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INVITED REVIEW

Effect of MIND diet on cognitive function in elderly: a narrative review with emphasis on bioactive food ingredients

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Abstract
As the world becomes a super-aged society, cognitive decline is public health problems that are increasing rapidly. A healthy diet has great potential for maintaining cognitive health. A diet that could delay the onset of neurodegenerative diseases has been developed: the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet, a hybrid form of the Mediterranean diet and the Dietary Approaches to Stop Hypertension (DASH) diet. In this review, the effects of the MIND diet on improving cognitive function, including memory, are summarized. In most studies, the higher the adherence to the MIND diet, the higher the cognitive function evaluation score, and the lower the incidence of dementia. This is because of the anti-inflammatory and antioxidant effects of the major nutritional components of the MIND diet: folate, carotenoids, polyphenols, and polyunsaturated fatty acids. Adherence to the MIND diet, containing various bioactive food ingredients, is related to cognitive improvement in the elderly population.

Keywords Bioactive food ingredients · Cognitive impairment · Dementia · MIND diet · Super-aged society

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Introduction

Currently, the global elderly population is rapidly increasing, leading to an aging society. As of 2020, there are 727 million people over the age of 65 years worldwide, and this number is estimated to double by 2050 (World Health Organization, 2020). Similarly, South Korea is rapidly becoming a super-aged society. As of 2022, the elderly population was 9.18 million people, accounting for approximately 17.5% of the total population (Statistic Korea, 2021). With the advent of an aging society, the prevalence of geriatric diseases is increasing rapidly, and degenerative neurological diseases such as dementia have recently been recognized as serious problems. As of 2020, the estimated number of patients with dementia aged 65 years and older in South Korea is over 840,000, and Alzhemer's is the leading cause of dementia (Korea Dementia Observatory, 2021). Dementia causes enormous economic losses, such as treatment, care, and labor losses for patients and their families (Lee and Seong, 2018). In South Korea, the annual management cost per dementia patient in 2010 was $13,055, estimated to increase to $14,540 in 2020, as the incidence of dementia increases (Korea Dementia Observatory, 2021). Given the increasing number of patients with dementia, their annual management costs are expected to increase (Lee and Seong, 2018). Therefore, active dementia management is the most effective way to reduce the number of patients with dementia and the burden of costs. As a cure for dementia has not yet been developed, research on the risk factors that can be altered is important to derive health recommendations and preventive interventions. In general, foreign and domestic intervention studies on cognitive function improvement that can prevent dementia include intervention methods such as single foods, mononutrients, dietary supplements, physical activity, and social activities (Jeong et al., 2019; Ngandu et al., 2015; Song et al., 2021).

Dementia mostly affects the elderly with multiple cognitive dysfunctions caused by degenerative brain diseases of the central nervous system. First, forgetfulness and cognitive decline occur, followed by declines in speech, thinking, judgment, and the appearance of Psychological Symptoms of Dementia (BPSD) (Jeong et al., 2019). The causes of dementia include age, ethnicity, sex, genetic factors, physical activity, smoking, drug use, educational level, alcohol consumption, body mass index (BMI), comorbidities, and environmental factors (Chen et al., 2009). Currently, the FDA-approved drugs for dementia include donepezil, galantamine, rivastigmine, and memantine. These drugs inhibit or help release more of the neurotransmitter acetylcholine into the brain. However, strict dosage control is required because of side effects, such as headache, dizziness, nausea, and constipation. Although drugs are effective in the short term, the long-term effects of dementia drugs remain unclear. Drugs for the treatment of dementia have many side effects, and because the efficacy of curative drugs or pharmacological treatments is limited, it is important to find a preventive method for cognitive decline or dementia (Kang et al., 2022).

