REVIEW ARTICLE

Evidence for Improved Cognitive Health with Diet: A Narrative Review

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ABSTRACT

Background • Despite growing interest in nutrition as a behavioral intervention to improve cognitive health in clinical populations, many providers find it challenging to provide specific nutritional recommendations. We aimed to review and synthesize current empirical research on this topic and provide considerations for healthcare providers working with adults who wish to optimize their cognition via dietary improvements.

Methods • We performed a narrative review of research published between January 2009 and May 2021 on 5 popular dietary interventions: the Mediterranean diet, Dietary Approaches to Stop Hypertension (DASH), the Mediterranean-DASH Intervention Diet for Neurodegenerative Delay (MIND), the ketogenic diet and intermittent fasting.

Results and Conclusions • Of the 5 dietary interventions, the Mediterranean diet has been the most extensively investigated, and there is evidence supporting its cognitive benefits. However, operationalization of the Mediterranean diet varies across studies, rendering the results inconclusive. The DASH diet and the MIND diet have stronger operationalization and showed evidence of cognitive benefits. More longitudinal studies and/or randomized clinical trials should be conducted on these 2 relatively new interventions. Finally, there is limited research with human participants regarding the ketogenic diet and intermittent fasting, which are found to be cognitively protective within stringent parameters. Definitions for these 5 dietary patterns and practice tips and recommendations are provided. (*Altern Ther Health Med.* 2023;29(7):12-17).

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INTRODUCTION

Dietary interventions are an area of increasing interest given the potential role of nutrition in improving physical[1,2] and mental health.[3,4] We are particularly interested in nutrition as a modifiable factor for improving cognitive health, which is a common concern in individuals with neurological and/or psychiatric illnesses. Despite the consensus that nutrition has the potential to have a positive impact on cognition, many providers find it challenging to provide specific nutritional recommendations. This is due, in part, to poor understanding of the mechanisms by which nutritional interventions may prevent cognitive decline. There are 2 prevailing hypotheses regarding the relationship between diet and cognition: (1) Nutritional interventions improve cognition through cardiovascular health because cardiovascular diseases (eg, hypertension, hyperlipidemia and diabetes) and midlife obesity are well-established risk factors for vascular dementia and Alzheimer's disease in older adults[5]; (2) There are several factors that may have an impact on daily cognitive functioning by way of mediators such as mood, stress, energy level and fatigue. For example, nutrition can have almost an immediate impact (ie, within minutes) on changing blood glucose levels. Specific nutrients can also lead to the synthesis of neurotransmitters, which can potentially have an impact on cognitive performance.[6]

These hypothesized mechanisms are difficult to confirm as they are multifactorial or have an impact on multiple targets, particularly in human participants. Research has focused on 3 approaches that have inherent methodological limitations: a single nutrient approach, observational studies and interventional studies. Early research focusing on the protective effects of single food items and nutrients, including blueberry juice;[7] vitamins B9, B12 and E; polyunsaturated fatty acids (eg, omega-3 and DHA) and non-nutrient phytochemicals,[8] have had minimal effects. Unfortunately, the body of literature on a single nutrient approach with human participants is limited by synergistic effects with other dietary ingredients that are difficult to evaluate and/or control. As a result, more recent research has shifted away from evaluating single nutrients to more general dietary patterns that better reflect the complexity of diets and daily eating behavior.[9]

Observational and interventional studies are conducted to assess the effects of dietary patterns both as a static protective factor and a potential intervention to delay cognitive decline. This line of research is also complicated by multiple procedural problems. For instance, observational studies often face the inherent low reliability of self-reported data and high variability of confounding factors such as socioeconomic status and general lifestyle, rendering results difficult to interpret. Interventional studies face the challenge of consistently operationalizing and implementing dietary interventions, which are unlikely to reflect a true diet. These methodological challenges have limited the quality of evidence supporting nutritional and dietary interventions, and as a result, reduce providers' confidence in providing specific nutritional recommendations.

In our review, we aimed to summarize the relevant literature on the cognitive impact of commonly used nutritional interventions, as well as highlight the challenges we face in prescribing nutritional interventions based on the literature to date. This review focused on 5 dietary interventions that providers are likely to encounter during their interactions with patients: the Mediterranean diet, the Dietary Approaches to Stop Hypertension (DASH) diet, theMediterranean-DASH intervention for neurodegenerative delay (MIND) diet, the ketogenic diet and intermittent fasting. We also aimed to provide a list of practical recommendations for healthcare providers working with adults who wish to optimize their cognition via dietary improvements.

