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The role of nutrition in the prevention and treatment of Alzheimer's Disease

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Abstract

Alzheimer's Disease (AD) is characterized as a chronic and progressive neurodegenerative disease with well-defined pathophysiological mechanisms, mostly affecting medial temporal lobe and associative neocortical structures [1]. Since its discovery some hundred years ago, AD continues to pose problems for affected families and society, especially in developed countries [2]. AD begins gradually; advances; and eventually leads to confusion, personality and behavior changes, and impaired judgment. A loss of independence, disordered eating behavior, and weight loss may accompany other symptoms [3].

Manifestations of AD result in a progressive dementia, with increasing loss of memory, intellectual function, and disturbances in speech. Persons with poor physical function have been shown to be at higher risk for developing dementia and AD [4]. At first, daily events are forgotten while memories are retained. Cerebral function declines, but this decline only becomes evident after the loss in memory is pronounces. Speech becomes impaired. Overtime motor skills deteriorate, as evidenced by changes in reflexes and shuffling gate. Clinical findings are consistent when disease progression reaches the terminal stage. Bowel and bladder control is lost; limb weakness contractures occur; and intellectual activity ceases. The patient becomes totally incapacitated in a vegetative state as death approaches. The incidence and prevalence of AD rise with increasing age and are higher in women in part because women live longer than men. The incidence of AD ranges from 1% at ages 65 to 70 to approximately 4% over age 85 [5].

Pathophysiology

A variety of factors are indicated in the pathophysiology of AD, including the extracellular deposition of b-amyloid (Aβ) plaques, accumulation of intracellular neurofibrillary tangles, oxidative neuronal damage, and inflammatory cascades. It is widely thought, however, that higher production of the Aβ peptide, the main component of amyloid plaques, is central to the pathogenesis of the disease. Since the first description of the neurotoxic properties of the Aβ peptide, a vast number of studies have investigated the cellular and molecular pathology triggered by Aβ [5].

Medical treatment

At present, no cure exists for AD. It is diagnosed by histopathology. Clinically, the diagnosis is based on exclusion. As a result, studies may be subjected to criticism because of the absence of a confirmatory diagnosis. Treatment aiming at the impairment of brain metabolism may improve neuropsychological function. No definitive treatment currently exists; cerebral vasodilators; stimulants; levodopa; and mega-doses of vitamins B, C and E remain unproven therapies.

Drug treatment remains experimental, and Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) in combination with nutri-

tion supplements are currently believed to be most effective. Tacrine, the first cholinesterase inhibitor approved by the Food and Drug Administration (FDA) for use in the treatment of AD, gives only modest improvement in both function and cognition. Some other medications are used to suppress aberrant behavior, disturbed sleep, anxiety or agitation.

The connection between nutrition and AD has been discussed in several published studies [6]. Appropriate lifestyle behaviors, including good nutrition and physical activity, are the first steps in preventing chronic diseases and disabilities in old age [7,8]. Effect of Certain nutrients derived from the diet on the aging brain, including polyunsaturated fatty acids and polyphenolic compounds contained in fruits and vegetables, can lead to improved cognition and motor abilities [9]. In some quarters, curcumin, vitamins, and Mediterranean diet, which all exert potent antioxidant and anti-inflammatory activity, have been postulated as having a preventative role in AD [10-12]. However, their potential for improving cognition is not limited to their antioxidant properties, as they also involve specific molecular and cellular processes that support brain plasticity [9]. For example, neuronal plasticity improvement by omega-3 intake was found to be mediated by the upregulation of Brain-Derived Neurotrophic Factor (BDNF) [9,13].

