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Comparative analysis of the effect of the Mediterranean, Ketogenic, DASH and MIND diets on the prevention of Alzheimer Análisis comparativo del efecto de las dietas Mediterránea, Cetogénica, DASH y MIND

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	Abstract
Keywords: Cognitive decline, Alzheimer's disease, Alzheimer's prevention, Mediterranean diet, Ketogenic diet, DASH diet, MIND diet.	The aim of this literature review is to examine and contrast four dietary patterns to evaluate their influence on Alzheimer's prevention. The need for this study arises from the lack of a comprehensive analysis definitively confirming the effectiveness of these diets in preventing this disease. An exhaustive literature review was conducted, including clinical trials, systematic reviews, meta-analyses, online books, guidelines, etc. However, only articles from studies, clinical trials, and controlled randomized trials were used for discussion. Exclusion criteria were: publication period of 5 years, articles published in indexed journals and in databases such as PubMed, COCHRANE, or Google Scholar, with an impact factor equal to or greater than 1.5. It has been evidenced that the four diets can offer benefits in Alzheimer's prevention. However, when selecting the most effective diet in Alzheimer's prevention, it is necessary to consider different types of nutritional approaches such as engaging in physical activity to improve cognitive decline. It has been demonstrated that the four investigated diets offer significant benefits in Alzheimer's prevention. Although the MIND diet emerges as a promising strategy, combining the benefits of the Mediterranean and DASH diets. Integrating this diet with practices such as mindfulness and physical activity is important to promote long-term brain health and reduce the risk of cognitive decline, thus maximizing Alzheimer's prevention.
	RESUMEN
Palabras clave: Deterioro cognitivo, enfermedad de Alzheimer, prevención de Alzheimer, dieta Mediterránea, dieta Cetogénica, dieta DASH, dieta MIND.	El objetivo es examinar y contrastar cuatro patrones alimenticios para evaluar su influencia en la prevención del Alzheimer. La necesidad de este estudio surge de la falta de un análisis exhaustivo que confirme de manera definitiva la efectividad de estas dietas en la prevención de esta enfermedad. Se ha realizado una revisión bibliográfica exhaustiva en la que se han incluido ensayos clínicos, revisiones sistemáticas ,metaanálisis, libros online, guías etc. Sin embargo, para realizar la discusión solo se utilizaron artículos de estudios, ensayos clínicos y ensayos aleatorios controlados. Los parámetros de exclusión fueron:

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antigüedad de 5 años, artículos publicados en revistas indexadas o bases de datos como Pubmed, COCHRANE o Google Scholar, con un factor de impacto igual o superior a 1,5. Se ha evidenciado que las cuatro dietas pueden ofrecer beneficios en la prevención del Alzheimer. Sin embargo, para seleccionar la dieta más efectiva en la prevención de esta enfermedad es necesario tener en cuenta los diferentes tipos de abordajes nutricionales como la realización de actividad física conjunta para la mejora del deterioro cognitivo. Se ha demostrado que las cuatro dietas investigadas ofrecen beneficios significativos en la prevención del Alzheimer. Aunque la dieta MIND emerge como una estrategia prometedora, combinando los beneficios de las dietas Mediterránea y DASH. Es importante integrar esta dieta con prácticas como el mindfulness y la actividad física para promover la salud cerebral a largo plazo y reducir el riesgo de deterioro cognitivo, maximizando así la prevención del Alzheimer.

Introduction

Alzheimer's disease (AD) is the most common form of dementia, accounting for at least two-thirds of cases in people over the age of 65. It is characterized by a gradual onset and steady progression that adversely affects various cognitive and behavioral functions, interfering with daily activities. This disease is the sixth leading cause of death in adults and affects 50 million people worldwide, with a projection of 152 million by 2050 (1).

AD is a complex disorder influenced by genetic factors and modifiable lifestyle habits. Currently, there are no effective drugs to halt or slow its progression, highlighting the urgent need to better understand the disease and develop more effective therapies. Neuroimaging research has shown that dietary choices can significantly impact the brain, suggesting that dietary interventions may be preventative measures against AD.

To meet this public health challenge, it is essential to adopt comprehensive and multidisciplinary approaches. The adoption of healthy eating habits, regular exercise and cognitive stimulation are crucial strategies to reduce the incidence of dementia, especially in the elderly. One study has shown that lower adherence to the Mediterranean diet is associated with greater impairment in AD-related brain areas, indicating that following this diet may be beneficial for brain health (2-4).

Other studies have evaluated the impact of ketogenic diet and medium-chain triglycerides in people with mild to moderate AD, and it has been observed that folate deficiency increases the risk of Alzheimer's disease, highlighting the importance of adequate folate intake. The MIND diet, which combines aspects of the Mediterranean diet and the DASH diet, may improve cognitive ability in older people, suggesting that following these dietary guidelines may be an effective strategy to prevent cognitive decline (5-9).

Definition of Alzheimer's Disease

Alzheimer's disease (AD) is the most common form of dementia. The term "dementia" comes from the Latin "demens," meaning "to be out of one's mind", and has been used since the 13th century to describe mental disorders. AD was identified in 1906 with a case of presenile dementia. This disease progresses continuously and, on average, sufferers live between 4 and 8 years after diagnosis, although some cases can last up to 20 years.