METHODS

The literature review was performed between July and August 2019 and updated in July 2021 through HOLLIS and PubMed. Search terms included keto diet, ketogenic diet, ketosis, intermittent fasting, time-restricted feeding, alternate-day fasting, Mediterranean diet, the MIND diet, MeDi, DASH diet, cognition, cognitive decline, neurodegenerative disease, neurodegeneration, and cognitive function. An additional search was performed by reviewing the reference lists of the articles collected. Articles were included for review if they met the following criteria: (1) the manuscript was published in peer-reviewed journals in or after 2009, with the exception of articles on the ketogenic diet, which were accepted from 2004 to the present due to the smaller number of publications; (2) cognitive functioning was measured by objective tests including brief cognitive screens and/or domain-specific cognitive tests, or by behavioral testing in animal models. Studies were excluded if cognition was measured by self-report only. Different levels of evidence were reviewed and presented, including randomized controlled trials (RCTs) in which dietary interventions were implemented in an experimental paradigm, longitudinal evidence in which observational data were collected at multiple time points and cross-sectional evidence in which observational data were collected at a single time point.

RESULTS

Mediterranean Diet

The cognitive effects of the Mediterranean diet have been examined quite extensively (see Table 1 for the key components of the Mediterranean diet). Cross-sectional studies generally show favorable results for the Mediterranean diet in older adults (>age 50 years) across different countries/regions. For example, better adherence to the Mediterranean diet was found to be predictive of better global cognition,[10,11] better domain-specific cognition[12,13] and a lower rate of dementia onset.[12] However, 1 cross-sectional study that included a broad range of age groups (age 20 to 70 years) found that higher Mediterranean diet scores calculated via a self-report lifestyle questionnaire were not associated with better cognitive scores.[14]

Evidence from longitudinal studies and RCTs is still favorable but less conclusive. In some longitudinal studies, better adherence to the traditional Mediterranean diet was

Table 1. Mediterranean Diet Guidelines

General Guidelines		Specific Guidelines
Moderate-to-high Consumption	Plant-based foods	Whole grains: daily
	Minimally processed foods	Vegetables: daily
	Total fat	Fruits: daily
		Cheese and yogurt: daily
Low-to-moderate Consumption	Red meat	Fish and poultry: twice per week
	Fish	Red meat: a few times per month
	Poultry	Eggs: up to 7 per week
	Cheese and yogurt	Total fat: 25% to 35% of calories per day
		Saturated fat: <7% to 8% of calories per day
Limited Consumption	Refined foods with added sugar	Wine: 1 to 2 glasses per day for men; 1 glass per day for women, if at all

Note: Adapted from Cunningham[62]

found to predict slower global cognitive decline over approximately 5 years.[15,16] In another study,[17] a Mediterranean diet score was not predictive of the onset rate of MCI or Alzheimer's disease over 10-year follow-up. Samieri and colleagues[18] found that, although a higher Mediterranean diet score was predictive of better cognitive status, it was not predictive of a slower rate of cognitive decline. A large-scale RCT conducted over 5 years found that the Mediterranean diet intervention was associated with better outcomes on global cognition measures but not on single neuropsychological tests or rate of MCI onset.[19,20]

In fact, the studies on the Mediterranean diet and brain health are so abundant that several reviews exist that summarize the current evidence. A systematic review of RCTs[21] found a weak to nonsignificant association between the Mediterranean diet and improved cognitive performance. This weak link was partly attributed to inconsistent operationalization of the Mediterranean diet and methodological issues across studies reviewed, which compromises the comparability and generalizability of the RCT findings. Other reviews that included both observational and RCTs[22-24] reached more favorable conclusions, although all reviews urged better standardization in future studies and 1 review[24] pointed out a possible regional effect favoring individuals who live in the Mediterranean regions.

Studies also attempted to discover the mechanism via which the Mediterranean diet can be neuroprotective. A 2019 review[25] found that the Mediterranean diet may influence cognitive aging via several inflammatory pathways in animal models. Although the same pathways are not fully established in human subjects,[25] there is ample data linking the Mediterranean diet to a decrease in inflammatory markers.[26,27] The other related mechanism is cognitive protection via reduced markers of cardiovascular risk (eg, systolic blood pressure and cholesterol-to-high-density lipoprotein cholesterol ratio), which has been investigated extensively by the longitudinal Prevención con Dieta Mediterránea [PREDIMED] study.[28,29]

In summary, evidence appears to support the cognitive benefits of the Mediterranean diet. However, continued studies with better methodological standardization (eg, well-defined criteria for the diet) and better characterization of confounding factors (eg, Mediterranean vs non-Mediterranean diet) are called for to strengthen the evidence and establish a causal relationship.

