

Review

Can Nutrients Prevent or Delay Onset of Alzheimer's Disease?

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Abstract. Age-related changes in nutritional status can play an important role in brain functioning. Specific nutrient deficiencies in the elderly, including omega-3 fatty acids, B-vitamins, and antioxidants among others, may exacerbate pathological processes in the brain. Consequently, the potential of nutritional intervention to prevent or delay cognitive impairment and the development of Alzheimer's disease (AD) is a topic of growing scientific interest. This review summarizes epidemiological studies linking specific nutritional deficiencies to mild cognitive impairment (MCI), as well as completed and ongoing nutritional studies in prevention of MCI and AD. Processes that underlie AD pathogenesis include: membrane/synaptic degeneration, abnormal protein processing (amyloid- β , tau), vascular risk factors (hypertension, hypercholesterolemia), inflammation, and oxidative stress. Consideration of mechanistic evidence to date suggests that several nutritional components can effectively counteract these processes, e.g., by promoting membrane formation and synaptogenesis, enhancing memory/behavior, improving endothelial function, and cerebrovascular health. The literature reinforces the need for early intervention in AD and suggests that multi-nutritional intervention, targeting multiple aspects of the neurodegenerative process during the earliest possible phase in the development of the disease, is likely to have the greatest therapeutic potential.

Keywords: Alzheimer's disease, nutrition, primary prevention, Souvenaid^{®1}, synapse formation

INTRODUCTION

The call for primary prevention

With the number of Alzheimer's disease (AD) cases projected to reach 100 million worldwide by 2050 [1], it is recognized that one of the major challenges facing health and social care professionals over the next decades will be the management of this growing population of AD sufferers. Alongside the search for more effective therapies, the quest for primary prevention is

imperative. Even a very small reduction in the rate of development of AD pathology would have enormous public health benefits.

The changes underlying AD are thought to be active for many years before the characteristic symptoms of loss of attention and memory impairment manifest. This is reflected in the transitional phase of mild cognitive impairment (MCI) preceding AD, representing a continuum of progressive synaptic and neuronal loss, particularly in the temporal and parietal lobes. Although the pathogenic mechanisms are unclear, key pathological features are extraneuronal senile plaques consisting of amyloid- β (A β) and intraneuronal neurofibrillary tangles consisting of phosphorylated tau protein. Other pathologies hypothesized to be involved include oxidative stress, mitochondrial and vascular dysfunction (e.g., blood pressure), and insulin resistance.

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Among other factors, ample evidence suggests that cognitive function is influenced by nutrition [2]. As the dry weight of the brain is composed of 60% fat, it is not surprising that dietary fatty acids strongly influence the structure and composition of brain cell membranes [3]. Membrane and neurotransmitter precursors (e.g., docosahexaenoic acid [DHA], uridine, choline, tyrosine, and tryptophane) are required to maintain electrical signaling and the constant restructuring of interconnected neurons. The potential influence of nutrition on cognitive impairment and on the development and prevention of AD in particular, is a topic of increasing interest in the scientific community. This review summarizes the key research findings in this growing field of investigation.

NUTRITION AND BRAIN FUNCTION

Multiple roles for nutrients in the brain

The formation and maintenance of neurons rely upon adequate provision of precursor and building block molecules, most of which are provided by diet. For example, around 20% of the fat in the human brain is composed of omega-3 (n-3) and omega-6 (n-6) essential fatty acids that must be provided by diet. Phospholipids form the backbone of neuronal membranes and are required for membrane receptor and enzyme functions, with phosphatidylcholine (PC) being the most abundant membrane phosphatide. Formation of the neuronal membrane is driven by the Kennedy pathway. In animal models, Wurtman and colleagues showed that administration of choline, uridine, and DHA, precursors to PC, synergistically accelerate brain phosphatide synthesis [4]. Membrane lipids may also play a role in cell signaling by acting as cofactors for second messengers or as precursors for the synthesis of cytokines and prostaglandins [5,6].

