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REVIEW ARTICLE

Dietary pattern in relation to the risk of Alzheimer's disease: a systematic review

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Abstract

Alzheimer's disease (AD) is a progressive neurodegenerative disease leading to a gradual and irreversible loss of memory, linguistic skills, and perception of time and space, thinking, and behavior. Dietary pattern has been presented as a contributor to the incidence of Alzheimer's. This study aimed at reviewing the evidence on the relation between dietary pattern and AD. This systematic search was performed on the articles available in PubMed, Scopus, and Web of Sciences databases until May 2019 using keywords, including (diet, food, dietary pattern, food pattern) and (Alzheimer's disease) among observational studies. After excluding duplicated, and irrelevant studies, 26 studies were eligible for this review study. We categorized the studied dietary patterns into two groups: healthy and unhealthy diet. This study reviewed two case-control, five cross-sectional, and 19 prospective studies. Eight studies assessed unhealthy diet (high-fat diet, high-glycemic diet, sweetened sugary beverage, etc.) and the risk of AD. In addition, the other studies considered the effect of healthy diet such as Mediterranean diet, dietary approaches to stop hypertension (DASH), Mediterranean-DASH intervention for neurodegenerative delay, and seafood-rich diet on AD. This literature review indicated that adherence to a healthy dietary pattern has neuroprotective effects on AD prevention, while unhealthy diet can cause neurodegenerative effects in AD etiology. In conclusion, our findings showed that adherence to healthy diet can decrease oxidative stress and inflammation and accumulation of amyloid-β and consequently can decrease the risk of AD.

Keywords Dietary pattern · Alzheimer disease · Inflammation · Oxidative stress

Introduction

Alzheimer's disease (AD) is a complex, progressive, and disabling neurodegenerative disease with no cure, leading to cognitive impairment and memory loss. It is also the most common cause of dementia. AD is characterized by the deposition of extracellular amyloid β plaques and the presence of neurofibrillary tangles. This disease affects millions of people around the world [1, 2]. In 2017, it was estimated that 5.5 million Americans of all ages lived with Alzheimer's dementia [3]. Every 66 s, one person in the USA develops Alzheimer's dementia, and by 2050, one person in the USA will develop Alzheimer's dementia every 33 s [2]. Like other common chronic diseases, AD develops as a result of multiple factors rather than a single cause [2]. The greatest risk factors for late-onset Alzheimer's are older age (being aged 65 or older) [3, 4], having a family history of Alzheimer's [5, 6], and carrying the APOE e4 gene [7, 8].

Despite the lack of change or modification, the mentioned risk factors to reduce the risk of AD [2], various studies have indicated that factors such as management of cardiovascular risk factors (diabetes, obesity, smoking, and hypertension), regular physical activity, and healthy diet may reduce the risk of dementia [9]. Diet may play an important role in the incidence and prevention of AD and can have considerable potential for nonpharmacological prevention [10]. Some epidemiological evidence has suggested that adherence to a diet

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with low glycemic index [11], higher consumption of omega-3 polyunsaturated fatty acids [12], calorie restriction [13], and Mediterranean diet (MD) [14] was associated with delay in the onset of dementia and a decrease in AD biomarker burden; however, some studies have showed that a high-glycemic diet and high cholesterol intake as unhealthy diet do not affect the risk of AD [15, 16].

Although many studies have been assessed the association between each of the mentioned dietary patterns alone and AD [17–19], no studies have been conducted to summarize findings about this association. According to the high prevalence of AD, assessment of a dietary pattern and its relationship to AD is important, since it can help to decrease the risk of AD. Therefore, the objective of present study was to conduct a systematic review of the findings on dietary pattern and the risk of AD.

Methods

This study was designed based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocol [20]. In one review study, we performed a literature search on electronic databases, including PubMed, Scopus, Web of Sciences, and Google Scoular for related publications until May 2019.

Search strategy A systematic search was performed by two researchers independently using Medical subject headings (MeSH) and non-MeSH keywords as follows: (diet, food, dietary pattern, food pattern) and (Alzheimer's disease). Furthermore, references of these articles were examined to identify other relevant articles that we had not found them in our initial search. In addition, we did not consider any language, location, and time restrictions in the search strategy.

Inclusion and exclusion criteria In this review, inclusion criteria were (1) studies examining all dietary patterns using dietary assessment tools, including FFQ, food record and so on; (2) studies conducted on adults (no rat and animal studies); (3) studies assessing the risk of AD; and (4) studies designing observation (prospective or retrospective or cross-sectional or case-control studies). In accordance with the purpose of the study, we considered studies with a long time exposure (dietary pattern). Therefore, we did not include a randomized clinical trial evaluating the effect of diet in a short time. Additionally, we did not include letters, comments, and short communication, since the study method and results were not written completely. Furthermore, we considered only original studies (no review or meta-analysis). Overall, in the initial search, we found 1401 relevant articles that, after removing duplicated studies and screening for interest topic, we selected 119 articles for review with more details. Among these articles, we excluded 30 irrelevant studies. A total of 44 articles were excluded since they did not examine AD and mentioned other cognitive disorders. A total of 18 articles were excluded due to no dietary pattern measured. Furthermore, 19 articles were excluded, since diet was not examined. Finally, 26 studies were included in the current review study (Fig. 1).