Dietary Approaches to Stop Hypertension (DASH)

DASH was developed in the context of a well-founded link between high blood pressure and the risk for stroke, dementia and neurocognitive dysfunction[30] (see Table 2 for the key components of the DASH diet). Using data from multiple longitudinal cohorts, higher DASH diet scores predicted better global cognitive function.[31,32] One study found slower cognitive decline or reduced rate of dementia onset,[15] but others did not replicate the finding.[17,31] An interventional study[30] found that a 4-month DASH diet intervention improved processing speed and sustained attention in patients with existing hypertension and obesity compared with normal diet controls. Additional cognitive improvements were found when DASH was combined with exercise and caloric restriction. Available evidence supports the potentially positive impact of the DASH diet, although these findings are preliminary. Mechanistically, cognitive benefit is directly related to a reduced risk for hypertension and resulting cardiovascular risks for cognitive impairment, such as stroke and small vessel disease.

Table 2. Dietary Approaches to Stop Hypertension (DASH) Diet Guidelines

General Guidelines		Specific Guidelines (2000-calorie diet)
High Consumption	Produce	Whole grains: 6 to 8 servings per day
	Low-fat dairy	Vegetables: 4 to 5 servings per day
	Whole grains	Fruits: 4 to 5 servings per day
	Fish and poultry	Low-fat or fat-free dairy: 2 to 3 servings per day
	Nuts	Poultry and fish: fewer than 6 one-ounce servings per day
		Nuts and seeds: 4 to 5 servings per week
Low Consumption	Red meats	Monounsaturated fats: 2 to 3 servings per day
	Processed sugars and sodium	Sodium: 1500 to 2300 mg per day
	Total fat	Sweets and added sugars: 5 or fewer servings per week

Note: Adapted from the Mayo Clinic.[63]

Mediterranean-DASH Intervention for Neurodegenerative Delay

Similar to DASH, the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet is a relatively new dietary intervention that was developed to emphasize the presumed neuroprotective dietary components from the Mediterranean and DASH diets[33] (see Table 3 for the key components of the MIND diet). Morris and colleagues[33] found that older adults with higher MIND diet scores exhibited a slower rate of global cognitive decline and have a reduced rate of developing Alzheimer's disease. Furthermore, they found that although individuals with higher MIND diet scores presented with a more favorable risk profile for cognitive health (eg, higher education, greater participation in cognitive and physical activities and lower prevalence of cardiovascular conditions), the relationship between the MIND diet and cognitive function remained when these factors were controlled.

Replication of these longitudinal findings was equivocal. Hosking and colleagues[34] found that a higher MIND score was predictive of reduced odds of the 12-year incidence of MCI/dementia in older adults, but not Mediterranean diet

Table 3. Mediterranean-DASH Intervention for Neurodegenerative Delay Diet Guidelines (MIND)

Limited Consumption	High Consumption
Butter and margarine: <1 Tbs per day	Leafy greens: ≥6 servings per week
Cheese: <1 serving per week	Other vegetables: ≥7 servings per week
Red meat: <4 servings per week	Berries: ≥2 servings per week
Fried food: <1 serving per week	Nuts: ≥5 servings per week
Pastries and sweets: <5 servings per week	Beans: 4≥ servings per week
	Whole grains: ≥3 servings per day
	Fish: ≥1 times per week
	Poultry: ≥2 times per week
	Wine: max 1 glass per day
	Olive oil: main source of dietary fat
	Leafy greens: ≥6 servings per week

Note: Adapted from Morris, et al.[33]

Table 4. Ketogenic Diet Guidelines

General Guidelines		Specific Guidelines
High Consumption	Low Consumption	Fat: 55% to 60% of daily calories
Meats and fish	Fruit	
Eggs	Sugar	Protein: 30% to 35% of daily
Dairy	Grains and starches	calories
Nuts and seeds	Beans and legumes	
Plant-based oils and avocados	Root vegetables	Carbohydrates: 5% to 0% of
Low-carb vegetables	Alcohol	daily calories

Note: Adapted from Masood, et al.[65]

scores. Another group using data from the Nurses' Health Study found that greater long-term adherence to the MIND diet was not predictive of cognitive decline over 6 years in older American women.[35] Cross-sectional evidence supported lower subjective memory complaints related to better adherence to MIND.[36] At this stage, evidence for MIND appears inconclusive. Longitudinal RCTs are needed to determine whether and how this diet improves cognitive health. The mechanism of cognitive benefit for MIND is believed to be the combined mechanisms of cognitive protection from the Mediterranean and DASH diets described above.

