Chapter

Influence of Bioactive Components of the Mediterranean Diet on Inflammation and Healthy Aging

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Abstract

The Mediterranean diet is characterized by an increased consumption of fruits, vegetables, grains, and fish. Olive oil and herbs and spices are also essential components of this food regimen. Such a diet is associated with a reduced risk of cardiovascular disease, overall mortality, reduced incidence of Parkinson's and Alzheimer's diseases, and reduced cognitive impairment. Some of the bioactive components that exert beneficial effects are ω-3 fatty acids, polyphenols, and alkaloids that have neuroprotective, anti-inflammatory, antioxidant, antimicrobial, and gluco-regulating properties. These beneficial effects contribute to improved health including organ health and cognitive function. While the number of such bioactive plant constituents is numerous, this review will examine the role of specific bioactives and vitamins and assess the molecular mechanisms including the antioxidant and anti-inflammatory beneficial effects of the bioactive components in the Mediterranean diet.

Keywords: polyphenols, inflammation, fatty acids, kidney health, cognition

1. Introduction

The Mediterranean diet (MedDiet) is characterized by an increased consumption of olive oil, fruits, vegetables, grains, and fish. It is defined as including olive oil as the main added lipid, two or more servings of vegetables at every meal, 1–2 servings of fruit at every meal, and two or more servings of fish on a weekly basis [1]. These ingredients impart specific nutrients which are the means for the MedDiet to have its beneficial effect. There are clearly advantageous consumptions of specific fatty acids such as oleic acid, a monounsaturated fat (MUFA) in olive oil, and the ω-3 fatty acids (polyunsaturated fat, PUFA) associated with fish consumption. Also, the plant-based ingredients: vegetables, breads and cereals, fruits, nuts, herbs, and spices which are components of the MedDiet impart specific nutrients that have a direct biological activity to enhance antioxidant support and reduce inflammation. This direct effect of the specific nutrients is likely the means to the reduced risk of cardiovascular disease, overall mortality, reduced incidence of Parkinson's and Alzheimer's diseases, and reduced cognitive impairment with aging.

A challenge in discovering the actual nutrients and their mode of action is that the MedDiet is often defined by a group of people consuming that food and then comparing that group to a cohort that is not consuming the MedDiet [2, 3]. This can generate likely benefits and an understanding of the ingredients which result in the observed beneficial effects of the MedDiet. It is apparent that these benefits come from specific ingredients. This leads to specific avenues of understanding of the biology behind the benefit of consuming the MedDiet. For example, some of the specific nutrients, which have been stated to be important components, are resveratrol from grapes, anthocyanins from vegetables and fruits, and polyunsaturated fatty acids especially those from olive oil and fish [4]. These nutrients were discussed in a recent review as well as the antioxidant nutrients such as selenium, the vitamins A, C, E, and the bioactive antioxidants of lycopene and the carotenoids [5]. These authors also stated that the increased consumption of specific phytochemicals played a role in the effectiveness of the MedDiet including resveratrol and epigallocatechin gallate, retinoids, phenolic acids, terpenes, isoflavones, and polyphenols.

These possibilities can then be further elucidated by specific individual factor experiments with focused outcomes in both human and nonhuman animals. This review will assess the molecular mechanisms of some of the most likely compounds which through their influence on the oxidant and inflammatory pathways result in the beneficial effects of the MedDiet.