Assessment of the study quality The Newcastle-Ottawa scale, for assessing the quality of non-randomized studies in review studies [21], was used to assess the study quality. Based on this scale, all the reviewed studies had an appropriate quality.

Data extraction and dietary pattern evaluation The studies' information was extracted in a checklist designed for this review study. This checklist included the first author, year of publication, study design, country of origin, sample size, gender, studied age range, dietary pattern assessment tools, kind of diet, and the most important outcome.

The introduced dietary patterns of these studies were categorized by two researchers independently into 2 groups: healthy and unhealthy diet. Healthy diet was tended to contain high intake of fruits, vegetables, fish, poultry, whole grain, and liquid oil, particularly olive oil. Unhealthy diet was characterized by high intake of red and processed meat, Sugar-sweetened beverage (SSB), refined grain, high-fat foods such as high-fat dairy, high intake of egg, and high-sugar foods. Based on these definitions among 26 studies, 8 studies were examined unhealthy diet and 19 studies examined healthy diet. (Table 1).

Results

In this literature review, we found 26 relevant studies. A total of 2 studies were case-control [27, 29], 5 studies [37, 38, 44–46] were cross-sectional, and other studies were designed prospectively [24, 26, 31, 35, 36, 41, 42, 47–59]. There were a total of 52–5395 participants per study. These studies were conducted in Australian [24, 32, 38], America [26, 27, 29, 31, 36, 37, 44, 46–48, 50–53, 57, 58], Asian [42, 45], and European countries [35, 49, 54, 59]. The ages in the studies were 25 years old and older in all of the studies. All of the studies examined sexual distribution except studies by Ylilauri et al. [16] and Olsson et al. [35] that participants in this study were male, and Hill et al. [24] examined only females.

All the studies assessed dietary intake by the food frequency questionnaire (FFQ) except four studies [16, 23, 35, 54]. Dietary assessment tools in the studies conducted by Laitinen [23] and Eskelinen [54] were the dietary habit questionnaire, and in studies conducted by Ylilauri [16] and Olsson [35], they were as food record. A total of 8 studies examined the risk of AD and unhealthy dietary patterns, including high-fat

