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Effects of Different Dietary Patterns on Alzheimer's Disease

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Abstract: Alzheimer's disease (AD) is a neurodegenerative disease commonly known as dementia, and its prevalence is increasing with age. The prevalence of AD is increasing year by year, and with age, the symptoms of brain atrophy in AD patients seriously affect their ability to take care of themselves, and the high level of difficulty in treating AD poses a great economic burden to the global healthcare system. Currently, drug therapy, such as β-amyloid (Aβ) targeting and Tau protein targeting, is the mainstay of clinical practice. However, the limitation is that drug therapy cannot influence the course of the disease and is expensive. Therefore, more and more doctors and patients pay more attention to the prevention of AD such as dietary pattern changes. This study found that dietary changes can not only effectively prevent the occurrence of AD, but also have a certain auxiliary effect on the treatment of AD. Its mode of action includes inhibiting inflammatory pathways, reducing the production of Aβ, or enhancing the antioxidant capacity of cells. It is believed that improved dietary patterns, which are safe, inexpensive, and have fewer side effects, will be used more often in clinical treatments and public prevention of AD, helping more people to get rid of the distress and fear of AD.

Keywords: Alzheimer's disease, Neurodegenerative disease, Dietary patterns, Mediterranean diet.

1. Introduction

Alzheimer's disease (AD) is a type of progressive neurodegenerative disorders that account for 60-80% of all dementia diseases [1]. The prevalence rate increases with age and has shown a continuous upward trend in recent years in all population groups [2]. Clinically, patients with mild symptoms present with memory loss and insomnia. Severe cases are characterized by loss of self-care, deterioration of speech and motor skills [1,2], and eventual death due to complications. The high prevalence of the disease and the difficulty of treating put a serious burden on patients and their families and also, on global healthcare system.

In view of the pathogenesis of AD, most clinical treatments at present are based on the use of medication, which is not ideal for the condition of massive neuronal death. Therefore, in order to keep more healthy people away from the risk of the disease, and to supplement clinical patients' medications to avoid rapidly increasing of the disease, scientific diet is getting more and more attention as an effective treatment for AD [3].

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There have a large number of epidemiologic and intervention studies that have already found that many patients' cognitive decline are relieved in different degrees because of different dietary patterns [3]. behavior of scientific diet can achieve effective target-specific control of AD-related pathways. However, the limitation is that the specific implementation of dietary patterns varies greatly among different physical conditions. Patients' adherence to long-term adherence is poor. In order to achieve a good therapeutic effect, a high degree of self-awareness is necessary

This article will let you know how different dietary approaches will work and be effective for people with AD, with the aim of exploring the current progress of research on dietary modulation of AD and helping those in need to prevent AD before it occurs. The aim is to explore the progress of current research on dietary modification of AD and help people in need to prevent AD before it occurs.

2. Characteristics and mechanisms of AD

2.1. Symptoms of AD

AD is a disease of cognitive decline that occurs most often in the older population, with 10.8% of people over the age of 65 in the U.S., and the prevalence continues to rise [4]. In Asian countries, for example in China, with the development of aging, the prevalence is increasing more obviously [5]. The continued rise in AD prevalence places a heavy economic burden on society, with healthcare costs for treating people with AD in the United States projected to reach $600 billion by 2050 [6]. Clinically, patients present with memory loss, impaired language skills, reduced discrimination, and tendencies such as depression and anxiety [2]. Eventually, they lose normal mobility and self-care ability [1] and die from complications caused by AD such as cardiovascular and respiratory diseases. Diagnostic modalities generally rely on clinical scales [7], which include a test about the patient's memory. Biological diagnostic modalities mainly include cerebrospinal fluid (CSF) testing [1], it is the gold standard for determining AD. In addition, there is the use of medical image to detect Aβ plaques, or neuronal fiber tangles to diagnose [1,8]. However, due to the high cost of testing, the advanced diagnostics is not sufficient to generalize to global applications, and cases of misdiagnosis still existing. The level of diagnosis is still highly limited.

Amyloid-β pathwayThis section must be in one column.

2.2. Amyloid-β pathway

β-secretase and γ-secretase cleave amyloid precursor protein to form Aβ [9]. Abnormal cleavage and overproduction of Aβ42 due to changes in γ-secretase specificity results in significant aggregation of Aβ to form protofibrils, leading to nerve damage [10]. Abnormal aggregation of Aβ forms Aβ plaque deposition, and Aβ binds to prominent adhesion molecules prompting calcium ion inward flow, causing cognitive impairment [9]. Deposited Aβ activates microglia, and gliosis induces pruning elimination of synapses, resulting in loss of neurons and synapses damage, ultimately causing cognitive impairment and memory decrease [9]. At this time, the cystatin F dimer of AD patients binds to Aβ, and the receptor that promotes Aβ input and output is abnormal [11]. Aβ not only aggregates but also cannot be cleared normally, and the brain is caught in a vicious cycle of Aβ deposition. Accelerated neuronal death.