In aging societies, cognitive decline is a major public health problem (Kheirouri and Alizadeh, 2021). Mild cognitive impairment refers to an intermediate state between natural cognitive decline and cognitive function that satisfies the diagnosis of dementia (Petersen, 2016). It is a disease characterized by a clear decrease in memory and concentration and subtle changes in personality and emotional regulation. Unlike dementia, mild cognitive impairment (MCI) does not significantly interfere with activities of daily living. However, since more than half of the elderly with MCI are likely to progress to dementia within five years, it can be viewed as a strong risk factor for dementia (Gauthier et al., 2006). Therefore, the prevention of cognitive decline can alleviate irreversible dementia.

Recently, the use of specific diets as a non-invasive treatment method to prevent cognitive decline and dementia has received increasing attention. Among them, the Mediterranean diet and Dietary Approaches to Stop Hypertension (DASH) are frequently studied because they are related to slowing the rate of cognitive decline (Berendsen et al., 2017; Lourida et al., 2013). However, neither diet contains specific ingredients that optimize brain health. A diet that protects the brain and delays dementia and cognitive decline has recently been developed in the US, based on a literature review of the Mediterranean diet and the DASH diet to prevent cognitive decline and dementia and maintain brain health (Liu et al., 2021). Foods and nutrients were found to complement the two diets, and a new hybrid Mediterranean-DASH diet intervention for neurodegenerative delay (MIND) was developed based on the aging brain and the nutrients that can protect it (Morris et al., 2015a). The MIND diet emphasizes a limited intake of natural plant foods, animal-based, and high saturated fat foods (Morris et al., 2015b). This diet is rich in antioxidant, anti-inflammatory, and nutritious ingredients that delay cognitive decline, such as vitamin E, flavonoids, folate, and carotenoids, and can help prevent cognitive decline and dementia, including providing brain protection.

Therefore, this study summarizes whether the MIND diet has better neuroprotection than other diets, helps improve "memory," the decline of which is one of the prominent early symptoms of dementia, and can also help healthy elderly and patients suffering from mild cognitive impairment (MCI). In addition, it summarizes the mechanisms by which the constituent foods of the MIND diet protect patients with MCI and dementia as well as the results that will be produced when they are changed to suit the traditional diet of each country.

Development of a MIND diet

Cardiovascular disease and hypertension are widely known to predict the early onset of cognitive impairment (Smith et al., 2010a, b), and studies have shown that patients with cardiovascular disease have a high incidence of dementia (Newman et al., 2005). Accordingly, the Mediterranean diet is known to lower the risk of cardiovascular and various chronic diseases, and it has recently been shown that it not only reduces the risk of Alzheimer's disease but also delays the rate of cognitive decline (Jeong et al., 2019). The Mediterranean diet is a diet based on the food of populations living in Mediterranean coastal countries, emphasizing the intake of mainly antioxidant-rich fruits and vegetables, monounsaturated fats (MUFA), and polyphenols and significantly lowering animal fats and transfats. Therefore, it is thought to reduce vascular and brain damage caused by reactive oxygen species (ROS) by lowering lipid oxidation and platelet aggregation (Vinciguerra et al., 2020). In addition, the DASH diet is defined as a diet that protects against hypertension, cardiovascular disease, and diabetes in Americans, and has recently been shown to improve cognition and increase executive function and attention (Tangney, 2014). The DASH diet also recommends the consumption of fruits, vegetables, nuts, beans, fish, poultry, and low-fat dairy products and avoids saturated fat and sodium consumption (Azadbakht et al., 2005).

Both diets have demonstrated protective effects against cardiovascular diseases that can negatively affect brain health; however, their dietary components are not specific to the composition and amount of food optimized for brain health (Morris et al., 2015b). Therefore, the MIND diet, developed based on these two diets, was sponsored by the National Institute on Aging (NIH) and researchers from the RUSH University Medical Center for Brain Health, Dr. Martha Clare Morris, and Harvard School of Public Health (Morris et al., 2015a, 2015b).