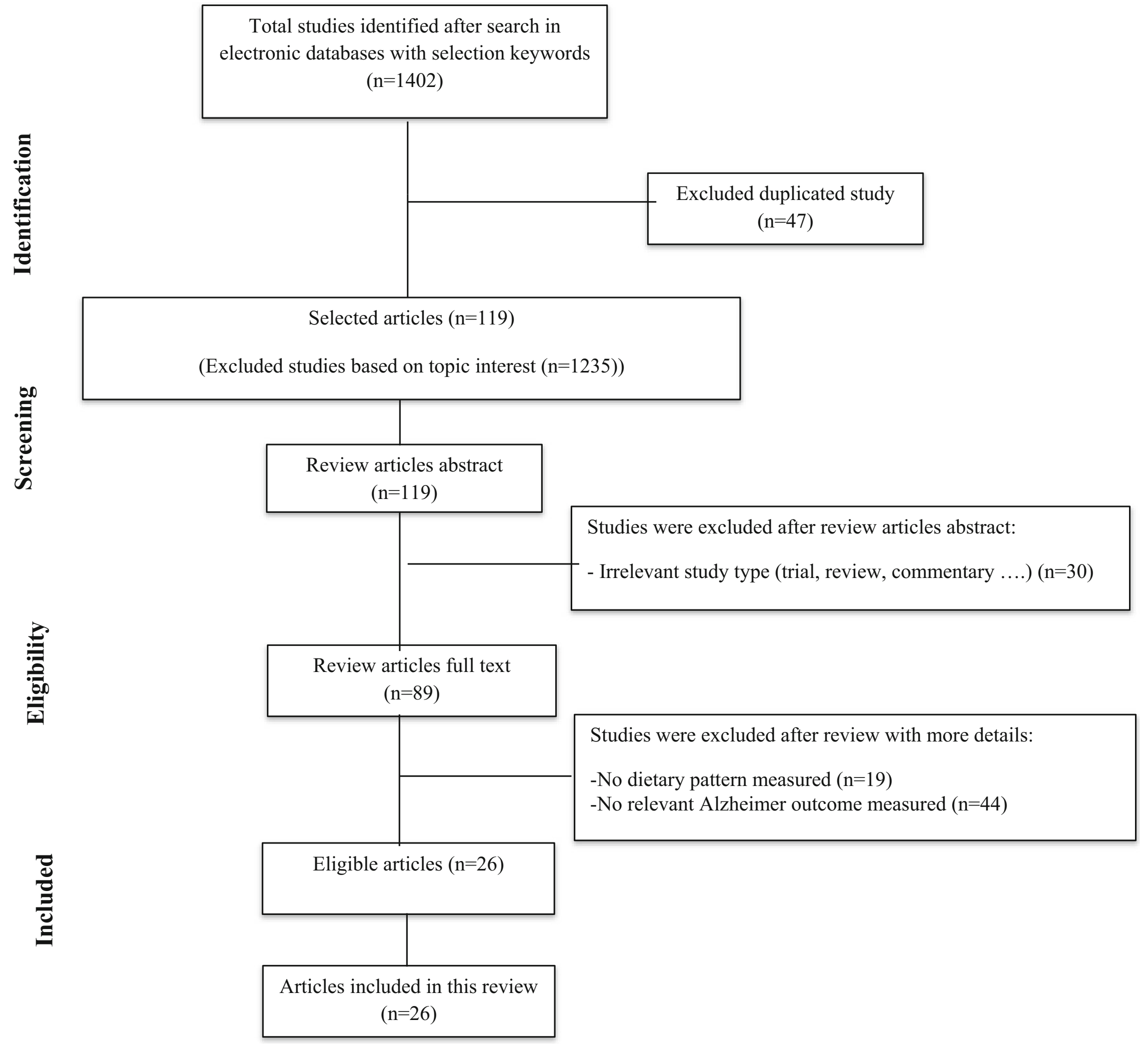

Fig. 1 Diagram of study selection

diet [22, 23], high-glycemic diet [15], SSB [25], high-cholesterol diet [16], DIF [26], and Western diet [27] (Table 2). Healthy diet and the risk of AD were assessed by 19 studies consisting of MD [19, 24, 28, 29, 32–37, 52, 55], dietary approaches to stop hypertension (DASH) [34], Mediterranean-DASH intervention for neurodegenerative delay (MIND) [34, 37], HEI [35, 54], seafood-rich diet [39–41], soy-based food diet [42], capsaicin-rich diet [43], high-protein diet [35, 38], and low-fat diet [24]. (Table 3).

In the literature review, we found that high-fat diet was associated with the risk of AD [22, 23]. Both of studies indicated that saturated fats, especially trans-fat, could increase the risk of AD [22, 23], while Hill et al. [24] did not observe any association between high-fat diet and AD. Luchsinger et al. [15] showed that high-glycemic diet as unhealthy diet did not affect the risk of AD even after being adjusted for potential confounders, including age, sex, diabetic, and APOE-ε4. We observed that, in the study by Pase et al. [25] in the community-based Framingham Heart Study, high intake of total sugary beverages, fruit juice, and sugar-sweetened soft drinks in diet increased with the presence of pre-clinical symptom of AD. In another population-based Kuopio Ischaemic Heart Disease Risk Factor study by Ylilauri et al. [16], high cholesterol intake of diet was not associated with the incidence of AD. However, they recommended moderate consumption of egg and other sources of cholesterol to improve cognitive function. DIF as another unhealthy dietary pattern was introduced by Gu et al. [26] that did not observe any association between adherence to DIF and AD. [27] In the study by Gustaw-Rothenberg et al. [27], patients with Alzheimer's tended to follow Western dietary patterns (Table 2).

Among healthy dietary patterns, MD was studied more than other dietary patterns [19, 24, 28, 29, 32–37, 52, 55]. Each of 12 studies reported that MD was associated with the decrease of AD risk [19, 28, 32–34]. Morris et al. [34] examined 3 dietary patterns and the risk of AD that, in this study, higher adherence to MD and DASH and moderate adherence to MIND might decrease incidence of AD. Morris et al. in two

