

The Effect of Mediterranean Diet on Depression

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Abstract. In recent years, the relationship between Mediterranean diet (MD) and mental health has attracted much attention as a healthy diet model. This paper systematically explores the potential impact of MD on depression and its mechanism of action. The current research focuses on the various biologically active ingredients of the MD and the connection between their nutritional components and physical health. The impact of its food combination on the risk of chronic diseases such as cardiovascular disease (CVD) was analyzed. However, existing studies have focused on observational analysis, and the evidence on the association of MD and depression is still insufficient. This paper analyzes the potential impact of MD on depression and its mechanism of action, and draws the results: MD may provide innovative nutritional intervention strategies for depression prevention and treatment through triple pathways of anti-inflammatory, neuroprotection and metabolic regulation. However, existing studies still have limitations such as sample heterogeneity, subjectivity of dietary compliance measurements, and insufficient evidence for the effect of long-term interventions. Future research can focus on combining multiomics technology and precise nutrition strategies to deeply analyze the interaction mechanisms of diet, microorganisms, and brain axis to provide a more solid scientific basis for dietary intervention in depression.

Keywords: Mediterranean diet, depression, dietary intervention.

1. Introduction

Depression is a common mental health problem with various symptoms and can be manifested in many aspects such as emotions, cognition, behavior and body. It not only affects the patient's emotional state, but also has a profound impact on the patient's daily life, interpersonal relationships, physical health, etc. Depression is one of the main causes of disability worldwide. The recurrence rate of first-stage depression within one year was 30%, and the recurrence rate increased significantly after multiple attacks. The cost of treating depression is high, and it is affected by factors such as the condition, treatment method, region, and treatment cycle. About 3.8% of the world's population suffers from depression, and about 577 million people are affected each year. In recent years, the incidence of depression has been on the rise, especially in developing countries and urbanization [1].

Current status with the deepening of medical research and the advancement of science and technology, significant progress has been made in the treatment methods and technologies of depression. Although the treatment methods are diverse, the coverage of treatment for depression worldwide is still relatively low. Many patients fail to receive timely treatment due to financial conditions, insufficient medical resources or insufficient awareness of depression. In addition, the treatment effect is limited, and the side effects are more common, so some patients cannot take medication for a long time. In addition, long-term use may lead to drug resistance problems.

The Mediterranean diet (MD) is a healthy diet based on traditional dietary patterns. It is not only famous for its deliciousness, but also widely studied and respected for its multiple benefits to health. A randomized controlled trial (RCT) showed that a MD reduced the risk of CVD by 30% [2]. However, there are still relatively few studies on the relationship between MD and depression.

Therefore, this article aims to explore the characteristics and main nutritional components of the MD, analyze its potential impact mechanism on depression, and review relevant clinical studies to provide a scientific basis for dietary intervention in depression.

2. Mechanism of Action of Depression

Regarding the mechanism of action of depression, existing research mainly involves multi-dimensional factors such as neurotransmitters, neuroendocrine and immune inflammation.

2.1. Neurotransmitter

Studies have shown that functional defects of monoamine transmitters lead to emotional, cognitive and motivational disorders, manifested as reduced serotonin synthesis, abnormal receptors and inhibition of norepinephrine release; hyperglutamatergic in amino acid transmitter systems triggers neuronal toxicity, while insufficient inhibition of γ -aminobutyric acid aggravates emotional imbalance; neuroendocrine disorders with impaired neurotrophic factor signal and hyperactivation of hypothalamic-pituitary-adrenal axis are intertwined through mechanisms such as synaptic plasticity changes, metabolic pathway shifts and blood-brain barrier destruction, and together constitute the biological basis of depression symptoms [3]. Food quality can regulate neurotransmitters. Unhealthy diets, such as high-fat and high-sugar diets, may disrupt the balance of neurotransmitters and lead to emotional and behavioral problems. On the contrary, a balanced diet helps improve the function of neurotransmitters [4]. Therefore, through reasonable dietary structure adjustment, we can effectively promote the balance of neurotransmitters, thereby improving mental health and behavioral performance.

2.2. Neuroinflammatory

Studies have shown that neuroinflammation is closely related to depression and has an impact on symptoms through multiple pathways. Inflammation may shift tryptophan metabolism to the kynurenine pathway by activating tryptophan dioxygenase, leading to a reduction in serotonin and accumulation of excitatory neurotoxic metabolites, forming a "neuroinflammatory-kynurenine-depression" cascade. There is a complex connection between neurogenesis and depression, and there are two pathways of action. The direct pathway is that proinflammatory factors directly inhibit hippocampal neurogenesis, leading to depressive behavior. The synergistic pathway is that reduction of neurogenesis needs to be combined with activation of the kynurenine pathway and abnormal hypothalamic-pituitary-adrenal axis to induce depression [5]. There is a wealth of evidence that dietary restrictions can alleviate age-related neuroinflammation [6]. Therefore, by choosing anti-inflammatory foods, maintaining a balanced diet, controlling weight, and avoiding bad foods, it can effectively reduce neuroinflammation and thus maintain the health of the nervous system.