Diet also provides precursors for the adequate supply and release of neurotransmitters [7], e.g., synthesis of acetylcholine is controlled by dietary intake of choline (given as lecithin), but can also be made available from membrane phospholipids. Changes in the brain content of n-3 and n-6 fatty acids bring about changes in membrane composition that in turn influence the fluidity and function of the neuronal membrane [8]. It is now recognized that homeostasis of membrane lipids in neurons is essential to prevent loss of synaptic plasticity, apoptosis, and neurodegeneration [9].

Aging, nutrition, and risk of developing AD

Dietary habits, nutritional intake, and the aging process are closely interrelated. With decreasing activity levels and a decline in basal metabolic rate, older people tend to consume less food, and consequently fewer nutrients. Aging also brings changes in taste and smell, and possibly impairments in digestion, absorption, and metabolism of nutrients because of chronic disease, changes in emotional wellbeing, and loss of independence. The demand for specific nutrients may increase. Consequently, the quality of dietary intake becomes increasingly important with advancing age, sometimes requiring supplementation to ensure adequate nutrients are consumed within a limited caloric intake.

Not surprisingly, therefore, many epidemiological studies indicate that older populations have higher rates of nutritional deficiencies than younger age groups, in particular deficiencies of B-vitamins, the antioxidant nutrients (vitamins C and E, selenium) [10], and omega-3 polyunsaturated fatty acids (PUFAs) [11,12], and reduced intake of choline [13]. Unfortunately, markers to identify nutrient deficiencies vary widely, making comparison of studies difficult.

Although levels of protein and nutrient malnutrition, i.e., weight loss, do not seem to differ between individuals with early-stage AD and the general elderly population, those with AD are more likely to be subclinically deficient in specific nutrients such as n-3 fatty acids; low intakes of n-3 fatty acids are associated with an increased risk of developing MCI or AD [14,15]. It follows therefore that cognitive decline may be accelerated if nutritional deficiencies are not adequately met by the diet. Table 1 provides a summary of studies that have identified specific nutrient deficiencies in individuals with MCI. These findings are important as this is a key area for future AD intervention or secondary prevention studies.

There is also evidence available suggesting that normal plasma or tissue levels of nutrients may not be adequate in certain individuals with elevated requirements resulting from chronic disease. It has been argued that AD patients may have specific nutrient needs that could be a consequence of the disease process itself, or a reflection of low nutrient intake or reduced bioavailability of specific nutrients required for brain function [16].

Epidemiological studies linking nutrition and AD

Likewise to coronary heart disease and diet, there is a growing wealth of evidence supporting a modifiable,

Table 1
Studies assessing nutrient deficiencies in MCI

Study	Subjects	Measure	Conclusion
Conquer et al., 2000 [11]	36 MCI 19 Control	Plasma phospholipid fatty acid composition	MCI showed reduced DHA content in phospholipids compared with control
Rinaldi et al., 2003 [66]	25 MCI 53 Control	Plasma antioxidant levels	Vitamin A, C & E, lutein, zeaxanthin and α -carotene were reduced in MCI
Quadri et al., 2004 [67]	81 MCI 55 Control	Plasma folate and vitamin B12 levels	Folate was reduced in MCI whereas vitamin B12 was unchanged
Baldeiras et al., 2008 [68]	85 MCI 37 Control	Plasma vitamin E	Vitamin E was reduced in MCI

Abbreviations: DHA, docosahexaenoic acid; MCI, mild cognitive impairment.

