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The role of dietary for the prevention and treatment of Alzheimer's disease

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Abstract

There are numerous scientific evidences suggesting that nutritional consumption plays a significant role in the development and progression of Alzheimer's Disease (AD). Since the major cause of AD and other dementias is aging, some dietary compounds are proved to be promising against the development and progression of AD. Various dietary compounds have been shown to diminish the risk of AD, including antioxidants, vitamins, polyphenols, and seafood, whereas saturated fatty acids, high-calorie diets, and alcoholic imbalance have been recognized as risk factors. Fortunately, several studies established a positive relationship between adhering to some dietary patterns and avoiding AD such as Mediterranean diet (MD) and DASH-Style Diets. These patterns consist of a high intake in fruits, vegetables, fish, nuts, monounsaturated fats, whole grains, and legumes whereas limiting intake of red meat, saturated fats, dairy, and refined grains. Furthermore, it is reported that adherence to MD or DASH-Style Diets are beneficial in minimizing the risk of developing vascular diseases and other cardiovascular risk variables such as cholesterol, blood glucose, and blood pressure, which corresponded with the development and progression of many neurological conditions including AD. In conclusion, certain dietary patterns are shown to be an effective and secure approach against AD. It has the potential to operate as a complementary strategy in the prevention and treatment of AD. Nonetheless, the scientific knowledge in the field of dietary compounds remains underexplored and large randomized trials with well-characterized variables are still required to conduct a perfect strategy.

Keywords: Alzheimer Disease; Mediterranean diet; DASH-Style Diets; Aging; Neurodegenerative disorders

Introduction:

A dietary strategy to reduce, minimize or stop the disease's progression is an effective tactic that has been globally explored (1). There exists a great deal of scientific evidence suggesting that dietary factors may influence the initiation and severity of Alzheimer's Disease (AD) (1). Metabolic disturbance, one of the prevalent triggers of AD, as a result of nutritional deficiency or excess which could be treated by diet and lifestyle alteration or nutritional supplementation (2). Aging is a leading factor of AD and also causes various negative adjustments to the brain (3). Aging interventions including dietary modification (such as caloric restriction or fasting) appear to be promising in increasing lifespan in model organisms such as mice (4). Since the primary risk factor regarding the occurrence of neurodegenerative conditions is aging, some nutritional adjustments can be evaluated since they could potentially be used as a possible therapeutic approach for patients with AD (5). Various nutrients that provide a positive impact to our health(such as anti-oxidants, vitamins, trace minerals, flavonoids, lipids) are presented in many nutritional supplements that might affect cellular rejuvenation and vitality, the aging process, or may directly halt the development or progression of AD (6). Dietary adjustments provide the benefits from being financially effective, easy to execute, socially satisfied, totally safe ,and free from the contrary

incidents in the majority of cases (7, 8). Various nutritional approaches have been explored and trialled in order to find a reliable agent which can be utilized to prevent or treat AD (9, 10). This review aims to find a successful dietary approach that can be used effectively to prevent or treat AD.

Nutrition and risk of AD:

AD is a chronic neurological condition that is the dominant causation of dementia across the world (2). The condition is expected to attain 106.8 million globally by 2050, making it a worldwide public health concern with serious socioeconomic implications (2, 11). Currently, licensed medications have shown only minimal therapeutic efficacy in halting the neurodegenerative progression, and the AD epidemic encountered two significant roadblocks (12). The shortage of disease-modifying medications and the necessity to stall cognitive impairment and frailty trajectories define the importance of developing nonmedicinal approaches to deal with this global epidemic that is rapidly growing (13). There has been a great deal of attention on disease-modifying and risk factors for AD (14, 15). Cognitive engagement and physical exercise have been attributed to a reduced risk of Alzheimer's disease (AD), while diabetes, smoking, and depression have been corresponded to an increased risk of AD (16). Recently, there has been an increase in evidence reported that nutrition plays a significant role in AD (17, 18). A wide range of dietary factors have been shown to diminish the risk of AD, including antioxidants, vitamins, polyphenols, and seafood, whereas saturated fatty acids, high-calorie diets, and alcoholic imbalance have been recognized as risk factors (19, 20). In recent years, there have been an appearance of dietary patterns that precisely reflect the complexity of diet to investigate the correlation between diet and AD (21, 22).

