

Chapter 16

Nutrition and Nutritional Supplements to Promote Brain Health

Abhilash K. Desai, Joy Rush, Lakshmi Naveen, and Papan Thaipisuttikul

Abstract New scientific evidence strongly suggests that a variety of nutritional strategies can promote brain health and slow the course of Alzheimer's disease and related dementias (ADRD). Improving nutrition is, thus, a critical component of any comprehensive strategy to slow the course of ADRD. This chapter presents recommendations designed to meet this objective. Specific goals are to consume a balanced diet with particular focus on increasing consumption of brain power foods. Examples of brain power foods include oily fish (to be consumed at least twice a week), berries (especially blueberries), green leafy vegetables, legumes, and turmeric. In addition, some nutritional supplements (especially vitamin D and vitamin B12) are also necessary to promote brain health. Multinutritional intervention, targeting multiple aspects of processes causing ADRD, instituted as early as possible is likely to have the greatest beneficial effect. Staying physically and mentally active and maintaining a healthy weight can greatly enhance the beneficial effects of nutritional interventions on brain health.

Introduction

Cognitive impairment associated with Alzheimer's disease and related dementias (such as Vascular dementia, Dementia with Lewy Bodies, Parkinson's Disease Dementia, Fronto-Temporal Dementia) (ADRD) causes impairment in daily functioning and significant emotional distress. New scientific evidence has indicated that appropriate changes in a person's diet *can* enhance their cognitive abilities, protect brain from damage, and may counteract the effects of dementia (Morley, 2010).

A.K. Desai (✉)

Medical Director, Geriatric Psychiatry Director, Memory Clinic, Sheppard Pratt Health Systems, Associate Professor, Department of Neurology and Psychiatry, Division of Geriatric Psychiatry, Saint Louis University School of Medicine, 605 N. Charles St., Baltimore, MD 21285, USA
e-mail: adesai@sheppardpratt.org

Nutrition researchers and scientists have identified foods and eating patterns that both increase and decrease the risk of ADRD (Gu, Nieves, Stern, Luchsinger, & Scarmeas, 2010). The effect of brain healthy food can be enhanced by combining it with other healthy lifestyle strategies such as regular exercise and engagement in intellectual and social activities (Kidd, 2008). Clinical trials to date investigating drugs for Alzheimer's disease (AD) have found that 25% of patients with AD do not worsen over 18-month period (Schneider & Sano, 2009). This allows time for nutritional and other lifestyle interventions to be instituted and have their impact.

Mechanisms of Diseases Causing Dementia and Nutrition

Processes that underlie ADRD pathogenesis include oxidative stress, chronic inflammation, accumulation of toxic mis-folded proteins, impaired utilization of glucose by brain cells, mitochondrial dysfunction, toxicity due to excess neurotransmitters (e.g., glutamate), and inadequate blood and oxygen supply to the brain cells (neurons) and brain connections (synapses) (Querfurth & LaFerla, 2010). These processes lead to loss of brain cells and brain connections, eventually leading to memory and other problems characteristic of ADRD. Growing research suggests that several nutritional components (e.g., anthocyanins, sulforaphane, curcumin) can effectively counteract these processes, e.g., by reducing oxidation and inflammation, decreasing accumulation of toxic proteins, promoting membrane formation and formation of new synapses and new brain cells, prolonging life of existing brain cells, improving function of inner lining (endothelial lining) of blood vessels, and thus improving blood and oxygen supply to the brain cells (Kamphuis & Scheltens, 2010). The suggested synergy between nutritional components to improve neuronal plasticity (i.e., capacity of the brain to change with experience and environment) and brain function is supported by epidemiological studies as well as experimental studies in animal models, although randomized controlled trials (RCTs) are lacking (van der Beek & Kamphuis, 2008).

The brain is particularly susceptible to oxidative damage. Brain activity consumes a lot of energy, and the reactions that release this energy also generate oxidizing chemicals. In addition, the brain contains a great amount of oxidizable tissue, particularly in the fatty membranes surrounding nerve cells. Tissue-damaging free radicals (reactive oxygen species and reactive nitrogen species formed during oxidation) become more prevalent as we age and their harmful effects are promoted by accumulation of toxic proteins and decrease blood circulation seen in ADRD (Desai, Grossberg, & Chibnall, 2010). This has led to the attempt to slow the progress of ADRD by using antioxidants (class of chemicals that protect brain cells and other tissues in the body against free radicals). Although research to date using antioxidants in the form of pills (e.g., vitamin E) to treat ADRD has been disappointing, studies to promote brain health through increasing intake of food high in antioxidants (e.g., Mediterranean diet) continue to be encouraging. Fruits and vegetables are the primary source of antioxidants. Over-eating increases oxidative stress on the brain and thus risks undoing the work of antioxidants and exercise. High blood sugar can also cause oxidative stress on the blood vessels and the brain.

Dietary Patterns and Brain Health

Mediterranean diet: The Mediterranean diet is characterized by high intake of vegetables, legumes, fruits, and cereals; high intake of unsaturated fatty acids (mostly in the form of olive oil), but low intake of saturated fatty acids; a moderately high intake of fish; a low-to-moderate intake of dairy products (mostly cheese or yogurt); a low intake of meat and poultry; and a regular but moderate amount of ethanol, primarily in the form of wine, which is generally consumed during meals. The Mediterranean diet has been found to improve cholesterol levels, blood sugar levels, and overall health of blood vessels. It has been associated with longer life, decreased heart disease and strokes, and reduced risk of obesity and diabetes. Recent studies have found that higher adherence to Mediterranean diet was associated with lower risk for both AD and Mild Cognitive Impairment (Scarmeas et al., 2009). Other studies have found that higher adherence to the Mediterranean diet was associated with lower mortality in AD in a possible dose–response effect. The Mediterranean diet may slow the progression to dementia. The potential mechanisms for Mediterranean diet to promote brain health includes antioxidant effect, anti-inflammatory effect, reducing destructive effects of toxic proteins (e.g., beta amyloid and hyperphosphorylated tau in AD), and improved blood supply to brain cells.

DASH diet (dietary approaches to stop hypertension): The DASH diet is a diet rich in fruits and vegetables, and low-fat dairy products, and low in saturated and total fat. The DASH diet comprises 4–5 servings of fruit, 4–5 servings of vegetables, 2–3 servings of low-fat dairy per day, and <25% fat. Besides lowering blood pressure, the DASH diet may also directly promote brain health through its high antioxidant effects.