The effect of the MIND diet on healthy elderly

Aging leads to physical and functional changes in tissues and organs of the body. Neurodegenerative diseases, cardiovascular diseases, and hypertension occur mostly due to oxidative stress, mitochondrial dysfunction, inflammation, and immune disorders (Barbalho et al., 2022). In the elderly, an unhealthy lifestyle (malnutrition, lack of exercise, etc.) can lead to nerve loss and, in severe cases, can lead to dementia (Wajman et al., 2018). Therefore, to achieve healthy aging, it is important to cultivate healthy lifestyles. Among these, a healthy diet is known to have a positive effect on cognitive function as a lifestyle pattern closely related to our lives (Yeung et al., 2021).

In the cohort studies, a comparative analysis was conducted on healthy elderly individuals (average age, 65 years)

Table 1 Summary and characteristics of the studies assessing the relationship of the MIND diet and healthy elderly

Author (year)	Design and location	Population and sex	Age	Follow-up time	Method of food intake assessment	Method of cognitive assessment	Outcomes
Morris et al. (2015a, b)	Prospective cohort/US	923	81.2 ± 0.7	4.5 yr	144-item FFQ[1]	Neuropsychological battery test	Significant reduction in incidence of AD[2]; Moderate and high adherence to MIND diet reduced 35% and 53% incidence of AD
McEvoy et al. (2017)	Cross-sectional/US	5907 (3548 women, 2359 men)	67.8 ± 10.8	-	163-item FFQ	Global cognitive function	MIND diet had 30% lower odds of having poor cognitive performance Each 1 SD increase in MIND diet reduced 14% odds of poor cognitive performance
Berendsen et al. (2018)	Prospective cohort/US	16,058 women	74.3 ± 2.3	12.9 yr	116-item FFQ	TICS[3]	Improved verbal memory
Nishi et al. (2021)	Cohort/Spain	6647 (3218 women, 3429 men)	65.0 ± 4.9	2 yr	143-item FFQ	Neuropsychological test	Improved DST[4] test
Dhana et al. (2021)	Cohort/US	569 (401 women, 168 men)	90.8	12 mo	144-item FFQ	Neuropsychological battery test	Increased global cognitive function score
Liu et al. (2021)	RCT[5]	295 (200 women, 95 men)	69.8 ± 4.2	3 yr	142-item FFQ	Neuropsychological test	α-Carotene↑, global cognition&semantic memory↑; Lutein&zeaxanthin↑, semantic memory↑
de Crom et al. (2022)	Cohort/Netherland	Baseline1: 5375 Baseline2: 2861	67.7/75.3	15.6 yr	170-item FFQ	MMSE[6], GMS[7]	Reduction of incidence of AD

FFQ Food Frequency Questionnaire, *AD* Alzheimer disease, *TICS* The Telephone Interview for Cognitive Status, *DST* Digit Span Test, *RCT* Randomized Controlled Trial, *MMSE* Mini-Mental State Examination, *GMS* Geriatric Mental Schedule, ↑ means it has the effective outcome with MIND and other neuroprotective diets (Table 1). The cognitive function evaluation score was significantly higher in the MIND diet group than in the other diet groups (Munoz-Garcia et al., 2020), and the MIND diet significantly improved memory (Nishi et al., 2021). According to a cohort study conducted by Morris et al., the extent to which the incidence of AD improved at an average age of 81 years when MIND, Mediterranean, and DASH diets were observed. The study showed that the incidence of AD decreased by 53% when comparing the group with the highest and lowest MIND diet scores and by 35% when comparing the group with the highest and middle MIND diet scores. In comparison, the incidence of AD decreased to 54% and 39% only in the groups with the highest and lowest dietary scores, respectively, in the Mediterranean and DASH diets (Morris et al., 2015a). The MIND diet is a hybrid of the Mediterranean and DASH diets, which is effective in improving cognitive function because it emphasizes the number of foods and specific intake related to nerve protection effects and dementia prevention. Therefore, mild compliance with the MIND diet, rather than high compliance with the Mediterranean and DASH diets, showed a neuroprotective effect.

