

Nutritional aspects of cognitive impairment

Ivana Đuričić

University of Belgrade - Faculty of Pharmacy, Department of Bromatology,
Vojvode Stepe 450, 11221, Belgrade, Serbia

Corresponding author: Ivana Đuričić, PhD
email: ivana.djuricic@pharmacy.bg.ac.rs

Summary

Many scientific arguments in this area, implicate low level of important nutrients in cognitive decline, simultaneously suggesting better nutritional status as an important goal in the management of cognitive aging.

Key nutrients for the protection of cognitive function are B-group vitamins, polyphenols, vitamin D, and omega-3 polyunsaturated fatty acids (PUFAs). The body of scientific evidence widely supports the roles of folic acid and metabolically related B6 and B12 vitamins in protecting cognitive function in old age. High concentrations of polyphenols in dementia therapy showed a significant increase in cerebral blood volume. Although low vitamin D blood levels were associated with a higher risk of developing dementia, vitamin D supplementation alone was not sufficient to improve cognitive outcomes. In relation to the role of omega-3 PUFAs, research findings indicate protective effects in individuals with cognitive decline. The importance of diets and a healthy lifestyle in the prevention of cognitive impairment are extensively accepted. The Mediterranean diet is the most investigated dietary pattern in observational studies. MIND diet (Mediterranean-DASH Intervention for Neurodegenerative Delay) is updated dietary approach of the Mediterranean-DASH diets. Its components are linked to dementia prevention and overall neuroprotection. It is also reported that regular physical activity maintains the brain function improving blood flow and oxygen supply.

Keywords: aging, cognition, dementia, nutrients, diet

Introduction

In many countries average lifespan is increasing, thus life expectancy actually exceeds 80 years (1). Noncommunicable diseases increase with age such as diabetes, cardiometabolic diseases, neurological and musculoskeletal disorders, therefore the World Health Organization (WHO) outlines a model of healthy aging in its 'World Report on Ageing and Health' (2). The report highlights two primary factors 'intrinsic capacity' and 'functional ability' as the most important considerations of healthy aging. Intrinsic capacity is a term that describes all physical, mental, and psychosocial capacities of an individual at one point in time. Intrinsic capacity varies across the lifespan and presents one aspect of the functioning of a person during growth and development (3). The environmental characteristics are in close interaction with intrinsic capacity and together determine an individual's functional ability. Environmental factors in a different life-stages may influence the maximum intrinsic capacity of tissues and organ systems, affecting later its rate of decline (4). Factors running in earlier life-stages may contribute to the satisfying functional capacity for older people. A holistic approach to healthy aging has primarily focused on lifestyle, physical performance, natural and socio-cultural environment, and nutritional factors rather than the presence and treating disease (5). Diet is a changeable environmental factor that has been associated with protective relations against cognitive impairment. At present, dementia affects about 50 million people and is expected to reach 80 million by 2030 and 150 million by 2050 worldwide. It is verified that cognitive function declines with age, indicating a preclinical silent phase, subjective cognitive decline as a further stage, mild cognitive impairment (MCI), and major neurocognitive impairment-severe enough to interfere with functional abilities. About 50% of patients with MCI are predetermined to develop dementia within 5 years (6). Managing risk factors may be an efficient approach in the prevention and treatment of the progressive cognitive decline associated with dementia (7).

Many scientific arguments, derived mostly from observational studies, implicate a low level of important nutrients in cognitive decline, simultaneously suggesting better nutritional status as an important goal in the management of cognitive aging (8, 9). Emerging aspects of nutrition research such as individual food components, food groups, and dietary patterns are covered in this Review.

Nutrients related to cognitive functions

Much research has been focused on the roles of specific nutrients concerning cognition in older age. Increased use of drugs, reduced food intake and compromised nutrient absorption may cause deficiencies of many micro- and macronutrients and consequently complex metabolic changes in older adults.

B vitamins

Researchers have been long time interested in the potential connection between B vitamins deficiency and dementia (10, 11). Folic acid, vitamins B6, and B12 are required for homocysteine metabolism and even moderately raised homocysteine levels might be related to increased risk of dementia in people older than 65 years (12). Elevated homocysteine levels may impair the brain function by affecting methylation processes, in turn disturbing gene expression in the β amyloid pathway and leading to neuronal cell death due to cerebrovascular ischemia (11). It seems that the homocysteine level increases with aging in cerebrospinal fluid, amplifying intracellular and extracellular accumulation of β amyloid, therefore causing harmful effects on the endothelial cells of small brain blood vessels (13). Homocysteine is produced by methyl transfer reactions during the metabolism of methionine and its elimination from the body may be performed in two pathways, one of which takes vitamin B6 and the other folate and vitamin B12 (14). Results of a recent meta-analysis confirmed minor effects of vitamin B on preventing cognitive decline (15). Available data certified significant cognitive decline in individuals with high homocysteine levels and B vitamins supplementation were found to improve cognition particularly in this subgroup (12).