AD is complex and is characterized by multiple interrelated pathological events, such as metabolic, neurovascular, inflammatory, bioenergetic and systemic processes, including ischemic white matter lesions. Unlike normal aging, AD is a progressive neurodegenerative condition that affects memory, thinking, decision making, communication, problem solving, personality and mobility (1,4).

In addition to these changes, there is a significant loss of neurons, chronic inflammation, extensive DNA damage, mitochondrial dysfunction, alterations in energy metabolism and prolonged oxidative stress. Oxidative damage is one of the earliest events in the progression of AD. These processes contribute to the complexity of the disease and its devastating impact on cognitive function and quality of life (1).

However, not all people with brain pathologies experience cognitive dysfunction; some maintain their function through cognitive resilience (10). Cognitive and physical activities in old age are associated with better cognitive scores, independently of brain pathologies. Identifying modifiable lifestyle factors is crucial in AD research. Diet, in

particular, has been linked to cognitive decline and AD, so it is essential to delve deeper into how diet influences cognitive health and the prevention of neurodegenerative diseases such as Alzheimer's disease.

Causes

Low cognitive reserve, often associated with low educational level, is one of the main hypotheses explaining early cognitive impairment and the onset of AD. Adult hippocampal neurogenesis (AHN) is essential for maintaining cognitive reserve, and diet plays a critical role in creating an environment conducive to AHN. A diet rich in essential nutrients such as monounsaturated (MUFA) and polyunsaturated (PUFA) fats, fiber-rich carbohydrates and protein, along with probiotics and prebiotics, has been found to correlate with improvements in mental health (2). In addition, maintaining an adequate sleep pattern and regular exercise are also associated with these mental health benefits (10).

The most reliable method of identifying mild cognitive impairment in the early stages of Alzheimer's disease is through neuropsychological testing. Recently, volumetric magnetic resonance imaging has emerged as an accurate tool for measuring volume changes in the brain (1). In Alzheimer's patients, this technique shows specific shrinkage in the medial temporal lobe, although hippocampal atrophy is also related to normal age-related memory decline, limiting its usefulness as a definitive method for early detection of the disease (4).

The exact role of volumetric magnetic resonance imaging in the diagnosis of Alzheimer's is not yet fully defined, and although it provides valuable information on brain structural changes, its definitive contribution to diagnosis is still under study (1). Functional brain imaging techniques such as PET, fMRI and SPECT are also being investigated to analyze dysfunction in specific regions of the medial temporal and parietal lobe. Although they hold promise in early detection and monitoring of the disease, their definitive role in diagnosis is yet to be determined, and their integration into full clinical diagnosis is an active area of research (13).

Even with a thorough history, complete physical exam, and high-quality testing, diagnosing the specific type of dementia with certainty can be challenging (4). Some patients may experience cognitive decline that, although objective, is not severe enough to affect daily tasks, being categorized as mild cognitive impairment. However, a significant proportion of people with mild cognitive impairment will develop dementia within 5 to 7 years (1).

According to the stage of cognitive impairment, they can be classified into: Preclinical or presymptomatic (13), mild cognitive impairment (12), dementia (6).

Treatment and Prevention

Alzheimer's disease currently lacks a definitive cure, but there are treatments that help alleviate symptoms and improve patients' quality of life (1). These treatments include cholinesterase inhibitors and partial NMDA receptor antagonists (4), which work by increasing acetylcholine levels and blocking specific receptors to reduce calcium accumulation in nerve cells.

Since there are no specific treatments to stop Alzheimer's disease, increasing emphasis has been placed on its prevention. Evidence suggests that a diet rich in antioxidants can improve cognitive function, highlighting the importance of adopting healthy dietary habits to reduce the risk of developing this disease (6). The Mediterranean, DASH and MIND diets have been shown to be associated with protection against cognitive decline, suggesting that following these dietary patterns may help preserve cognitive function and delay the development of neurodegenerative disorders (14).

Prospective studies have confirmed that reducing the intake of saturated and transunsaturated fats, and increasing the intake of antioxidant nutrients and B vitamins, can slow cognitive decline. These findings underscore the importance of maintaining healthy eating habits to optimize cognitive function (12).

Diet plays a crucial role in the generation of new neurons, while cognitive training facilitates the integration of these neurons into existing neural networks. Therefore, it is essential to combine proper nutrition with mental exercise to maintain and improve brain function (12).

Effective prevention of cognitive decline and dementia requires comprehensive approaches that address several aspects of lifestyle simultaneously. This includes interventions in areas such as physical activity (15), diet, mental exercise, social relationships, and stress management, with the goal of promoting long-term brain health and reducing the risk of cognitive decline and dementia (13).

Dietary Intervention

Diet plays a crucial role in the prevention of Alzheimer's disease (AD) through lifestyle changes (16) through lifestyle changes. The literature on dietary interventions has grown, showing that modifying diet can improve cognitive function and reduce the risk of mental decline. However, variability in evaluation methods limits the ability to draw robust conclusions about the brain health benefits of these interventions (17).

Evidence suggests that a healthy diet may prevent cognitive decline related to aging (18), based on prospective epidemiological studies. Although these studies have been encouraging, more research is needed to fully understand this relationship and to establish precise guidelines on the most beneficial diet in the long term (16).