In another cohort study, memory improvement was associated with the MIND diet, which improved working memory, temporarily storing, and manipulating information needed for complex cognitive tasks such as language understanding, learning, and reasoning (Baddeley, 1992), despite a shorter follow-up period of 2 years than other previous studies. This study further analyzed the relationship between diet components and cognitive function and found that working memory had a beneficial relationship with olive oil and red wine intake, as well as with eating white meat rather than red or processed meat. Additionally, refraining from eating snacks improves memory (Nishi et al., 2021). A cross-sectional study of an average 67-year-old healthy elderly showed a 35% decrease in cognitive decline when comparing the highest and lowest MIND dietary scores, and a 15% decrease when comparing the highest and middle MIND dietary scores (McEvoy et al., 2017).

Taken together, the above studies show that when the MIND diet is applied to healthy elderly compared to other healthy diets, the higher the compliance to the MIND diet, the lower the incidence of dementia and rate of cognitive and memory decline, which is one of the early symptoms of AD. This is because the MIND diet emphasizes the consumption of green leafy vegetables and berries more than do other healthy diets, and thus has an excellent neuroprotective effect (de Crom et al., 2022). Therefore, the MIND diet is rich in antioxidants, vitamins, probiotics, plant proteins, and unsaturated fatty acids and can have a good effect on neurocognitive aging (Nishi et al., 2021). The MIND diet reduced the incidence of dementia-associated cognitive decline. However, it seems that the verification of the improvement effect on memory is still insufficient; therefore, further research is needed to prove this in detail.

The effect of the MIND diet on elderly patients with MCI

According to the Ministry of Health and Welfare, the estimated number of patients with mild cognitive impairment (MCI) aged 65 years and older in South Korea in 2020 was approximately 2.54 million, accounting for 22.7% (Ministry of Health and Welfare, 2020). Approximately 12% of patients with MCI develop AD or other types of dementia; this is higher than the annual incidence of dementia in healthy elderly individuals, which is less than 2% (Furio et al., 2007). Therefore, the incidence of dementia decreases if the number of patients with MCI decreases. Similarly, there is currently no proven effective treatment for MCI; therefore, it is best to maintain a healthy diet and lower the risk of progression (Oh and Lee, 2016). Therefore, the association between MCI and the MIND diet was examined (Table 2).

Morris et al. conducted a cohort study of healthy elderly individuals and those with MCI, with an average age of 81. Consequently, a higher MIND diet score was associated with a decreased rate of cognitive decline. The cognitive level of those with high MIND scores was 7.5 years younger than those with the lowest dietary score. In addition, episodic memory, semantic memory, and perceptual speed significantly improved. Dietary changes were also observed over time and global cognitive scores increased (Morris et al., 2015b).

In the absence of dementia, it has been reported that higher MIND diet scores are associated with better memory in subjective cognitive decline (SCD), MCI, and AD in relatives and in healthy elderly individuals. In addition, dietary components related to memory were analyzed, and the ingredients of 'alcoholic beverages, vegetables, cereals, and nuts' were related to the improvement of memory (Wesselman et al., 2021).

In a similar study, a low-calorie MIND diet (reducing the participants' total energy intake by 20%) and a low-calorie MIND diet + aerobic exercise intervention were recently conducted in menopausal women aged 65 on average who were experiencing MCI in Egypt. Both groups showed significant differences before and after the intervention, and since the experiment used a low-calorie MIND diet, both groups lost weight after the intervention, and BMI also decreased. Both cognitive function and functional activity level evaluation scores improved. This study showed that the MIND diet and light exercise had a positive effect on cognitive function in menopausal women (Elsayed et al., 2022).