Table 1 Dietary patterns and their main component from the reviewed studies

Kind of diet	Frist author, year	Main component of the dietary pattern
Unhealthy diet		
High-fat diet	Morris, 2003 [22]	Dairy products, removal fat or poultry skin, specified brand name products for cereals, margarine, oil, and multivitamins.
	Laitinen, 2006 [23]	Milk, sour milk, eggs, coffee, tea, and sugar in tea/coffee
	Hill, 2018 [24]	Processed meats, fried fish, red meats, fried potatoes, and poultry
High-glycemic diet	Luchsinger, 2007 [15]	Carbohydrate and sugary food intake
SSB-rich diet	Pase, 2017 [25]	Total sugary beverages, fruit juice, sugar-sweetened soft drinks
	Hill, 2018 [24]	Takeaway foods, added sugar, confectionary and cakes, biscuits, and sweet pastries
High-cholesterol diet	Ylilauri, 2017 [16]	Cholesterol and egg
DII	Gu, 2011 [26]	Amount and type of fat, essential fatty acids, vitamins, minerals and antioxidants, glycemic index, and anti-inflammatory compounds
Western diet	Gustaw-Rothenberg, 2009 [27]	Processed meat, butter, high-fat dairy products, eggs, and refined sugar
Healthy diet		
MD	Scarmeas, 2006 [28]	Fruits, vegetables, legumes, cereals, fish, meat and dairy products
	Scarmeas, 2006 [29]	Fruits, vegetables, legumes, cereals, fish, meat and dairy products
	Scarmeas, 2009 [30]	Dairy, meat, fruits, vegetables, legumes, cereals, and fish
	Gu, 2010 [19]	Fruits, vegetables, legumes, cereals, fish, meat and dairy products
	Gu, 2010 [31]	Higher intakes of salad dressing, nuts, fish, tomatoes, poultry, cruciferous vegetables, fruits, and dark and green leafy vegetables and a lower intake of high-fat dairy products, red meat, organ meat, and butter
	Gardener, 2012 [32]	Fruits, vegetables, legumes, cereals, fish, meat and dairy products
	Mosconi, 2014 [33]	Fruits, vegetables, legumes, cereals and fish or detrimental (meat and dairy products)
	Morris, 2015 [34]	Fruits, vegetables, legumes, cereals, fish, meat, and dairy products
	Olsson, 2015 [35]	PUFA/SFA (ratio), fruits, vegetables, legumes, cereals, fish, meat, dairy products, and alcohol
	Vassilaki, 2018 [36]	Fruits, vegetables, legumes, cereals, fish, meat, and dairy products
	Calil, 2018 [37]	Fruits, vegetables, legumes, cereals, fish, meat, and dairy products
	Hill, 2018 [24]	Whole grains, vegetables, nuts, fish, and wine as the main source of alcohol
DASH	Morris, 2015 [34]	7 food groups and 3 dietary components (total fat, saturated fat, and sodium)
MIND	Morris, 2015 [34]	10 brain healthy food groups (green leafy vegetables, other vegetables, nuts, berries, beans, whole grains, fish, poultry, olive oil, and wine) and 5 unhealthy food groups (red meats, butter and stick margarine, cheese, pastries and sweets, and fried/fast food)
	Calil, 2018 [37]	Whole wheat bread (whole grains group); lettuce, endive, cress and wild chicory (group of green leaves); broccoli, carrot, beet, zucchini, eggplant, tomato, cucumber, chard, cabbage, pumpkin (group of other vegetables), and strawberry (red fruit group)
HEI	Eskelinen, 2011 [38]	Beneficial components (vegetables and roots, berries and fruits, bread, fish, coffee drinking, monounsaturated fatty acids (MUFAs), and PUFAs from milk products and spreads) and unhealthy (sausage foods, eggs, candies, sweet soft drinks, sugar lumps in coffee, salty fish, and SFAs from milk products and spreads)
	Olsson, 2015 [35]	WHO dietary guidelines
Seafood-rich diet	Morris, 2003 and 2016 [39, 40]	Tuna sandwich; fish sticks, cakes, or sandwich; fresh fish as a main dish; and shrimp, lobster, or crab
	Devore, 2009 [41]	Total fish intake and intake of different fish types (e.g., salmon)
Soy-based food diet	Ozawa, 2013 [42]	High intake of soybeans and soybean products, vegetables, algae, and milk and dairy products and a low intake of rice
Capsaicin-rich diet	Liu, 2016 [43]	Chili pepper
High-protein diet	Olsson, 2015 [35]	Carbohydrate and protein intake
	Fernando, 2018 [38]	Grams per day intake of protein and fiber
Low-fat diet	Hill, 2018 [24]	Low-fat dairy products, vegetables, and unsaturated spreads

SSB, Sugar-sweetened beverage; *DII*, dietary inflammatory index; *MD*, Mediterranean diet; *DASH*, Dietary Approaches to Stop Hypertension; *MIND*, Mediterranean-DASH Intervention for Neurodegenerative Delay; *HEI*, Healthy Eating Index

independent studies [39, 40] showed that intake of all seafoods could decrease AD risk, while Devore et al. [41] did not observe any association between seafood and AD. Liu et al. [43] reported that capsaicin-rich diet had positive effects on biomarker's AD and cognitive performance. Furthermore, high intake of soy-based food, high protein, and adherence to healthy dietary patterns showed prevention effects on AD [38, 42, 54] (Table 3).

Table 2 The studies were examined unhealthy dietary pattern and AD

First author/year	Study population/study design/country	Age (year)	Sample size	Dietary pattern assessment tools	Kind of diet	Comparison	ES	CI	Outcome*
Morris, 2003 [22]	Chicago Health and Aging Project/prospective study/Chicago	Age ≥ 65	815 subjects (101 men and 713 women)	FFQ	High-fat diet	Q1	1		W
						Q2	RR:1.1	0.4–2.7	
						Q3	RR:0.9	0.3–2.3	
						Q4	RR:0.7	0.3–1.6	
						Q5	RR:0.9	0.4–1.8	
					High animal fat diet	Q1	1		W
						Q2	RR:0.6	0.2–1.7	
						Q3	RR:0.7	0.3–1.7	
						Q4	RR:0.6	0.2–1.7	
						Q5	RR:0.7	0.3–1.6	
					High vegetables fat diet	Q1	1		P
						Q2	RR:0.9	0.4–2	
						Q3	RR:0.3	0.1–0.8	
						Q4	RR:0.4	0.2–1.3	
						Q5	RR:0.2	0.1–0.7	
Laitinen, 2006 [23]	The Cardiovascular Risk Factors, Aging and Incidence of Dementia (CAIDE) study/prospective study/Finland	65–80	1449 subjects (549 men and 900 women)	Dietary habit questionnaire	High-fat diet	Q1	1		W
						Q2	OR:0.52	0.2–1.36	
						Q3	OR:1.36	0.61–3.06	
						Q4	OR:0.79	0.29–2.12	
Luchsinger, 2007[15]	Prospective study/Northern Manhattan	Age ≥ 65	939 subjects (549 men and 390 women)	FFQ	High-glycemic diet	Q1	1		W
						Q2	HR:1	0.7–1.6	
						Q3	HR:0.9	0.6–1.5	
						Q4	HR:1.1	0.7–1.7	
Gustaw-Rothenberg, 2009 [27]	Badanie Epidemiologiczne Rozpowszechniena Choroby Alzheimera i innych form demencji w Województwie Lubelskim (BERCAL)/case-control/-USA	> 55	71 subjects (29 men and 42 women)	FFQ	Western	–	–	–	–
Gu, 2011 [26]	1992 (WHICAP 1992) and 1999 (WHICAP 1999)/prospective study/New York	Age ≥ 65	2258 subjects (1526 men and 732 women)	FFQ	DII	Continuous	HR:0.99	0.99–1	W
Pase, 2017 [25]		Age ≥ 30	4276 subjects	FFQ	SSB-rich diet	–	–	–	–