Dietary patterns with high vegetable and fruit consumption correlate with better cognitive scores. Diets such as Mediterranean, DASH, and MIND have been associated with improved cognitive, behavioral and brain function. These findings support the idea that a healthy diet can preserve cognitive function and delay neurodegenerative processes, although more research is needed to confirm them (2).

Several dietary patterns, such as the Mediterranean diet and the DASH diet, have demonstrated neuroprotective properties, reducing the risk of cognitive impairment (19). The ketogenic diet may improve cognition in mild cognitive impairment by regulating brain metabolism and reducing inflammation (20). The MIND diet, combining principles of the Mediterranean and DASH diets, may decrease the risk of cognitive decline, offering a promising strategy to prevent dementia (13).

Mediterranean Diet

The Mediterranean diet, typical of coastal regions of the Mediterranean Sea such as Greece (21), Italy, southern France, Crete, Spain, and some areas of the Middle East, is considered a model of healthy eating in modern Western society. It is characterized by the abundant consumption of plant foods, moderate intake of dairy products, fish and poultry, and the use of olive oil as the main source of fat, while limiting the consumption of eggs and red meat (22).

Foods in the Mediterranean diet include green leafy vegetables, legumes, nuts, almonds, pistachios, fresh fruits and whole grains (6). Olive oil, a monounsaturated fat rich in alpha-linoleic acid (an omega-3 fatty acid), is essential in this diet because of its cardioprotective benefits (14). Marine products provide omega-6 fatty acids, which further enhance their cardioprotective properties. Moderate consumption of wine, especially red wine, is also associated with metabolic benefits, such as improved lipid metabolism (22).

It is recommended to consume three to nine servings of vegetables per day, onehalf to two servings of fruit, and one to 13 servings of cereals, in addition to up to eight servings of olive oil daily. It is suggested to include at least three servings of oily fish and legumes per week, to use white meat instead of red meat, and to moderate the consumption of red wine at meals (22).

This diet provides approximately 2200 calories per day, with 37% of total fat intake (18% monounsaturated and 9% saturated) and 33 grams of fiber, benefiting digestive and metabolic health. It is advised to limit consumption of soft drinks to less than one per day, baked goods and commercial sweets to less than three times per week, and fat spreads to less than one serving per day. In addition, the intake of red and processed meats should be restricted to less than once a day (23).

Following the Mediterranean diet correlates with a slowing of cognitive decline and a lower incidence of AD. Epidemiological studies have shown that high adherence to this diet in older adults is associated with a lower risk of cognitive decline (24). Recent research indicates that adopting a healthy diet such as the Mediterranean diet could have a significant impact on cognitive health during aging, demonstrating potential in the prevention of neurodegenerative diseases such as Alzheimer's disease (25). One specific study suggested that extra virgin olive oil therapy may reduce the risk of progression from mild cognitive impairment to AD by decreasing fibrinolytic factors and AD-associated proteins such as tau and A β amyloid, as well as the oxidative stress biomarker MDA (26).

These findings highlight the importance of healthy dietary choices and specific interventions to preserve cognitive health during aging (23).

Ketogenic Diet

In 1921, Russell Wilder introduced the ketogenic diet to treat epilepsy and coined the term "ketogenic diet" (27). In the 1970s, the diet gained popularity and has been the subject of numerous studies as a treatment for various medical conditions (28). This dietary approach is characterized by high fat and low carbohydrate intakes (29) and low carbohydrate intake, with the goal of facilitating weight loss, improving mental clarity and increasing energy levels (30).

The exact cause of weight loss induced by the ketogenic diet is not completely clear. It is suggested that this could be due to water loss, fat oxidation, or a reduction in total caloric intake. The diet typically involves 55% to 60% fat, 30% to 35% protein and 5% to 10% carbohydrates. On a 2,000 calorie diet, this equates to about 20 to 50 grams of carbohydrates per day (29).

Normally, carbohydrates are the main source of energy for the body. However, by reducing their intake to less than 50 grams per day, insulin secretion decreases, leading the body into a catabolic state (31). This depletes glycogen stores and activates gluconeogenesis and ketogenesis in body tissues (20).

There are four types of ketogenic diets: the standard long-chain triglyceride (LCT), the medium-chain triglyceride (MCT) ketogenic, the modified version of the Atkins diet (MAD) and the low glycemic index approach (LIG) (9).

In studies with animal models of Alzheimer's disease (AD), the ketogenic diet has been shown to delay cognitive decline (32). In humans, a reduction in neuroinflammation and amyloid and tau accumulation has been observed. In addition, ketone bodies may have a neuroprotective effect against beta-amyloid toxicity (27).

DASH Diet

The dietary approach known as DASH got its start in the 1990s with funding from the National Institutes of Health (NIH) to investigate dietary interventions to treat hypertension (33). This dietary approach promotes a balanced diet(33), which includes a variety of foods such as vegetables, fruits, lean meats and dairy products, as well as the incorporation of essential micronutrients (34). A cornerstone of the DASH diet is the reduction of sodium intake to about 1,500 mg per day, along with a preference for fresh and minimally processed foods, similar to other dietary patterns recommended for cardiovascular health (35).

