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Key neuroprotective mechanisms of the MIND diet - a review paper

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Abstract

Introduction and purpose:

Impaired cognitive function is a growing public health problem, where dementia is affecting about 47 million people worldwide, and that number is expected to triple by 2050. The MIND (Mediterranean-DASH Intervention for Neurodegenerative Delay) diet is intended to overcome this problem. This article aims to raise awareness of the MIND diet, highlighting how dietary choices can promote cognitive health and delay disease progression.

Brief description of the state of knowledge:

The MIND diet focuses on foods that support cognitive health and may mitigate these degenerative processes. It emphasizes green leafy vegetables, berries, nuts, olive oil, whole grains, fish, and poultry while limiting red meat, dairy, sweets, and fried foods. These products contain several components with multidirectional neuroprotective effects.

Material and method:

This work was based on material found on Google Scholar. Articles were selected based on citation counts, publication dates, and relevance, ensuring a comprehensive review of recent findings on the MIND diet's impact on cognitive health.

Summary:

The MIND diet enhances brain health by incorporating nutrient-dense foods that reduce inflammation, combat oxidative stress, and support neuronal function. Green leafy vegetables, berries, nuts, whole grains, and healthy fats work together to improve cognitive function, support synaptic plasticity, and protect brain structure, leading to slower cognitive decline and a lower risk of neurodegenerative diseases.

Keywords: MIND, diet, brain, neurodegeneration, neuroprotection

Introduction

Cognitive performance encompasses various mental abilities, such as learning, reasoning, memory, and decision-making. Maintaining strong cognitive function is crucial for a healthy and active lifestyle, in older adults. However, cognitive decline, closely tied to aging, is a growing public health concern. [1] According to the World Alzheimer Report 2016, around 47 million people worldwide have dementia, a number that is expected to rise to more than 131 million by 2050. [2] Following research, one of the factors influencing the efficient functioning of the brain is diet. A diet specifically dedicated to neuroprotection is the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet, a blend of the Mediterranean and DASH diets.

The aim

This study aims to raise awareness of the prevention of neurodegenerative diseases and the possibility of improving brain function through diet, as well as what the beneficial properties of the given products recommended in the MIND diet are.

Material and methods

The paper was created by searching on Google Scholar for keywords such as "mind diet", "neuroprotection", "neurodegeneration", “cognition”, and "diet" and then selecting articles. The articles were selected based on the number of citations, date of publication, and fit with the topic of the paper and the content of the information needed.

Neurodegeneration

Neurodegeneration is a process in which there is gradual and irreversible damage and loss of function of nerve cells. [3] The mechanisms underlying neurodegeneration are complex and multifaceted, including abnormal protein metabolism, oxidative stress, mitochondrial

dysfunction, and inflammatory processes, among others. One key element of the neurodegeneration is the accumulation of abnormally folded proteins, such as beta-amyloid in Alzheimer's disease and alpha-synuclein in Parkinson's disease, which lead to the formation of toxic aggregates that disrupt neuronal function. [4,5] Another mechanism is associated with dysfunction of mitochondria (a source of cellular energy), resulting in oxidative stress, that leads to increased production of reactive oxygen species (ROS), damaging nerve cells and causing neuronal loss. [6] Neuroinflammation is also a cause of neurodegeneration. Inflammation is a protective response in the body that aims to repair, regenerate, and eliminate damaged tissues, cells, or infectious agents. However, in the central nervous system (CNS), once neurons are damaged or degenerate, they cannot be repaired or regenerated. This process is mediated by inflammatory and neurotoxic mediators that are released by microglia, astrocytes, neurons, T lymphocytes and mast cells, as well as immune cells and inflammatory mediators that have passed through the damaged blood-brain barrier (BBB). [7] Targeting mechanisms is key to developing effective nutritional therapies that could slow or stop the progression of neurodegenerative diseases and improve cognitive function.