Diet, Aging, and AD:

Since aging is the major cause of neurodegenerative disorder, a strategy could be to aim for agents that stall the aging processes and finalize the effect on progression of AD and other dementias (23, 24). According to researchers, diet plays a significant role in the progression of AD (25). There exists scientific evidence for particular dietary strategies that could be implemented, such as Mediterranean diet (MD) and vitamin supplementation, offering protection opposing the development of dementias (26, 27). Nonetheless, the impact of dietary adjustment against AD is still underexplored (28). Studies have shown a correlation between ketogenic diet to improving cognition in AD patients (29). These results appeared to be assisted by researches illustrating AD patients constantly presented shrinkage in cerebral glucose utilization despite variation regarding brain ketone metabolism (30, 31).

More specifically, dietary has a direct effect on several of the primary symptoms of AD development–including amyloid genesis, oxidative stress, and inflammation (32). Certain nutrients had been widely investigated for their possible influences regarding the development and/or progression of AD (33). To illustrate, rising cholesterol levels cause the increase of amyloid beta production due to the growth in activity of APP cleaving enzymes γ-secretase and BACE1 (34). Cholesterol reduction via statin therapies has also presented a relation with lowering of amyloid beta accumulation and AD development (35). Nevertheless, a progressive drop in serum cholesterol commonly appeared with dementias showing the diversity of AD pathogenesis (36). Research on fatty acids shows contradictory results (37). While Saturated fats, trans-fats, and ω-6 fatty acids provide no advantage or may cause negative drawbacks in terms of AD, ω-3 fatty acids have exhibited potential therapeutic benefits (38, 39). The correlation between carbohydrates-rich diet and AD progression is significant and there exists a hypothesis as to whether impaired glucose metabolism could be contributively in AD (40). Continuously high levels of glucose is associated with insulin resistance, which is being stated as a contributing variable for AD progression (41, 42). Surprisingly, brains of AD patients have represented a decline in glucose transporters level (GLUT1 and GLUT3) allowing glucose to pass the blood brain barrier and supply resources to the CNS (43). Lowered rate of glucose delivery to the brain causes glucose deprivation and AD neuropathology stimulation, vascular degradation, and cognitive impairment (44, 45). In addition, a brain with AD disrupts insulin signalling, which has also been proposed for proper control of amyloid beta and tau proteins. Insulin resistance also stimulates inflammation, which might worsen AD pathology (46).

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Generally, modification in dietary protein consumption improves lifespan (4). Mice that has been fed with one of the multiple diets altering in the proportion of macronutrients and net energy content (47, 48). As a result, those fed with low protein to high carbohydrate (LPHC) diets had an extraordinary advancement in lifespan and overall health in comparison to all other diets (47, 49). In humans, a research conducted with the United States population consisting of 6,381 individuals (aged 50 years and above) stated that although one who had protein as their primary calorie source had tremendously heightened risk of all-cause cancer and other mortality associated with cancer, it only limited to individuals under 66 years of age (1). On the contrary, those who are older expressed a decrease in all-cause mortality when consuming protein as their primary source of calories (50). The positive outcome of increased dietary protein intake represented in the older batch could be clarified by the disturbance of the sarcopenia and frailty development, which appears prevalent with older age (51). Moreover, the source of protein is paramount, as a study with a large group of participants reported a correlation of increased intake of animal protein to increased risk of all-cause mortality, in comparison to plant-based protein consumption (52, 53). Whether protein consumption affects AD directly is a field that is currently under discovered (54, 55).