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2.3. Tau protein hyper-phosphorylation pathway

Tau protein is phosphorylated and detached from microtubules by the kinase glycogen synthase kinase-3β (GSK-3β), and cell cycle protein-dependent kinase 5 (CDK5) [12], The phosphorylated Tau then forms oligomers that aggregate to form protofibrils, which in turn form paired-helix fibers (PHFs), which tangle to form intracellular neural protofibrillar tangles (NFTs), which lead to abnormal neuronal transport and ultimately cause synaptic loss and neuronal death [12]. At the same time hyperphosphorylation of Tau also leads to mitochondrial damage, damages synapses and induces neuroinflammation and gliosis.In the end, this causes or worsens AD [13]. Abnormal phosphorylation of specific sites in the brain tissue of AD patients is significantly associated with neuronal damage.

2.4. Metabolic dysfunction pathway

Metabolic disorders in AD patients are mainly an imbalance in the regulation of mitochondria, metabolic syndrome (Mets) and neuroinflammation. Mitochondrial dysfunction occurs in association with an impaired electron transport chain in AD patients, which induces the production of excess reactive oxygen species (ROS) [14]. ROS contribute to metabolic disturbances in three ways. The first is mitochondrial damage, ATP production is inhibited triggering apoptosis [13]. Secondly, ROS inhibit PP2A phosphatase and activate the kinase GSK-3β, which hyperphosphorylates Tau proteins to form NFTs [15]. Finally it also causes the accumulation of Aβ protein to form amyloid plaques. This ultimately aggravates the condition. It has been found that antioxidant transcription factor nuclear factor E2-related factor 2 (Nrf2) activity is reduced in AD patients, ROS also accumulate, and glial cell inflammatory response is promoted [16]. Regarding Mets, it is mainly manifested as abnormal lipid metabolism activating inflammatory signaling pathways and mitochondrial oxidative stress resulting in Aβ deposition and Tau phosphorylation, which affects the brain environment triggering AD [17].

3. Dietary patterns in the treatment of AD

3.1. Mediterranean Diet (MD)

3.1.1. Principles of the MD

A traditional dietary pattern originating from the Mediterranean region, based on monounsaturated fatty acids (MUFAs). Olive oil is the main source of fat, with a high proportion of vegetables, fruits, whole grains and nuts. This diet also recommends the consumption of fish rich in Omega-3 fatty acids and the consumption of red wine in moderation. Studies have shown that this dietary pattern is good for the brain. Vegetables, fruits and whole grains are rich in polyphenols, which significantly reduce the levels of inflammatory factors and inhibit inflammatory pathways [18].

3.1.2. MD and AD

Studies have already pointed to the neuroprotective effects of the MD pattern in slowing down the progression of AD through multiple targets. For example, MUFAs and omega-3 polyunsaturated fatty acids (EPA/DHA), which are provided by olive oil and deep-sea fish, significantly reduce the levels of pro-inflammatory factors, such as IL-6 and TNF-α, thereby inhibiting neuroinflammatory pathways [19]. Polyphenols in fruits and vegetables can also cross the blood-brain barrier to inhibit

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β-amyloid aggregation and help loose cognitive decline. A 3-year follow-up of 537 dementia-free older adults found that for every 1-point increase in MD adherence (on a 9-point scale), the risk of AD incidence was reduced by 23% (HR=0.77, 95% CI 0.61-0.98) [20]. The MD is equally effective in the prevention of AD.

3.2. Ketogenic Diet (KD)

3.2.1. Principles of the KD

The KD is an extremely low-carbohydrate and high-fat eating pattern that forces the body to produce ketone bodies to supply the body's needs due to the absence of available glucose. It is mainly characterized by restricting carbohydrate and protein intake, allowing the body to consume large amounts of fat from natural foods such as olive oil and coconut oil, which make up 60-70% of the total calories. Low carbohydrates reduce the expression of beta-secretase, resulting in a decrease in Aβ. The production of ketone bodies can promote the efficiency of ATP synthesis by mitochondria to some extent thus stabilizing the synapse. And KD diet can also inhibit microglia activation and reduce the production of inflammatory factors [21]. These are the advantages of the KD model. Since the KD has to be controlled for calorie and carbohydrate intake, it can also cause some degree of damage to the human body and is less maneuverable. Generally this dietary pattern is used for the treatment of high body weight population.