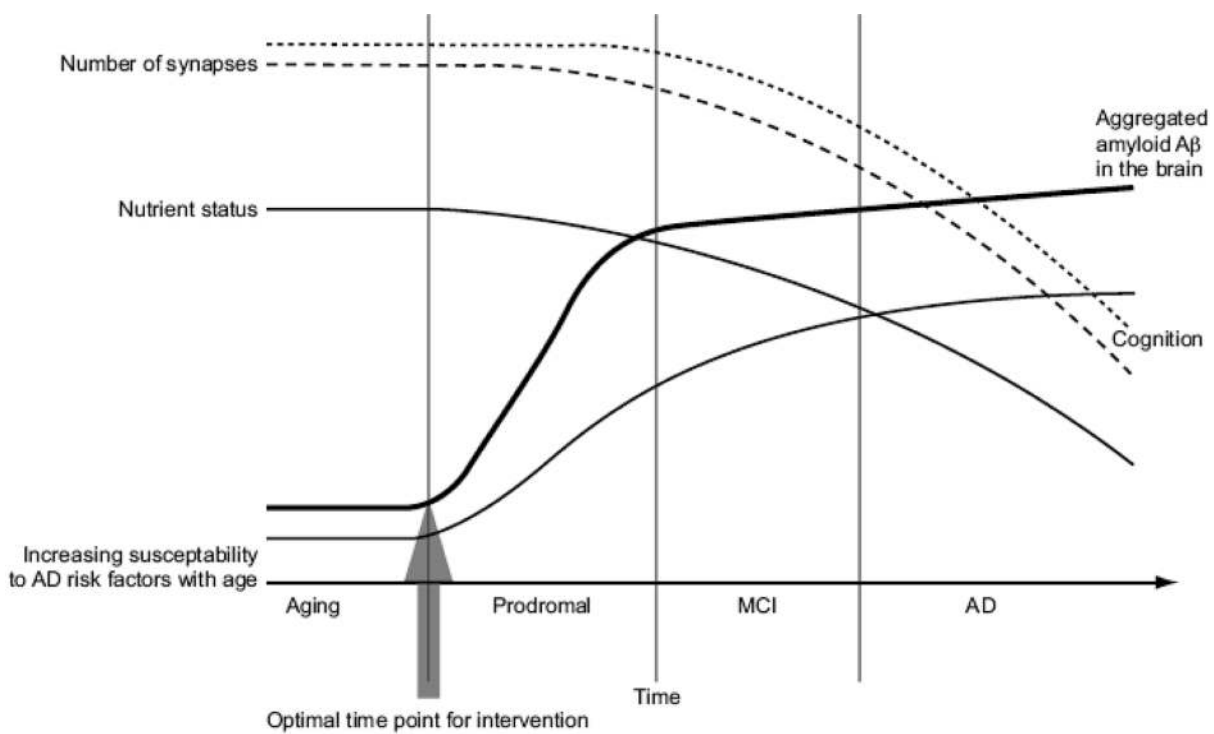


Fig. 1. Hypothesized relationship between nutritional biomarkers and neuropathological changes in the AD neocortex (adapted from Ingelsson et al. [18]).

causal link between diet/nutrition and the risk of developing age-related cognitive decline and subsequently AD. Studies suggest that dietary components such as n-3 fatty acids, B-vitamins, and antioxidants may help to lower the risk of developing AD. This epidemiological evidence has already been comprehensively reviewed [10,17]. Furthermore, patients with AD have been found to be clinically or subclinically deficient in certain nutrients [16]. The hypothesized relationship between nutritional status and increasing burden of AD pathology is depicted in Fig. 1 (adapted from Ingelsson et al. [18]).

Based on the evidence to date supporting a direct

relationship between diet and AD, improved nutrition in general and nutritional intervention, i.e., dietary supplementation, may benefit patients with cognitive decline by modifying the underlying disease process [19].

AD nutrient intervention studies

There are surprisingly few published studies that have reported on nutritional intervention in primary and secondary prevention of AD, and most of them have focused on supplementation of a single dietary component. Table 2 provides a topline overview of the

Table 2
 Topline overview of completed and ongoing nutritional intervention studies for prevention of cognitive decline or AD