Table 2 Summary and characteristics of the studies assessing the relationship of the MIND diet and MCI elderly

Author (year)	Design and Location	Population and Sex	Age	Follow-up time	Method of food intake assessment	Method of cognitive assessment	Outcomes
Morris et al. (2015a, b)	Cohort study/US	960 (883 women, 77 men)	81.4 ± 7.2	4.7 yr	144-item FFQ[1]	Neuropsychological battery test	Slower decline in global cognitive score
Calil et al. (2018)	Cross-sectional study/Brazil	96 (69 women, 27 men)	75.2 ± 6.5	-	98-item FFQ	MMSE[2], BCSB[3], VF[4], CDT[5], GDS[6]	Improved learning score in healthy elderly, but not in MCI or AD
Wesselman et al. (2021)	Cross-sectional study/Germany	395 (202 women, 193 men)	69.4 ± 5.6	-	148-item FFQ	CERAD[7], MMSE	Improved memory in all groups; Improved language in healthy elderly
Eslayed et al. (2022)	Randomized clinical trial/ Egypt	68 women	65.3 ± 0.2	8 mo	Perceived dietary adherence questionnaire	RUDAS[8]; cognitive function/ FIM[9]; functional activity	RUDAS score increase FIM scale increase

[1]FFQ, Food Frequency Questionnaire; [2]MMSE, Mini-Mental State Examination; [3]BCBS, Brief Cognitive Screening Battery; [4]VF, Verbal Fluency-Animal Category; [5]CDT, Clock Drawing Test; [6]GDS, Geriatric Depression Scale; [7]CERAD, Consortium to Establish a Registry for Alzheimer's Disease; [8]RUDAS, Rowland Universal Dementia Assessment Scale; [9]FIM, Functional Independence Measure

In contrast, in the results of a cross-sectional study by Calil et al., moderate compliance with the MIND diet was related to the learning score of the healthy elderly, but not in those with MCI or AD (Calil et al., 2018).

Mechanism of a MIND diet

AD and MCI have pathological causes commonly known as synaptic and neuronal loss, extracellular accumulation of β-amyloid (Aβ) proteins, senior plaque formation, and intracellular deposition of hyperphosphorylated tau proteins (neurofibrillary tangles) (Mecocci, 2004). The amyloid precursor protein (APP) is broken down in the extracellular environment or lumen of the Golgi apparatus due to risk genes (APOE, PSEN1, APP, etc.), traumatic brain injury, sleep apnea, diabetes, hypertension, and aging. Aβ consists mostly of Aβ1-40 and Aβ1-42, and fibers are a major feature of AD lesions (Korte et al., 2020). At the same time, when Aβ deposits in brain tissue, cell death occurs, and neurons are lost. In addition, the hyperphosphorylated Tau proteins bind together to form a neurofibrillary tangle in the nerve cell body, which destroys the function of the neuron by breaking down the microtubule and accumulates Aβ in the brain cell membrane (Mufson et al., 2012; Thal et al., 2002). Oxidative stress, mitochondrial dysfunction, and neuroinflammation are also associated. These causes can be partially corrected if a balanced diet is maintained (Vinciguerra et al., 2020). Therefore, although the mechanism of the neuroprotective effect of the MIND diet is not clearly defined, the components of the MIND diet have excellent antioxidant and anti-inflammatory effects that can reduce the essential pathological causes of neurodegenerative diseases. The MIND diet recommends 10 foods and limits the intake of 5 foods (Morris et al., 2015b). According to the recommended foods of the MIND diet, the most important dietary ingredients are Vitamin B, carotenoids, polyphenols, and polyunsaturated fatty acids (PUFA). It is rich in antioxidants and anti-inflammatory components and is a good nutrient for improving cognitive function and preventing dementia.