Ketogenetic Diet

The ketogenic diet and its variations, such as the modified Atkins® diet, are essentially high-fat, low-carbohydrate diets that are expected to induce ketosis, a process in which the body is forced to use ketone bodies yielded from fatty acids as the primary source of energy, as opposed to carbohydrates[37] (see Table 4 for the key components of the ketogenetic diet). The cognitive benefits of the ketogenic diet were initially studied in patients with drug-resistant epilepsy, a population in which patients often report subjective experience of improved alertness and global cognition after starting the ketogenic diet, although only improvement in alertness was confirmed by objective tests.[38]

More recently, studies have attempted to explore the neuroprotective effects of ketosis beyond epilepsy treatment. In rodent models, ketosis has been linked with improvements in cognitive function,[39,40] and several mechanisms were proposed for this, including reduced brain amyloid beta (Aβ) levels and protection from Aβ toxicity,[41,42] altered neurotransmission,[39] improved mitochondrial function,[43] anti-inflammatory action[44] and separate effects of carbohydrate restriction.[45] In human participants, studies were largely conducted in clinical populations with MCI or dementia. In these populations, there appears to be compelling evidence showing a link between ketosis and better cognitive outcomes, but only in individuals who are ApoE4-negative. However, it should be noted that these studies achieved ketosis through oral administration of a ketogenic compound (eg, medium-chain triglycerides)[46-49] rather than the traditional low-carbohydrate, calorie-restricted ketogenic diet. A few reviews regarding the ketogenic diet and dementia have been published[37,50,51] that agree upon the promising role of ketosis (not necessarily the ketogenic diet) in modifying cognitive outcomes related to dementia but also cautioning the risk for adverse events such as malnutrition. Studies with other clinical or non-clinical populations are rather limited. Cognitive benefits linked to the ketogenic diet were found in a cohort of older adults with HIV-associated neurocognitive disorder (HAND),[52] but not in a cohort of healthy adults.[53]

In summary, current evidence supports a link between ketosis and better cognitive outcomes in certain clinical populations (ie, patients with drug-resistant epilepsy, and ApoE4-negative patients with MCI or early-stage dementia, HAND) when ketosis is induced by the oral administration of ketogenic compounds.

Intermittent Fasting

Similar to the ketogenic diet, the effect of intermittent fasting on cognitive health has been more extensively studied in rodent models (see Table 5 for the key components of intermittent fasting). Often operationalized as alternate-day fasting (ADF) or daily time-restricted feeding (TRF), intermittent fasting has been associated with reduced neurodegenerative disease in rats,[54] increased neurogenesis and expression of brain-derived neurotrophic factor in healthy rats and a rat model of Huntington's disease[55,56] and reduced cognitive decline in a mouse model of Alzheimer's disease.[57] However, human studies were rather limited and the operationalization of intermittent fasting varied greatly across studies. Cognitive outcomes was directly assessed in only 1 study,[58] in which modified fasting (ie, fasting on Monday and Thursday) for a total of 4 years was related to a lower rate of disease conversion in adults with MCI. Other

Table 5. Intermittent Fasting Guidelines

	Alternate-Day Fasting	**Modified Fasting**	**Time-Restricted Fasting**
Schedule	Alternating non-fasting days and fasting days	5 non-fasting days and 2 fasting days	8 non-fasting hours and 16 fasting hours
Fasting Days/Hours	No food or beverages with calories	Small amounts of foods (eg, 500 calories)	No food or beverages with calories
	Allow calorie-free drinks (water, black coffee and tea)		Allow calorie-free drinks (water, black coffee and tea)
Non- Fasting Days/Hours	No limit on food intake but Following healthful eating guidelines recommended	No limit on food intake but following healthful eating guidelines recommended	No limits on food intake but recommended to follow healthful eating guidelines

Note: Adapted from Patterson, et al.[66]

evidence appears to support the cardiovascular benefits of ADF in individuals with obesity,[59,60] which may reduce vascular-related cognitive decline. The hypothesized mechanism for the impact of intermittent fasting on cognition can be extended to the neuroplastic effects of metabolic switching via dietary changes or exercise that has been thoroughly reviewed by Mattson and colleagues.[60] In brief, intermittent fasting triggers a biochemical cascade ending with the activation of mesial temporal lobe neurons important for cognition and which stimulate synaptogenesis and neurogenesis in brain regions.[60]

CONCLUSION

Despite evidence that nutrition/diet has an impact on cognition, there is an ongoing need for well-designed research studies on specific nutritional interventions. The present body of research consists of variable methodologies and mixed findings. In this context, the Mediterranean diet appears to be the dietary pattern with the most extensive research support, although longitudinal and RCTs are not unanimously positive. The MIND and DASH diets appear to be promising options for continued research because they were developed based on the positive evidence for the Mediterranean diet components and are better operationalized. However, given the relatively recent nature of these 2 interventions, more studies are needed before clinical implementation to improve cognition can be recommended. The ketogenic diet and intermittent fasting, despite their increasing popularity in the general population, have only been researched in specific populations. Operationalizations of these 2 diets are also quite loose in practice and even in research.

We generated the following recommendations for practitioners, especially practitioners working with clinical populations that exhibit cognitive deficits who are interested in providing more evidence-based guidance related to nutrition and cognition; however, it is important to note that a broad range of lifestyle factors (eg, sleep, social support, exercise) are likely necessary to have the greatest impact on cognition.