2. Discussion

The antioxidant defense system protects the body from free radical damage and is an essential component of the control of prooxidant damage and pro-inflammatory cytokines [6–8]. The active antioxidant nutrients in the MedDiet include a number of phytopolyphenols including quercetin, resveratrol, curcumin, apigenin, and epigallocatechin gallate [9, 10]. Quercetin, a flavonoid polyphenol, is a free radical scavenger and binds transition metal ions; both activities provide support for the antioxidant defenses [11]. The defense against low-density lipoprotein (LDL) oxidation provided by quercetin may be of significant benefit in reducing the risk of coronary heart disease [12]. Resveratrol, a stilbene polyphenol found in grapes and berries, is a potent antioxidant with multiple biological effects [13] which support its positive influence in the MedDiet [14]. For example, acting as an antioxidant resveratrol was shown to be effective in reducing the neuroinflammation and memory loss in aged mice [15]. The role of curcumin, a polyphenol found in turmeric, as an antioxidant has been frequently reviewed [16, 17]. In a recent review [18], it was concluded that curcumin was effective in reducing protein and lipid oxidation. They noted a reduction in nitrotyrosines, thiols, protein carbonyls, and malondialdehyde. This was accompanied with an increased activity of glutathione peroxidase and superoxide dismutase both effective antioxidant enzymes. This enhanced antioxidant status is consistent with curcumin being a positive component of the benefits for those consuming the MedDiet. Apigenin, a flavonoid found in parlsey and celery, has been shown to be both an antioxidant and an anti-inflammatory compound [19, 20]. These antioxidant and anti-inflammatory effects suggest that the MedDiet benefits in protecting against cancer, cardiovascular disease, and all-cause death are partially the result of its consumption. Epigallocatechin gallate (EGCG), a major polyphenol found in green tea, is an effective antioxidant [21] that has been shown to be a benefit in modulating the molecular and cellular mechanisms associated with obesity and hypertension [22, 23].

Because of these benefits, it is quite likely that epigallocatechin gallate has a positive role in the benefits of consuming the MedDiet. Taken as a group, the phytophenols associated with the MedDiet are a significant support for health outcomes through reduced oxidation and control of inflammation.

The vitamins including C, D, E, B_{12}, $B_{6,}$ and folic acid [8] which are found in abundance in the MedDiet also support the oxidant defense system and overall health. Vitamins E, C, and β-carotene are well-known antioxidants present in the MedDiet which have been shown to be significant antioxidants with health benefits [24–27]. Circulating vitamin D is increased in the MedDiet [28]. In addition to the antioxidant effect of vitamin D [29], this may be a direct benefit and a factor in the reduced risk of bone fracture associated with the MedDiet [30]. It is possible that the enhanced B_{12}, $B_{6,}$ and folic acid nutrition associated with the MedDiet have their beneficial effects through a reduction in homocysteine. These vitamins along with betaine (which is enhanced in the MedDiet because of the increased consumption of grains) are all influential in reducing homocysteine. This is a likely benefit associated with the consumption of the MedDiet because increased homocysteine is associated with more than 100 diseases [31].

The composition of olive oil is significant for understanding the role of fats in the MedDiet. Olive oil has as a majority fatty acid oleic acid (18:1) with between 2.8%–21.1% of linoleic and 0.49–1.9% linolenic [32]. Regarding the fatty acid composition of the MedDiet, the frequent servings of fish complement the ω-3 linolenic acid by adding EPA and DHA. In general, it is well known that the consumption of the ω-3 fatty acids (linolenic, EPA, and DHA) results in reduced inflammation as compared to the ω-6 fatty acids [33]. However, there are reports that oleic acid is also anti-inflammatory [34, 35] although it is not elongated or desaturated to the eicosanoids through which the ω-3 and ω-6 fatty acids have their effects [36]. The pro-inflammatory and regulatory effects of the eicosanoids have been reviewed showing the relative anti-inflammatory role of the ω-3 fatty acids [37].

A decline in certain domains of cognitive function including attention, memory, and executive function, with normal aging has been reported [38, 39]. Structural and functional changes in the brain associated with aging also contribute to a decline in cognitive performance. There is evidence to indicate that increased intake of antioxidant and polyphenol-rich MedDiet combined with physical activity may be associated with less brain atrophy in humans without dementia [39, 40]. While dietary interventions, in particular MedDiet, have shown promising results in improving cognitive function [41, 42], further studies are needed as results have been inconsistent. Nevertheless, a diet rich in polyphenols, vitamins, and essential fatty acids, which together form a core component of MedDiet, is an important interventional strategy to minimize the modifiable risk of aging-associated cognitive decline. **Table 1** highlights the role of the MedDiet ingredients dietary legumes and nuts on cognitive function.

3. Conclusions

This review highlights that the ingredients associated with the MedDiet impart specific nutrients. The nutrients discussed here do not explain all of the benefits of consuming the MedDiet. However, they have been shown to reduce systemic chronic inflammation and optimize the normal oxidative balance. These changes contribute to the enhanced length of life and well-being, including a beneficial effect on cognitive function, observed with this dietary regimen.