Completed studies	Subjects	Mean follow-up	Nutrient	Conclusion	Status
Crook et al., 1991 [69]	149 subjects with age-associated memory impairment 50–75 years	12 Weeks	Phosphatidylserine 3 × 100 mg/day	– PS improves memory in those performing at the low range of normality	Completed
Petersen et al., 2005 [70]	769 subjects with MMSE between 24 to 30 55–90 years	3 Years	Vitamin E 1.3 g/day	– Vitamin E had no effect on the rate of progression to AD	Completed
Wolters et al., 2005 [71]	220 healthy, free-living women 60–91 years	6 Months	Multi-vitamin Providing 11 vitamins and 2 minerals	– No effect on cognitive performance	Completed
Eussen et al., 2006 [72]	195 Free-living older persons and older persons living in care facility homes ≥ 70 years	24 Weeks	Vitamin B-12 with or without folic acid 1 mg + 0.4 mg/day	– Vitamin B-12 administered alone or in combination with folic acid showed no improvements in cognitive function in older persons	Completed
Kang et al., 2006 [73]	6377 women ≥ 65 years	4 Years	Vitamin E 600 mg/day	– Vitamin E did not reduce the rate of cognitive decline	Completed
Durga et al., 2007 [74]	818 healthy men and women with raised plasma total homocysteine 50–70 years	3 Years	Folic acid 0.8 mg/day	– Improved performance on tests that measure information-processing speed and memory, domains that are known to decline with age	Completed
McNeill et al., 2007 [75]	910 healthy men and women ≥ 65 years	1 Year	Multi-vitamin + multi-mineral Providing 11 vitamins and 5 minerals at 50–210% of the UK Reference Nutrient Intake	– No evidence for a beneficial effect of multi-vitamin + multi-mineral supplementation on cognitive function – Beneficial effects are possible in those at higher risk of nutritional deficiency	Completed
van de Rest et al., 2008 [76]	302 cognitively healthy subjects ≥ 65 years	26 Weeks	Fish oil 1800 or 400 mg/day	– No effect on cognitive performance	Completed
Yurko-Mauro et al., 2009 MIDAS	185 subject with a Logical Memory (WMS III) baseline score > 1 SD below the younger adult mean > 55 years	6 Months	DHA 900 mg/day	– DHA improved memory function in healthy older adults with age-related cognitive decline	Completed

Table 2, continued

Ongoing Studies	Subjects	Mean follow-up	Nutrient	Objective	Status
Alois de Montauban study	4000 individuals ≥ 67 years	5 Years	DHA	<ul style="list-style-type: none"> Prevent development of neurodegenerative disease Secondary outcome: prevent development of AD 	Ongoing Recruiting
EPOCH ACTRN12607000278437	400 elderly 65–90 years	1.5 Years	n3 PUFAs 450 mg DHA + 135 mg EPA	<ul style="list-style-type: none"> Decrease the rate of cognitive decline measured by working memory, reasoning, short-term memory, long-term memory and retrieval, speed of reasoning, inhibition, perceptual speed 	Ongoing Recruitment completed
LIPIDDIET NTRI705 [77]	Prodromal AD as defined by episodic memory disorder and evidence for underlying AD pathology MMSE ≥ 20 55–85 years	2 Years	125 mL of Souvenaid [®] once-a-day	<ul style="list-style-type: none"> Progression to dementia measured by MMSE and ADAS-cog 	Ongoing Recruiting
MAPT NCT00672685	1200 frail elderly with subjective memory complaints ≥ 70 years	3 Years	DHA 800 mg/day	<ul style="list-style-type: none"> Changes in memory function scores determined by Gröber & Buscke test 	Ongoing Recruiting
OPAL ISRCTN72331636	800 healthy volunteers aged between 70–79	2 Years	n3 PUFAs 700 mg/day	<ul style="list-style-type: none"> Slow the decline of cognitive function as determined by the California Verbal Learning Test 	Ongoing Recruitment completed
PREADVISE NCT00040378	10400 men with no neurological or psychiatric illness 60–90 years	7–12 Years	Vitamin E + Selenium 400 mg + 0.2 mg/day	<ul style="list-style-type: none"> Prevention of Alzheimer's disease as measured by Memory Impairment Screen (MIS) 	Ongoing Not recruiting
Royal Perth Hospital ACTRN12605000045617	300 older men with a previous history of hypertension ≥ 75 years	2 Years	B-vitamins 2 mg folate + 25 mg B6 + 0.4 mg B12/day	<ul style="list-style-type: none"> Prevention of cognitive impairment measured by MMSE, Clock Drawing Test, California Verbal Learning Test and Test of Attention 	Ongoing Recruitment completed
University of Otago ACTRN12605000030673	260 healthy elderly ≥ 65 years plasma homocysteine $\geq 13 \mu\text{M}$	2 Years	B-vitamins 1 mg folate + 10 mg B6 + 0.5 mg B12/day	<ul style="list-style-type: none"> Rate of cognitive performance impairment measured by a range of tests of cognition 	Ongoing Recruitment completed

Abbreviations: DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MCI, mild cognitive impairment; PS, phosphatidylserine; PUFAs, polyunsaturated fatty acids.

completed and ongoing clinical nutritional intervention studies to date.