Commitment to a Mediterranean diet (MD) leads to improved health outcomes (56). Recent studies are investigating whether MD also offers cognitive and/or neurological benefits (57). In general, MD consists of a high intake in fruits, vegetables, fish, nuts, monounsaturated fats, whole grains, and legumes whereas limiting intake of red meat, saturated fats, dairy, and refined grains (57). Outcomes of much research have been descriptive but still uncertain for MD to have a positive effect on neurological condition and enhanced cognitive capabilities along with aging (26, 57). The mechanism in which MD may have a protective effect on dementias is currently indefinite (57, 58). MD has been reported to minimize the risk of stroke and other vascular diseases (57, 58). Vascular diseases are corresponded with the development and progression of many neurological conditions and could define the benefits of MD to neuroprotection (26, 57, 58). Furthermore, antioxidants and anti-inflammatory components included in MD were proved to be beneficial (59). Mouse subject fed with extra virgin olive oil, which has high monounsaturated fats, had enhanced cognitive capabilities and diminished beta-amyloid and tau proteins (60). In addition, neurons reacting with oleocanthal (a polyphenol presented in extra virgin olive oil) results in reduced amyloid-beta oligomer-mediated astrocyte inflammation and synaptic proteins (61).

MD and AD Prevention:

MD appears to be beneficial for preventing AD (26). It is true that MD is based on the way people used to eat in Greece, Italy, and other Mediterranean areas, but there are some differences (58, 61). It has a lot of fruits and vegetables, cereals, legumes, olive oil, nuts, and seeds as the primary source of fats, much fish, and minimal dairy and alcohol (57). It is under the impression of a nutritional model for healthy diet because it includes all necessary nutrients, such as monounsaturated fatty acids (found primarily in olive oil), polyunsaturated fatty acids (found primarily in fatty fish), antioxidants (found in anthocyanins, beta-carotene-flavonoids, catechins, indoles, or lutein), vitamins A, B1, 6, 9, along with magnesium, potassium, calcium, iodine, zinc, and selenium (26, 57, 62). Growing evidence demonstrated that MD has protective properties , implying that MD may be an effective measure for preventing cognitive degeneration, mild cognitive impairment (MCI), and AD (63). Consistent habits regarding MD may have an effect not just on the risk of AD development but also on AD mortality (64). Numerous studies established a positive relationship between adhering to a Mediterranean diet and avoiding AD (57, 65). According to a meta-analysis of eighteen study designs involving 2,190,627 subjects, following MD was diagnosed with a major decrease in mortality and neurodegenerative condition (17, 66, 67). Since fruits and vegetables, fish, and reduced alcohol consumption decreased the risk of AD development, despite the paucity of data from interventional studies, MD may be promising against AD (68).

DASH-Style Diets:

It is recommended to consume plant-based food such as fruit and vegetables as well as fish, poultry, and whole grains, also consuming low-fat dairy products and nuts whereas reducing an intake of red meat,

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sodium, sweets, and sugar-sweetened beverages on a DASH diet, according to the American Heart Association (69). The clinical studies showed that representatives on the DASH diet showed more considerable improvements regarding neurocognition with raised blood pressure than those on the control diet (21, 70). Because high blood pressure is related to an elevated risk of AD, it is scientifically feasible that DASH could lower the risk of AD (68, 71).

Dietary Approaches to Stop Hypertension (DASH), is a modified nutritional pattern that was initially designed to recognize nutritional elements that affect blood pressure and is now recommended by the National Heart, Lung, and Blood Institute (NHLBI) (72). Fiber, potassium, and calcium are among the nutrients found in the DASH diet: fruits, vegetables, nuts, whole-grain products, low-fat dairy products, fish, and poultry (70). These nutrients, potassium, calcium, "lean proteins," minerals, and fibre, help lower blood pressure (70). Additionally, DASH diminished the use of foods such as red meats and processed meats, high-fat dairy products, and tropical oils, in addition to high-sugar beverages and desserts. As a result, DASH is customized to be low in sodium, total fats, and cholesterol (73). Several cardiovascular risk factors (such as high blood pressure) associated with AD development and other dementias have been shown to be protected by this type of dietary pattern, at least playing a role by manipulating the processes which are identified as the physiopathology of AD (74). Several food ingredients (such as whole grains, veggies, and nuts) are shared by DASH and MD, but there are some distinctions as well, such as the ratio in which low-fat dairy products are consumed in DASH versus MD are mild-to-high and low respectively (75).