The effect of vitamins on Alzheimer's disease

AD has been recognized as the most studied and common cause of dementia. Since available drugs are able only to improve cognitive symptoms temporarily, and no treatment can reverse, stop, or even slow the neurodegenerative process. Researches indicate that the main strategy of treating AD might be through optimal nutrition and exercise. The use of vitamin supplementation as an adjuvant intervention has been examined, some of which have been postulated to be effective [14]. Lopes et al.'s [15] systematic review indicated that AD population had significantly lower plasma levels of folate as well as vitamins B12, C, and E and suggested that vitamins, among other nutrients, play an extensive role in AD treatment and management. Antioxidants are molecules that inhibit oxidation of other molecules. They are widely employed and investigated for preventative benefits to diseases including AD, along with other neurodegenerative conditions. Antioxidants protect against extracellular and intracellular Reactive Oxygen Species (ROS) and H_2O_2-cell-damaging radicals, which are by products generated from normal cell metabolism [16]. Exogenous chain breaking antioxidants vitamin E (tocopherol), vitamin C, and retinoic acid lower free-radical-mediated damage caused by toxic chain reactions in neuronal cells, thus aiding in the inhibition of dementia pathogenesis in mammalian cells [17]. Also, vitamin D exhibits antioxidant properties that abate free-radical-mediated damage in neuronal cells, hereby assisting in the impediment of dementia and cognitive impairments [18]. Additionally, nicotinamide, the amide form of vitamin B3 (niacin), is the precursor for coenzyme -Nicotinamide Adenine Dinucleotide (NAD+) and is necessary for cellular function and energy metabolism. Nicotinamide treatment has been evinced to prevent cognitive deficits while improving short-term spatial memory in an AD mouse model, thus explicating potentiality as an AD therapy [19].

Vitamin A

Vitamin A as one of the most multi functional vitamins, succors in embryonic growth and development, immune competence, reproduction, conservation and maintenance of epithelial surfaces as well as proper functioning of adult brain [20]. Low levels of vitamin A are a risk factor for AD and a major problem in the aging population. A number of genes implicated in AD are maintained in the immune system by vitamin A [21]. The most useable form of vitamin A is retinol, which is converted by the body into retinal and retinoic acid (RA). In AD, there have been observations on the transport of retinoid from the intestine to target tissues, including the brain, being modified. Though distribution of RA within a mature human central nervous system is unknown, coupled with the impossibility of sampling live human brains as well as the rapid degradation of RA in autopsied brains, there is, albeit, indirect evidence endorsing lowered concentration of retinoic acid in AD brain. On the other hand, the enzymatic synthesizer of RA, Retinaldehyde Dehydrogenase (RALDH), has also been found to be elevated in AD brains, which further warrants the theory of AD patients having lower levels of RA. In occurrences where neuronal cell lines have been deprived of retinoid, higher levels of RALDH have been exhibited. However, these high levels would have been normalized by the addition of retinol through feedback mechanisms in healthy patients [14].

Vitamin B

Vitamin B, a notable contributor to the regulation of healthy levels of the amino acid, Homocysteine (HCy), also plays a synergistic role in the maintenance of cardiovascular and neural health [22]. In several aspects, information and controlled trial research efforts in this area has been conclusively limited. Majority of sources explored focused on a small subset of vitamin B (folate, vitamin B12, and, to a lesser extent, vitamin B6) as they play the most obvious role in HCy metabolism. Thus, the multifaceted inter-related roles of the other vitamin Bs have been largely over looked. Vitamin B1 (thiamine) plays an important role in Wernicke-Korsakoff syndrome (a form of amnesia caused by brain damage occurring in long-term alcoholics who rely mainly on alcohol for nutrition) [23]. The acute syndrome is normally reversible but may proceed to pro found dementia, although its progress can be stopped by a timely injection of a large dose of thiamine. There have been suggestions that thiamine may have a beneficial effect in Alzheimer's disease. One review [24] in 2011 examined the association between histopathogenesis and neurotransmitters to understand the relationship between thiamine and AD pathology. Oral thiamine trials have been shown to improve the cognitive function of patients with AD; however, absorption of thiamine is poor in elderly individuals. In the early stage of thiamine-deficient encephalopathy (Wernicke's encephalopathy), however, parental thiamine has been used successfully [24]. Nicotinamide (vitamin B3) participates in cellular energy metabolism, influences oxidative stress and modulates multiple pathways that are tied to cellular survival and death. This resilient cytoprotectant blocks cellular inflammatory cell activation, early apoptotic phosphatidylserine exposure and late nuclear degradation during disorders, including immune system dysfunction, diabetes, and age-related diseases [25]. Studies showed nicotinamide treatment to improve cognitive performance, along with extenuation of A and hyperphosphorylated tau pathologies in both the hippo campus and cerebral cortex of AD mice. Preserved mitochondrial integrity, improved autophagy function, and declined neuronal vulnerability to oxidative stress were also noted. Vitamin B3 presents extraordinary optimism in the development of dietary AD therapy and is expected to be further canvassed [26]. Vitamins B6, B9 (folate), and B12 have also been explored as possible therapeutic treatments for AD. These vitamins are inextricably linked