The results of nutritional intervention studies in AD prevention appear to be conflicting. Meta-analyses of clinical studies investigating the potential of cholesterol-reducing agents [20] and vitamin E [21] for the prevention of AD both failed to uncover clear benefits. Although effects are not overwhelmingly convincing, there are trends for potential benefits provided by n-3 PUFA, phospholipid, and B-vitamin supplementation. Difficulties establishing clear-cut evidence supporting efficacy in terms of cognitive impairment may be due to supplementary doses in clinical trials being much higher/lower than are physiologically required, or a consequence of the single-nutrient, single-target study designs. Furthermore, prevention of cognitive decline is not always the primary outcome of nutrient intervention studies in prevention of AD. Some intervention studies have utilized surrogate markers such as $A\beta$ to demonstrate that specific nutritional components are able to counteract underlying neurodegenerative and pathological processes in the AD brain. This will be considered in further detail within the mechanistic section of this review.

The importance of considering the diet as a whole (rather than single components) in observational-type studies is gaining increasing recognition. There is substantial evidence for the existence of food synergy – the additive or more-than-additive influences of foods and food constituents on health [22]. For example, the Mediterranean diet is characterized by a high intake of vegetables, legumes, fruits, cereals, and unsaturated fatty acids and fish, and low intake of saturated fatty acid; this incorporates many of the nutritional components considered potentially beneficial for cognitive decline. Adherence to a Mediterranean-style diet has been associated with a reduced risk for developing AD [23]. Based on studies comparing single *versus* multiple nutrient supplementation [24], there is a need for multi-nutrient, multi-target interventional AD management approaches.

MECHANISMS SUPPORTING THE ROLE OF NUTRITIONAL INTERVENTION IN AD PREVENTION

Multiple mechanisms underlie AD pathogenesis

The neurodegenerative and pathological processes that underlie the development of AD are complex and

interrelated. Consequently, targeting individual disease targets is unlikely to be an effective therapeutic approach. This is evidenced by recent systematic reviews focusing on individual nutrients: the reduction of cholesterol by statins [20] and reactive oxygen species (ROS) by the antioxidant vitamin E [21]. Although biologically it seems feasible that each of these interventions could potentially help to prevent or delay cognitive decline, individually their efficacy in randomized clinical trials has not been established.

In terms of helping to understand how specific dietary components impact the biochemical mechanisms responsible for disease processes, there is merit in examining individual nutrients. Aspects of AD pathogenesis that can be targeted from a nutritional perspective will be considered.

Amyloid- β /tau

A characteristic pathological feature of the AD brain is the accumulation and spreading of extracellular senile plaques consisting of $A\beta$ and neurotoxic intraneuronal neurofibrillary tangles consisting of phosphorylated tau protein (see Fig. 1). Generation of $A\beta$ /tau pathology may be prevented by targeting mechanisms at different levels in the progression of pathology.

Supplementation with the n-3 PUFA DHA has been shown to promote membrane fluidity [8]; this stimulates non-amyloidogenic amyloid- β protein precursor ($A\beta$ PP) processing resulting in reduced $A\beta$ production [25,26]. Additionally, DHA has been shown to inhibit $A\beta$ production by increasing the expression of LR11 (a protein involved in sorting and trafficking of $A\beta$ PP) [27], and reducing presenilin 1 levels (a component of the γ -secretase complex) [28,29]. DHA may also prevent $A\beta$ aggregation by stimulating the transcription of the $A\beta$ scavenger transthyretin [30] and through inhibition of $A\beta$ fibrillation, as well as disruption/destabilization of preformed $A\beta$ fibrils [31]. Uridine has been shown to specifically stimulate α -secretase activity [32] and when combined with DHA and B-vitamins also reduced activity of the γ -secretase complex (preliminary data) [33]. Administration of antioxidants in a transgenic mouse model of AD resulted in a significant reduction in $A\beta$ levels and amyloid deposition [34].