PRACTICE TIPS AND RECOMMENDATIONS FOR PROVIDERS

- Refer patients with nutrition questions to a registered dietitian (RD) for individualized, evidence-based nutrition counseling. Nutrition counseling with an RD is often covered by insurance (patients should check with their insurance provider, as some insurance may require a primary care physician [PCP] referral). Local hospitals, college/university nutrition departments and private medical practices often employ RDs and may accept insurance. The Academy of Nutrition and Dietetics website also provides an option to search for local dietitians (https://www.eatright.org/find-an-expert).
- Encourage patients to shift their focus from a single nutrient diet to more general healthful nutritional patterns that better reflect the complexity of one's diet and eating behavior.
- Encourage patients to focus on the *quality* of food, as opposed to the *quantity* of food they eat (eg, limit highly processed foods and incorporate more whole foods).
- Encourage sustainable eating behavior modifications, or setting realistic goals (eg, implement 1 nutrition change per week, such as consume a non-starchy vegetable [carrots, green beans or cauliflower] with dinner every night).
- Consult reliable sources for more practical guidelines, such as the Academy of Nutrition and Dietetics (https://www.eatright.org/), United States Department of Agriculture Choose MyPlate (https://www.choosemyplate.gov/) and a publication by the American Congress of Rehabilitation Medicine called "Food for Thought: Basic Nutrition Recommendations for the Mature Brain."[61]