due to their complementary roles in “folate” and “methionine” cycles [27]. It is, nonetheless, important to note that the existence of inadequate statistical control for dietary cofounders such as antioxidants and other vitamin B’s gives rise to inconsistent findings. Folate, for example, is correlated with other various preventative factors in AD therapy, which could possibly account for cofounding partiality. Such dietary cofounders should be carefully examined in requisite prospective studies so as to limit conflicting results [28,29].

Vitamin C

Vitamin C (ascorbic acid) as a water-soluble antioxidant prevents lipid peroxidation in biological systems and acts as a major defense against free radicals in whole blood and plasma. Like other antioxidant vitamins, plasma levels of vitamin C were found to be significantly curtailed in patients with AD despite adequate intake of this vitamin in diets. This concurred with the fact that antioxidant vitamins offer protection against damage instigated by oxidative stress [30]. The relationship between AD and vitamin C has been investigated in large population studies and clinical trials. Reports have evidenced neurodegenerative diseases, which exhibit high oxidative stress, to constantly consume ascorbic acid available in the brain, subsequently culminating in the oxidation of vitamin C. Additionally, in the presence of high levels of ROS, vitamin C becomes unavailable to modulate neuronal metabolism. Hence, breakdown of homeostatic systems for ascorbic acid recycling, oxidative stress, and elevated ROS production are essential aspects in the progression of neurodegeneration, more specifically AD. It is important, however, to note that avoiding vitamin C deficiency is likely to be more beneficial in having a protective function against age-related cognitive decline and AD than taking supplements in an already healthy diet. This is due to the ability of the transport of ingested vitamin C from the intestines into blood being limited by saturable sodium-dependent vitamin C transporter, subsequently resulting in the use of supplements being erroneously thought of having greater benefit than they really do [31-33].

Vitamin D

Vitamin D, a steroidal hormone, is important for physiological function and protection of the central nervous system as well as regulation of bone metabolism [34]. Deficiency in vitamin D is known to decrease bone density coupled with increasing risk of copious common forms of cancer and cognitive impairment in both young and old adults [35]. The active form of vitamin D, 1, 25 dihydroxy-vitamin D3, upregulates neurotrophin expression and glial-derived neurotrophic factor, while hypovitaminosis D has been associated with prevalent cognitive impairment and AD in older people [18]. The connection between vitamin D earth and AD has been made, where studies have discovered vitamin D levels to be conspicuously subservient in comparison to normal controls. What is more, vitamin D depletion has been linked to brain atrophy owing to inflammation of the different types of vitamin D receptors. A strong relationship between over expression of either vitamin D receptors or vitamin D supplementation and the suppression of Amyloid- Protein Precursor (AßPP) has also been noted [18,30,34,35]. One study demonstrated vitamin D3 supplementation improved cognition and memory in patients with moderate AD receiving memantine, which might be contingent on the synergistic neuroprotective effect of memantine plus vitamin D. This phenomenon typifies a new multi-target therapeutic class for AD treatment [36]. Besides, vitamin D affects several mechanisms of AD pathogenesis including production, clearance, phagocytosis, and enzymatic degradation of A peptides as well as tau phosphorylation [37]. Supplementation with vitamin D has been postulated to ameliorate cognitive deficit, more specifically AD. It is expected that detailed investigation a propos to the link between several gene-environment interactions and their influence on AD progression along with metabolic and endocrine etiological factors would be explored [36-38].