Specific Food Groups to Promote Brain Health

Fruits, vegetables, and legumes: Fruits, vegetables, and legumes contain a variety of phytonutrients that have strong antioxidant and anti-inflammatory properties. Phytonutrients (also called phytochemicals) are organic compounds of plants that are thought to promote health. Unlike the traditional nutrients (proteins, fat, vitamins, minerals), phytonutrients are not “essential” for life. Some common classes of phytonutrients that have been found to promote brain health include carotenoids, flavonoids (polyphenols), lignans, saponins, and terpenes. All types of fruits, vegetables, and legumes promote brain health. Preliminary research has suggested that certain fruits, vegetables, and legumes may have more nutritional punch in regard to brain health compared to others. Several studies have indicated that regular consumption of 5–10 servings per day of fruits, vegetables, and legumes enhances brain function and may slow cognitive decline. Polyphenols isolated from blueberries have been shown to demonstrate positive effects on cognitive functioning in persons with dementia. Among all fruits, berries have some of the highest amount of antioxidants. Many vegetables (e.g., broccoli) contain chemicals (e.g., sulforaphane) that encourage production of enzymes which protect the blood vessels, and thus

promote blood flow to the brain. Among vegetables, tomatoes and green leafy vegetables have some of the highest amount of nutrients (e.g., lycopene, folate) that are needed for brain to function well.

Omega-3 fatty acids (O3FA): O3FA are essential fatty acids (i.e., they cannot be synthesized by the body and need to be obtained from food). There are three O3FA, Docosahexanoic acid (DHA), Eicosapentanoic acid (EPA), and linoleic acid. DHA constitutes 40% of all fatty acids in the brain. DHA is found predominantly in marine fish and algae. DHA has antioxidant and anti-inflammatory properties and enhances synaptic function (function of brain cell connections). DHA provides synaptic membranes with “fluidity” – improved capacity to transmit signals from one cell to another. Therefore, decreased DHA in neuronal membranes may weaken the brain architecture and leave it vulnerable to diseases. Low levels of DHA have been found in persons with dementia. O3FA can improve memory in genetically modified Alzheimer’s mouse model. Best sources of O3FA include a variety of oily fish. It is important that fish is consumed either baked or broiled. When fish is fried, the nutritional value is lost (due to loss of omega 3 during the process of frying) and harmful chemicals (e.g., partially hydrogenated fatty acids) are created by frying process that may harm the brain by promoting inflammation. Other sources of O3FA include walnuts, Kiwi, flax seed, and omega-3 enriched food items (e.g., eggs, milk, cereals). It is important to eat a variety of fatty fish. Due to concern about mercury contamination of some fish, we recommend avoiding fish with high mercury content such as King Mackerel, swordfish, golden bass, shark, and tilefish.

Whole grains: Whole grains are another excellent source of phytonutrients. Whole grains pack more nutritional punch and fiber than refined grains (e.g., white bread, white rice). Whole grains are rich in B vitamins, fiber, and antioxidants and thus have significant beneficial effects on brain function. Whole grains include wheat, barley, oats, rye, kasha, bulgar, millet, quinoa, and maize. Commonly consumed food rich in whole grains include whole grain pasta, brown rice, whole wheat bread, and quinoa. We can make breads, muffins, and other home-made goods healthier by mixing whole-wheat flour with white flour. Higher intake of whole grains can help lower amounts of blood sugar, total body fat, and abdominal fat, which may be especially important for individuals with diabetes, obesity, and metabolic syndrome. Not all foods in the grocery store that claim to be “whole grain” are whole grain. Many include refined or enriched white flour. Foods with labels that say “100% whole wheat” (or oats or rye) are recommended.

Monounsaturated fatty acids (MUFA): MUFA, as part of traditional Mediterranean diet, have been found to promote brain health and slow cognitive decline. Animal studies support the concept that extra-virgin olive oil plays a central role in slowing the dementing process. Sources of MUFA include olive oil (preferably first cold-pressed extra-virgin olive oil), canola oil (cheaper than olive oil and equally beneficial) and avocados. Regularly adding a few olives in one’s salads or other food items is an easy way to improve intake of MUFA. MUFA are high in calories and thus excess consumption should be avoided.

Spices: Spices (e.g., turmeric, cinnamon, cloves, red pepper, black pepper, ginger, garlic) have all been found to contain phytonutrients with potential disease-modifying capabilities. Turmeric, or Indian saffron, is currently the most promising among all spices regarding potential benefits in AD. Several studies have pointed to curcumin, the active ingredient in turmeric, and its anti-inflammatory and anti-amyloid properties (Aggarwal & Sung, 2009). Turmeric is an orange-yellow powder commonly used as a spice in curries. Turmeric is present in many Asian curries. High Asian curry consumption has been found to be associated with improved memory and other cognitive functions. Most Asian curries prepared in US restaurants have high salt and saturated fat content and therefore are not good options to promote brain health. A pinch of turmeric may be mixed with home-made healthy curries and sauces. Turmeric is also found in some pickles and in yellow mustard that can be used in sandwiches.

Nuts: Nuts are also an excellent source of many phytonutrients. Tree nuts (e.g., walnuts, almonds, pecans, hazel nuts) have chemicals (e.g., O3FA in walnuts, vitamin E in almonds, MUFA in most of the nuts) that have been known to promote brain health. It is prudent to limit consumption of nuts to small amounts as they contain high amount of fat and thus, high amount of calories.

Green tea: Green tea has high content of polyphenolic flavanoids known as “catechins.” Catechin has been demonstrated to have potent antioxidant and anti-inflammatory properties. Sugar and saturated fat in many commonly consumed tea drinks (e.g., “chai tea” found in coffee houses) may not only cancel out the beneficial effects but may even be harmful to the brain. Caffeine content of tea can also cause insomnia, anxiety, tremors, and irregular heart beat.

Coffee: Some studies have found that regular consumption of coffee is associated with decreased future risk of AD. Sugar and saturated fat in many commonly consumed coffee drinks (e.g., “lattes” found in coffee houses) may not only cancel out the beneficial effects but may even be harmful to the brain. Caffeine content of coffee can also cause insomnia, anxiety, tremors, and irregular heart beat.