Study model	Methodology and results	Results for cognition or learning and memory	References
A cross-sectional study investigated the association between dietary patterns and cognitive function in older adults (n = 371, 65–74 yr) in New Zealand. REACH Study	Three dietary patterns: Mediterranean style, Western, and Prudent. Six cognitive domains (global cognition, attention and vigilance, executive function, episodic memory, working memory, and spatial memory) were tested using COMPASS.	No association was reported between any cognitive domain and dietary pattern scores.	[43]
Study investigated the association between dietary patterns and overall cognitive performance and cognitive change over time in community-dwelling older adults (n = 1037, 70–90 yr). Sydney Memory and Aging (SMA) Study	Study with 6 years follow-up. Mediterranean diet and Dietary Approaches to Stop Hypertension (DASH) diet scores were generated based on questionnaires. Neuropsychological tests assessed global cognition and 6 cognitive domains on 4 occasions, at baseline and 2, 4, and 6 yr.	No association reported for MedDiet or Dietary Approaches to Stop Hypertension with overall cognition or cognitive decline over 6 years. However, higher intake of legumes and nuts was related to better overall performance in global cognition	[44]
Cross-sectional investigated the dietary patterns associated with mild cognitive impairment (MCI) in hospitalized adults aged over 50 years in Korea	Diet information was obtained using a questionnaire with 112 food items and 24-h dietary recall. Principal component analysis, three dietary patterns, "legumes and vegetables," "beverage and nuts," and "white rice" Mini-Mental State Examination (MMSE) was used to assess global cognition	The "beverage and nuts" pattern was inversely associated with the prevalence of high MCI but the white rice pattern was associated with the prevalence of MCI. However, when adjusted for all confounding factors, no association was found.	[45]
Study analyzed data of Chinese adults (n = 4309, 55 yr and older) Community-based Cohort Study on Nervous System Diseases from 2018 to 2019.	Dietary information obtained using a food frequency questionnaire. Cognitive function of the subjects was measured by the Montreal Cognitive Assessment.	Increased consumption of rice, legumes, fresh vegetables, fresh fruit, pork, poultry, fish, and nuts was associated with higher scores of global cognitive function and domains, and lower odds of MCI.	[46]
A population-based, cross-sectional analysis (baseline phase) of non-demented community-dwelling individuals (n = 819, 70–90 yr) Sydney Memory and Aging (SMA) Study	Scores for Mediterranean diet, Dietary Approaches to Stop Hypertension (DASH) diet and the Dietary Guidelines Index (DGI 2013) were generated using a questionnaire. Neuropsychological tests were used for measuring global cognition and six cognitive domains.	Mediterranean and DASH diets were both positively associated with improved visuospatial cognition. Higher intake of legumes and nuts was also associated with better performance in global cognition, and other cognitive domains.	[44]