Vitamin E

Since vitamin E has anti-oxidative potential which protects lipids from peroxidation in membranes, its supplementation has been suggested to be beneficial in AD. More importantly, vitamin E molecules exert neuroprotective, anti-inflammatory, and hypo-cholesterolemic properties [39,40] along with its ability to modulate gene expression by influencing various transcriptional pathways [40]. Again, studies found vitamin E to suppress tau-induced neurotoxicity and provided a palpable level of neuroprotection against increased oxidative stress induced by A plaques, a known risk factor for neuronal death and resultant brain injury in AD [41]. Moreover, vitamin E deficiency can cause destruction of neurons and has been indicated in cases of cerebellar atrophy, with diminished vitamin E levels being found in the plasma of both AD patients and individuals with mild cognitive impairment. Inversely, higher plasma concentrations of vitamin E and improved dietary intake of either vitamin E or -tocopherol equivalents have been linked to lower AD risk [42].

The effect of Polyphenols on Alzheimer’s disease

Dietary polyphenols have been suggested as potential functional food candidates to prevent memory decline [43]. Polyphenols are natural substances present in plants, fruits, and vegetables. Some polyphenols, such as Epigallocatechin-3-Gallate (EGCG) found in green tea, 4-O-methyl honokiol found in Magnolia officinalis, resveratrol contained in grapes, and ginkgolide which found in ginkgo biloba, have been suggested to provide protection against AD. Their effects may be due to their modulation of enzyme activity and regulation of intracellular signaling pathways and gene expressionas well as antioxidant and anti-inflammatory properties [43,44]. Polyphenols, especially flavonoids, can modulate those neuronal signaling cascades altered with ageing by acting on ERK/CREB pathway involved in synaptic plasticity and long-term potentiation, improving learning and memory in both animals and humans [45-48]. Flavonoid supplementations can modulate specific signaling kinases like CaMKII and ERK, controlling the activation of CREB and the increase dexpression of BDNF and NGF at the brain level [45,47,49]. Infact, these compounds also exerta protective function in the hippo campus of middle age mice preserving and promoting the spatial learning strategies. Recently, Ono et al. [50] have corroborated the relevance of polyphenol supplementation for AD prevention. He demonstrated that wine-related polyphenols, including myricetin, quercetin, and kaempferol, inhibited Aβ oligomer formation in a dose-dependent manner from fresh monomeric Aβ, as well as destabilised preformed Aβ oligomers in invitro experiments. Furthermore, Bensalem et al. [51] demonstrated that a polyphenol-rich Oxidative Medicine and Cellular

Longevity extract from grape and blueberry (PEGB), with high contents of flavonoids, can facilitate the use of spatial strategies in both adult and middle-aged mice. In these animals PEGB supplementation was able to improve learning performance by restoring CaMKII mRNA levels and increasing NGF expression