3. Characteristics and Nutritional Content of MD

The MD originates from the traditional dietary model of Mediterranean coast countries, including major food categories such as olive oil, nuts and seeds, fruits and vegetables, whole grains, fish and red wine.

Its core feature is emphasizing the balance between plant-based foods and healthy fats. Specifically, it is manifested as a large intake of whole grains, beans, nuts and seasonal fruits and vegetables, using olive oil as the main source of fat to achieve a high proportion of unsaturated fatty acids; animal protein selection follows the "stage" intake principle - fish and poultry are given priority, eggs are appropriate, and red meat is strictly restricted; dairy products are mainly fermented, and cheese and yogurt are eaten daily to supplement calcium; fresh fruits are used instead of delicate desserts after meals, and natural sweeteners such as honey are consumed only in special occasions. This dietary model achieves the dual goals of nutritional balance and chronic disease prevention through scientific proportioning.

4. The Potential Mechanism of the Impact of MD on Depression

The MD may affect the occurrence and development of depression through a variety of mechanisms. First, its rich nutrients can regulate the synthesis and function of neurotransmitters. It has significant anti-inflammatory effects.

4.1. Omega-3 Fatty Acids

Studies have shown that Omega-3 fatty acids have anti-inflammatory effects and can fight inflammation and autoimmune diseases. They are crucial to the function of the cell membrane and the normal function of the central nervous system. They are involved in various important physiological processes of nerve cells and maintain homeostasis [7]. The balance between Omega-3 and Omega-6 fatty acids needs to be maintained in the diet, which is of critical significance to prevent central nervous system diseases. Adjusting the diet is the main way to achieve the above-mentioned health benefits, rather than relying on drugs or other interventions.

4.2. Polyphenols

Studies have found that higher polyphenol intake is significantly related to the reduced risk of depression. Studies have confirmed that specific polyphenols such as soy isoflavones, cocoa flavanol, and curcumin have therapeutic effects on alleviating depression symptoms. The protective mechanism of polyphenols for mental health may form a dual pathway of anti-inflammatory and neuroprotection by inhibiting the release of proinflammatory factors, scavenging free radicals and enhancing antioxidant activity. In particular, isoflavones may improve depression in menopause women through phytoestrogenic effects. Isoflavones can regulate the violent fluctuations of ovarian hormones during menopause and improve the symptoms of depression related to hormone imbalance through phytoestrogen effects. Specifically, isoflavones simulate endogenous estrogen activity by binding to estrogen receptors, thereby alleviating mood disorders caused by sudden drop in hormone levels [8].

Related studies have shown that the anti-inflammatory effect of the MD stems from its dietary structure with extra virgin olive oil as the core and rich in natural anti-inflammatory ingredients. Among them, monounsaturated fatty acids in olive oil reduce inflammatory responses by regulating lipid metabolism, while polyphenols reduce the production of proinflammatory factors by inhibiting signaling pathways such as NF- κ B [9].

4.3. Dietary Fiber

Related studies have shown that seaweed and mushrooms are important sources of fiber for diet, and their intake is significantly negatively correlated with the severity of depression symptoms, among which seaweed fiber is directly related to the reduction in the diagnosis rate of clinical depression. Its antidepressant mechanism may involve many levels. First, dietary fiber can promote the metabolism of intestinal flora. Seaweed polysaccharides are decomposed by the bacteria into short-chain fatty acids, which affect brain function by regulating histone acetylation, G protein signaling and immune balance; mushroom fiber promotes the proliferation of beneficial bacteria and inhibits pathogens. Secondly, dietary fiber has a protective effect on the nerves. Seaweed phenolic compounds have antioxidant and anti-inflammatory activities and may exert neuroprotective effects through inhibiting A β protein aggregation and other ways. On the other hand, fiber deficiency may trigger depletion of the intestinal mucus layer, leading to aggravation of systemic inflammation, while adequate intake can maintain immune homeostasis and reduce pro-inflammatory cytokine levels. It is worth mentioning that dietary fiber can intervene in serotonin metabolism, and the bacterial population affects serotonin synthesis by regulating tryptophan metabolism. This pathway is a key target of antidepressants [10].

