first two therapies, DBS produces fewer side effects and features strong recoverability, and causes less damage to the patient's brain.

4.2.3. Psychotherapy

Psychotherapy mainly includes cognitive therapy, behavioral therapy, interpersonal therapy, family therapy, supportive psychotherapy and some other therapies [7]. Currently, psychotherapy features short-lived effectiveness and is easy to recur, and it is generally used to treat depressed patients with mild symptoms or to supplement other therapies as adjuvant treatment.

5. Conclusion and Prospect

In the 21st century, depression remains a major problem for countless doctors and pathologists, and causes damage to hundreds of millions of people every day. This paper, concluding the latest research findings on depression which have been recognized by the mainstream society, gives a brief overview of the impact of depression on individuals and the entire society, and reviews the symptoms, pathogenesis, and treatments of depression known to the scientific world. It aims to contribute to future research on depression. Human beings have never ceased to do research on depression, as is evidenced by the "body-fluid balance theory" proposed by Hippocrates in ancient Greece, to the "genetic theory", "neurotransmitter theory" and "psychological theory" now accepted universally by the scientific community. As the modern neuroscience and psychology boom, a qualitative leap has been achieved in terms of theoretical knowledge, research methods and research instruments and equipment. Though a number of problems related to depression haven't been completely solved, progress has already been made. The future of research on depression is promising, and human beings haven't figured out the pathogenesis of depression, and it seems that the "neurotransmitter theory" is an important direction for future research on the pathogenesis of depression. At the same time, there is lack of both side-effect-free and effective treatments for depression. Physical therapies such as ECT, rTMS, DBS, etc. featuring little damage to the brain and strong curative effects, will become the priority of future research on depression treatment.

It is believed that, on the basis of previous studies, human beings can make further exploration in depression, identify the real pathogenesis of depression and find more effective methods to prevent and cure depression. It is hope that the depression will no longer be a perennial disease plaguing 300 million people, and people afflicted with depression can come out of the shadow of the disorder and move towards a brighter future.

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