exactly in the hippocampus. It is note worthy that this is the first nutritional intervention that, even if with a mix of different polyphenols at low doses, shows a rescue effecton those specific memory deficits [51]. Resveratrol,another wine related polyphenol abundant also in berries, protects neurons against Aβ-induced toxicity and attenuates behavioral impairment in rats [52]. Again, green tea's polyphenols, EGCG and Epicatechin (EC), showed their neuroprotective effects through out the free radical scavengers on in vitro oxidative stress and in neuro toxicity cellular models [53,54]. Curcumin also has a potential role in the prevention and treatment of AD. The biophenolic curcumin, isolated as the active yellow component of Curcum along a, has along history of use in traditional Asian medicines for its potent anti inflammatory, antioxidant, and anti cancer activities [55]. In AD animal models, curcumin reduced proinflammatory cytokines, oxidative damage, and beta-amyloid production, ameliorating cognitive deficits [56]. Ambegaokar et al. [57], using different doses of curcumin in a mixed colony of both neuronal and glial rat cells, showed that curcumin stopped the proliferation of neuroglial cells dose dependently, by differentiating them into mature cells or inducing apoptosis, resulting in inhibiting neuroinflammation. In addition, curcumin exerted an anti proliferative action on microglial cells preventing cytokine release. Another study conducted by Zhangetal. [58] demonstrated that macrophages derived from AD patients treated with curcum in showed an improved up take of beta-amyloid when compared with untreated cells. Further more, curcumin decreases the lipoprotein oxidation and the free radicals formation in AD and in other neurodegenerative disorders [59]. Because of its lipophilic nature, curcumin crossed the blood-brain barrier and reduced existing senile plaques, as demonstrated in APPswe/PS1dE9 mice [60]. Curcum in reduces senile plaques by binding with the Aβ oligomers, destabilising them and preventing their extension [61]. However, further studies on large population will be necessary inorder to demonstrate the effects of all these polyphenols in delaying or preventing AD.

The effect of Zinc on Alzheimer's disease

Different concepts of the etiology of AD exist including the 'metal hypothesis' which has attracted increasing scientific attention in recent years [62]. The hypothesis relies on the disease-associated alterations of metals in the brain which participate in the cascade of pathogenic events that finally cause the clinical symptoms. With regard to zinc (Zn), a plethora of evidence has arisen showing its involvement in AD [63,64]. For example, free, extra cellular Zn induces amyloid deposition [65], which is in line with strongly increased Zn concentration in senile plaques and neuropils of AD patients [66], and both the Amyloid Precursor Protein (APP) and Aβ have Zn binding sites [67,68]. Moreover, Zn is an ionic signalling messenger, participates in diverse non enzymatic biological reactions and serves as a crucial component in catalytic, co-active or structural functions of hundreds of proteins [69], facilitating manifold biological processes such as anti oxidative function, immunity, DNA metabolism, vision, taste, neurotransmission, neurogenesis, or neuronal growth [69-71]. Effects of malnutrition may be particularly relevant for neurodegenerative diseases as the brain is the organ with the highest Zn levels (in mean: approx. 150 µmol /l) separated in delicately balanced pools [72]. Dietary zinc deficiency is a world wide problem [73] and is estimated to affect more than two billion people [74]. Importantly, elderly and particularly institutionalized subjects are at high risk of Zn deficiency [75,76]. In the only reviewed evidence of an association between zinc (Zn) nutrition and Alzheimer's disease (AD) or age-associated cognitive decline by Martin Loef et al. [77], from fifty-five studies which met the inclusion criteria, neither randomized controlled trials nor observational studies provide conclusive evidence whether Zn in the diet is associated with cognitive decline or AD. Case-control and autopsy studies suggest decreased systemic and increased brain Zn levels, respectively. The current state of evidence does not allow conclusions to be drawn on whether supplementation of Zn is beneficial for the prevention or treatment of AD, although a subclinical deficiency appears common in the elderly and subjects with AD. Dietary studies with animals suggest that the impact of dietary Zn on cognitive performance depend on additional nutrients [77]. Further studies are necessary to determine whether Zn deficiency is a risk factor for AD in general terms or under certain dietary circumstances only.