Study model	Methodology and results	Results for cognition or learning and memory	References
Study investigated the relation between food patterns and mild cognitive impairment (MCI) among elderly Chinese population (n=2311, 60–88 yr participants from 760 communities of six districts in China)	A 49-item food frequency questionnaire survey was administered and 4 dietary patterns were identified. Chinese version of the Mattis Dementia Rating Scale (CDRS) was used to assess the general cognitive status as well as the Chinese version of MMSE.	Food pattern that included a higher intake of legumes, vegetables, fruits, milk and dairy products, nuts but a low intake of noodles and cereals was significantly correlated with better cognitive function including memory and language function.	[47]
Study investigated the cross-sectional association between adherence to MedDiet and cognitive performance (n= 1607 men and women, 20–70 yr) in Holland. Study conducted using the cross-sectional data of the Nutrition Questionnaires plus (NQplus) study	Dietary intake was assessed using a 183-item Food Frequency Questionnaire. MedDiet intakes were measured on a scale based on consumption of vegetables, legumes, fruits/nuts, cereals, fish/seafood, meat/poultry, dairy, ethanol and the MUFA:SFA ratio. Cognitive function was assessed using three standardized neuropsychological tests including the Letter Fluency test (LFT), Symbol Digit Modalities Test (SDMT), and the Rivermead Behavioral Memory Tests (RBMT)	Increased adherence to MedDiet was associated with poorer everyday memory. While higher vegetable intake was associated with better processing speed in cognitive tests, higher legume intake was with related to poorer processing speed.	[48]
Study analyzed the consumption of foods among elderly Italian individuals (n = 214 subjects, aged ≥65 years) and cognitive function over a period of 12 months.	Food choice was measured by a combination of the dietary intake data, assessed by a 24-h recall and a seven-day diet record. MMSE and the cognitive sub-test of ADA Scale were used to detect cognitive decline progression over 12 months.	While there was a positive association between a food pattern that included high legume consumption and improved MMSE after an interval of 1 year, there was an inverse association with basal and 1 year ADAS-cog test. Dietary pattern that included plant proteins and PUFAs was independently associated with an improvement on ADAS-cog after 1 year.	[49]
Study assessed the efficacy of a MedDiet approach to reduce the onset of cognitive decline, and promote optimal cognitive performance among healthy older adults (n = 137 men and women, >65 yr) in Australia The MedLey Study	A randomized 2-cohort parallel group intervention trial, examining the effect of a Mediterranean dietary pattern (MedDiet) for six months that extended for a duration of 18 months Experimental group consumed traditional Cretan MedDiet (i.e. vegetables, fruits, olive oil, legumes, fish, whole grain cereals, nuts and seeds and low consumption of processed foods, dairy products, red meat and vegetable oils). Control group were asked to maintain their customary lifestyle and diet. A neuropsychological test battery that included 11 individual tests.	MedDiet group did not perform significantly better than control group in tests to assess executive functioning, speed of processing, memory, visual-spatial ability. Thus, there was little evidence of a beneficial effect of a MedDiet intervention on cognitive function among healthy older adults.	[50]

Study model	Methodology and results	Results for cognition or learning and memory	References
This prospective study investigated the relationship between cognitive performance and dietary intake in community dwelling adults (n=333 participants) in New York. Maine-Syracuse Longitudinal Study.	Wechsler Adult Intelligence Scale (WAIS) was assessed at baseline, and dietary intake was measured using the Nutrition and Health Questionnaire measured 18 years later.	Higher WAIS Scores at baseline were prospectively associated with higher intakes of vegetables, meats, nuts and legumes, and fish.	[51]
Study examined prospectively the association between Mediterranean-style dietary pattern, Dietary Approaches to Stop Hypertension (DASH), and age-related cognitive change (n = 3831 men and women ≥65 y of age in Utah). The Cache county Study on Memory, Health, and Aging.	Dietary intake was assessed at baseline by using a 142-item self-administered FFQ. DASH and Mediterranean diet accordance scores were computed from food and nutrient components emphasized or minimized in the dietary patterns. Cognitive function was assessed using the Modified Mini-Mental State Examination ≤4 times over 11 yr.	Whole grains and nuts and legumes were positively correlated with higher cognitive function. Higher levels of adherence to both the DASH and MedDiet patterns were associated with better cognitive function in elderly men and women over an 11-y period.	[52]
Study examined the association of adherence to the Mediterranean diet with cognitive performance (n = 6174 participants, aged 65+ years) Part of the Women's Health Study.	Alternate MedDiet adherence score was constructed based on intakes of vegetables, fruits, legumes, whole grains, nuts, fish, red and processed meats, moderate alcohol, and the ratio of monounsaturated-to-saturated fats. Women provided dietary information at baseline and completed a cognitive battery consisting of 5 tests, 5 years later, followed by two assessments at 2-year intervals.	The alternate MedDiet score was not associated with overall global cognition and verbal memory.	[53]

Table 1.
The role of Mediterranean diet ingredients on cognitive function.

4. Future perspective of the Mediterranean Diet

This review brings to light the specific attributes of reduced chronic inflammation and normalized oxidative balance. Future research could enhance the available knowledge through the investigation of the interaction of chronic inflammation and oxidative damage in the specific biological benefits associated with the MedDiet such as the control of energy use (and thus insulin resistance and diabetes), the control of renal function (and therefore chronic kidney disease), and enhancement of cognitive function (and therefore control of Alzheimer's disease).

Conflict of interest

The authors declare no conflict of interest.

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