Dark chocolate: Dark chocolate (true dark chocolates are bitter) has been found to have beneficial effects on heart health and brain health. Stearic acid in pure chocolate is a saturated fat that acts more like unsaturated fat in that it lowers LDL levels and reduces atherosclerosis. An exact amount is not clear; hence their use is recommended only in very modest amounts. For example, an ounce of dark chocolate (at least 70% cocoa) per day may be appropriate. Note that many “dark chocolates” may not have flavonols (one group of phytonutrients) (removed by their manufacturers because of their bitter taste) but have abundant saturated fat, refined sugar, and calories – all three proven to be harmful to the blood vessels, the heart, and the brain. Even with flavonols present, chocolate lovers should be mindful of the other contents. Those who eat a moderate amount of flavanol-rich dark chocolate may need to balance the calories by reducing their intake of other foods.

Sweeteners: Splenda is recommended over other sweeteners such as aspartame or stevia. This is because splenda has been researched the most among all sweeteners

and to date, it has not been linked to any adverse direct effects on the brain or body. We recommend using only modest amounts of sweeteners because eating sweet food regularly can train the brain to crave for sweet food which in turn can lead to consumption of calorie dense sweet foods.

Alcohol: Modest alcohol intake has been associated not only with improved heart health but also with reduced risk of future dementia and slower cognitive decline in patients with MCI. However, by the time a person develops dementia, the brain is significantly damaged and thus becomes very sensitive to toxic effects of even modest amounts of alcohol. Brain damage is a common and potentially severe consequence of long-term, heavy alcohol consumption. Even social drinkers who consume more than 21 drinks per week are at high risk for cognitive impairment in the long run. Excessive alcohol use can cause structural and functional abnormalities of the brain. These changes are more severe and other brain regions are also damaged in patients drinking excessive alcohol who have additional vitamin B1 (thiamine) deficiency (Wernicke–Korsakoff syndrome). The more alcohol consumed, the smaller the total brain volume. Thus, the negative effect of excessive, at-risk alcohol consumption and binge drinking habits is of much greater concern than possible beneficial effects of light drinking. At-risk and binge drinking are frequently reported by middle-aged and elderly adults nationwide (Blazer & Wu, 2009). Therefore, advice about alcohol consumption should be tempered by the known risks of excessive use in terms of neurologic and other organ damage as well as increased risk of injury from intoxication. Also, alcohol interacts with many medications routinely taken by middle aged and older adults with potentially serious adverse health consequences. Persons with dementia should be recommended to avoid intake of alcohol. For those adults with dementia who drink regularly and wish to continue, we recommend that men avoid drinking more than 7 U/week (maximum of 1/day). Women should avoid drinking more than 4 U/week (maximum of 0.5/day). All adults with dementia should avoid drinking 3 or more units of alcohol at 1 time. One unit of alcohol is equal to 12 oz of beer, 4–5 oz of wine and 1 oz of distilled spirit.

Medical Foods and “Memory Shakes”

Medical food is defined as a medical product intended for the dietary management of a disease or a specific condition. Medical foods are available by prescription only and should be taken only under the supervision of a physician or a physician extender (nurse practitioner or physician assistant). Axona is the only medical food currently available for clinical management of mild-to-moderate stage AD. Hypometabolism may be involved in the pathogenesis of AD. Hypometabolism involves brain’s impaired ability to breakdown and/or utilize glucose as source of energy. Axona is thought to promote brain health by providing an alternative source of glucose that the brain can use for energy. A small study found that there was slower decline in memory and other cognitive functions compared to placebo in subjects with mild-to-moderate Alzheimer’s disease who were APOE e4 negative (Henderson et al., 2009).

Adverse effects reported include diarrhea, flatulence, and abdominal distress. We recommend starting with half a packet shaken with milk, fruit juice, or water daily in the morning for a week before trying one packet daily. In individuals with protein calorie malnutrition, Axona can be mixed with health shakes such as Ensure, Boost, or Carnation Instant Breakfast. Patients with uncontrolled diabetes, alcohol abuse, and liver disease are recommended to avoid Axona.

The three compounds – O3FA, uridine, and choline – are all needed by brain cells to make phospholipids, the primary component of cell membranes. Increasing intake of these compounds has been found to dramatically increase the amount of membranes that form brain cell connections. Loss of brain cell connections is believed to cause memory loss and other cognitive impairments seen in ADRD. Souvenaid is a “memory shake” rich in these three compounds. It is currently being studied for potential benefits to persons with AD. There are animal studies supporting its potential effects on memory (Morley, 2010). Preliminary analysis of the study suggested that in patients with early AD, there was an improvement in verbal memory (Scheltens et al., 2010). Benevia is a drink containing lutein and DHA. It is available over the counter and advertised as a “memory boosting” drink. It contains high amounts of sugar, so caution is needed in patients with diabetes. It also contains a good amount of protein and thus may be particularly beneficial to individuals with protein calorie malnutrition.

Nutritional Supplements

Nutritional supplements are often needed to supplement diet in order to promote brain health. They are recommended because even older adults who eat a brain healthy and well-balanced diet may not absorb necessary nutrients because of age and disease-related problems with absorption. There are several widely marketed nonprescription nutritional supplements claimed to be memory enhancers and treatments for cognitive decline associated with ADRD (McDaniel, Maier, & Einstein, 2003). Supplements may promote brain function through a variety of mechanisms including antioxidant, anti-inflammatory, and metabolic regulation. Besides cognition, some supplements (e.g., Vitamin D, O3FA, B12, Folate, Acetyl L Carnitine) may have antidepressant effects (Yashodhara et al., 2009). Table 16.1 lists commonly used supplements, their doses, and common adverse effects. There are also supplement products available that combine a variety of supplements. Studies in animals indicate that some combinations of supplements may decrease oxidative stress and prevent cognitive decline (Suchy, Chan, & Shea, 2009). Caution in using such combination products should be urged due to risks that have not been identified due to a lack of rigorous studies on such products. There is also a potential for many such supplements to interact with prescription medications commonly used by persons with ADRD (e.g., combination of huperzine and antimentia drugs [e.g., donepezil, galantamine, rivastigmine] can lead to vomiting and diarrhea) (Desai & Grossberg, 2003). There are no RCTs to support the use of any herbal remedies and