Elevated plasma homocysteine is often regarded a risk factor for the development of AD. In a study of elderly men randomized to two years of treatment with folate plus vitamins B6 and B12, or placebo, those who received B-vitamins had significantly lower plasma ho-

homocysteine levels and tended to have reduced plasma A β compared with the placebo group [35]. However, findings from the large, randomized Vitamin Intervention for Stroke Prevention (VISP) trial suggest that homocysteine is a marker for, rather than a risk factor for, vascular disease [36]. A strong correlation exists between plasma homocysteine and A β levels in individuals with vascular disease [37]. Yet while high-dose vitamin supplementation in ischemic-stroke patients lowers plasma homocysteine levels, it has no influence on plasma A β levels. On this basis, it seems that despite an association, plasma homocysteine and A β levels are most likely regulated via independent pathophysiological mechanisms [36].

The first experimental demonstration of a reduction in tau pathology involved co-supplementation of DHA and n-6 fatty acid docosapentaenoic acid (DPA) in a mouse model of AD. This effect was thought to be mediated via a reduction in activated (phosphorylated) c-Jun N-terminal kinase (JNK, a member of the stress-activated mitogen-activated protein kinase family) [28]. Studies implicating protein phosphatase 2A methyltransferase-dependent methylation of tau and A β PP suggest that folate deficiency may trigger/hasten accumulation of phosphorylated A β PP and tau in the brain, favoring neurofibrillary tangle formation and amyloidogenesis [38].

Synaptic loss

Even in the absence of AD, the aging process alone is associated with a gradual loss of neurons in various brain regions [39]. Decreased ability to create new synapses and biochemical changes that directly influence the fluidity of neuronal membranes has a negative effect on numerous synaptic processes. These include communication (axonal signal transduction), regulation of membrane-bound enzymes, ion channel structure, and maintenance of various receptors [40]. In individuals with AD, decline in the number of brain synapses (see Fig. 1) is a major contributing factor to the development of cognitive impairment [41]. Counteracting this decline may have the potential to prevent the onset of cognitive decline and AD-type dementia.

Synapses and neurites consist of neuronal membranes which are composed of phosphatides. Synthesis of brain membrane phosphatides is dependent on circulating nutritional precursors: DHA, uridine, and choline. In experimental animals, oral administration of these three compounds increased levels of phosphatides and synaptic proteins in the brain and per brain cell,

as well as the numbers of the membranous protrusions from dendrites known as dendritic spines on hippocampal neurons, which form the anatomical precursors of synapses [42,43]. In transgenic mice, DHA supplementation has demonstrated protective effects against dendritic pathology, and increased levels of DHA in the brain have been shown to significantly enhance hippocampal dendritic spine formation leading to improved spatial learning [43,44]. Combined administration of uridine and choline has also been shown to improve selective attention and spatial learning in a rat model of cognitive impairment [45].

B-vitamins and antioxidants also play a crucial role. B-vitamins are involved as co-factors in methylation processes that drive cellular metabolism and membrane phosphatide formation in the Kennedy pathway. Antioxidants reduce ROS-induced damage and stabilize membranes, suppressing synaptic loss. *In vitro* studies with PUFAs combined with a vitamin and mineral complex, or supplementation with a vitamin-B complex (B₁, B₆, and B₁₂) have been shown to increase neurite formation [46,47]. Administration of multiple nutrients (including DHA, choline, uridine, and B-vitamins) promotes receptor-mediated (e.g., P₂Y and syntaxin) synthesis of synaptic membranes and neurite outgrowth [48]. Indicative of the functional potential of newly formed membranes, dendritic spines and synaptic proteins increase in parallel with increases in membrane phosphatides [49].

Nutrients stimulating the formation of neuronal membranes and synapses also enhance evoked release of neurotransmitters like acetylcholine and dopamine [50,51]. In terms of receptor function, neurite-promoting nutrients have been associated with increased agonist binding to serotonergic 1A and muscarinic 1 receptors through changes in membrane fluidity [52]. DHA phospholipids appear to optimize the propagation of G-protein-coupled receptor signaling [53].