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REFERENCES

1. Marsh K, Zeuschner C, Saunders A. Health implications of a vegetarian diet: A review. *Am J Lifestyle Med*. 2012;6(3):250-267. doi:10.1177/1559827611425762
2. Serra-Majem L, Roman B, Estruch R. Scientific evidence of interventions using the Mediterranean diet: a systematic review. *Nutr Rev*. 2006;64(suppl 1):S27-S47. doi:10.1111/j.1753-4887.2006.tb00232.x
3. Harbottle L, Schonfelder N. Nutrition and depression: A review of the evidence. *J Ment Health*. 2008;17(6):576-587. doi:10.1080/09638230701677746
4. O'Neil A, Quirk SE, Housden S, et al. Relationship between diet and mental health in children and adolescents: A systematic review. *Am J Public Health*. 2014;104(10):e31-e42. doi:10.2105/AJPH.2014.302110
5. Allès B, Samieri C, Féart C, Jutand M-A, Laurin D, Barberger-Gateau P. Dietary patterns: a novel approach to examine the link between nutrition and cognitive function in older individuals. *Nutr Res Rev*. 2012;25(2):207-222. doi:10.1017/S0954422412000133
6. Stevenson RJ, Prescott J. Human diet and cognition: Human diet and cognition. *Wiley Interdiscip Rev Cogn Sci*. 2014;5(4):463-475. doi:10.1002/wcs.1290
7. Shukitt-Hale B, Thangthaeng N, Miller MG, Poulose SM, Carey AN, Fisher DR. Blueberries improve neuroinflammation and cognition differentially depending on individual cognitive baseline status. *J Gerontol Ser A*. 2019;74(7):977-983. doi:10.1093/gerona/glz048
8. Poulose SM, Miller MG, Scott T, Shukitt-Hale B. Nutritional factors affecting adult neurogenesis and cognitive function. *Adv Nutr Int Rev J*. 2017;8(6):804-811. doi:10.3945/an.117.016261
9. van de Rest O, Berendsen AA, Haveman-Nies A, de Groot LC. Dietary patterns, cognitive decline, and dementia: A systematic review. *Adv Nutr*. 2015;6(2):154-168. doi:10.3945/an.114.007617
10. Hernández-Galiot A, Goñi I. Adherence to the Mediterranean diet pattern, cognitive status and depressive symptoms in an elderly non-institutionalized population. *Nutr Hosp*. 2017;34(2):338. doi:10.20960/nh.360
11. McEvoy CT, Guyer H, Langa KM, Yaffe K. Neuroprotective diets are associated with better cognitive function: The health and retirement study. *J Am Geriatr Soc*. 2017;65(8):1857-1862. doi:10.1111/jgs.14922
12. Anastasiou CA, Yannakoulia M, Kosmidis MH, et al. Mediterranean diet and cognitive health: Initial results from the Hellenic Longitudinal Investigation of Ageing and Diet. *PLoS ONE*. 2017;12(8). doi:10.1371/journal.pone.0182048
13. Shannon OM, Stephan BCM, Granic A, et al. Mediterranean diet adherence and cognitive function in older UK adults: the European Prospective Investigation into Cancer and Nutrition–Norfolk (EPIC-Norfolk) Study. *Am J Clin Nutr*. 2019;110(4):938-948. doi:10.1093/ajcn/nqz114
14. Brouwer-Brolsma EM, Benati A, van de Wiel A, et al. Higher Mediterranean diet scores are not cross-sectionally associated with better cognitive scores in 20- to 70-year-old Dutch adults: The NQplus study. *Nutr Res*. 2018;59:80-89. doi:10.1016/j.nutres.2018.07.013
15. Tangney CC, Li H, Wang Y, et al. Relation of DASH- and Mediterranean-like dietary patterns to cognitive decline in older persons. *Neurology*. 2014;83(16):1410-1416. doi:10.1212/WNL.0000000000000884
16. Trichopoulou A, Kyrozis A, Rossi M, et al. Mediterranean diet and cognitive decline over time in an elderly Mediterranean population. *Eur J Nutr*. 2015;54(8):1311-1321. doi:10.1007/s00394-014-0811-z
17. Haring B, Wu C, Mossavar-Rahmani Y, et al. No association between dietary patterns and risk for cognitive decline in older women with nine-year follow-up: data from the Women's Health Initiative Memory Study. *J Acad Nutr Diet*. 2016;116(6):921-930.e1. doi:10.1016/j.jand.2015.12.017
18. Samieri C, Okereke OI, E. Devore E, Grodstein F. Long-term adherence to the Mediterranean diet is associated with overall cognitive status, but not cognitive decline, in women. *J Nutr*. 2013;143(4):493-499. doi:10.3945/jn.112.169896
19. Martínez-Lapiscina EH, Clavero P, Toledo E, et al. Mediterranean diet improves cognition: the PREDIMED-NAVARRA randomised trial. *J Neurol Neurosurg Psychiatry*. 2013;84(12):1318-1325. doi:10.1136/jnnp-2012-304792
20. Valls-Pedret C, Sala-Vila A, Serra-Mir M, et al. Mediterranean diet and age-related cognitive decline: A randomized clinical trial. *JAMA Intern Med*. 2015;175(7):1094-1103. doi:10.1001/jamainternmed.2015.1668
21. Radd-Vagenas S, Duffy SL, Naismith SL, Brew BJ, Flood VM, Fiatarone Singh MA. Effect of the Mediterranean diet on cognition and brain morphology and function: a systematic review of randomized controlled trials. *Am J Clin Nutr*. 2018;107(3):389-404. doi:10.1093/ajcn/nqx070
22. van den Brink AC, Brouwer-Brolsma EM, Berendsen AAM, van de Rest O. The Mediterranean, dietary approaches to stop hypertension (DASH), and Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diets are associated with less cognitive decline and a lower risk of Alzheimer's disease—A review. *Adv Nutr*. 2019;10(6):1040-1065. 2019. doi:10.1093/advances/nmz054