The effect of Omega-3 fatty acids on Alzheimer's disease

The role of nutrition in prevention of dementia and AD arouses increasing hope with particular interest in dietary intake of omega-3 fatty acids, for brain tissue membranes rich in omega-3 fatty acids, including Docosahexaenoic Acid (DHA) and Eicosapentaenoic Acid (EPA) with protective roles for nervous system [78]. Experimental evidence indicates brain protection from cognitive decline and neurodegenerative pathology reduction in aged rats with a DHA-enriched diet [79]. However, evidence from observational and epidemiological studies suggests an inconsistent relationship between dietary intake of omega-3 fatty acids and risk of dementia and AD. Some human studies suggest that higher intakes of omega-3 fatty acids from dietary sources are related to reduced risk of dementia and AD [80,81], while other studies failed to find this association [82,83]. In this regard a systematic and meta-analysis found that a higher dietary intake of long-chain omega-3 fatty acids was not associated with lower risk of dementia or AD compared with the respective lower exposure category. A previous randomized trial indicated that supplementation with DHA compared with placebo did not slow the rate of cognitive and functional decline in patients with mild to moderate AD [84]. Nevertheless, most of the individual studies evaluating the relationships between long-chainomega-3 fatty acids intake and risk of dementia or AD, suggest that there was may be potential protective effect of long-chain omega-3 fatty acids on incidence of dementia and AD, although no significant statistical differences were identified in the pooled analyses. The biological mechanisms could support beneficial effects of long-chain omega-3 fatty acids on the risks of dementia and AD. Indeed, long-chain omega-3 fatty acids are major components of neuron membranes, and they have vascular and anti-inflammatory properties which have a protective effect against dementia and AD [80,85-88]. A dose–response meta-analysis showed that each 100 g per week higher intake of fish was associated with an 11% lower risk of AD. The protective effect of fish intake was mainly attributed to its high content in long-chain omega-3 fatty acids, in particular DHA [89], and the biological mechanisms are similar as we mentioned above. However, this protective effect may have several alternative explanations. Firstly, fish is also a good source of other nutrients, such as vitamins, essential amino acids and trace elements, and these nutrients may also contribute to cognitive function improvement [90,91]. Secondly, a higher fish intake may simply be an indicator of a healthier dietary pattern or higher socio economic status, which themselves are associated with better cognitive performance [92,93] . Thirdly, a higher fish intake may

associate with a lower intake of other type of fat such as saturated fat. According to the inverse effect of saturated fatty acids on the risk of dementia, protective effect of fish intake may also due to the lower intake of other type of fat [94].

The discordant results observed for long-chain omega-3 fatty acids intake compared with fish intake may also have several potential explanations. Firstly, it is not well-known about what foods contain long-chain omega-3 fatty acids and the food composition tables are often incomplete, and this would lead to an underestimation of the true long-chain omega-3 fatty acids intake. Secondly, dietary intake of long-chain omega-3 fatty acids may also be accompanied by the intake of other nutrients simultaneously such as saturated fat, which may attenuate the associations between longchain omega-3 fatty acids and risk of dementia or AD. Thirdly, the categories of long-chain omega-3 fatty acids intake and fish intake are quite different, and this may also be responsible for the inconsistent results in studies concerning long-chain omega-3 fatty intake and in those concerning fish intake. Findings of this meta-analysis are in line with three cross sectional studies [80,95,96], which described better cognitive performance on various neuropsychological tests in middle-aged and older persons who regularly consumed fish. Despite the association between higher fish intake and better cognitive performance was reported in these cross-sectional studies, this type of study can not as certain causality. In contrast, in prospective studies, long chain omega-3 fatty acids and fish intake was monitored in a cohort that was followed-up to determine which subjects developed dementia or AD. Thus, the results in the meta-analysis could be used to identify a causal relationship between dietary intake of omega-3 fatty acids and risks of dementia and AD. Due to positive effects of higher fish intake on reduction the risk of AD, mechanistic researches are essential to explain this protective effect. Well-designed randomized controlled trials that address a specific mechanism of fish intake and reduced risk of AD are urgently needed.