Western World's Diet :

Western diets are characterized by increasing consumption of red meats and processed meats, refined cereals, and desserts (76). A high-fat Western diet may encourage the development of AD by altering accumulation and oxidative stress (77). There were no epidemiological studies linking the Western diet to an increased risk of AD (78).

Japanese Diet :

Fishery and plant-based foods (such as soy products, seaweed and vegetables) are the mainstays of the traditional Japanese diet, whereas refined carbohydrate and animal fats are minimized (79). A study involving 1006 Japanese patients over 15 years of age revealed that a diet high in soybeans and soybean products, vegetables, algae, and dairy products but low in rice was linked to a lower risk of AD (80).

Alzheimer's Disease Prevention Through Healthy Eating Habits:

A research conducted with 525 participants created a healthy-diet index to examine the components of healthy and poor diets; persons who ate healthy (index >8 points) had a reduced risk of AD (64). Fruit, whole grains, fresh dairy, veggies, breakfast cereal, tea, vegetable oil, nuts, and fish were all associated with a healthy diet (81). Meat and poultry consumption was associated with unhealthy diets, whereas refined grains and animal fat consumption was associated with poor diets that followed the health diet more strictly than those who did not have improved cognitive performance (81). Improvements in cognitive function have been found to be associated with a healthy diet, which is described by men's greater consumption of fish and women's increased intake of food (21, 81).

Dietary Patterns and the Brain: The Underlying Mechanisms:

Several studies have shown the modified nutritional pattern outlined above, such as MD, and DASH diet, can help prevent or reduce neurological diseases, such as AD (82). Advantages of these modified strategies stems from their versatility (82). Indeed, nutrient-dense diets may synergistically interact with various metabolic and cellular signalling mechanisms, resulting in brain health maintenance and protection (31). This evident conviviality is a hallmark of this nutritional way of life (58). Initiating in vitro and in vivo research to observe the results of such dietary patterns on the brain, on the other hand, presents significant methodological challenges, owing to the inherent diversity of an overall diet, the micro-and macronutrient constituents, the critical role of culinary preparation techniques, and, at least for MD's popularity (75). These variables are challenging to replicate and access in analytical settings (83). Until now, the underlying mechanisms of the MD's and other dietary patterns' neuroprotective effects are unknown (68). Despite

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widespread agreement that they help prevent several biological processes associated with AD pathogenesis, including oxidative stress, neuroinflammation, neurovascular dysfunction and hypoperfusion, disruption of the gut-brain axis, and dysfunction of hippocampal neurogenesis (68). They may also have a systemic effect on the brain by decreasing cardiovascular risk variables such as cholesterol, blood glucose, and blood pressure (68, 84). Additionally, these dietary patterns may affect Tau metabolism, even though the data for these pathways is primarily based on animal research and requires additional examination and validation (21).

Conclusion:

A dietary method to prevent AD has proven to be a promising and secure approach that has the potential to be highly cost-effective, simple to administer, and, most importantly, operate as a globally acceptable technique or complementary strategy in the prevention and treatment of AD. Despite decades of scientific, medical, and therapeutic progress in this sector, much about specific nutritional therapy for AD prevention remains unknown and unproven. Additional experiment is required to bolster the evidence for a link between AD and various dietary habits. To establish a causal relationship between specific nutrients, foods, and dietary patterns and the etiology of AD, adequately powered, large randomized research with a well-characterized patient group and intervention are necessary.

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