Table 2 (continued)

First author/year	Study population/study design/country	Age (year)	Sample size	Dietary pattern assessment tools	Kind of diet	Comparison	ES	CI	Outcome*
	Framingham Heart Study (FHS)/prospective study/USA		(1965 men and 2311 women)						
Ylilauri, 2017 [16]	The Kuopio Ischemic Heart Disease Risk Factor Study/prospective study/Kuopio	42–60	2497 subjects (2497 men)	Food record	High-cholesterol diet	Q4 vs. Q1	HR:0.79	0.53–1.19	W
					High dietary egg	Q4 vs. Q1	HR:0.85	0.59–1.23	W
Hill, 2018[24]	The Women's Health Aging Project/prospective study/Australia	45–55	115 subjects (115 women)	FFQ	High fat	Liner	Coefficient:− 0.007	− 0.09–0.07	W
					Junk food	Liner	Coefficient:− 0.09	− 0.18-(−0.008)	N

FFQ, food frequency questionnaire; *DII*, dietary inflammatory index; *SSB*, sweetened sugary beverage; *ES*, effect size; *CI*, confidence interval; *RR*, relative risk; *OR*, odds ratio; *HR*, hazard ratio

*Outcome: P, protective effect; W, without effect; N, neurodegenerative effect

Discussion

Our findings based on the literature review showed that adherence to healthy diet could decrease the risk of AD, while people with unhealthy diet are at an increased risk of AD. Healthy diet was defined as a dietary pattern that helps to maintain and improve the general health of the body with the least harmful effects [60]. Based on this definition, healthy diet was tended to be a regular intake of fruits, vegetables, whole grains, and white meat (fish and poultry) [61]. The major healthy dietary patterns were studied in relation to the risk of AD, including MD [19, 24, 28, 29, 32–37, 52, 55], DASH [34], MIND [34, 37], HEI [35, 54], seafood-rich diet [39–41], soy-based food diet [42], capsaicin-rich diet [43], high-protein diet [35, 38], and low-fat diet [24].

Mediterranean diet in relation to risk of AD

The expression "Mediterranean diet" refers to the dietary habits of the Mediterranean countries that are characterized by high intake of fruits, vegetables, whole grains, legume, nuts, olive, and olive oil, as well as moderate consumption of fish and fat-free and low-fat dairy products and a decrease of red and processed meat. In this pattern, it is acceptable to have a moderate intake of alcohol and wine, but it is forbidden in some religions [17]. MD has been associated with decrease of cardiovascular disease (CVD), diabetes, metabolic syndrome, cancer, and cognitive disorders [62–65]. An investigation of the reviewed articles showed that greater adherence to MD was associated with a decrease of AD [19, 24, 28, 29, 32–37, 52, 55]. Results of the ATTICA study after 10-year follow-up showed that greater adherence to MD could decrease the level of interleukin 6, human tumor necrosis factor-α, C-reactive protein, and oxy low-density lipoprotein (ox LDL) [66]. High intake of antioxidant foods in this dietary pattern plays a key role in the induction of oxidative stress and inflammatory disorders [28, 30]. High levels of reactive oxygen species and reactive nitrogen were seen in the brain of patients with AD. Inflammation and oxidative stress play a role in AD pathogenesis [32, 67] (Fig. 2). Therefore, MD is known as a neuroprotective dietary pattern due to high intake of fruits, vegetables, polyunsaturated fat, and low alcohol and wine intake that can lead to decrease of inflammation and oxidative stress.

DASH diet in relation to risk of AD

DASH diet is effective in the treatment of hypertension and is recommended for CVDs [68]. This diet emphasizes low consumption of saturated fat, total fat, and red and processed meat and promotion of intake of fruits, vegetables, low-fat dairy, and whole grains [68, 69]. In other words, this approach can increase intake of potassium, calcium, and magnesium and