Antioxidants

The brain is most liable to oxidative damage, causing the neuroimmune response to stress, vascular and neuronal disorders, and induction of mechanisms foregoing the onset of cognitive decline. Consumption of potent antioxidants, such as vitamin C, E, and carotenoids are effective in a struggle with the pathogenesis and progression of dementia (16). The brain has a high ability to maintain homeostasis of vitamin C, particularly during prolonged vitamin C deficiencies, indicating the importance of the biological role of vitamin C in central nervous functioning (17). Vitamin C is a co-factor in numerous processes such as the biosynthesis of tyrosine, carnitine, collagen, peptide hormones, and myelin (18, 19). Vitamin E has varying functions like potent antioxidant and anti-inflammatory properties, showing beneficial effects in the treatment of dementia associated pathology (20). Carotenoids are an important representative of plant pigments, especially those found in dark leafy greens (21). Results of a recent meta-analysis of a few cohort studies have shown borderline significance regarding dietary intake of carotenoids and its protective effect on the risk of dementia. Taking beta-carotene has not confirmed the slowing down of cognitive decline in some longitudinal studies (22, 23). A recent study reported a moderate decrease in cognitive decline with higher consumption of lutein+zeaxanthin and total carotenoids, but significant decrease with greater intakes of lycopene (24).

Non-nutrient bioactive compounds, most notably polyphenols and anthocyanins have direct antioxidant features. Essential elements such as zinc, copper, selenium serve

as cofactors for enzymes and proteins with antioxidative activity. It has been suggested that the pathogenesis and progression of dementia might be mediated by oxidative stress or inappropriate antioxidant defense (25). Polyphenols intake ranging from 200 and 300 mg per 100 g of fresh weight is associated with the consumption of fruits such as grapes, berries, and various non-berry fruits (apples, plums, cherries) (26). Additionally, a cup of coffee or tea contains around 100 mg of polyphenols. Chocolate, nuts, legumes, particularly red wine also contribute to the polyphenol intake.

Vitamin D

Vitamin D plays an important role in the protection of neurons and maintains normal brain functions. Its receptors are present in brain regions involved in cognition. Vitamin D is included in the regulation of immune function, cellular homeostasis, and modulation of synaptic structure (27). Proposed mechanisms for the protective effects of metabolically active 1,25-dihydroxy vitamin D against cognitive decline include antioxidative activity, decreasing ischemia, clearing β amyloid peptide, regulating intraneuronal calcium, and choline acetyltransferase neurotrophic factors (28). Although lower vitamin D blood level is associated with a higher risk of developing dementia, it is shown that vitamin D supplementation alone is not sufficient to improve cognition. According to the Vitamin D Council recommendations middle-aged and older adults should have serum vitamin D level in a range of 70-80 ng/mL (28).

Polyunsaturated fatty acids (PUFAs)

Omega 3 PUFAs, especially docosahexaenoic acid (DHA), have an essential role in the central and peripheral nervous system metabolism. DHA is mostly accumulated in the brain and the relation between omega-3 PUFAs intake and brain function is reasonably well accepted. Omega-3 PUFAs play a role in many aspects of brain physiology such as membrane fluidity, synaptic function, inflammation, cerebral blood flow, and neurotrophic effects. Linked to their structural role in neuronal membranes omega-3 PUFAs communicate directly with membrane-bound proteins, transporters, and ion channels, glucose transporters, thus affecting signal transduction and synaptic activity (29, 30). Omega-3 PUFAs may impact cerebral blood flow influencing endothelial function (31). They perform powerful antiapoptotic effects and help to maintain healthy neurons and synaptic structures. The very recent review encompasses inconsistent results from large observational studies and clinical trials of omega-3 fatty acids and cognitive function in elderly participants (9). Even though no effect was found in some observational studies, the relationship between higher blood concentrations of omega-3 fatty acids and decreased risk of cognitive decline was confirmed. In one clinical trial, 6 months supplementation with 900 mg/day DHA was linked with improved 'immediate and delayed Verbal Recognition Memory scores' in both genders, age ≥ 55 (32). In a beneficiary sense, another study found improvement in

executive function after supplementation with 800 mg docosahexaenoic acid and 225 mg eicosapentaenoic acid a day for 3 years in non-demented older adults with low baseline omega-3 index (33).

Food groups related to cognitive functions

Fruits and vegetables

Epidemiological studies based on fruit and vegetable intake and cognition have extensively established that adequate consumption may prevent cognitive impairment, while the low intake has been associated with a higher risk for cognitive decline. In most observational studies benefit were highest for dark leafy greens and berries, good sources of folate, and antioxidants (34, 35).

Fish and seafood

The results of a 2017 meta-analysis supported the potential preventive role of fish and seafood consumption in age-related cognitive decline (36). Slower decline in semantic memory and perceptual speed was found in individuals with habitual consumption of one or more seafood meals compared to those with less than one seafood meal intake (37). The certain genetic background might be a reason for a different response on fish consumption in individuals.

Nuts and olive oil

Few studies have explored nuts and olive oil intake with cognitive outcomes but not separately, merely in the context of a Mediterranean dietary pattern. JAMA Internal Medicine reported results of a randomized clinical trial that improved cognitive function concerning long-term consumption of the Mediterranean diet with either extra virgin olive oil (1L per week) or nuts (30 g per day) (38).