The DASH diet recommendations encourage a balanced, nutrient-rich, low-sodium diet to maintain healthy blood pressure and promote overall wellness. It is suggested to consume at least five daily servings of a variety of vegetables and fruits, opting for those with a low glycemic index to stabilize blood sugar levels. As for carbohydrates, it is recommended to consume about seven servings a day of healthy options such as whole grains, legumes and fiber-rich vegetables. It is also advisable to limit lean meat consumption to approximately two servings per day, preferring options such as skinless chicken, turkey and lean cuts of meat (33).

It is also recommended to incorporate nuts and seeds in the diet 2 to 3 times per week as a source of healthy fats, proteins and fiber. The DASH diet emphasizes the consumption of healthy fats such as extra virgin olive oil, avocados, nuts and fish rich in omega-3 fatty acids to promote cardiovascular health (23). As for proteins, it is suggested to prioritize vegetable sources such as legumes, soy products, nuts and seeds, and to limit the consumption of processed and cured meats (36).

Both the DASH and Mediterranean diets offer protection against several health conditions, including hypertension, obesity, cardiovascular disease and diabetes. These conditions have also been associated with increased cognitive impairment. However, studies have shown that physical activity combined with the DASH diet can improve neurocognition in adults at risk for Alzheimer's disease, suggesting that the two should be maintained in tandem for optimal benefits in metabolic function and quality of life (37). The combination of these healthy diets can play a crucial role in protecting both the body and mental health over time (23).

MIND Diet

The MIND diet, a fusion of the Mediterranean and DASH diets (38), has been associated with decreased cognitive decline and reduced risk of Alzheimer's dementia in older adults. This diet, influenced by the dietary patterns of both of the above diets, includes a variety of foods and nutrients considered beneficial to brain health (39). Research has revealed that following the MIND diet can slow cognitive decline in older

adults and reduce the likelihood of developing Alzheimer's dementia, according to four relevant domains: executive function, perceptual speed, episodic memory and semantic memory. These results suggest that the MIND diet may be a promising strategy for maintaining brain health and preventing cognitive decline associated with aging (17).

The MIND diet is based on a set of 10 food groups considered beneficial for the brain, such as green leafy vegetables, additional varieties of vegetables, nuts, berries, legumes, whole grains, fish, poultry, olive oil and moderate consumption of wine (12). On the other hand, 5 unhealthy food groups that should be limited are identified, such as red meat, butter and margarine sticks, cheeses, bakery products and sweets, as well as fried and fast foods (12).

The MIND diet offers detailed nutritional recommendations, such as daily consumption of three or more servings of whole grains and at least six servings per week of leafy green vegetables, along with an additional variety of vegetables per day (12). Weekly consumption of berries, fish and poultry, as well as beans and nuts, is also recommended. Olive oil is promoted as the main source of fats, while moderation in alcohol consumption is suggested, allowing for one daily serving of wine (12).

On the other hand, the consumption of foods such as red meat, fast food, fried foods and pastries is discouraged, limiting them to specific weekly portions. These nutritional recommendations are based on dietary guidelines of the Mediterranean and DASH diets (12).

The MIND diet promotes the consumption of foods rich in nutrients such as vitamin E, folate, β -carotene, lutein-zeaxanthin and flavonoids, which possess antioxidant, anti-inflammatory and neuroprotective properties. For example, vitamin E, present in green leafy vegetables and nuts, acts as an antioxidant, protecting neurons from damage caused by oxidative stress (39).

Method

This paper focuses on a literature review that analyzes the impact of the Mediterranean, ketogenic, DASH and MIND diets in the prevention of Alzheimer's disease. The aim is to determine which of these diets has a greater preventive effect against this disease. An exhaustive search of scientific articles related to the topic was conducted, including clinical trials, systematic reviews and meta-analyses, among other resources. Studies published in the last five years, from 2019 to 2024, in English or Spanish, and available in indexed journals and databases such as PubMed, COCHRANE and Google Scholar, with an impact factor equal to or greater than 1.5 were selected.

The literature search was conducted from November 20, 2023 to June 2, 2024. The following are the terms used in the search for articles.

• "Cognitive impairment": a total of 2,450 articles were obtained from this search, of which 6 were used for this review.

• "Alzheimer disease": a total of 1,082 articles were obtained from this search, of which 5 were used for this review.

• "Alzheimer prevention": a total of 324 articles were obtained from this search, of which 2 were used for this review.

• "Mediterranean diet": a total of 441 articles were obtained from this search, of which 2 were used for this review.

• "Ketogenic diet": a total of 166 articles were obtained from this search, of which 1 was used for this review.

• "DASH diet": a total of 108 articles were obtained from this search, of which 1 was used for this review.

• "MIND diet": a total of 42 articles were obtained from this search, of which 3 were used for this review.



Figure 3 - Decision tree for choosing used articles searched with keywords.

Finally, 11 experimental articles were used for the discussion section.

Results

A randomized trial by Hoscheidt et al (2022) (24) examined the impact of the Mediterranean diet compared with the Western diet on amyloid beta (A β) levels in cerebrospinal fluid and cerebral perfusion. The results suggest that the Mediterranean diet may benefit adults with normal cognition by increasing A β levels, whereas, in those with mild cognitive impairment, a decrease in these levels is observed. In addition, the Mediterranean diet was found to increase cerebral perfusion, in contrast to the Western diet which reduces it. These findings underscore the neuroprotective potential of the Mediterranean diet and its ability to counteract the negative effects of the Western diet on cognitive health.