Table 16.1 Nutritional supplements commonly used to promote brain health

Nutritional supplement	Recommended daily dosage	Adverse effects and toxicity symptoms
Vitamin D	Ranges from 1,000 IU once daily to 50,000 IU once a week depending on how low vitamin D blood levels are	Toxicity symptoms: Excessive thirst, dehydration, anorexia, nausea, vomiting, headache, constipation, weakness, increase levels of calcium in the blood, kidney stones
Vitamin B12	500–1,000 µg	No known toxicity or serious side effects
Folic acid	Ranges from 400 to 1,000 µg/depending on blood levels	Large doses can mask symptoms of vitamin B ₁₂ deficiency
Nicotinamide	300–500 mg	Toxicity symptoms: increased heart rate, anxiety, bloating, flatulence, nausea, tingling and numbness in extremities, blurred vision
Vitamin B1	100 mg	No known toxic effects from oral intake
Vitamin B3 Niacin	Unclear	Toxicity symptoms: headache, nausea, skin flushing and tingling, sweating
Omega-3	500–1,000 mg of DHA ^a in two divided doses	Adverse effects: eructation, dyspepsia, taste perversion, bleeding time prolonged
Ginkgo Biloba	40–80 mg 3 times/day Standardized to contain 24–27% ginkgo flavone glycosides and 6–7% triterpenes per dose	Adverse effects: nausea, and dyspepsia, prolongs bleeding time and thus avoided in patients at risk of bleeding (e.g., patients taking anticoagulants, or with clotting disorders)
Huperzine A	50 µg 1–3 times/day	Nausea, vomiting, and abdominal distress and interacts with commonly used antidementia drugs
Alpha lipoic acid	20 mg–900 mg/	Low blood sugar, skin rash
Acetyl L Carnitine	500–2,000 mg/ in divided doses; up to 3 g daily have been used	Mild abdominal discomfort, restlessness, vertigo, and headache
Vinpocetine	10–40 mg twice daily	Nausea, vomiting, and abdominal distress

^aDHA docosahexanoic acid

supplements for the treatment of ADRD. Hence, no supplements are recommended for routine treatment of ADRD. HCPs may consider judicious use of supplements in selected patients with ADRD, especially if there is great interest from the patient and/or the family to try supplements to promote brain health. In patients with ADRD who have documented deficiencies of certain nutrients (e.g., vitamin B12, D), replacement therapy may improve cognitive function and/or slow cognitive decline. Guidance and ongoing follow up from healthcare provider who is knowledgeable about risks and potential benefits of supplements are recommended before initiation of supplement therapy.

1. *Vitamin D (Calciferol)*: Vitamin D helps to maintain normal blood levels of calcium and phosphorus which strengthens bones. Vitamin D is fat soluble vitamin and thus is stored in fat cells. Well-recognized effects of vitamin D deficiency include hip fractures, falls, functional deterioration, muscle pain, and increased mortality. Thus, maintaining adequate levels of vitamin D may improve overall musculoskeletal health and thus, indirectly promote brain function. Recent studies have found that deficiency of 25(OH) vitamin D is associated with cognitive impairment (Morley, 2010). Vitamin D may have a protective role in neurodegenerative diseases. Meeting the recommended daily requirements of vitamin D (1,000–2,000 IU) is a challenge. Foods rich in vitamin D include egg yolks, oily fish (e.g., salmon, sardines), fortified cereal, and dairy products. Sun exposure for about 15 min daily works, too. Salmon has one of the highest natural food sources of vitamin D, with 360 IU per 3.5 oz. Vitamin D deficiency occurs as a result of restricted sunlight exposure, reduced capacity of the skin to produce vitamin D, and reduced dietary intake. The prevalence of vitamin D deficiency is common in elderly, affecting up to 50% of older adults and a much higher percentage of nursing home residents. Hypercalcemia can cause cognitive impairment and vitamin D supplementation may exacerbate hypercalcemia. For this reason, it is essential to measure 25(OH) vitamin D and calcium levels. Most Americans seem to have enough calcium, but vitamin D is a bigger concern. Adequate level should be maintained over 32 ng/mL.
2. *Vitamin B12 (Cyanocobalamin)*: Vitamin B12 assists in making new brain cells and new brain connections. It also prolongs life of existing brain cells, helps production of red blood cells (cells that carry oxygen in the body), and decreases homocysteine levels. Vitamin B12 deficiency is common in older adults and even more prevalent in individuals with ADRD. It is classically on the list of reversible dementia. Other psychiatric symptoms of vitamin B12 deficiency are depression, psychosis, and delirium. Longer periods of deficiency lead to irreversible damage. Vitamin B12 supplements come in injectable, oral, and nasally inhaled form. Whatever the replacement method, vitamin B12 should be monitored to ensure adequate supplement.
3. *Folic acid (folate, folacin, vitamin B 9)*: Folic acid deficiency is uncommon in Americans because of fortification of food (e.g., bread) with folate. Folic acid deficiency can cause cognitive impairment and depression. In addition, deficiency of folic acid results in high concentration of homocysteine through different pathways. An increase in homocysteine level contributes to the AD pathology by vascular mechanisms or as a neurotoxin. A high intake of folate seems to help decrease the homocysteine level. Recent studies in patients with ADRD have found a relationship between low serum folate level and cognitive impairment. A study also found that higher folate intake is related to lower risk of AD. The small number of studies done to date provides no consistent evidence either way that folic acid supplementation, with or without vitamin B12, has a beneficial effect on cognitive function of unselected healthy or cognitively impaired older people (Malouf & Grimley Evans, 2008). In a preliminary study, folic acid was associated with improvement in the response of people with AD to cholinesterase inhibitors.

In another study, long-term use appeared to improve the cognitive function of healthy older people with high homocysteine levels. Folic acid supplementation may exacerbate vitamin B12 deficiency in patients with preexisting, uncorrected vitamin B12 deficiency. Thus, all patients receiving folate supplementation should have vitamin B12 levels checked and if low corrected prior to folate supplementation.

