

Cognitive deficits in depressive disorder

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Abstract. Depression is a globally prevalent mental disorder, often accompanied by various cognitive impairments. Cognitive impairment in depression is related to brain dysfunction, resulting from focal brain damage affecting cognitive functions. Its primary manifestations include memory loss, visual disturbances, hallucinations, executive function deficits, and difficulties in sustaining attention. Cognitive functions encompass perception, cognition, and interaction with the external environment, constituting complex brain processes. Presently, our understanding of cognitive impairment in depression remains somewhat limited, underscoring the importance of further in-depth research. Damage to specific brain regions such as the amygdala, hippocampus, and medial temporal lobe can result in cognitive deficits in severe depression patients. Interventions tailored to these lesions, such as computerized cognitive tasks and brain stimulation techniques, contribute to cognitive improvement in depression patients. Cognitive-behavioral therapy and relaxation techniques, including breath control, assist patients in reducing stress and negative emotions. Cognitive bias modification and creative art therapy promote both mental and physical well-being. Moreover, exposure to pleasant music and engaging in aerobic exercise facilitate the recovery of depression patients with cognitive impairments. Regarding pharmacological treatments, duloxetine, vortioxetine, liraglutide, intranasal insulin, and intracerebral insulin can be employed for intervention in cognitive impairment associated with depression.

Keywords: Depression, Cognitive Impairment, Cognitive Intervention, Mechanism.

1. Introduction

Depression is a highly typical mental disorder characterized by diminished interest in life, prolonged emotional low moods, and attention deficits lasting for more than two weeks. To date, approximately 350 million people worldwide suffer from depression [1]. Depression often accompanies high incidence rates and mortality rates. In 2016, severe depression caused economic losses of \$201.5 billion in the United States and \$32.3 billion in Canada. It is anticipated to become a leading cause of functional disability worldwide in the coming decades, posing a significant economic burden to society [1]. According to the World Health Organization's projections, severe depression is expected to become a primary contributor to the global disease burden by 2030 [2].

Depression, as a multidimensional mental disorder impacting human psychology and cognition, notably affects cognitive functions. Consequently, it is included in the International Classification of Diseases-10 and the Diagnostic and Statistical Manual of Mental Disorders-5 [1]. Furthermore, cognitive impairment is recognized as a core diagnostic criterion for severe depression within the

research community. Despite alleviating depressive symptoms in patients, the cognitive deficits resulting from depression remain inadequately addressed. These persistent cognitive impairments stemming from severe depression hinder complete patient recovery and worsen with increased recurrence rates [2]. Hence, further understanding of cognitive impairment is imperative. Cognitive impairment is characterized by the disruption of cognitive functions due to focal brain lesions, which can lead to impairments in memory, vision, language, among others, either singly or in combination. Presently, our understanding of cognitive impairment is relatively limited, and there exists a substantial demand for research in this domain [3]. The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders mentions impairments in attention, memory, and executive functions as determinants of whether an individual meets the criteria for cognitive impairment in severe depression [2]. Cognitive functions are widely regarded as the most intricate functions within the brain, primarily responsible for perception, cognition, and interaction with the external environment [3]. The operation of attention, memory, and executive functions differs, as these cognitive phenomena are interconnected yet separable, often with neurobiological foundations [2]. Data indicate that approximately 85-90% of the time during depressive episodes, patients with severe depression experience cognitive issues, and during remission, approximately 39-44% of the time. Notably, around 20-30% of patients exhibit significant cognitive deficits. Furthermore, the more frequent the episodes of severe depression, the more pronounced the decline in cognitive abilities, as demonstrated by several studies. One study found that declarative memory decreases by approximately 2-3% with each depressive episode in patients. Additionally, research suggests that prolonged depressive episodes in patients with severe depression lead to hippocampal dysfunction and bilateral hippocampal volume reduction, resulting in memory impairments [4]. This study aims to conduct a more in-depth examination of the presentation, mechanisms, and interventions for cognitive impairment in depression.

2. Cognitive impairment in depression

Cognitive impairment in depression is closely related to the brain. In 1861, Paul Broca provided the first empirical evidence linking cognitive functions to specific regions within the brain's cortex [5]. According to literature, the severity, duration, and frequency of depressive episodes affect the functions of the prefrontal cortex, the amygdala, and the hippocampus within the brain. These, in turn, influence cognitive functions such as working memory, executive function, and contextual responses. The reduction in hippocampal volume is closely associated with the frequency of severe depression episodes. Bilateral hippocampal volume reduction typically occurs in patients with severe depression. Research suggests that as the number of depressive episodes increases in these patients, their memory functions decline [2].