Vascular system

Epidemiological evidence suggests that risk factors for vascular disease and stroke are associated with cognitive impairment and AD, and that the presence of cerebrovascular disease intensifies the presence and severity of the clinical symptoms of AD [54]. Susceptibility to vascular risk factors tends to be prevalent in the elderly, so they often have one or more increased risk factors. Hypertension and hypercholesterolemia are well-known risk factors for cognitive decline, which

have been shown to be reduced by intervention with fish oil-derived PUFAs [55], B-vitamins [56–58], or phospholipids [59]. Evidence suggests that alleviating these risk factors may improve endothelial function by reducing the number of microvessels with degenerative pericytes [60], increasing cerebral endothelial nitric oxide synthase, and glucose transporter-1 expression, and decreasing vascular cell adhesion molecule-1 expression [58]. Together, these changes may lead to improved condition of the blood-brain barrier [60].

Inflammation and oxidative stress

Proinflammatory cytokines, e.g., interleukin-1 β (IL1 β) modulate central nervous system functions and may contribute to the etiology of MCI and AD. Animal studies suggest that intervention with specific nutrients (PUFAs, B-vitamins, and phosphatidylserine) has the potential to reduce plasma levels of inflammatory IL1 β and thereby attenuate associated behavioral changes by counteracting its neuroendocrine and immune effects [61,62]. On the other hand, dietary supplementation with eicosapentaenoic acid can stimulate the formation of the anti-inflammatory cytokine IL10 [61,63].

Oxidative stress is also known to increase in the aging brain. Therefore, antioxidant supplementation may help to scavenge ROS formation in the brain and offer protection by reducing ROS-induced lipid/protein peroxidation and DNA/RNA damage [64].

Rationale for a multi-target approach

To summarize, nutrition is complex with individual nutrients acting on multiple targets. For example, based on current understanding: DHA lowers cholesterol, blood pressure, and A β ; B- vitamins reduce homocysteine, improve endothelial function, and play a role in phospholipid formation; and antioxidants reduce ROS-induced damage and stabilize membranes.

Having considered the mechanisms that underlie AD pathogenesis, it is clear that there exists a wealth of preclinical evidence supporting a role for nutrients in the prevention of MCI and AD. Demonstrated additive/synergistic effects by combining nutritional components underline the importance of a multi-nutrient, multi-target approach to achieve optimal therapeutic benefits in the prevention of AD [24].

IMPLICATIONS AND CONCLUSIONS

Epidemiological evidence suggests that specific nutrients such as PUFAs, vitamins, and antioxidants can affect the risk of cognitive decline and prevent the development of AD. Age-related changes in nutritional status play an important role in brain functioning. Susceptibility of the elderly population to specific nutrient deficiencies may exacerbate pathological processes in the brain.

The potential of nutritional supplementation to prevent cognitive decline by counteracting deleterious neurodegenerative and pathological processes is of great public and scientific interest. Current understanding suggests that multi-nutritional (rather than single nutrient) intervention, targeting multiple disease aspects – A β , synaptic loss, vascular system, inflammation, and oxidative stress – may have the greatest therapeutic potential. A recent 12-week proof-of-concept study with multi-nutrient drink Souvenaid[®], designed to meet the increased demand of particular nutrients, suggested that it was well-tolerated and improves memory in patients with mild AD [56]. Especially given the synergy seen to occur between nutrients in many studies, there is no reason why nutrient supplementation should exceed physiological levels. From a safety perspective, nutritional supplements could conceivably be administered as an add-on therapy to AD patients already receiving anti-AD medication.

Pathological changes in the brains of persons at risk for developing AD can develop as early as 20 to 30 years prior to clinical dementia symptoms [65]. Therefore, the earlier that nutritional supplementation can be initiated the greater the potential to prevent/delay cognitive decline and AD. Protecting neuronal tissue, cells, and synapses when damage is minimal may offer the most meaningful long term outcomes. Preventing or delaying the onset of AD would enable higher functional levels to be maintained and help to preserve quality of life and independence. There is a need for the development of earlier detection of neurodegenerative processes, especially in individuals who are at particular risk of developing AD. However, even further along in the disease process, supplementation of specific brain-supportive nutrients may still be able to prevent further deterioration or improve brain function.

DISCLOSURES

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