4. *Vitamin B1 (Thiamine)*: Vitamin B1 deficiency is uncommon in patients with ADRD unless they have diabetes or alcohol abuse problems. Thiamine deficiency causes “beri-beri” syndrome, which can involve neurologic and cardiovascular symptoms. Neurologic symptoms include peripheral neuropathy, Wernicke’s encephalopathy (confusion, double vision, and impaired balance), and Korsakoff syndrome. Thiamine deficiency often occurs in patient with alcohol addiction. Korsakoff syndrome is characterized by severe memory loss, both anterograde and retrograde, confabulation which is invented memories that are taken as true because of the gap in memories, and apathy which is loss of interest and appear indifferent to change. It may be mistaken for ADRD. Vitamin B1 deficiency induces oxidative stress, increases inflammation, and may exacerbated toxic amyloid beta levels. Treatment of thiamine deficiency involves oral supplementation.
5. *Vitamin B3 (Niacin/Nicotinamide)*: Niacin deficiency is uncommon in individuals with ADRD. Deficiency of niacin can cause “pellagra,” a disease with rough scaly skin, diarrhea, muscle weakness, mental confusion, and dementia. Early treatment with niacin can reverse some or all of these problems. Niacin is an effective treatment for high cholesterol and low high-density lipoprotein (HDL) as well. Preliminary data suggest that those with the high intake of niacin were less likely to have developed AD or decline in memory during the 5-year period. In an animal study, niacin was found to restore cognitive deficit in AD associated with tau protein pathology.
6. *Vitamin B6 (pyridoxine, pyridoxal, pyridoxamine)*: Vitamin B6 helps make red blood cells and is important for normal brain function. It helps lower homocysteine levels. It also promotes immune system function. Most Americans do not have B6 deficiency.
7. *Omega-3 fatty acids supplements (O3FA)*: Patients with ADRD who do not eat fish regularly may benefit from O3FA supplements. DHA supplement positively affected weight and appetite in patients with mild-to-moderate AD. Research to date has not clarified its optimal dose. We recommend 500–1,000 mg of DHA per day in divided doses. O3FA can cause abdominal discomfort and slight increase in risk of bleeding. Hence, they should be used with caution in patients on blood thinners (e.g., warfarin). Its use should be discontinued 7–14 days prior to surgery.
8. *Vitamin E (Tocopherol)*: In general, the outcomes of these studies have been disappointing. There is no evidence to date of efficacy of Vitamin E in the prevention or treatment of people with AD or MCI (Isaac, Quinn, & Tabet, 2008). Vitamin E at doses above 400 IU is associated with an increase in all-cause mortality. Vitamin E use was associated with improved survival of people with AD and thus did not support concerns over increased mortality with high-dose vitamin E supplementation in this population (Pavlik, Doody, Rountree, &

- Darby, 2009). Vitamin E is associated with increased risk of falls and bleeding. It should be used with caution in patients on blood thinners such as warfarin.
9. *Ginkgo biloba (GB)*: GB is perhaps the most widely used herbal treatment consumed specifically to prevent age-related cognitive decline and slow progression of ADRD. Putative mechanisms of action on brain functioning include vascular effects such as increased blood flow to the brain, decreased blood viscosity (i.e., thinning of the blood so that it is less likely to clot), reduction of oxygen free radicals, and neurotransmitter effects. Evidence to date indicates that ginkgo does not slow decline in memory/cognition in patients with AD, MCI, or older adults with normal cognition (Dekosky et al., 2008; Snitz et al., 2009). There are constraints to the generalizability of research to date due to underrepresentation in the cohort of individuals with divergent ethnic-cultural backgrounds and relatively few participants with lower educational levels. There are some data to suggest that ginkgo can increase bleeding risk, so people who take antiplatelet drugs (e.g., acetyl salicylic acid, clopidogrel), anticoagulant drugs (warfarin), have bleeding disorders. Patients should discontinue the use of ginkgo at least 36 h and preferably 7 days prior to surgery or dental procedure to reduce potential risk of excessive bleeding. Interaction potential exists between GB and commonly used drugs, such as aspirin and warfarin.
 10. *Alpha-Lipoic Acid (ALA)*: ALA is a more powerful antioxidant (free radical scavenger) than Vitamin E. Preliminary data suggest beneficial effects in memory and other cognitive performance in mouse models of AD and human studies (Morley, 2010).
 11. *Huperzine A (HupA)*: HupA is an herbal remedy used for centuries in China for its medicinal properties. It has cholinesterase inhibition properties similar to prescription antimentia drugs (specifically cholinesterase inhibitors [ChEIs]) such as donepezil (Aricept), galantamine (Razadyne), and rivastigmine (Exelon) that are currently approved by US FDA for the treatment of AD. Thus, HupA promotes cholinergic neurotransmission that is thought to be impaired in AD. Cholinergic neurotransmission is necessary for optimal functioning of memory and other cognitive processes.
 12. *Acetyl L Carnitine*: Acetyl L Carnitine is an amino acid nutrient that has important roles in improving mitochondrial function and thus has potential for cognitive benefits in persons with ADRD.
 13. *Vinpocetine*: Vinpocetine increases blood circulation in the brain, and in animal studies has been shown to reduce the loss of brain cells due to decreased blood supply (McDaniel et al., 2003).

A Systematic Approach to Promote Brain Health with Nutritional Strategies

Comprehensive nutritional strategies to promote brain health involve several steps. Please see Table 16.2. These steps need to be individualized and should be in keeping with the goals of overall care. Also, the beneficial effects are greatest if nutritional

Table 16.2 Ten steps to promote brain health

Step 1: comprehensive assessment of nutritional status
Step 2: eating a balanced diet
Step 3: eating food that is appetizing and cooked in healthy ways
Step 4: increasing intake of brain power foods
Step 5: reducing intake of food that is bad for the heart
Step 6: eating frequent small meals with optimal calories to achieve and maintain healthy weight
Step 7: eating a variety of foods
Step 8: monitoring food-medication and food-medical condition interaction
Step 9: proactively addressing unique challenges that dementia poses
Step 10: focusing on small steps

strategies are initiated in the earliest stages of dementia and combined with active physical, intellectual, and social life. For many individuals with ADRD in advanced stages, liberalization of diet (i.e., providing food that they enjoy irrespective of the nutritional value of the food) may have a better effect on improving their quality of life than food that is brain healthy but not enjoyed by the individual.