Table 3 The studies were examined healthy dietary pattern and AD

Study/year	Study population/study design/country	Age (year)	Sample size	Dietary pattern assessment tools	Kind of diet
Morris, 2003[48]	Chicago Health and Aging Project/prospective study/Chicago	Age ≥ 65	815 subjects (101 men and 713 women)	FFQ	Seafood-rich diet
Scarmeas, 2006 [28]	1992 (WHICAP 1992) and 1999 (WHICAP 1999)/prospective study/New York	Mean age 77.2	2226 subjects (720 men and 1506 women)	FFQ	MD
Scarmeas, 2006 [29]	1992 (WHICAP 1992) and 1999 (WHICAP 1999)/case-control/New York	Mean age 76.3	1984 subjects (630 men and 1354 women)	FFQ	MD
Devore, 2009 [41]	Ommoord cohort study/prospective study/Rotterdam, Netherlands	Age ≥ 55	5395 subjects (2211 men and 3184 women)	FFQ	Seafood-rich diet
Scarmeas, 2009 [30]	1992 (WHICAP 1992) and 1999 (WHICAP 1999)/prospective study/New York	Mean age 77.2	1880 subjects (587 men and 1293 women)	FFQ	MD
Gu, 2010 [31]	WHICAP II/prospective study/Columbia	Age ≥ 65	1219 subjects (407 men and 812 women)	FFQ	MD
Gu, 2010[53]	1992 (WHICAP 1992) and 1999 (WHICAP 1999)/prospective study/Northern Manhattan, New York	Age ≥ 65	2148 subjects (691 men and 1457 women)	FFQ	MD
Eskelinen, 2011 [38]	The Cardiovascular Risk Factors, Aging and Dementia (CAIDE) study/prospective study/Sweden	65–79	525 subjects (201 men and 324 women)	Dietary habits questionnaire	HEI
Gardener, 2012 [55]	The Australian Imaging, Biomarkers and Lifestyle Study of Ageing (AIBL)/prospective study/Australia	Age ≥ 60	970 subjects (402 men and 568 women)	FFQ	MD
Ozawa, 2013 [42]	Hisayama Study/prospective study/Japan	60–79	1006 subjects (433 men and 573 women)	FFQ	Soy-based food and diary
Mosconi, 2014 [44]	Cross-sectional/Manhattan	25–72	52 subjects (16 men and 36 women)	FFQ	MD
Olsson, 2015 [35]	The Uppsala longitudinal study of adult men (ULSAM)/prospective study/Sweden	60–70	1602 subjects (1602 men)	Food record	HEI MD LCHP
Morris, 2015 [57]	Rush Memory and Aging Project/prospective study/Chicago	58–98	923 subjects (232 men and 691 women)	FFQ	MD DASH MIND
Morris, 2016 [46]	Rush Memory and Aging Project/cross-sectional/Chicago	Mean age 89.9 years	286 subjects (93 men and 193 women)		Seafood-rich diet DHA + EPA food sources α-Linolenic 18:3 n-3
Liu, 2016 [45]	Cross-sectional/China	Age ≥ 40	388 subjects (156 men and 232 women)	FFQ	Capsaicin-rich diet
Vassilaki, 2018 [36]	Mayo Clinic Study of Aging (MCSA)/prospective study/USA	70–89	278 subjects (155 men and 123 women)	FFQ	MD
Calil, 2018 [37]	The Paulista Institute of Geriatrics and Gerontology Jos e Ermírio de Moraes (IPGG)/cross-sectional/Sao Paulo	Age ≥ 60	96 subjects (27 men and 69 women)	FFQ	MD MIND
Fernando, 2018 [38]	The Australian Imaging, Biomarkers and Lifestyle Study of Ageing (AIBL)/cross-sectional/Australia	age ≥ 60	541 subjects (222 men and 319 women)	FFQ	High protein High fiber
Hill, 2018 [24]	The Women's Health Aging Project/prospective study/Australia	45–55	115 subjects (115 men)	FFQ	MD Low fat

Table 3 (continued)

Study/year	Comparison	ES	CI	Outcome*
Morris, 2003[48]	Q1	RR:1		P
	Q2	RR:0.6	0.3–1.3	
	Q3	RR:0.4	0.2–0.9	
	Q4	RR:0.4	0.2–0.9	
Scarmeas, 2006 [28]	Continuous	HR, 0.91	0.83–0.98	P
Scarmeas, 2006 [29]	T1	1		
	T2	OR, 0.48	0.29–0.79	P
	T3	OR, 0.31	0.16–0.58	
Devore, 2009 [41]	T1	1		
	T2	HR, 1.07	0.83–1.37	W
	T3	HR:0.99	0.76–1.29	
Scarmeas, 2009 [30]	Continuous	HR, 0.87	0.77–0.99	P
Gu, 2010 [31]	Continuous	HR, 0.87	0.78–0.97	P
Gu, 2010[53]	T1	1		
	T2	HR, 0.81	0.59–1.12	
	T3	HR, 0.62	0.43–0.89	
Eskelinen, 2011 [38]	High adherence vs. low	OR, 0.08	0.01–0.89	P
Gardener, 2012 [55]	Continuous	OR, 0.806	0.71–0.92	P
Ozawa, 2013 [42]	Q1	1		
	Q2	HR, 0.64	0.39–1.04	W
	Q3	HR:0.74	0.46–1.18	
	Q4	HR, 0.65	0.4–1.06	
Mosconi, 2014 [44]				
Olsson, 2015 [35]	Continuous	HR, 0.95	0.75–1.22	W
	Continuous	HR, 1	0.75–1.33	W
	Continuous	HR, 1.16	0.95–1.43	W
Morris, 2015 [57]	T1	1		P
	T2	HR, 0.64	0.42–0.97	
	T3	HR, 0.48	0.29–0.79	
	T1	1		P
	T2	HR, 0.98	0.64–1.46	
	T3	HR, 0.6	0.37–0.96	
	T1	1		P
	T2	HR, 0.81	0.53–1.21	
	T3	HR, 0.49	0.29–0.85	
Morris, 2016 [46]	Continuous	Beta, 0.2	− 0.04–0.43	P