Homocysteine, a risk factor for dementia, can directly cause brain damage through several mechanisms, including hypersecretion of the neurotransmitter glutamate through excessive activation of the N-methyl-D-aspartate receptor, and improve γ-amyloid peptide production, DNA repair disorders, and brain atrophy (Ravaglia et al., 2005). Among these B vitamins B, B12 and folate act as coenzymes that convert homocysteine to methionine (Kang et al., 2021). Also, vitamin B is widely known as a component that can reduce these risk factors. Folic acid inhibits Aβ production and plaque accumulation by regulating the expression of β-secretase (BACE1) and γ-secretase, which decompose APP, and inhibit tau hyperphosphorylation and neurofibrillary tangles by regulating the activities of protein phosphatase cyclin-dependent kinase and glycogen synthase kinase (Zhang et al., 2021). When comparing patients with dementia and MCI with healthy elderly individuals, plasma homocysteine levels were high in patients with dementia and MCI, whereas plasma folate levels were low (Ravaglia et al., 2005). In patients with MCI, when comparing the vitamin B (folic acid, vitamin B_{12}, vitamin B_6) administration group with the placebo administration group for 24 months, plasma homocysteine levels decreased in the vitamin B administration group and holo-transcobalamin (vitamin B_{12} biomarker) levels increased (Smith et al., 2010a, b). The intake of green leafy vegetables increases plasma folate levels in the elderly and improves cognitive function (Morris et al., 2018). In addition, in a study that provided folic acid for two years, Verbal IQ (VIQ), information, and digit span test results improved with folic acid intake, and the dementia prevalence factors homocysteine, Aβ, and APP decreased (Ma et al., 2019) (Table 3).

Carotenoids interact with various types of cell membranes, including plasma, mitochondria, and nuclei. Also, they may act indirectly through interactions with cell signaling cascades including nuclear factor erythroid 2-related factor 2 (Nrf2), NF-κB, or MAPK. Carotenoid is absorbed by micelle and then activated with β-carotene oxygenase 1 (BCO1) and β-carotene dioxygenase 2 (BCO2) to remove ROS (Mohammadzadeh Honarvar, 2017). In addition, lutein has been shown to reduce phospholipid peroxidation in human erythrocytes, oxidative stress, mitochondrial dysfunction, and neuroinflammation (Morris et al., 2018). When carotenoid-based foods are consumed by healthy older adults, cognitive function and memory are improved, and lutein components are highly related to cognitive function (Liu et al., 2021; Morris et al., 2019; Yuan C et al., 2021) (Table 3).

Polyphenols with strong antioxidant components play a role in inhibiting the expression of Aβ-producing BACE1 (Williams and Spencer, 2012). Resveratrol interferes with amyloid cascade, reducing tau protein phosphorylation and accumulation, and reducing Aβ-induced production of ROS. In addition, polyphenols, such as anthocyanins and catechins, pass through the blood–brain barrier, protect neurons from neurotoxicity-induced lesions, and protect the brain by weakening the signaling cascade of oxidative stress and inflammatory reactions in the brain (Reale et al., 2020). In addition, isoflavones exert beneficial effects on dementia by improving apoptosis in Aβ-induced cells (Reale et al., 2020). In general, isoflavone levels increase in the elderly who consume a lot of soy products (e.g., tofu and natto), and the incidence of dementia decreases (Kishida et al., 2022).

Among PUFA, ω-3 fatty acids, docosahexaenoic acid (DHA), and eicosapentaenoic acid (EPA) are the main components of membrane phospholipids that regulate membrane fluidity and signal transmission. DHA is synthesized and absorbed by hippocampal neurons and incorporated into membrane phospholipids, especially phosphatidylethanolamine, to improve neuronal growth and synaptic production (Su, 2010). In addition, α-linolenic acid has a strong anti-inflammatory effect, and by down-regulating iNOS, COX-2, and inflammatory cytokines (IL-1β, IL-6, TNF-α), it suppresses the fibrosis of Aβ and solubilizes the already formed Aβ fiber (Chauhan A and Chauhan V, 2020). When DHA and EPA were administered in all three RCT studies, they mainly improved memory (Bo et al., 2017; Tokuda et al., 2020; Yurko-Mauro et al., 2010).

Development of region-based MIND diets

The MIND diet is a hybrid of the Mediterranean and DASH diets, and the Mediterranean diet pattern has already been included in the diet patterns of European and Asian countries (Cena and Calder, 2020). Therefore, if the standard MIND diet for Americans is changed according to the traditional dietary pattern of each country, and the diet is applied, more synergistic effects will be produced (Table 4). Huang et al. analyzed the Chinese MIND diet (C-MIND diet) for the Chinese elderly, with an average age of 84 years, in a cross-sectional study. Higher C-MIND diet scores were associated with male sex, higher education, urban living, regular exercise, cognitive impairment, and Instrumental Activities of Daily Living (IADL) scores. However, the lower the C-MIND diet scores, the greater the number of women, lower the education level, and greater the likelihood of rural living and lack of regular exercise. Therefore, the dietary score, was associated with different characteristics of the population group and the improvement of cognitive decline and daily living performance, physical motor performance, cognitive impairment, and IADL scores (Huang et al., 2022).