Step 1: Comprehensive Assessment of Nutritional Status

Persons with dementia should undergo a comprehensive evaluation of their nutritional status during initial assessment and periodically thereafter (Pepersak, 2009). The goal of such assessment is to identify and treat nutritional deficiencies and disorders early. Such assessment also allows better understanding of the person's food preferences, food habits, and comorbid medical conditions that may influence any future dietary recommendations. Specific nutritional deficiencies (e.g., protein energy malnutrition, dehydration, O3FA deficiencies, vitamin deficiencies [especially Vitamin D, B12, folate, B1, B6, nicotinamide]) may exacerbate pathological processes in the brain that are causing ADRD. In addition, nutritional deficiencies can directly cause memory loss, dementia, and even delirium (sudden onset of confusion). Nutritional deficiencies are common in people with ADRD. Specific nutritional disorders (such as celiac disease) are often overlooked in persons with ADRD. Celiac disease (also called Celiac Sprue/Gluten Sensitive Enteropathy) is associated with many nutritional deficiencies and impaired brain function (e.g., memory problems). It commonly manifests as bloating (especially after eating wheat products), abdominal discomfort, and diarrhea and is often misdiagnosed as irritable bowel syndrome. Treatment of Celiac disease involves avoiding food containing gluten (e.g., wheat products). Hypoglycemia (low blood glucose) and hyperglycemia (high blood glucose) can also cause memory impairment (Morley, 2010). Nutritional problems in individuals with ADRD may reflect years of subclinical malnutrition, possibly paired with nutritional abuse (Baker, 2007). By identifying and correcting nutritional disorders, we have seen dramatic improvement in memory and other cognitive functions of many of our patients with ADRD.

Step 2: Eating a Balanced Diet

To promote brain health, it is important to eat a balanced diet, maintain healthy weight (Body Mass Index between 20 and 25), and consume appropriate amount of calories that are required for weight maintenance. The new Food Pyramid (MyPyramid) for older adults is a useful guide for planning a healthy and well-balanced diet. It emphasizes the importance of consuming nutrient-dense foods (i.e., foods with a higher nutrient value per calorie) by outlining specific recommendations for the basic food groups. Brightly colored vegetables, deep-colored fruits, whole grains and fiber, lean proteins, and healthy types of fats are recommended (http://nutrition.tufts.edu/docs/pdf/releases/071220_ModifiedMyPyramid.pdf). Using packaged (frozen and canned) fruits and vegetables – specifically those without added salt or sugar – can be just as healthy as their fresh counterparts, while also being less expensive and more convenient.

My pyramid also recommends sufficient fluid intake. Adequate daily intake of water is necessary for the brain to function well. Inadequate consumption can lead to dehydration, which in turn can impair the ability to pay attention and remember.

Eating frequent, small meals instead of one or two large meals is recommended. Going more than 3 h without eating should be avoided when possible in order to provide the brain with a steady supply of energy.

The most appropriate ratio of omega-6 fatty acids (O6FA) to O3FA is approximately 4:1 (Rakel & Rindfleisch, 2005). Thus, in order to have a balanced diet, increasing the intake of O3FA and reducing the intake of O6FA are recommended, since the typical American diet is low in O3FA and high in O6FA. Protein content of the diet should be around 12% of the total calories consumed (Baker, 2007). Consuming 21–30 g of dietary fiber per day is recommended. Table 16.3 lists recommended amounts of daily food items for a 1,500-cal intake. Older people simply need fewer calories than younger people, and many individuals with ADRD become physically inactive, in which case energy needs decline further. Adequate consumption

Table 16.3 Brain power foods and daily recommended intake (based on 1,500 cal/day)

Food category	Brain power foods	Recommended intake
Fruits	Berries (especially blueberries), avocados	4–6 servings/day
Vegetables	Green leafy vegetables (e.g., broccoli, spinach), tomatoes	4–6 servings/day
Legumes	Beans, lentils, peas	1–2 servings/day
Fatty fish (omega-3 rich food)	Pacific herring (sardine), sablefish (black cod), European anchovies, Spanish Mackerel, wild sockeye salmon, and farmed rainbow trout	2–4 servings/week
Whole grains	Quinoa, barley, oats, maize, brown rice, buckwheat	3–6 servings/day
Spices	Turmeric	A pinch/day
Tree nuts	Walnuts, almonds, pecans, hazelnuts	3–5 pieces
Fluids	Green tea	4–8 oz
	Water	24–40 oz

of calories is critical because brain is an energy hog. Brain consumes 20% of energy despite constituting just 2% of body weight.

Step 3: Eating Food That Is Appetizing and Cooked in Healthy Ways

Many older adults share the common complaint of food no longer tasting as good as it once did. Age and disease-related loss of certain taste functions needs to be addressed to make food more appealing. An example of this can be seen with sweet, which is preserved while there is increased sensitivity to bitter with aging. However, these changes are highly individualistic. Thus, it is important to talk to older adults to find out what specifically they can and cannot sense in a food or dish. This can help design meals that are best suited to their individual perceptions and expectations.

It is important to decrease the salt, sugar, and fat in our menus while not compromising the flavor. Herbs and spices can not only enhance flavor but also have brain health promoting potential. Therefore, herbs and spices can partially or wholly replace less desirable ingredients such as salt, sugar, and added saturated fat in dishes including, marinades and dressings, stir-fry dishes, casseroles, soups, and curries (Tapsell et al., 2006). Vegetables and vegetarian dishes may be more appetizing when prepared with herbs and spices. Researchers have tested extracts of cinnamon, cloves, fennel, ginger, lavender, parsley, rose, rosemary, sage, and thyme and found that simmering, soup-making, and stewing significantly increase the disease-preventing antioxidant capacity of these herbs and spices, while grilling and stir-frying decrease. Allowing fresh garlic to stand for 15 min after crushing it can boost its content of allicin, a phytonutrient that can reduce blood clots and prevent oxidative damage to the brain blood vessels. Some older adults complain of heartburn when they eat onions. Yet swapping sweet for more pungent yellow onions can overcome this without sacrificing the healthful dose of sulfur-containing phytonutrients in this vegetable. Making comfort foods healthier is another good strategy (e.g., putting fresh rosemary and lemon on rotisserie chicken, substituting half of the ground beef for turkey in meatloaf). Replacing sweet potatoes for white or russet or red potatoes, steel-cut oats for instant oatmeal are simple strategies to try out. Cooking pasta *al dente* rather than overcooking it until it is swollen and soft is also a healthier alternative.

Many older adults are open to trying new foods and flavors. Offering them new healthy food options may not only be good for the brain but also be fun!