Table 3 (continued)

	Continuous	Beta, 0.81	− 0.63–2.25	
	Continuous	Beta:− 0.37	− 0.93–0.18	
Liu, 2016 [45]	–	–	–	P
Vassilaki, 2018 [36]	Continuous	OR, 0.76	0.58–0.99	P
Calil, 2018 [37]	–	–	–	–
	–	–	–	–
Fernando, 2018 [38]	T1 vs. T3	OR, 12.594	1.7–93.01	P
	T1 vs. T3	OR:2.106	0.51–8.64	W
Hill, 2018 [24]	Liner	Coefficient, 0.06	− 0.02–0.14	W
	Liner	Coefficient, 0.023	− 0.05–0.1	W

FFQ, food frequency questionnaire; *MD*, Mediterranean diet; *DASH*, Dietary Approaches to Stop Hypertension; *MIND*, Mediterranean-DASH Intervention for Neurodegenerative Delay; *HEI*, Healthy Eating Index; *LCHP*, low carbohydrate high protein; *ES*, effect size; *CI*, confidence interval; *RR*, relative risk; *OR*, odds ratio; *HR*, hazard ratio

*Outcome: P, protective effect; W, without effect

fiber, and simultaneously decrease intake of sodium, refined grains, and saturated fat [69]. Similarly to MD, it seems that DASH diet with effects on inflammatory pathways and oxidative stress can prevent AD (Fig. 2) [70].

High intake of antioxidants, including vitamin C, vitamin E, beta carotene, and flavonoids from fruits, vegetables, and vegetable oils, can enhance antioxidant capacity and reduce inflammation [71]. On the other hand, results from a Québec Longitudinal Study on nutrition and successful aging (NuAge Study) showed that high intake of sodium was associated with the risk of cognitive maintenance in elders [72]. Inconsistent with the results, the study “Health, Aging and Body Composition (Health ABC)” (2018) did not confirm the finding that decrease of sodium and increase of potassium intake were associated with the risk of cognitive disorders [73]. Although no studies have examined the effect of dietary sodium and potassium on AD in elderly population, DASH diet is an appropriate approach to prevent AD due to high intake of dietary antioxidants and anti-inflammatories.

MIND in relation to risk of AD

This dietary pattern has been developed by Morris in Chicago for the first time emphasizing the intake of natural and plant-based foods and limitation of animal food source and saturated fat intake [74]. This healthy diet has 15 components, including 10 brain healthy food groups (green leafy vegetables, other vegetables, nuts, berries, beans, whole grains, white meat (fish and poultry), olive oil instead of other oil, and wine intake limitation) as well as decrease of 5 unhealthy food groups, including red meats, butter and stick margarine, cheese, pastries and sweets, and fried/fast food [34]. The possible mechanisms for the effect of this diet on AD were associated with the high intake of n-3 fatty acids from fish consumption, leading to decrease of amyloid-β formation, oxidative stress, and inflammation [75] (Fig. 2). In addition, these complications related to AD were improved with a high intake of flavonoids, beta carotene, folate, and carotenoids from green leafy vegetables and other vegetables [34].

Other healthy dietary patterns in relation to risk of AD

Other healthy dietary patterns were examined in this review, including seafood, soy-based foods, capsaicin-rich, and high-protein diet that can reduce the risk of AD [38, 39, 42, 43]. Seafood is a source of n-3 fatty acids that can decrease inflammation, oxidative stress, and formation of amyloid-β [75–77]. Similarly, capsaicin, as an active ingredient in chili pepper, has effective beneficial effects on AD, which was mediated by a decrease of inflammation and oxidative stress, and neuroprotective effects [78, 79] (Fig. 2). Liu et al. showed that capsaicin-rich diet leads to decrease of amyloid-β formation and can delay AD [43]. Therefore, it seems that adherence to