Dietary patterns and lifestyle habits

The importance of nutrition and a healthy lifestyle in the prevention of cognitive impairment is widely accepted. Numerous observational studies have reported a generally beneficial effect of sticking to the Mediterranean diet on reducing the risk of MCI, dementia, or overall neurodegenerative diseases (39-41). The Mediterranean diet is the most investigated dietary pattern which is based on a high intake of fruits and vegetables, whole grains, olive oil, legumes and fish instead of red meat, regular consumption of fermented dairy, seeds, nuts, moderate consumption of red wine (42-44). The Mediterranean diet emphasizes a high intake of folic acid and other vitamins B, vitamin E, carotenoids, flavonoids, dietary fiber, and monounsaturated fatty acids, a balanced intake of unsaturated and reasonably low intake of saturated fatty acids. Omega-3 fatty acids are highly recommended in the Mediterranean dietary approach

(42-44). Other dietary patterns have been also taken into consideration for cognitive outcomes. Beneficial associations between cognitive outcomes and adherence to the Dietary Approaches to Stop Hypertension (DASH) diet in both genders have been reported in two observational studies (45, 46), whereas one study found no association (47). The DASH diet emphasizes a high intake of fruits, vegetables, whole grains, lean animal protein, and reasonably low consumption of red meat, foods that are low in saturated and trans-fatty acids, sugar, and sodium. This dietary approach is reached in calcium, potassium, magnesium, fiber, and protein intake, but low in saturated and total lipids, cholesterol, and sodium (48). The updated dietary approach called MIND diet (Mediterranean-DASH Intervention for Neurodegenerative Delay) is a hybrid of the Mediterranean-DASH diets. Its components are linked to dementia prevention and overall neuroprotection. The MIND diet score emphasizes natural foods originated by plants and limited intakes of animal foods. It authentically specifies consumption of berries and green leafy vegetables, but not high fruit consumption like in the Mediterranean and DASH diets (3-4 servings per day) high dairy (more than 2 servings per day in DASH), high potato consumption (2 servings per day in the Mediterranean) or more than 1 fish meal per week (in the Mediterranean diet recommendation may reach greater than 6 meals per week) (49). The MIND diet approach was related to a lower risk of Alzheimer's disease and a slower decline in cognitive outcome in four observational studies (47, 49-51).

Besides, the health condition depends on numerous aspects of lifestyle habits. At the same time, education about nutrition and physical activity is crucial for cognitive function. The importance of regular physical activity should be pointed out to individuals with cognitive disorders. It is advisable to exercise 2 or 3 times a week for more than 60 min in order to improve physical performance. The exercise should be supervised by professional guide (52). It is also reported that regular physical activity maintains the brain function improving blood flow and oxygen supply. Consequently, the danger of Alzheimer's type dementia might be decreased (53).

Having in mind the complexity of biological interactions between various components of the diet, the whole diet approach should be in the focus of further investigations rather than individual nutrients or food groups. Such an investigation would enable better understanding of the nutrition role in chronic diseases like age-related cognitive impairment.

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Nutritivni aspekti poremećaja kognitivnih funkcija

Ivana Đuričić

Univerzitet u Beogradu - Farmaceutski fakultet, Katedra za Bromatologiju,
Vojvode Stepe 450, 11221, Beograd, Srbija

Autor za korespondenciju: ivana.djuricic@pharmacy.bg.ac.rs

Kratak sadržaj

Novi naučni dokazi u ovoj oblasti ukazuju na nedostatke određenih hranljivih materija u opadanju kognitivnih funkcija, istovremeno pokazujući da bolji nutritivni status može biti važan u očuvanju kognicije kod starijih osoba.

Ključni nutrijenti za zaštitu kognitivnih funkcija su vitamini B grupe, polifenoli, vitamin D i omega-3 polinezasićene masne kiseline (PMK). Sveukupnost naučnih dokaza u ovom trenutku najjače podržava uloge folata i metabolički povezanih vitamina B6 i B12 u zaštiti kognitivnih funkcija u starijoj životnoj dobi. Visoke koncentracije polifenola u terapiji demencije pokazale su značajno povećanje volumena cerebralne krvi. Iako su niže koncentracije vitamina D u serumu bile povezane sa većim rizikom za razvoj demencije, suplementacija vitaminom D nije bila dovoljna za poboljšanje kognitivnih ishoda. U vezi sa ulogom omega-3 PMK, rezultati istraživanja ukazuju na zaštitne efekte kod osoba sa kognitivnim smetnjama. Dijetarni režim i zdrav stil života igraju značajnu ulogu u prevenciji kognitivnih poremećaja. Mediteranska ishrana je najčešće ispitivani dijetarni obrazac u observacionim studijama. Pokazano je da je koncept MIND dijeta (*Mediterranean-DASH Intervention for Neurodegenerative Delay*) u vezi sa neuroprotektivnim efektima i prevencijom demencije. Redovna fizička aktivnost predstavlja značajnu komponentu zdravog životnog stila u održanju vitalnosti moždanih funkcija.

Ključne reči: starenje, kognicija, demencija, nutrijenti, dijeta