The MIND diet

The MIND diet (Mediterranean-DASH Diet Intervention for Neurodegenerative Delay) is a diet designed to reduce the risk of neurodegenerative diseases such as Alzheimer's disease. It combines elements of the Mediterranean diet and DASH (Dietary Approaches to Stop Hypertension), emphasizing the consumption of foods beneficial to brain health. [8] The MIND diet recommends regular consumption of green leafy vegetables, berries, nuts, olive oil, whole grains, fish, and poultry while limiting consumption of red meat, dairy products, sweets, and fried foods. [9] Studies have shown that those who follow the MIND diet have a lower risk of developing dementia and better cognitive function compared to those who don't. [10] The MIND diet is a source of many essential vitamins, minerals, flavonoids and antioxidants, and limits products that are unhealthy for the brain, making it an antioxidant and anti-inflammatory diet, which is responsible for its neroprotective properties. [11]

Green leafy vegetables

Green leafy vegetables play a key role in the MIND diet, being one of the most important ingredients for supporting brain health. Vegetables such as spinach, kale, lettuce, collards, greens, and lettuce are rich in vitamins, minerals, and antioxidants that have beneficial effects on cognitive function and neuronal protection. They contain large amounts of vitamin K (phylloquinone), lutein, beta-carotene, nitrate, folate, kaempferol (flavonoid), and vitamin E (alfa-tocopherol) which promote neuroprotective processes and reduce inflammation in the brain. Nutrients found in green leafy vegetables may work together through different mechanisms to protect the brain. Regular consumption of green leafy vegetables, recommended at least 1 serving per day, is associated with a slower cognitive decline with aging and has protective relations against dementia. [12]

Berries

Berries play an important role in the MIND diet, being one of the most important ingredients for promoting brain health. Berries such as blueberries, raspberries, strawberries, cranberries, blackcurrants, and blackberries, are rich in vitamins, fibers, and minerals, that support neuroprotective processes. Strawberries have the highest amount of vitamin C compared to other berries. Strawberries, blackberries, and raspberries are the best folate sources. Vitamin K is present in high levels in blackberries and blueberries, while cranberries are rich in vitamin E. Blackberries are an abundant source of beta-carotene, lutein, and zeaxanthin. [13] Berries are rich in phytochemicals such as anthocyanins, caffeic acid, catechin, quercetin, kemferol and tannin. [14] They contain various polyphenol compounds that can interact and synergistically affect the central nervous system (CNS). [15]

Nuts

Nuts are nutrient-dense foods high in fats, particularly monounsaturated and polyunsaturated fatty acids (MUFAs and PUFAs), such as alpha lipolic acid (ALA), linoleic acid (LA), oleic acid and palmitic acid. [16] They also provide a significant amount of plant-based protein, including tryptophan, arginine, and lysine, as well as essential vitamins like folate, riboflavin, and various tocopherols (alpha, beta, gamma, and delta). Additionally, nuts are rich in minerals (such as calcium, phosphorus, magnesium, potassium, and sodium), trace elements (including zinc, copper, and selenium), soluble fiber (raffinose and stachyose), and other compounds that may protect brain health, such as melatonin and various polyphenols. Regular

consumption of nuts has been linked to increased levels of brain-derived neurotrophic factor (BDNF), which is crucial for cognitive function and neuroprotection. Nuts, especially walnuts, are associated with improved memory, working memory, and overall cognitive performance, likely due to their high polyphenol content. Furthermore, nuts may significantly reduce the risk of stroke, a major contributor to cognitive decline. [17]

Olive oil

Olive oil's primary active ingredients are oleic acid, a type of monounsaturated fatty acid, and squalene. Additionally, olive oil contains at least 30 different phenolic compounds [18] that offer potential for both prevention and treatment of neurodegenerative disorders. Consuming olive oil leads to better blood-brain barrier (BBB) function and enhances cognitive performance and memory in people with mild cognitive impairment (MCI). [19]