Cognitive impairment in patients with severe depression is linked to damage to their working memory. After damage to the working memory of patients with severe depression, some negative information is retained, stored in long-term memory, and has lasting effects. A study conducted at the University of Bergen's Neuropsychology Clinic involved patients with severe depression who underwent encoding working memory intervention for the initial two weeks. Following the intervention, they received approximately three weeks of treatment. Throughout this period, these patients interacted with researchers on a weekly basis and received feedback. Subsequently, they underwent a battery of objective neuropsychological tests and self-report measurements both during the intervention and at the conclusion of treatment, with an average completion time of approximately five weeks. During this time, these patients were subjected to standard tests, including working memory, which was assessed based on the number of mistakes made; the more mistakes, the lower the inhibitory capacity. California Verbal Learning Test and the D-KEFS Tower Test evaluated participants' language long-term memory and planning abilities, respectively. Besides memory-related tests, participants' intelligence and processing speed were assessed using the Wechsler Abbreviated Scale of Intelligence and the D-KEFS Color-Word Interference Test, respectively. Lastly, they completed self-reports concerning self-awareness and reflection. Through a series of data statistics and analyses, researchers concluded that patients who

participated in encoding working memory training showed significant improvement in their memory functions [6].

In addition to memory, the vision of patients with severe depression can also be affected due to damage to the hippocampus and medial temporal lobe. A prior study involving patients with medial temporal lobe (MTL) damage was tasked with scene recognition tests. These patients were required to observe and identify distorted scenes and determine which one closely resembled the endpoint scene on the screen. Results indicated that compared to patients with focal hippocampal lesions, those with medial temporal lobe damage exhibited cognitive deficits in more areas. Furthermore, the hippocampus is involved in scene construction. In an experiment, participants were asked to vividly imagine a more elaborate scene based on a given scene prompt. Results from this experiment demonstrated that patients with hippocampal damage lacked a sense of immersive perception of imagery. Another experiment required participants to identify which one of four given scenes did not belong with the others. This study revealed that patients with focal hippocampal damage had impairments in scene recognition, although not as severe as expected. Additionally, within the realm of visual science, an emerging area of study focuses on how eye movements unfold. Memory is also influenced by the role of the hippocampus in eye movements [7]. In another piece of literature, researchers determined that during depressive episodes, patients with severe depression exhibited normal retinal processing but altered cortical processing of visual contrast, based on brightness sensitivity tests and visual contrast suppression tests conducted on the patients' retinas [8].

Apart from memory and vision, patients with severe depression also experience anomalies in other aspects. Hallucinations may occur, wherein they may see images that cry or laugh, or even move. In their eyes, the size and shape of the surrounding environment may change. At times, patients may struggle to distinguish between left and right. Furthermore, in their view, the environment can rapidly shift like a movie scene, or the night may seem exceptionally prolonged. Patients often experience fear, loss of self-confidence, loss of desire, and even self-implosion [9]. Patients with severe depression also face difficulties in executing tasks and problem-solving, termed as executive function deficits. Additionally, they typically struggle to maintain attention while reading or watching television. Research indicates that attention deficits are associated with depression, whether in acute or remission phases. Initial depression patients do not exhibit attention deficits when processing information, whereas recurrent depression patients often experience attention deficits during information processing. In the realm of processing speed, patients with depression require more time to process information. Generally, initial patients show normal processing speed during remission, whereas recurrent patients typically experience a slowdown [10].

3. Intervention methods

Cognitive impairment has been identified as a primary mediator of health outcomes in severe depression. Furthermore, cognitive impairment is associated with the overall social and psychological functioning of patients with severe depression. A previous meta-analysis indicated that the deterioration of function and metabolism is related to a decline in cognitive function. According to research from the International Mood Disorders Collaborative Project conducted jointly by the University of Toronto and the Cleveland Clinic, cognitive function in patients with severe depression is more influential than the severity of depression in determining overall work function. Computerized cognitive tasks can improve cognitive function, with reports suggesting that mental arithmetic is beneficial for improving the intelligence quotient of patients with severe depression. Siegle et al. reported that rhythm serial addition tests can alleviate depressive symptoms and enhance cognitive skills in patients, although the specific effects of this therapy on patients remain unclear. Studies have shown that brain stimulation techniques such as repetitive transcranial magnetic stimulation can improve cognitive function in the depression population. Cognitive remediation therapy has a positive effect on treating cognitive function impairment in severe depression, primarily by enhancing learning and cognition. In this therapy, patients are required to complete computerized tasks to stimulate brain nerves. Currently, cognitive activation in cognitive remediation therapy is used in clinical treatment. Aerobic exercise can help patients improve cognition,

so an alternative treatment approach is to combine aerobic exercise with resistance training. According to a study by Stanton and Reaburn, after nine weeks of moderate aerobic exercise, patients exhibited significant improvements in depression symptoms and cognitive function [2].