Step 4: Increasing Intake of Brain Power Foods

Within the category of healthy food items, there are certain foods that are thought to have a higher effect in promoting brain health compared to others. Ensuring consumption of such brain power foods is recommended to further improve the beneficial

effects of balanced diet on brain health. Table 16.3 lists brain power foods. Soy has not been shown to have any specific brain health promoting effect but is recommended because it remains a healthy alternative to red meat (as an excellent source of protein).

Step 5: Reducing Intake of Food That Is Bad for the Heart

Improving diet is a critical component of the American Heart Association's strategy to improve heart health (Lichtenstein et al., 2006). Research in the last decade has shown that what is good for the heart is good for the brain and what is bad for the heart is bad for the brain. We recommend reducing intake of saturated fat (less than 7% of daily caloric needs), trans fat (less than 1% of daily caloric needs), cholesterol (less than 300 mg/day) by choosing lean meats and vegetable alternatives, fat-free (skim) or low-fat (1% fat) dairy products and minimizing intake of trans fats; minimizing intake of beverages and foods with added sugars; choosing and preparing foods with little or no salt. Such nutritional strategies can not only promote heart health but also brain health (Lichtenstein et al., 2006; Morley, 2010).

Foods rich in saturated fat and trans fat (e.g., butter, margarine) increase inflammation and lead to elevated levels of cholesterol (Rakel & Rindfleisch, 2005). Elevated cholesterol can cause cognitive impairment through inflammation of the blood vessels and atherosclerosis. The saturated fat found in beef, butter, whole milk, cheese, and other dairy products increases low-density lipoproteins and promotes atherosclerosis (inflammation in wall of blood vessels leading to its narrowing). Trans fats (partially hydrogenated oils) in small amounts occur naturally in red meat. Other common sources of trans fats include packaged baked products such as cookies, cakes, breads, and crackers, as well as fast foods, and some dairy products. Trans fats are even more unhealthy than saturated fats. They directly promote inflammation, besides increasing LDL and worsening atherosclerosis. There is no safe level of trans fat and there are no known health benefits. People also more likely to eat foods high in saturated and trans fats when they have consumed more than healthy amount of alcohol. We also recommend minimizing consumption of fried foods and food with long shelf life. Eating charred, grilled, or burnt foods also increase inflammation. Reducing dietary intake of O6FA (which in US is normally much higher than what is needed for maintaining health) may reduce memory problems because excess amount of O6FA promotes dysfunction in hippocampus (seat for memory formation). O6FA is found in red meat and most vegetable oils.

The American Heart Association recommends reduction in the intake of added sugars to reduce the risk of a variety of metabolic disorders (e.g., metabolic syndrome, diabetes, obesity). Besides promoting oxidation and inflammation, high intake of refined sugars can lead to hypertriglyceridemia. Hypertriglyceridemia can lead to delirium and cognitive impairment in animals and humans (Morley, 2010). A prudent upper limit of intake for most American women is no more than 100 cal/day and for most American men is no more than 150 cal/day from added sugar.

A 330 mL container of a soft drink has on average (unless designed to be sugar-free) the equivalent of ten tea-spoonsful of sugar in it. Simple health promotion campaigns to improve the public's awareness of how much sugar there is in soft drinks is recommended in order to encourage changing to alternatives. Fructose-sweetened foods and drinks (e.g., many yogurts, soft drinks) have a negative effect on body's sensitivity to insulin and its ability to handle fats, increasing the risk of strokes. Many cereals are high in sugar and thus should be selected carefully. Americans are consuming 50 additional calories of sweetened beverages daily compared to 2 decades ago, for an average of about 300 cal daily coming from such drinks. Although less than younger population, baby boomer generation and older adults continue to consume substantial amount of sweetened beverages (12–18% of daily caloric intake) (Storey, Forshee, & Anderson, 2006). Glycemic load and glycemic index are measures for how quickly a serving of food is converted to blood sugar during digestion and how high the spike of blood sugar is. Foods with high glycemic load are digested more quickly, thus rapidly flooding the blood stream with sugar. Sudden high spikes of blood sugar trigger release of insulin to clear the sugar from one's blood. This quick surge of insulin can clear blood sugar dramatically, leaving the blood sugar too low. When our blood sugar is low, we feel hungry and if blood sugar is low soon after a meal, we are apt to overeat. Consumption of refined grains such as white rice, white flour, white bread and pasta (nonwhole wheat varieties), and other foods with high glycemic load (e.g., bagels, cakes, ice-cream, French fries, white potatoes, crackers, soft drinks, refined grains) should be reduced because they also promote inflammation and free radical production.

Low carbohydrate diets may also impair mental acuity and hence not recommended. Glucose is the primary source of energy for brain cells. Intake of food containing coloring agents should be minimized as some coloring agents have been linked to attentional problems. Many soft drinks (e.g., diet coke, diet pepsi) contain advanced glycation end products (AGEs) that promote inflammation and thus are potentially harmful. Many soft drinks also contain high fructose corn syrup, and high intake of fructose may also lead to excessive inflammation and oxidative stress on the brain. In general, older men (especially those with higher alcohol consumption) are more likely to consume food that is unhealthy (e.g., high in saturated fat and refined sugars) compared to older women (Robinson et al., 2009). In terms of everyday consumption, we recommend reducing intake of food that is bad for the heart. On special occasions such as Thanksgiving or birthdays, there is no need to pass up apple pie or cake. For everyday eating, choosing desserts with less fat and refined sugars is recommended (see Table 16.4).