23. Petersson SD, Philippou E. Mediterranean Diet, cognitive function, and dementia: A systematic review of the evidence. *Adv Nutr*. 2016;7(5):889-904. doi:10.3945/an.116.012138
24. Aridi YS, Walker JL, Wright ORL. The Association between the Mediterranean dietary pattern and cognitive health: A systematic review. *Nutrients*. 2017;9(7):674. doi:10.3390/nu9070674
25. McGrattan AM, McGuinness B, McKinley MC, et al. Diet and inflammation in cognitive ageing and Alzheimer's disease. *Curr Nutr Rep*. 2019;8(2):53-65. doi:10.1007/s13668-019-0271-4
26. Casas R, Sacanella E, Urpí-Sardà M, et al. The effects of the Mediterranean diet on biomarkers of vascular wall inflammation and plaque vulnerability in subjects with high risk for cardiovascular disease. A randomized trial. *PLOS ONE*. 2014;9(6):e100084. doi:10.1371/journal.pone.0100084
27. Bonaccio M, Pounis G, Cerletti C, Donati MB, Iacoviello L, Gaetano G de. Mediterranean diet, dietary polyphenols and low grade inflammation: results from the MOLI-SANI study. *Br J Clin Pharmacol*. 2017;83(1):107-113. doi:10.1111/bcp.12924
28. Estruch R. Effects of a Mediterranean-style diet on cardiovascular risk factors: A randomized trial. *Ann Intern Med*. 2006;145(1):1. doi:10.7326/0003-4819-145-1-200607040-00004
29. Ros E, Martínez-González MA, Estruch R, et al. Mediterranean diet and cardiovascular health: Teachings of the PREDIMED study. *Adv Nutr*. 2014;5(3):330S-336S. doi:10.3945/an.113.005389
30. Smith PJ, Blumenthal JA, Babyak MA, et al. Effects of the dietary approaches to stop hypertension diet, exercise, and caloric restriction on neurocognition in overweight adults with high blood pressure. *Hypertension*. 2010;55(6):1331-1338. doi:10.1161/HYPERTENSIONAHA.109.146795
31. Berendsen AAM, Kang JH, van de Rest O, Feskens EJM, de Groot LCPGM, Grodstein F. The dietary approaches to stop hypertension diet, cognitive function, and cognitive decline in American older women. *J Am Med Dir Assoc*. 2017;18(5):427-432. doi:10.1016/j.jamda.2016.11.026
32. Wengreen H, Munger RG, Cutler A, et al. Prospective study of dietary approaches to stop hypertension – and Mediterranean-style dietary patterns and age-related cognitive change: the Cache County Study on Memory, Health and Aging. *Am J Clin Nutr*. 2013;98(5):1263-1271. doi:10.3945/ajcn.112.051276
33. Morris MC, Tangney CC, Wang Y, et al. MIND diet slows cognitive decline with aging. *Alzheimers Dement*. 2015;11(9):1015-1022. doi:10.1016/j.jalz.2015.04.011
34. Hosking DE, Eramudugolla R, Cherbuin N, Anstey KJ. MIND not Mediterranean diet related to 12-year incidence of cognitive impairment in an Australian longitudinal cohort study. *Alzheimers Dement*. 2019;15(4):581-589. doi:10.1016/j.jalz.2018.12.011
35. Berendsen AM, Kang JH, Feskens EJM, de Groot CPGM, Grodstein F, van de Rest O. Association of long-term adherence to the MIND diet with cognitive function and cognitive decline in American women. *J Nutr Health Aging*. 2018;22(2):222-229. doi:10.1007/s12603-017-0909-0
36. Adjibade M, Assmann KE, Julia C, Galan P, Hercberg S, Kesse-Guyot E. Prospective association between adherence to the MIND diet and subjective memory complaints in the French NutriNet-Santé cohort. *J Neurol*. 2019;266(4):942-952. doi:10.1007/s00415-019-09218-y
37. Rusek M, Pluta R, Ułamek-Kozioł M, Czuczwar SJ. Ketogenic diet in Alzheimer's disease. *Int J Mol Sci*. 2019;20(16):3892. doi:10.3390/ijms20163892
38. van Berkel AA, IJff DM, Verkuyl JM. Cognitive benefits of the ketogenic diet in patients with epilepsy: A systematic overview. *Epilepsy Behav*. 2018;87:69-77. doi:10.1016/j.yebeh.2018.06.004
39. Hernandez AR, Hernandez CM, Campos K, et al. A ketogenic diet improves cognition and has biochemical effects in prefrontal cortex that are dissociable from hippocampus. *Front Aging Neurosci*. 2018;10. doi:10.3389/fnagi.2018.00391
40. Xu K, Sun X, Eroku BO, Tsipis CP, Puchowicz MA, LaManna JC. Diet-induced ketosis improves cognitive performance in aged rats. *Adv Exp Med Biol*. 2010;662:71-75. doi:10.1007/978-1-4419-1241-1_9
41. Van der Auwera I, Wera S, Van Leuven F, Henderson ST. A ketogenic diet reduces amyloid beta 40 and 42 in a mouse model of Alzheimer's disease. *Nutr Metab*. 2005;2(1):28. doi:10.1186/1743-7075-2-28
42. Kashiwaya Y, Bergman C, Lee J-H, et al. A ketone ester diet exhibits anxiolytic and cognition-sparing properties, and lessens amyloid and tau pathologies in a mouse model of Alzheimer's disease. *Neurobiol Aging*. 2013;34(6):1530-1539. doi:10.1016/j.neurobiolaging.2012.11.023
43. Nylen K, Velazquez JLP, Sayed V, Gibson KM, Burnham WM, Snead OC. The effects of a ketogenic diet on ATP concentrations and the number of hippocampal mitochondria in Aldh5a1−/− mice. *Biochim Biophys Acta*. 2009;1790(3):208-212. doi:10.1016/j.bbagen.2008.12.005