Whole grain

Whole grain cereal products play an important role in the MIND diet, supporting brain health and lowering the risk of developing neurodegenerative diseases. Products such as oatmeal, brown rice, quinoa, barley, and whole-grain bread, are valuable sources of dietary fiber and contain several micronutrients, such as B vitamins and vitamin E compounds (tocopherols and tocotrienols), which are linked to a lower risk of dementia. Whole grains are rich in various non-nutrient phytochemicals, including flavonoids, phenolic acids, phenolic lipids, carotenoids, and phytosterols, which may have direct or indirect effects on cognitive function. For example, brown rice has higher levels of the neurotransmitter γ-amino butyric acid, which, along with ferulic acid, has been linked to improved spatial learning in Alzheimer’s disease models. [20] Also consumption of whole grains, such as rye, may significantly contribute to reducing the accumulation of beta-amyloid (Ab) in the brain, which is a key factor in the development of Alzheimer's disease. For instance, 5-heptadecylresorcinol, a biomarker for whole grain rye consumption, has been shown to markedly decrease the formation of beta-amyloid plaques and improve cognitive function in mice. As a vital component of the MIND diet, whole grains may play a protective role in brain health by inhibiting the formation and accumulation of beta-amyloid, thereby reducing the risk of neurodegenerative diseases like Alzheimer's. [1]

Fish and poultry

Regular consumption of poultry and fish, which are key sources of protein and beneficial fatty acids, plays an important role in the MIND diet. Poultry provides high-quality protein, B vitamins, and minerals such as iron and zinc to support neurological function. [21] Fish are rich in vitamin D, B vitamins and polyunsaturated fatty acids, such as DHA and EPA (omega-3 acids), which have well-documented neuroprotective properties and are beneficial in the treatment of Alzheimer's disease. The combination of EPA and DHA from fish oil can improve plasma lipid profiles and dopamine levels, which is advantageous for neuroprotection in Parkinson's disease. Studies also indicate that bioactive peptides from fish protein hydrolysates can enhance memory and learning abilities while reducing oxidative stress in the brain, making them potentially useful in treating neurodegenerative disorders. The integration of poultry and fish in the MIND diet is therefore an important part of a nutritional strategy to preserve brain health and delay the aging processes of the nervous system. [22]

Mechanisms that support brain health in the MIND diet

Products in the MIND diet contain many essential vitamins, elements, fats and other components that affect brain health. Phytochemicals, such as anthocyanin and caffeic acid, positively impact brain aging and neurodegenerative diseases due to their antioxidant, anti-inflammatory, antiviral, and antiproliferative effects. [14] Polyphenols exhibit neuroprotective properties through several mechanisms that warrant further exploration. One key aspect of their neuroprotective effect is their ability to cross the blood-brain barrier (BBB). Phenolic sulfate metabolites, such as Pyr-sulf, demonstrate significant neuroprotective potential at physiologically relevant concentrations. These metabolites can modulate cellular metabolism, protect BBB integrity, and influence inflammatory and oxidative stress responses. For instance, Pyr-sulf has been shown to reduce TNF-α release, interfere with NF-κB nuclear translocation, and enhance cellular resilience to oxidative stress and excitotoxicity. [23] Flavonoids can enhance synaptic plasticity by modulating neuronal receptors, signaling pathways, and gene expression, which improves memory and learning in both animals and humans. Additionally, they positively affect peripheral vascular health, leading to improved