Through an experiment conducted at the First Affiliated Hospital of Bengbu Medical College in Anhui Province, it was found that cognitive-behavioral therapy can effectively improve the psychological health of patients with depression, alleviate insomnia symptoms, and reduce stress and anxiety. Therefore, adopting cognitive-behavioral therapy for severe depression patients with cognitive impairment can greatly enhance their quality of life. Additionally, relaxation breathing training can reduce patients' negative emotions. Furthermore, interventions for cognitive impairment in depression can also include listening to pleasant music and engaging in communication with family members [11]. Another method is cognitive bias modification, which requires the assistance of computer intervention programs. Patients need to modify information processing through repeated practice to achieve cognitive improvement [12]. Creative art therapy can effectively improve the physical and mental health of patients, offering a non-pharmacological treatment method. Through this approach, patients can alleviate depression, reduce stress and fatigue, and strengthen the immune system, all while achieving relaxation [13].

The symptoms of depression and cognitive deficits in patients can also be improved through medication. Currently, several drugs are used for treatment. For instance, sertraline can improve psychomotor function, and aniracetam can help improve memory. Here, we focus on two drugs: duloxetine and vortioxetine. Duloxetine is produced by the reuptake of serotonin and norepinephrine and can improve patients' memory and language functions. Vortioxetine is similar to duloxetine, and both can improve depression and cognition. Compared to duloxetine, vortioxetine has a broader impact on memory and shows more significant improvements in other cognitive functions. Currently, the FDA has approved vortioxetine as the only antidepressant [2].

Cognitive function can also be improved through insulin promotion, which is a metabolic hormone involved in regulation. According to research findings, depression and cognitive impairment can also be improved by using 1.8 mg of liraglutide, an exogenous glucagon-like peptide-1 receptor agonist that has been FDA-approved for treating diabetes. Additionally, intranasal insulin and cerebral insulin are beneficial for the cognition of patients with severe depression. For patients with severe depression accompanied by diabetes, intranasal insulin can better improve their cognition. Numerous insulin receptors related to cognition are distributed in the brain, and insulin plays a significant role in brain nerve growth and other aspects. Therefore, the use of cerebral insulin can effectively treat cognitive impairment in patients with severe depression [2].

4. Conclusion

This article primarily investigated the manifestations, mechanisms, and intervention methods for cognitive impairment in depression. Through an extensive review of literature, it can be concluded that the main manifestations of cognitive impairment in depression include a decline in memory function, visual impairment [3], hallucinations, executive function deficits, and attention deficits. The onset of these cognitive impairments is related to the brain, with a decrease in hippocampal volume and damage in the brain leading to defects in memory and visual functions [2]. Additionally, damage to the medial temporal lobe can also lead to visual impairments in patients with severe depression, and compared to patients with focal hippocampal lesions, those with medial temporal lobe damage experience more extensive cognitive impairments [7].

There are corresponding intervention methods for addressing cognitive impairment in depression. These studies indicate that computerized tasks like mental arithmetic are beneficial for the cognition of patients with severe depression. According to research by Siegle et al., cognitive interventions can be conducted through rhythmic serial addition tests. Furthermore, brain stimulation techniques like cognitive remediation therapy can also improve the cognitive function of the depression population. Stanton and Reaburn's research suggests that aerobic exercise plays an important role in improving cognitive impairment in patients with depression [2]. Patients can also benefit from cognitive-behavioral

therapy and relaxation breathing training to improve both depression and cognition [11]. Creative art therapy is an innovative treatment method, providing a non-pharmacological approach to effectively intervene in the cognitive impairment of depression patients [13]. In terms of pharmacological interventions, both duloxetine and vortioxetine have been shown to help improve cognition. Among them, vortioxetine has a broader impact on memory function and is the only antidepressant approved by the FDA. Liraglutide, an FDA-approved drug for diabetes treatment, has also been found to be effective in addressing cognitive impairment in depression. Additionally, intranasal insulin and cerebral insulin play important roles in intervening in the cognitive impairment of patients with severe depression [2].

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