On the other hand, a randomized trial carried out by Tsolaki and colleagues (2020) (21) suggests that consumption of extra virgin olive oil and a higher intake of polyphenols may have a positive impact on preventing or slowing cognitive decline. Both studies highlight the importance

of the Mediterranean diet, rich in olive oil and polyphenols, as an effective strategy in the prevention of Alzheimer's disease and the maintenance of cognitive health.

The clinical trial by Ruiz-Rizzo et al (2024) (13) highlights the importance of physical activity and adherence to the Mediterranean diet in improving cognitive health, especially verbal memory over time. It suggests that the combination of a Mediterranean diet and an active lifestyle may be an effective strategy for preserving cognitive function in aging.

Finally, a cohort study based on a randomized controlled clinical trial conducted by Domínguez-López et al (25) focused on vitamin B12 provides additional insight. It suggests that, in an elderly Mediterranean population at high cardiovascular risk, changes in blood vitamin B12 levels are linked to improvements in memory function, but this effect is only apparent in those with high adherence to the Mediterranean diet. This finding highlights the importance of the interaction between specific nutrient intake and overall dietary pattern in the protection of cognitive functioning.

In summary, these studies support the idea that the Mediterranean diet not only promotes cardiovascular health, but may also play a crucial role in the prevention of cognitive decline and Alzheimer's disease.

As for the ketogenic diet, it has emerged as a possible intervention in the prevention and management of Alzheimer's disease (AD). Two recent studies provide valuable insights into the role of ketosis in this pathology.

The randomized crossover trial by Phillips MCL et al. 2021 (7) explored the effects of a modified ketogenic diet for 12 weeks in patients with AD in a hospital clinic. The results indicated positive changes in cardiovascular risk factors, together with mild adverse effects. This study highlighted high retention, adherence and safety rates, suggesting that the ketogenic diet can improve daily function and quality of life in patients with AD, crucial aspects for those living with dementia.

On the other hand, the clinical trial by Fortier M et al. 2021 (8) examined the effects of a ketogenic beverage with medium-chain triglycerides on mild cognitive impairment. The results revealed significant improvements in cognitive outcomes, possibly due to increased blood ketone levels. These findings highlight the importance of further research on the impact of diet-induced ketosis on the progression of AD.

Research conducted by Wright KD et al. 2021 (38) presents findings regarding the prevention of Alzheimer's disease through the implementation of the DASH diet. This pilot study evaluated the feasibility and acceptability of a combined intervention, Mindfulness in Motion (MIM) and Dietary Approaches to Stop Hypertension (DASH), specifically in older African Americans with both mild cognitive impairment and hypertension.

The results obtained indicate a significant improvement in adherence to the DASH diet, as well as in mindfulness, stress management and systolic blood pressure.

On the other hand, the two randomized clinical trials with 2x2 factorial design conducted by Smith PJ et al. (37) and Blumenthal JA et al. (36)investigated the independent and combined effects of aerobic exercise (AE) and the DASH diet in older adults with mild cognitive impairment and cardiovascular risk factors.

Only one of them showed that both physical activity and the DASH diet had beneficial effects on metabolic function (37). However, the other found significant improvements in executive functioning associated with physical activity, while the DASH diet showed no significant effect (36).

These findings suggest good potential for the DASH diet as a preventive strategy for Alzheimer's disease in individuals with mild cognitive impairment.

In the context of the MIND diet and its role in the prevention of Alzheimer's disease, a randomized controlled trial was conducted by Barnes LL et al. 2023 (34) which compared the cognitive effects of the MIND diet with a similar control diet, both with mild

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caloric restriction. Participants were randomly assigned to follow one of the two diets, with the aim of promoting weight loss.

The results revealed improvements in global cognition scores in both groups up to year 3. However, for those with cognitive impairment and a family history of dementia, no significant differences were observed between those following the MIND diet and those following the control diet during the same period.

On the other hand, another randomized control trial by Krueger KR et al. 2022 (17) focused on the relative efficacy of the MIND diet in preventing cognitive decline and reducing brain atrophy in older adults at risk for Alzheimer's dementia.

The results indicated that the MIND cognitive battery is complete and valid, covering four different domains of cognitive function.

Discussion and Conclusions

In this literature review based on current scientific evidence, it has been shown that the four diets investigated: the Mediterranean diet, the Ketogenic diet, the DASH diet and the MIND diet, may offer significant benefits in the prevention of Alzheimer's disease.

Articles on the Mediterranean diet highlight its numerous benefits, which go beyond the promotion of cardiovascular health. This diet is rich in antioxidants, monounsaturated (MUFA) and polyunsaturated (PUFA) fats, fiber-rich carbohydrates and proteins, as well as probiotics and prebiotics, which are associated with the reduction of oxidative stress, the prevention of which is crucial, since oxidative damage is one of the first events in the progression of neurodegenerative diseases such as AD.