endothelial function and increased nitric oxide (NO) availability. This, in turn, enhances cerebral blood flow (CBF). Improved CBF is significant because it helps counteract the declines in brain perfusion associated with aging and neurodegenerative diseases. [24] B vitamins are essential for cellular function, acting as co-enzymes in a wide range of catabolic and anabolic enzymatic processes, with their combined impact being particularly significant for various aspects of brain function. Vitamin B1 influences the synthesis of neurotransmitters and other bioactive compounds essential for brain function. It also has a neuro-modulatory effect on the acetylcholine neurotransmitter system and plays a part in maintaining the structure and function of cellular membranes, including neurons. Vitamin B6 is a crucial cofactor in amino acid metabolism, making it essential for the synthesis of neurotransmitters such as dopamine, serotonin, GABA, noradrenaline, and melatonin. Additionally, vitamin B6 plays a role in immune function, gene expression, and brain glucose regulation, and its levels are linked to inflammation, which is associated with various pathological conditions, including cognitive decline and dementia. Folate is important for brain health, as it supports purine and pyrimidine synthesis and methylation processes in brain tissue. A folate deficiency can reduce DNA stability and repair, disrupt gene expression, and hinder neuronal differentiation and repair. This may lead to hippocampal atrophy, demyelination, and compromised membrane phospholipid integrity, which can impair nerve signal transmission. [25] Folate is also involved in the prevention of Alzheimer's disease through its effects on key proteins, such as inhibition of tau protein phosphorylation. [26] Vitamin E has been linked to improved cognitive function and mitochondrial function, and its deficiency may lead to memory impairment in the elderly. Although the mechanisms of action of vitamin E are not fully understood, it may promote synaptic plasticity by protecting synaptic membranes from oxidation. [27] Vitamin C, one of the most important antioxidants in biological systems, neutralizes reactive oxygen species (ROS) by directly interacting with hydroxyl radicals, superoxide, and singlet oxygen. [15] Vitamin K appears to exert anti-apoptotic and anti-inflammatory effects through the activation of Growth Arrest Specific Gene 6 and Protein S. Additionally, this vitamin plays a role in sphingolipid metabolism, a group of lipids that are crucial for the proliferation, differentiation, and survival of brain cells. Changes in sphingolipid expression have been associated with neuroinflammation and neurodegenerative diseases. [28] Vitamin D, specifically in its active form 1,25(OH)2D3, is considered neuroprotective due to its ability to regulate neurotrophic factors and modulate inflammation. Studies have shown that pre-treatment with 1,25(OH)2D3 can reduce glutamate-induced cell

death in neurons from the cortex, hippocampus, and midbrain. This neuroprotective effect is largely attributed to the regulation of proteins that decrease the levels or mitigate the toxicity of reactive oxygen species (ROS), leading to reduced ROS-induced cell death and increased antioxidant activity in glial cells and neurons. [29] Fatty acids are abundant in neuronal membranes, where they contribute to structural integrity, regulate enzyme activity, and produce secondary messengers and other signaling molecules. The level of PUFAs in neuronal membranes decreases with age, leading to a decline in neuronal function. Therefore, increasing the availability of PUFAs may help prevent their depletion in neuronal membranes. PUFAs like ALA are converted into EPA and DHA in the liver. EPA and DHA are crucial for brain health, as they reduce oxidative stress, modulate immune function, and support synaptic plasticity, neuronal membrane stability, gene expression, and neurogenesis. They also have an anti-inflammatory effect as precursors of eicosanoids and neuroprotection D1 (NPD1), respectively. NPD1 has been demonstrated to reduce the activation of inflammatory signaling molecules, such as prostaglandins, which are produced from arachidonic acid (a long-chain n–6 PUFA) by the enzyme COX-2. [16] DHA has been also shown to increase hippocampal BDNF levels. [22]

Summary

The MIND diet supports brain health through a synergy of nutrient-rich foods that engage several neuroprotective mechanisms. Green leafy vegetables, berries, nuts, whole grains, and healthy fats provide essential vitamins, antioxidants, and polyphenols that work together to reduce inflammation, combat oxidative stress, and support neuronal function. These foods help maintain cognitive function by enhancing synaptic plasticity, improving cerebral blood flow, and protecting the brain's structural integrity. By modulating inflammatory responses, supporting brain cell metabolism, and maintaining vascular health, the MIND diet contributes to slower cognitive decline and lowers the risk of neurodegenerative diseases such as Alzheimer's.

Disclosure

Author's contribution

Conceptualization: Weronika Szafrańska and Dominika Poborowska; methodology: Weronika Kahan; software: Magdalena Kras and Marcin Łata; check: Katarzyna Polańska and Magdalena Kras; formal analysis: Agnieszka Kosińska and Katarzyna Lelek; investigation: Piotr Niedbał and Agnieszka Kosińska; resources: Marta Wojaczek; data curation: Marta Wojaczek; writing - rough preparation: Weronika Kahan; writing - review and editing, Katarzyna Polańska and Marcin Łata; visualization: Piotr Niedbał; supervision: Weronika Szafrańska and Dominika Poborowska; project administration, Agnieszka Kosińska and Katarzyna Lelek; receiving funding - no specific funding.

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The data presented in this study is available upon request from the corresponding author.

Conflict of interest

The authors deny any conflict of interest

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