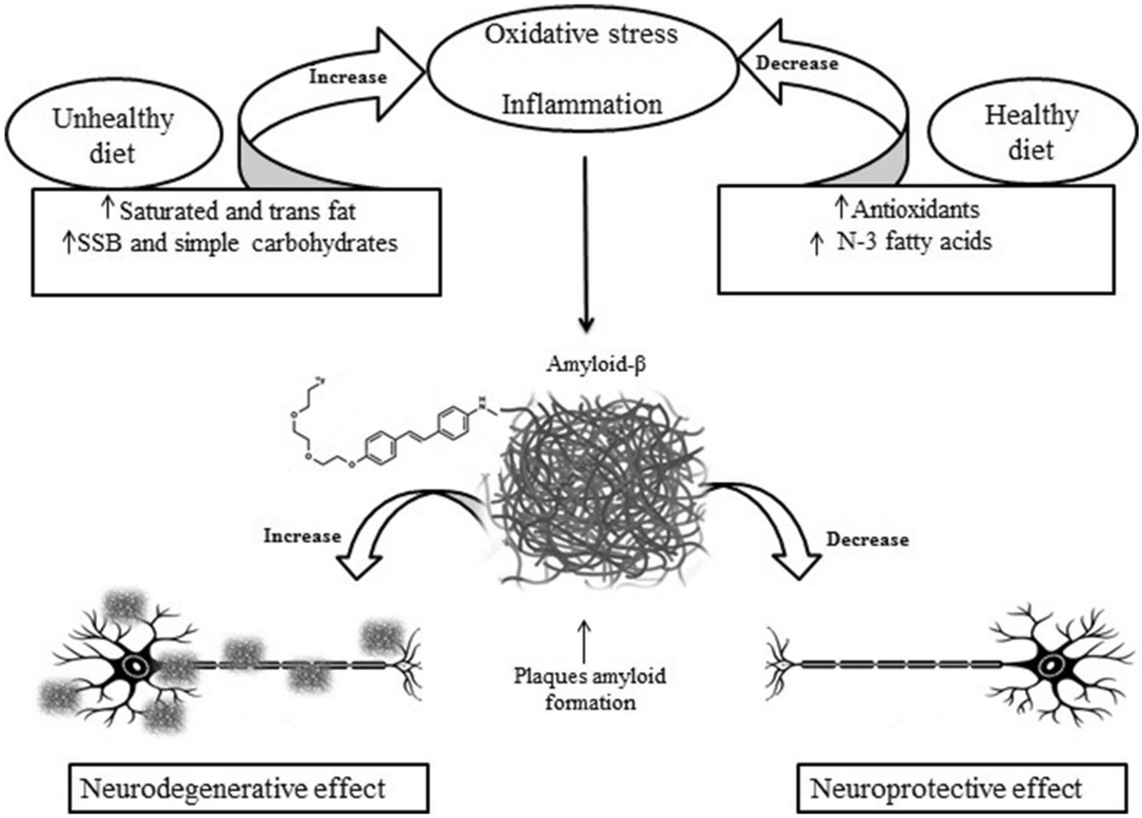

Fig. 2 Healthy and unhealthy diet in relation to AD

this healthy diet to decrease AD has beneficial effects; however, further studies are required in this field.

Unhealthy diet, Western diet in relation to risk of AD

In the literature review, we observed that 8 studies examined unhealthy dietary patterns and the risk of AD [15, 16, 22–27]. These unhealthy dietary patterns included dietary high-fat diet [22, 23], high-glycemic diet [15], SSB [25], high-cholesterol diet [16], DIF [26], and Western diet [27]. In the literature, a high intake of total fat, saturated fat, cholesterol, sodium, processed foods, refined grains, and simple carbohydrates and high sugar intake were considered Western diet [68, 80]. Manzel et al. [81] in their review study stated that Western diet led to increase in inflammatory diseases consisting of obesity, metabolic syndrome, and cardiovascular disease. In another review study, we observed that Western diet can degenerate the blood-brain barrier and a subsequent risk of dementia is mediated by damaging the hippocampus in the brain [82]. To the best of our knowledge, no study has assessed Western diet in relation to the risk of AD and its biological mechanism is still unknown. However, some studies have suggested that a higher intake of saturated and trans fat can increase inflammation and oxidative stress. As stated in healthy dietary patterns, inflammation and oxidative stress play a key role in etiology of AD [22, 23]. Gustaw-Rothenberg et al. [27] evaluated a high intake of processed meat, butter, high-fat dairy products, eggs, and refined sugar and the risk of AD. These foods are the components of Western diet that had harmful effects on AD. Therefore, based on these results, consumption of unsaturated fat, especially n-3 fatty acids instead of saturated and trans fat, to promote neuroprotective effects is recommended (Fig. 2).

Furthermore, despite the role of dietary cholesterol in inflammatory disorders [83], Ylilauri et al. [16] did not observe a significant association between dietary cholesterol and the risk of AD. In his opinion, dietary cholesterol has no effect on the human brain and subsequently cognitive diseases. The other components of Western diet are SSB and increase of glycemic load, which were examined by Pase [25], Luchsinger [15], and Hill [24]. In animal studies, a high intake of sugar enhances the accumulation of amyloid-β and damage of the hippocampus, leading to an increased risk of AD [18, 84]. In the study by Pase et al. [25], a higher SSB intake could cause brain atrophy and increased preclinical AD. While Luchsinger et al. [15] did not find a significant association between high glycemic load diet and the risk of AD, they reported that the lack of an association may be due to the measurement error of the glycemic index and the under-reporting of carbohydrate intake by the studied population. Hill [24] introduced these foods as "junk foods," which were significantly associated with amyloid-β deposition.

Conclusion

In conclusion, our findings based on the literature review showed that adherence to a healthy dietary pattern has neuroprotective effects on AD prevention. These major healthy dietary patterns include MD, DASH, MIND, HEI, dietary seafood, soy-based foods, capsaicin-rich, high-protein, and low-fat diet that can decrease oxidative stress and inflammation and accumulation of amyloid-β, while, among these reviewed studies, we observed that unhealthy dietary patterns, particularly in a high intake of fat and SSB, can promote oxidative stress and inflammation and accumulation of amyloid-β and subsequent development of AD. However, more studies are required in other components of dietary patterns in relation to AD. Overall, according to the limited number of studies on AD and dietary patterns, the definition of a healthy and unhealthy diet is too little specified. Therefore, further well-designed and controlled studies seem to be needed to identify a healthy diet in this population.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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