Regarding the articles on the ketogenic diet, evidence suggests that this diet may have beneficial effects in several aspects, such as improving cardiovascular risk factors or increasing cognitive function in patients with mild cognitive impairment.

A study in animal models of Alzheimer's disease has shown a delay in cognitive decline, while in humans a reduction in neuroinflammation and amyloid and tau accumulation has been observed. In addition, it has been shown that ketone bodies could exert a neuroprotective effect against beta-amyloid toxicity.

However, it is important to note that this dietary approach should not be applied in isolation, nor maintained over time, as it can produce different nutritional deficits, and in specific cases, can produce fatigue, headaches, nausea and dizziness, in addition to being a very restrictive diet and can be very limiting when making nutritional choices.

Avoidance of ischemic white matter injury is crucial in the prevention of Alzheimer's disease. Although the DASH diet has been promoted for this purpose, there is insufficient scientific evidence to support the application of the DASH diet on an individual basis to prevent Alzheimer's disease.

Therefore, it is recommended to adopt a holistic approach that combines the Mediterranean diet with complementary practices such as mindfulness, physical activity, among others.

Regarding the MIND diet, significant improvements in global cognition are shown compared to a similar control diet, although benefits may vary depending on certain factors. Studies highlight the relevance of diet as a viable strategy to prevent Alzheimer's disease, combining the benefits of the Mediterranean diet and the DASH diet.

This diet is composed of 10 food groups beneficial to the brain, rich in polyphenols and micronutrients such as vitamin E, folate, β -carotene, lutein- zeaxanthin and

flavonoids, which possess antioxidant, anti-inflammatory and neuroprotective properties. Vitamin E acts as an antioxidant protecting neurons from damage related to oxidative stress caused by free radicals.

In conclusion, the four diets investigated have been shown to offer significant benefits in the prevention of Alzheimer's disease. Although the MIND diet emerges as a promising strategy, combining the benefits of the Mediterranean and DASH diets.

Likewise, it is essential to adopt a holistic approach that combines this diet with other complementary interventions such as mindfulness and physical activity to promote long-term brain health and reduce the risk of cognitive decline and thus maximize the prevention of Alzheimer's disease.

References

- Kumar A, Sidhu J, Goyal A, Tsao JW. Alzheimer Disease. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [citado 14 de marzo de 2024]. Retrieved from: <u>https://www.ncbi.nlm.nih.gov/books/NBK499922/</u>
- 2. Dissanayaka DMS, Jayasena V, Rainey-Smith SR, Martins RN, Fernando WMADB. The Role of Diet and Gut Microbiota in Alzheimer's Disease. Nutrients. 31 de enero de 2024;16(3):412. Retrieved from: <u>https://pubmed.ncbi.nlm.nih.gov/38337696/</u>
- 3. Rolandi E, Dodich A, Galluzzi S, Ferrari C, Mandelli S, Ribaldi F, et al. Randomized controlled trial on the efficacy of a multilevel non-pharmacologic intervention in older adults with subjective memory decline: design and baseline findings of the E.Mu.N.I. study. Aging Clin Exp Res. mayo de 2020;32(5):817-26. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/31749018/
- 4. Enfermedad de Alzheimer | Publicaciones de exones. [citado 16 de junio de 2024]; Retrieved from: <u>https://exonpublications.com/index.php/exon/issue/view/11</u>
- Dhana K, James BD, Agarwal P, Aggarwal NT, Cherian LJ, Leurgans SE, et al. MIND Diet, Common Brain Pathologies, and Cognition in Community-Dwelling Older Adults. J Alzheimers Dis. 2021;83(2):683-92. Retrieved from: <u>https://pubmed.ncbi.nlm.nih.gov/34334393/</u>
- Cherian L, Wang Y, Fakuda K, Leurgans S, Aggarwal N, Morris M. Mediterranean-Dash Intervention for Neurodegenerative Delay (MIND) Diet Slows Cognitive Decline After Stroke. J Prev Alzheimers Dis. 2019;6(4):267-73. Retrieved from: <u>https://pubmed.ncbi.nlm.nih.gov/31686099/</u>
- Phillips MCL, Deprez LM, Mortimer GMN, Murtagh DKJ, McCoy S, Mylchreest R, et al. Randomized crossover trial of a modified ketogenic diet in Alzheimer's disease. Alzheimers Res Ther. 23 de febrero de 2021;13(1):51. Retrieved from: <u>https://pubmed.ncbi.nlm.nih.gov/33622392/</u>