Step 6: Eat Frequent Small Meals with Optimal Calories to Achieve and Maintain Healthy Weight

It is important to not go more than 3 h without eating, so one's brain has a steady energy supply. Also, to maintain brain health, it is equally important for persons

Table 16.4 Healthy snacks/meals

Examples of healthy snacks

- Hummus with vegetables or whole grain crackers
- Small amount of nuts
- Cottage cheese (fat-free)
- Fruits
- Fat free or low fat (1%) milk (sweetened with Splenda if necessary)
- Oat meal with fruits
- Yogurt
- Trail mix with walnuts and dried fruits
- Some health bars
- Fruit and vegetable juices may be substituted for fruits and vegetables if necessary

Examples of healthy meals

Breakfast

- Skim milk
- Scrambled eggs
- Multigrain cereal with raisins
- Pancakes made from multigrain pancake mix
- Fruits (or if necessary, fruit juices)
- Tomato juice (low salt)

Salads

- Avocado, spinach, and lettuce salad, with a scattering of walnuts and toasted crumbled anchovies, and dressed with canola oil and balsamic vinegar
- Broccoli salad with olive oil – balsamic dressing
- Tossed salad with Romaine lettuce, tomatoes, nuts, olives, and low fat dressing

Main course

- Salmon in a curry made with turmeric, broccoli, brown rice served with lentil daal
- Chicken/Turkey sandwich with whole-wheat bread
- Three-grain pilaf with canola oil and mixed vegetables

Dessert

- Dark chocolate with cut up fruits, berries, and almonds

with dementia to maintain healthy weight and to consume appropriate amount of calories that are needed to maintain healthy weight. Weight maintenance is important, even when dealing with those who are overweight or obese. Weight loss within this population is somewhat controversial and not always desirable. Excess amount of calories in older adults who are obese (BMI above 30) should be avoided because it increases oxidative stress and promotes inflammation by increasing body fat stores. Many patients with Fronto-temporal dementia and some patients with AD develop hyperphagia with disabling obesity-related health complications (e.g., impaired mobility). If weight loss is recommended, it can be accomplished through minor changes to the diet and the addition of a light exercise regimen. Modest weight loss strategies (e.g., portion control, replacing calorie dense food with fruits and vegetables) in this group may not only improve mobility but also promote heart and brain health.

Step 7: Eating a Variety of Foods

We recommend eating a variety of brain healthy foods (i.e., variety of fruits, vegetables, whole grains, and fish) to facilitate consumption of a variety of brain healthy nutrients (polyphenols, curcumin). Consuming high amount of only certain foods (even if the food has beneficial effects on brain) can be potentially harmful. For example, nuts in excess amount can dramatically increase total amount of calories consumed and subsequent oxidative stress may override any beneficial effects. In addition, due to potential for mercury toxicity in many fish, a variety of fish should be consumed rather than just one kind on a regular basis. Often, the combination of healthy foods (e.g., unique combination of food items constituting the Mediterranean diet) may have a much bigger impact on brain health than individual food items (Jacobs, Gross, & Tapsell 2009).

Step 8: Monitoring Food-Medication and Food-Medical Condition Interaction

Many food items can interact with prescription and over-the-counter medications leading to harmful consequences. For example, common fruit juices (e.g., orange, apple, grape) have significant brain health promoting effects. However, these juices also have the potential (especially if consumed with medications) to limit the body's absorption of certain commonly prescribed drugs for the treatment of blood pressure, infection, and allergies (e.g., tenormin, levofloxacin, fexofenadine), compromising their effectiveness. Patients with Celiac disease need to avoid food containing gluten (e.g., wheat products). Patients on blood thinners such as warfarin need to minimize intake of food high in vitamin K such as spinach and broccoli. Appropriate precautions should be taken (e.g., input of one's physician, pharmacist) to minimize this risk.

Step 9: Proactively Addressing Unique Challenges Posed by Dementia

In order to create an environment that promotes consumption and enjoyment of meals and snacks by persons with dementia, thoughtful planning and some simple strategies are recommended. Socialization is very important to the elderly and may positively affect the amount of food eaten. However, distractions should be limited to maintain focus on the meal. Televisions ideally should be turned off. Soft music may help to relax those dining. Sometimes, it may be helpful to have everyone seated and ready for the meal a few minutes prior to it being served. This may also help to alleviate any stress or distractions caused during the transition from an activity to mealtime.

As to the actual food that is served, it is usually best to keep the food simple and easily recognizable. Individuals with moderate-to-severe dementia may be more likely to eat something familiar that needs no explanation. Also, the food should be easy to eat. Foods that require tedious manipulation of utensils may not be a reasonable option unless assistance is readily available. Providing utensils that are not only food appropriate, but personally appropriate, is very important. Some may require cups with handles or lids while others may be fine with traditional glasses. Finger foods may also be a good choice, especially if there is limited assistance available to help with feeding. Finger foods also help to maintain some autonomy because no one is really needed to help eat these kinds of foods. Because those with moderate-to-severe dementia tend to be most lucid during the morning with waning alertness throughout the day, breakfast may truly be the most important meal of the day! A full, hearty breakfast should be encouraged daily, even to those who traditionally did not eat in the mornings. Many individuals with dementia suffer from protein energy malnutrition and may need energy-dense foods. This is also helpful to those with early satiety. Foods that can be altered to increase the nutritional content without increasing the actual volume of the food can help better meet their needs.

Step 10: Focusing on Small Steps

Change is hard, especially when it involves changing what we eat. However, even small changes in ones diet (say 20% change) can have a significant effect on brain health (say 80% benefit). Thus, it is best to focus on making small steps (e.g., increasing the amount of fruits and vegetables by one serving per day; adding blueberries to cereal). Adding small amounts of nuts, raisins, and various spices, like cinnamon to one's cereal can dramatically boost their phytonutrient content. Handful of tree nuts or trail mix is a better snack than a cookie made with butter or trans fats. Regular input from a registered dietician at an individual and group level is strongly recommended in order to make changes in daily diet practical and effective. Table 16.5 lists resources (books and websites) we recommend to promote brain health.

Table 16.5 Resources to promote brain healthy nutrition

Healthy eating. A guide to the new nutrition. A special health report from Harvard Medical School. 2006 Harvard Health Publications, Boston, Massachusetts. www.health.harvard.edu
Casey A, Benson H. Mind Your Heart: a mind/body approach to stress management, exercise, and nutrition for heart health. New York: Free Press; 2004
Websites
Pritikin Longevity Center: www.pritikin.com
DASH diet: www.dashdiet.org

Conclusion

Healthy food is essential for all the functions of the body and this is especially true of the brain. Appropriate changes in a person's diet can enhance their cognitive abilities, protect the brain from damage and counteract the effects of aging. Maximizing foods that are brain healthy (e.g., nutrient and fiber-rich fruits, vegetables, whole grains, fatty fish, and legumes) and minimizing foods that put the brain at risk (e.g., fatty meat, high-fat dairy, refined, processed foods) may help to slow cognitive decline in persons with ADRD. It is never too late to make positive changes. Older adults with dementia can make changes today that will improve their brain health tomorrow, which may help them lead a better quality of life.

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