Similarly, in a large population-based French cohort study, a French MIND diet (F-MIND diet) analysis was performed on healthy elderly individuals with an average age of 75 years without dementia. The higher the F-MIND diet score, the lower the incidence of dementia and Alzheimer's disease. In addition, higher MIND diet scores were positively associated with gray matter in the left temporal superior pole and left anterior cingulate cortex and a positive association with lower mean and radial diffusivities in the splenium of the corpus callosum of white matter (Thomas et al., 2022). Recently, in South Korea, interventions have been conducted for elderly people with risk factors for dementia through programs to prevent dementia, such as nutrition, exercise, cognitive training, and vascular disease, including the Korean MIND diet (K-MIND diet). The results of the study showed that it had a positive effect on the improvement of the nutrition quotient for the elderly and the evaluation of cognitive function in the high-risk dementia group (Song et al., 2021). According to our previous study, the K-MIND diet, tailored for the elderly Korean population, showed significant improvements in subjects' orientation to place and was associated with upregulation of genes related to mitochondrial respiration and immune system processes, as well as modulation of metabolic pathways linked to cognitive function (data not shown).

Table 3 Summary and characteristics of major nutrient ingredients in a MIND diet

Author (year)	Design and location	Population and sex	Age	Follow-up time	Method of food intake assessment	Method of cognitive assessment	Outcomes
Vitamin B							
Ravaglia et al (2005)	Cohort/Italy	816 (434 women, 382 men)	74	4 yr	-	NINDS-AIREN[1]	Incidence of 112 dementia, among them, plasma folic acid in dementia patients significantly decrease compared to healthy elderly
Smith et al. (2010a, b)	RCT[2]/ UK	168 (102 women, 66 men)	76.2 ± 4.5	2 yr	Folic acid 0.8 mg + cyanocobalamin 0.5 mg + pyridoxine 20 mg	-	Homocysteine↓, holo-transcobalamin↑
Morris et al. (2018)	Cohort/ US	960 women	81	4.7 yr	144 items FFQ[3]	Batter cognitive tests	Folate↑, cognitive function↑
Ma et al. (2019)	RCT/China	180 women	74.9	2 yr	Folic acid 0.4 mg	MMSE[4], FSIQ[5], VIQ[6], PIQ[7]	VIQ↑, information↑, digit span↑, homocysteine↓, Aβ[8]-42↓, APP[9]↓
Carotenoids							
Liu et al. (2021)	RCT	295 (200 women, 95 men)	69.8 ± 4.2	3 yr	142-item FFQ	Neuropsychological test	α-Carotene↑, global cognition&semantic memory↑ Lutein&zeaxanthin↑, semantic memory↑
Morris et al. (2018)	Cohort/ US	960 women	81	4.7 yr	144 items FFQ	Batter cognitive tests	Lutein↑, cognitive function↑
Yuan et al. (2021)	Cohort/ China	927 (694 women, 233 men)	81 ± 7	7 yr	144 items FFQ	CEARD[10]	Lutein&zeaxanthin↑, CERAD↓
Polyphenol							
Kishida et al. (2022)	Cohort/ Japan	3739	40–64	9.2 yr	24 h dietary recall	-	Bean consumption↑, isoflavone↑, incidence of dementia↓
PUFA							
Bo et al. (2017)	RCT	86 (35 women, 51 men)	71	6 mo	DHA[17] 480 mg + EPA[18] 720 mg	BCAT[19]	Perceptual speed↑, space imagery efficiency↑, working memory↑, total BCAT↑
Tokuda et al. (2015)	RCT	76 (47 women, 29 men)	59	1 mo	DHA, 300 mg + EPA, 100 mg + ARA[20], 120 mg	MMSE, BDI-II[21]	Improve cognitive function
Yurko-Mauro et al. (2010)	RCT	485	70	24 wk	DHA, 900 mg	MMSE	Learning&memory↑
Polyphenol							
Kishida et al. (2022)	Cohort/ Japan	3739	40–64	9.2 yr	24 h dietary recall	-	Bean consumption↑, isoflavone↑, incidence of dementia↓