- 8. Fortier M, Castellano CA, St-Pierre V, Myette-Côté É, Langlois F, Roy M, et al. A ketogenic drink improves cognition in mild cognitive impairment: Results of a 6-month RCT. Alzheimers Dement. marzo de 2021;17(3):543-52. Retrieved from: <u>https://pubmed.ncbi.nlm.nih.gov/33103819/</u>
- 9. Buchholz A, Deme P, Betz JF, Brandt J, Haughey N, Cervenka MC. A randomized feasibility trial of the modified Atkins diet in older adults with mild cognitive impairment due to Alzheimer's disease. Front Endocrinol (Lausanne). 2024;15:1182519. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10949529/
- 10. Li B, He Y, Ma J, Huang P, Du J, Cao L, et al. Mild cognitive impairment has similar alterations as Alzheimer's disease in gut microbiota. Alzheimers Dement. octubre de 2019;15(10):1357-66. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/31434623/
- 11. Scafato E, Solfrizzi V, Custodero C, Casieri G, Falco C, Maggipinto R, et al. Associations of a biopsychosocial frailty phenotype with all-cause dementia, Alzheimer's disease, vascular dementia, and other dementias: the Italian PRoject on the Epidemiology of Alzheimer's disease (IPREA). Geroscience. junio de 2023;45(3):2037-49. Retrieved from: <u>https://pubmed.ncbi.nlm.nih.gov/37014539/</u>
- 12. Clark DO, Xu H, Moser L, Adeoye P, Lin AW, Tangney CC, et al. MIND food and speed of processing training in older adults with low education, the MINDSpeed Alzheimer's disease prevention pilot trial. Contemp Clin Trials. septiembre de 2019;84:105814. Retrieved from: <u>https://pubmed.ncbi.nlm.nih.gov/31326523/</u>
- 13. Ruiz-Rizzo AL, Finke K, Damoiseaux JS, Bartels C, Buerger K, Cosma NC, et al. Fornix fractional anisotropy mediates the association between Mediterranean diet adherence and memory four years later in older adults without dementia. Neurobiol Aging. abril de 2024;136:99-110. Retrieved from: https://www.sciencedirect.com/science/article/pii/S0197458024000241
- 14. Liu X, Morris MC, Dhana K, Ventrelle J, Johnson K, Bishop L, et al. Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) study: Rationale, design and baseline characteristics of a randomized control trial of the MIND diet on cognitive decline. Contemp Clin Trials. marzo de 2021;102:106270. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/33434704/
- 15. Elsayed MM, Rabiee A, El Refaye GE, Elsisi HF. Aerobic Exercise with Mediterranean-DASH Intervention for Neurodegenerative Delay Diet Promotes Brain Cells' Longevity despite Sex Hormone Deficiency in Postmenopausal Women: A Randomized Controlled Trial. Oxid Med Cell Longev. 2022;2022:4146742. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/35419166/
- 16. Liu X, Dhana K, Furtado JD, Agarwal P, Aggarwal NT, Tangney C, et al. Higher circulating α-carotene was associated with better cognitive function: an evaluation among the MIND trial participants. J Nutr Sci. 2021;10:e64. Retrieved from: <u>https://pubmed.ncbi.nlm.nih.gov/34527222/</u>

(2025) MLSHNR, 4(1),

- 17. Krueger KR, Dhana K, Aggarwal NT, Arfanakis K, Carey VJ, Sacks FM, et al. Properties of the Cognitive Function Battery for the MIND Diet Intervention to Prevent Alzheimer's Disease. J Int Neuropsychol Soc. septiembre de 2022;28(8):790-7. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8983783/
- Komulainen P, Tuomilehto J, Savonen K, Männikkö R, Hassinen M, Lakka TA, et al. Exercise, diet, and cognition in a 4-year randomized controlled trial: Dose-Responses to Exercise Training (DR's EXTRA). Am J Clin Nutr. 1 de junio de 2021;113(6):1428-39. Retrieved from: <u>https://pubmed.ncbi.nlm.nih.gov/33742194/</u>
- 19. Paknahad Z, Sheklabadi E, Derakhshan Y, Bagherniya M, Chitsaz A. The effect of the Mediterranean diet on cognitive function in patients with Parkinson's disease: A randomized clinical controlled trial. Complement Ther Med. mayo de 2020;50:102366. Retrieved from: <u>https://pubmed.ncbi.nlm.nih.gov/32444045/</u>
- 20. Masood W, Annamaraju P, Khan Suheb MZ, Uppaluri KR. Ketogenic Diet. En: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [citado 5 de mayo de 2024]. Retrieved from: <u>http://www.ncbi.nlm.nih.gov/books/NBK499830/</u>
- 21. Tsolaki M, Lazarou E, Kozori M, Petridou N, Tabakis I, Lazarou I, et al. A Randomized Clinical Trial of Greek High Phenolic Early Harvest Extra Virgin Olive Oil in Mild Cognitive Impairment: The MICOIL Pilot Study. J Alzheimers Dis. 2020;78(2):801-17. Retrieved from: <u>https://pubmed.ncbi.nlm.nih.gov/33044178/</u>
- 22. Rishor-Olney CR, Hinson MR. Mediterranean Diet. En: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [citado 14 de marzo de 2024]. Retrieved from: <u>http://www.ncbi.nlm.nih.gov/books/NBK557733/</u>
- 23. Tangney CC, Li H, Wang Y, Barnes L, Schneider JA, Bennett DA, et al. Relation of DASHand Mediterranean-like dietary patterns to cognitive decline in older persons. Neurology [Internet]. 14 de octubre de 2014 [citado 17 de junio de 2024];83(16):1410-6. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4206157/
- 24. Hoscheidt S, Sanderlin AH, Baker LD, Jung Y, Lockhart S, Kellar D, et al. Mediterranean and Western diet effects on Alzheimer's disease biomarkers, cerebral perfusion, and cognition in mid-life: A randomized trial. Alzheimers Dement. marzo de 2022;18(3):457-68. Retrieved from: <u>https://pubmed.ncbi.nlm.nih.gov/34310044/</u>
- 25. Tzekaki EE, Tsolaki M, Pantazaki AA, Geromichalos G, Lazarou E, Kozori M, et al. Administration of the extra virgin olive oil (EVOO) in mild cognitive impairment (MCI) patients as a therapy for preventing the progress to AD. Hell J Nucl Med [Internet]. 2019;22 Suppl 2:181. Retrieved from: <u>https://pubmed.ncbi.nlm.nih.gov/31802059/</u>
- 26. Domínguez-López I, Casas R, Chiva-Blanch G, Martínez-González MÁ, Fitó M, Ros E, et al. Serum vitamin B12 concentration is associated with improved memory in older individuals with higher adherence to the Mediterranean diet. Clin Nutr. diciembre de 2023;42(12):2562-8. Retrieved from: <u>https://pubmed.ncbi.nlm.nih.gov/37948836/</u>