The effect of saturated fatty acids: Caprylic acid and coconut oil on Alzheimer's disease

Caprylic acid is a medium-chain triglyceride (fat) produced by processed coconut oil or palm kernel oil, and is an active ingredient of the "medical food" Axona, which targets the nutritional needs of AD patients [97]. In the metabolization of caprilyc acid in the body, Ketone bodies are produced which thought to provide an alternative energy source for impaired brain cells in AD patients that have lost their ability to utilize glucose, which is the brain's chief source of energy. In a study, patients taking Axona displayed improvement in cognition when measured at 45 and 90 days of supplementation. However, benefits were only seen in ApoE4 negative patients and were short lived. Axona was eventually discontinued due to its adverse side effects such as diarrhea, flatulence, and dyspepsia [97]. Coconut oil is a less expensive source of caprylic acid and has been reported to help AD patients. Definitive scientific and/or clinical evidences on the effectiveness of coconut oil for either the prevention or treatment of AD are limited, as no clinical trial data, as of yet, is available to substantiate or refute these claims [98,99].

Dietary patterns

Dietary patterns have been associated with protective relations to cognitive decline and incident dementia in epidemiological studies [12,100]. Encouraging support for these findings was recently provided by reports of secondary analyses of two dietary intervention trials. In the PREDIMED trial [101], participants at high vascular risk were randomized to dietary counseling of either the Mediterranean diet (supplemented with either extra-virgin olive or mixed nuts) or a low-fat control diet. After 6.5 years of nutritional intervention, those randomized to the Mediterranean diet had significantly higher scores on the Mini-Mental State Examination (MMSE) and Clock Drawing Test (CDT) compared to the control diet participants. In the second trial [102], 124 overweight participants with elevated blood pressure were randomized to the DASH diet (Dietary Approaches to Stop Hypertension) alone or in combination with exercise and caloric restriction, or to a usual diet control group. After 4 months of the intervention, the participants on the DASH diet exhibited greater improvements in psychomotor speed compared with the usual diet control. The results of these dietary intervention trials provide evidence that dietary patterns may reduce the risk of dementia. However, whereas both the cultural-based Mediterranean diet and the blood pressure-lowering DASH diet have demonstrated protective effects on cardiovascular conditions that can adversely affect brain health, their dietary components may not specifically capture the levels and types of foods shown to optimize brain health. In a previous study, a hybrid of the Mediterranean-DASH diets, called MIND (Mediterranean-DASH Intervention for Neurodegenerative Delay) that emphasizes the dietary components and servings was linked to neuroprotection and dementia prevention. Similar to the Mediterranean and DASH diets, the MIND diet score emphasizes natural plant-based foods and limited intakes of animal and high saturated fat foods but uniquely specifies consumption of berries and green leafy vegetables, and does not specify high fruit consumption (3-4 servings/d in the DASH and Mediterranean diets), high dairy (2+ servings/d in DASH), high potato consumption (2 servings/d in the Mediterranean) or greater than 1 fish meal per week (>6 meals/week in the Mediterranean). The MIND diet score was associated with a slower rate of cognitive decline equivalent to 7.5 years of younger age among the participants in the top third of MIND diet scores compared with the lowest third [103].

Same authors related these three dietary patterns to incident Alzheimer's disease [104]. The diet-AD relations was investigated in a prospective study of 923 participants, ages 58 to 98 years, followed on average 4.5 years. In adjusted proportional hazards models, the second and highest tertiles of MIND diet scores had lower rates of AD versus tertile 1 whereas only the third tertiles of the DASH Mediterranean diets were associated with lower AD rates. It was concluded that High adherence to all three diets may reduce AD risk and Moderate adherence to the MIND diet may also decrease AD risk [104].

Conclusion

A plethora of research work has been and is still being conducted to elucidate the complexities of AD pathology. Some mechanisms relating to AD, together with the connection of the disease to other diseases as well as possible preventive mechanisms of AD, continue to be untangled. Nonetheless, until effective treatments and preventative mechanisms are ascertained, AD will continue to pose a great burden to aging people, especially those in Western Europe, where the disease is thought to be prevalent. Wishing that the intake of bioactive nutrients in preventing/delaying AD will be confirmed, nutritional intervention might be considered a promising strategy to reduce AD prevalence.

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