NINDS-AIREN National Institute of Neurological Disorders and Stroke and the Association Internationale pour la Recherche et I'Enseignement en Neurosciences, *RCT* Randomized Controlled Trial, *FFQ* Food Frequency Questionnaire, *MMSE* Mini-Mental State Examination, *FSIQ* Full Scale IQ, *VIQ* Verbal IQ, *PIQ* Performance IQ, *Aβ* β-amyloid, *APP* Amyloid Precursor Protein, *CEARD* Consortium to Establish a Registry for Alzheimer's Disease, *MDA* malondialdehyde, *SOD* Superoxide Dismutase, *GSH* Glutathione, *CTL* Control group, *VD* Vascular Dementia group, *RES* Vascular Dementia + Resveratrol treatment group, *DHA* Docosahexaenoic acid, *EPA* Eicosapentaenoic acid, *BCAT* Brief Cognitive Assessment Tool, *ARA* α-linolenic acid, *BDI-II* Beck Depression Inventory-Second Edition; ↑ means it has increase scores or levels; ↓ means it has decrease scores or levels

[*]In Table 3, we deleted two studies

Table 4 Summary and characteristics of the studies assessing the relationship of region-based MIND diet

Author (yr)	Design and Location	Population and Sex	Age	Follow-up time	Method of food intake assessment	Method of cognitive assessment	Outcomes
Song et al. (2021)	RCT/South Korea	136 (100 women, 36 men)	70.8 ± 4.83	1 yr	MIND diet meal check, NQ-E[1], MNA[2], Meal diary	RBANS[3], K-MMSE[4], CCI[5]	RBANS, K-MMSE, CCI↑, NQ-E↑
Huang et al. (2022)	Cross-sectional/China	11,245 (6155 women, 5090 men)	84.1 ± 11.5	-	144-item FFQ[6]	MMSE[7], IADL[8]	Improve cognitive decline rate and IADL
Thomas et al. (2022)	Cohort/French	1412 (890 women, 522 men)	75.8 ± 4.8	9.7 yr	148-item FFQ	MMSE, MRI[9]	Reduction of incidence dementia rate Positive association with gray matter and white matter

NQ-E Nutrition Quotient for Elderly, *MNA* Mini Nutritional Assessment, *K-MMSE* Korean version Mini-Mental State Examination, *CCI* Cost of Care Index, *FFQ* Food Frequency Questionnaire, *MMSE* Mini-Mental State Examination, *IADL* Instrumental Activities of Daily Living, *MRI* Magnetic Resonance Angiography, ↑ means it has the effective outcome

This review aims to help improve cognitive function and lower the incidence of dementia in healthy elderly and those with MCI when following a MIND diet and help improve memory as a major early symptom of Alzheimer's dementia. In addition, the MIND diet is richer in vitamin B, carotenoids, polyphenols, and PUFA components than other diets, which have been shown to improve cognitive functions in patients with MCI and dementia with anti-inflammatory and antioxidant effects. The advantages of this study are summarized for the effectiveness of the MIND diet in healthy and elderly individuals with MCI, and the mechanism is described for the most prominent nutrients in the MIND diet. However, the cognitive function evaluation and diet criteria of all the experimental studies summarized in this review were slightly different. In addition, there is a lack of research on interventions using the MIND diet by itself, and the results of research on specific areas of cognitive function are insufficient. Therefore, it will be necessary to demonstrate consistency in future studies.

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Declarations

Conflict of interest The authors declare that there are no conflicts of interest.

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