- 27. Hersant H, Grossberg G. The Ketogenic Diet and Alzheimer's Disease. J Nutr Health Aging. 2022;26(6):606-14. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/35718870/
- 28. Myette-Côté É, St-Pierre V, Beaulieu S, Castellano CA, Fortier M, Plourde M, et al. The effect of a 6-month ketogenic medium-chain triglyceride supplement on plasma cardiometabolic and inflammatory markers in mild cognitive impairment. Prostaglandins Leukot Essent Fatty Acids. junio de 2021;169:102236. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/33906081/
- 29. O'Neill B, Raggi P. The ketogenic diet: Pros and cons. Atherosclerosis. enero de 2020;292:119-26. Retrieved from: <u>https://pubmed.ncbi.nlm.nih.gov/31805451/</u>
- 30. Hall KD, Guo J, Courville AB, Boring J, Brychta R, Chen KY, et al. Effect of a plant-based, low-fat diet versus an animal-based, ketogenic diet on ad libitum energy intake. Nat Med. febrero de 2021;27(2):344-53. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/33479499/
- 31. Antonio Paoli A, Mancin L, Caprio M, Monti E, Narici MV, Cenci L, et al. Effects of 30 days of ketogenic diet on body composition, muscle strength, muscle area, metabolism, and performance in semi-professional soccer players. J Int Soc Sports Nutr. 16 de septiembre de 2021;18(1):62. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/34530857/
- 32. Schönknecht YB, Crommen S, Stoffel-Wagner B, Coenen M, Fimmers R, Stehle P, et al. APOE ε4 Is Associated with Postprandial Inflammation in Older Adults with Metabolic Syndrome Traits. Nutrients. 2 de noviembre de 2021;13(11):3924. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/34836179/
- 33. Challa HJ, Ameer MA, Uppaluri KR. DASH Diet To Stop Hypertension. En: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [citado 14 de marzo de 2024]. Retrieved from: <u>http://www.ncbi.nlm.nih.gov/books/NBK482514/</u>
- 34. Filippou CD, Tsioufis CP, Thomopoulos CG, Mihas CC, Dimitriadis KS, Sotiropoulou LI, et al. Dietary Approaches to Stop Hypertension (DASH) Diet and Blood Pressure Reduction in Adults with and without Hypertension: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Advances in Nutrition [Internet]. 1 de septiembre de 2020 [citado 2 de junio de 2024];11(5):1150-60. Retrieved from: https://www.sciencedirect.com/science/article/pii/S2161831322000473
- 35. SL I. Todo lo que deberías saber sobre la dieta DASH. [Internet]. [citado 17 de junio de 2024]. Retrieved from: <u>https://www.seen.es/portal/hablemos-de-nutricion/todo-lo-que-deberias-saber-sobre-la-dieta-dash</u>
- 36. Blumenthal JA, Smith PJ, Mabe S, Hinderliter A, Lin PH, Liao L, et al. Lifestyle and neurocognition in older adults with cognitive impairments: A randomized trial. Neurology. 15 de enero de 2019;92(3):e212-23. Retrieved from: <u>https://pubmed.ncbi.nlm.nih.gov/30568005/</u>

- 37. Smith PJ, Mabe SM, Sherwood A, Doraiswamy PM, Welsh-Bohmer KA, Burke JR, et al. Metabolic and Neurocognitive Changes Following Lifestyle Modification: Examination of Biomarkers from the ENLIGHTEN Randomized Clinical Trial. J Alzheimers Dis. 2020;77(4):1793-803. https://pubmed.ncbi.nlm.nih.gov/32925039/
- 38. Wright KD, Klatt MD, Adams IR, Nguyen CM, Mion LC, Tan A, et al. Mindfulness in Motion and Dietary Approaches to Stop Hypertension (DASH) in Hypertensive African Americans. J Am Geriatr Soc [Internet]. marzo de 2021;69(3):773-8. Retrieved from: <u>https://pubmed.ncbi.nlm.nih.gov/33227157/</u>
- 39. Barnes LL, Dhana K, Liu X, Carey VJ, Ventrelle J, Johnson K, et al. Trial of the MIND Diet for Prevention of Cognitive Decline in Older Persons. N Engl J Med. 17 de agosto de 2023;389(7):602-11. Retrieved from: <u>https://pubmed.ncbi.nlm.nih.gov/37466280/</u>