3.2.2. KD and AD

Since AD patients have impaired glucose metabolism, the KD enables AD patients to produce ketone body-supplied energy metabolism to replace the original glucose, which creates a new pathway of metabolism for AD patients. The KD diet effectively reduces the activity of GSK-3β and inhibits the phosphorylation of Tau, and the study found that serum β-hydroxybutyrate levels were significantly increased in AD patients, effectively improving synaptic transmission and providing new energy for neuronal metabolism. levels were significantly elevated, effectively improving synaptic transmission and providing new energy for neuronal metabolism [21]. A four-month KD diet was found to reduce Aβ deposition and microglia increase in APP/PS1 mice, inhibit tau protein hyperphosphorylation, significantly reduce the expression of pro-inflammatory factors such as IL-1β and TNF-α in the hippocampus, and alleviate neuroinflammation [22]. Although the KD protects synapses to a certain extent, the exact mechanism is not fully understood and the limitation of poor experimental adherence occurs in the clinical setting. Therefore, more experimental data are needed to prove the specific effects and safety of KD on AD.

3.3. DASH diet

3.3.1. Principles of the DASH diet

Emphasize the daily diet should low in sodium and high in potassium, with a reduced intake of processed foods, red meat, and additives, and an increased intake of potassium through a high consumption of vegetables, fruits, and grains. Vegetable oils are recommended for large intake, and high quality protein such as fish and poultry should be consumed as much as possible for protein intake. It is possible to reduce high blood pressure and the risk of developing cardiovascular disease. Dietary flavonoids can inhibit inflammatory pathways to protect neurons and reduce microglial

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activation [23]. Antioxidants such as omega-3 and vitamin E can reduce the inflammatory response and Aβ deposition to some extent.

3.3.2. DASH diet and AD

A study of non-AD patients found that individuals with low DASH dietary adherence had significantly lower relative alpha power in the Default Mode Network (DMN) region (OR=3.22, 95% CI 1.08-9.59) [24], and DMN abnormality is one of the early pathological hallmarks of AD. It suggests that DASH may delay cognitive decline in patients by maintaining normal DMN. A cohort study found that for every 1-point increase in DASH dietary adherence, the risk of AD was reduced by approximately 7% [25]. DASH is also involved in antioxidant and anti-inflammatory pathways to protect the brain. However, the current role of DASH is still at the level of AD prevention, and for AD prevention, MIND is more advantageous and has more significant efficacy.

3.4. MIND diet

3.4.1. Principles of the MIND diet

The diet is a fusion of both the MD and the DASH eating pattern. The diet emphasizes one serving of vegetables per day and five servings of nuts and two servings of berries per week. Try to avoid red meat, processed foods, etc. in your daily diet.Similar to the DASH diet, its composition includes a large number of antioxidant foods such as berries and vegetables whose carotenoids, among others, can reduce levels of pro-inflammatory factors and improve neuroinflammation. Similar to the MD, omega-3 fatty acids in fish have an inhibitory effect on Tau phosphorylation [19,20].MIND can be used in the prevention and treatment of cognitive disorders and has been shown to be effective in the protection of brain health.

3.4.2. MIND diet and AD

The anti-inflammatory and antioxidant properties of antioxidant-rich foods in the MIND diet helped to reduce β-amyloid deposition and hyperphosphorylation of tau proteins in the brain, which delayed cognitive decline. For example, anthocyanins in berries can enhance cellular antioxidant capacity to reduce Aβ-induced oxidative damage by activating the Nrf2/ARE pathway and up-regulating glutathione peroxidase (GPx) and superoxide dismutase (SOD) expression [26]. Polyphenols (e.g. hydroxytyrosol) in olive oil inhibit β-secretase activity, reduce Aβ production, and promote Aβ clearance by microglia [26]. After controlling for other variables, both adherence and moderate adherence showed a 53% and 35% reduction in the risk of developing AD within the older age group, in sequence [25]. It combines the advantages of MD and DASH's effects on AD with notable preventive and protective effects against AD.

4. Conclusion

In summary, the different dietary patterns characterized and such as the four types of dietary patterns to protect the brain have been clarified. It is not necessary to follow any one dietary pattern in order to prevent AD. Since there are commonalities in all four dietary patterns, you can judge how to make adjustments according to your own health condition and needs.

The above four dietary patterns can reduce the risk of AD to different degrees. In addition, the use of medication during the treatment phase can effectively inhibit the expression of pro-

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inflammatory factors and improve the brain environment, thereby slowing down cognitive decline. Compared with medication, dietary modification is safer and more economical, and can improve cognition while preventing and controlling cardiovascular disease and diabetes. Provides new ideas for the prevention and combined treatment of AD.

It is important to note that for patients with advanced AD, changing dietary patterns will not provide relief or treatment for the patient's condition. As long as the disease is present, then the possibility of treatment in any disease state cannot be pinned on dietary patterns. Dietary modifications have a limited role in the treatment of AD patients and in the prevention of the disease in high-risk individuals, and not all patients are physically capable of practicing dietary patterns. To achieve real delay and prevention of the disease, a combination of exercise and medication, as well as other behavioral modifications, is needed to achieve the best results.

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