44. Yang X, Cheng B. Neuroprotective and anti-inflammatory activities of ketogenic diet on MPTP-induced neurotoxicity. *J Mol Neurosci MN*. 2010;42(2):145-153. doi:10.1007/s12031-010-9336-y
45. Broom GM, Shaw IC, Rucklidge JJ. The ketogenic diet as a potential treatment and prevention strategy for Alzheimer's disease. *Nutr Burbank Los Angel Cty Calif*. 2019;60:118-121. doi:10.1016/j.nut.2018.10.003
46. Reger MA, Henderson ST, Hale C, et al. Effects of β-hydroxybutyrate on cognition in memory-impaired adults. *Neurobiol Aging*. 2004;25(3):311-314. doi:10.1016/S0197-4580(03)00087-3
47. Henderson ST, Vogel JL, Barr LJ, Garvin F, Jones JJ, Costantini LC. Study of the ketogenic agent AC-1202 in mild to moderate Alzheimer's disease: a randomized, double-blind, placebo-controlled, multicenter trial. *Nutr Metab*. 2009;6:31. doi:10.1186/1743-7075-6-31
48. Rebello CJ, Keller JN, Liu AG, Johnson WD, Greenway FL. Pilot feasibility and safety study examining the effect of medium chain triglyceride supplementation in subjects with mild cognitive impairment: A randomized controlled trial. *BBA Clin*. 2015;3:123-125. doi:10.1016/j.bbacli.2015.01.001
49. Taylor MK, Sullivan DK, Mahnken JD, Burns JM, Swerdlow RH. Feasibility and efficacy data from a ketogenic diet intervention in Alzheimer's disease. *Alzheimers Dement Transl Res Clin Interv*. 2017;4:28-36. doi:10.1016/j.trci.2017.11.002
50. Lilamand M, Porte B, Cognat E, Hugon J, Mouton-Liger F, Paquet C. Are ketogenic diets promising for Alzheimer's disease? A translational review. *Alzheimers Res Ther*. 2020;12:42. doi:10.1186/s13195-020-00615-4
51. Davis JJ, Fournakis N, Ellison J. Ketogenic diet for the treatment and prevention of dementia: A review. *J Geriatr Psychiatry Neurol*. 2021;34(1):3-10. doi:10.1177/0891988720901785
52. Morrison SA, Fazeli PL, Gower B, et al. Cognitive effects of a ketogenic diet on neurocognitive impairment in adults aging with HIV: A pilot study. *J Assoc Nurses AIDS Care JANAC*. 2020;31(3):312-324. doi:10.1097/JNC.0000000000000110
53. Iacovides S, Goble D, Paterson B, Meiring RM. Three consecutive weeks of nutritional ketosis has no effect on cognitive function, sleep, and mood compared with a high-carbohydrate, low-fat diet in healthy individuals: a randomized, crossover, controlled trial. *Am J Clin Nutr*. 2019;110(2):349-357. doi:10.1093/ajcn/nqz073
54. Mattson MP. Emerging neuroprotective strategies for Alzheimer's disease: dietary restriction, telomerase activation, and stem cell therapy. *Exp Gerontol*. 2000;35(4):489-502. doi:https://doi.org/10.1016/S0531-5565(00)00115-7
55. Duan W, Guo Z, Jiang H, Ware M, Li X-J, Mattson MP. Dietary restriction normalizes glucose metabolism and BDNF levels, slows disease progression, and increases survival in huntingtin mutant mice. *Proc Natl Acad Sci U S A*. 2003;100(5):2911-2916. doi:10.1073/pnas.0536856100
56. Lee J, Duan W, Long JM, Ingram DK, Mattson MP. Dietary restriction increases the number of newly generated neural cells, and induces BDNF expression, in the dentate gyrus of rats. *J Mol Neurosci*. 2000;15(2):99-108. doi:10.1385/JMN:15:2:99
57. Halagappa VKM, Guo Z, Pearson M, et al. Intermittent fasting and caloric restriction ameliorate age-related behavioral deficits in the triple-transgenic mouse model of Alzheimer's disease. *Neurobiol Dis*. 2007;26(1):212-220. doi:10.1016/j.nbd.2006.12.019
58. Ooi TC, Meramat A, Rajab NF, et al. Intermittent fasting enhanced the cognitive function in older adults with mild cognitive impairment by inducing biochemical and metabolic changes: A 3-year progressive study. *Nutrients*. 2020;12(9):2644. doi:10.3390/nu12092644
59. Stockman M-C, Thomas D, Burke J, Apovian CM. Intermittent fasting: Is the wait worth the weight? *Curr Obes Rep*. 2018;7(2):172-185. doi:10.1007/s13679-018-0308-9
60. Mattson MP, Longo VD, Harvie M. Impact of intermittent fasting on health and disease processes. *Ageing Res Rev*. 2017;39:46-58. doi:10.1016/j.arr.2016.10.005
61. Philippou E, Polak R, Michunovich A, et al. Food for thought: Basic nutrition recommendations for the mature brain. *Arch Phys Med Rehabil*. 2019;100(8):1581-1583. doi:10.1016/j.apmr.2019.01.006
62. Cunningham E. I have a client who wants to follow the Mediterranean diet—Where do I start? *J Acad Nutr Diet*. 2014;114(8):1312. doi:10.1016/j.jand.2014.06.004
63. DASH diet: Guide to recommended servings - Mayo Clinic. Accessed February 1, 2022. https://www.mayoclinic.org/healthy-lifestyle/nutrition-and-healthy-eating/in-depth/dash-diet/art-20050989
64. Marcason W. What are the components to the MIND Diet? *J Acad Nutr Diet*. 2015;115(10):1744. doi:10.1016/j.jand.2015.08.002
65. Masood W, Annamaraju P, Uppaluri KR. Ketogenic Diet. [Updated 2021 Nov 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan.
66. Patterson RE, Laughlin GA, LaCroix AZ, et al. Intermittent fasting and human metabolic health. *J Acad Nutr Diet*. 2015;115(8):1203-1212. doi:10.1016/j.jand.2015.02.018