4.4. Protein

Protein is significantly negatively correlated with depression symptoms, and the effects of specific protein sources have differential amino acid metabolism effects, such as milk and dairy intake negatively correlated with depression risk. The mechanism of action may be the effect of amino acid metabolism on it. For example, the conversion of tryptophan into serotonin can regulate mood. The conversion of tyrosine to dopamine can affect motivation and pleasure. Small molecule peptides may regulate monoamine metabolism. In addition, dairy products may have special effects, such as α -whey protein in milk is a major source of tryptophan and may reduce the risk of depression by improving cognitive function under stress [11].

In addition, the MD has a dual regulatory effect on improving symptoms in patients with depression. Studies have shown that patients increase their daily intake of fruits, nuts and vegetables, among which the risk of depression in deep-sea fish decreases by 12% for every 20g/day. Whole grains and legumes affect serotonin secretion by regulating intestinal flora [12]; on the other hand, controlling red meat processed products and excessive alcohol intake can reduce the risk of depressed diseases.

5. Clinical Study on the Relationship Between MD and Depression

In recent years, several observational studies and clinical trials have explored the relationship between MD and depression. A prospective cohort study of 15,000 adults without depression for 10 years followed up on 15,000 baseline adults without depression and assessed MD adherence screening scoring system (MEDAS score), a tool used to assess individual adherence to MD patterns. The high adherence group (≥ 10 points) was found to have a 33% lower risk of depression compared with the low adherence group (≤ 5 points), and a 18% lower risk for every 3 points, especially in women and people aged ≥ 50 years [13]. Despite observational studies of residual confounding, dietary self-report bias and geographical restrictions, the results still support the MD as a mental health intervention strategy, and its components such as polyphenols and dietary fiber may reduce the risk of depression through multiple pathways. Another longitudinal study analyzed the degree of depression in patients through the most widely used questionnaire (PHO-9) to evaluate depression in pharmacological and psychological studies, and quickly and effectively assessed the effect of MD on depressive symptoms in combination with MEDAS scores. Studies have shown that people who strictly followed the MD showed better mental health status in the assessment of PHQ-9 depression symptoms, with an average score of 4.01 points (standard deviation 4.56), significantly lower than the 4.68 points (standard deviation 5.09) in the non-strictly followed group, and statistically significant differences [14]. This result suggests that the MD model may have a positive intervention effect on depressive symptoms by regulating inflammatory response, improving intestinal flora or promoting neuroprotection mechanisms. However, the current research still faces certain limitations. First, most studies use observational designs, which to some extent limits the confirmation of causality. Second, due to the diversity of dietary assessment methods, the conclusions of these studies may differ, which in turn affects the accuracy of the results. In addition, factors such as individual genetic background and living habits may also have an impact on the relationship between diet and depression. Therefore, in order to gain a deeper understanding of the prevention and treatment effects of MD on depression and its potential mechanism of action, more large-scale, long-term and rigorously designed RCTs are needed.

6. Conclusion

This study systematically explores the potential impact of MD on depression and its mechanism of action, revealing the important value of dietary intervention in the field of mental health. Comprehensive evidence shows that the MD has a protective effect on depression through multi-dimensional biological pathways, and its core mechanisms involve neurotransmitter regulation, anti-

inflammatory effects, neuroprotection and intestinal-brain axis function optimization. Specifically, the rich Omega-3 fatty acids, polyphenols, dietary fiber and high-quality proteins in this dietary model work together to synergize neurotransmitter synthesis, inflammatory factor inhibition and intestinal flora balance, forming a multi-target intervention network. At the same time, clinical studies further support this association. However, there are still some limitations in the current study: First, most of the evidence comes from observational studies, and it is difficult to rule out the interference of confounding factors on causality. Secondly, insufficient standardization of dietary assessment methods may affect the comparability of results. In addition, individual genetic differences may regulate the effect of dietary interventions, but relevant research is still blank. Later studies can verify their efficacy through double-blind RCTs, and combine metabolomics and microbiomics techniques to analyze the molecular mechanisms of diet-host interaction. In addition, personalized dietary plans designed for different groups of people may become the key to improving the accuracy of intervention.

From a public health perspective, promoting MD has significant cost-effective advantages. Compared with traditional drug treatment, the risk of side effects of dietary intervention is lower, and it can achieve wide coverage through community nutrition education. It is recommended to include dietary assessment in the clinical management process of depression and to develop improved MD guidelines based on regional ingredients. It is worth noting that dietary interventions need to form a synergy with psychotherapy and drug therapy, rather than a single alternative. In summary, this study provides theoretical basis and practical direction for dietary intervention in depression. With the rapid development of the field of nutritional psychiatry, MD is expected to become an important part of the mental health promotion system. Its concept of "food-based medicine" not only expands the treatment path for depression, but also provides interdisciplinary inspiration for chronic disease prevention and control. Follow-up studies should focus on establishing a dose-effect relationship model and explore differentiated application strategies of dietary intervention in depression prevention, treatment and recurrence control.

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