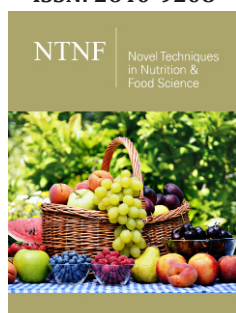


Does Food Have Anything to Do with Memory and Intelligence? A Review on Alzheimer's Disease Fighting

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Abstract

Alzheimer's disease is a neurological disorder that causes the brain to gradually and irreversibly shrink, atrophy, and die. There is no successful treatment for Alzheimer's disease to this day, which makes it necessary to reduce its occurrence rather than treat the disease after it has occurred. Therefore, it became necessary and priority to focus on preventing it and knowing the causes that lead to the deterioration of the brain after it was fully active and strong. Back in the early stages of brain development, food plays an important role. The focus comes on the important elements and materials that increase intelligence, skills, brilliance of thinking and memory, which continue with the person throughout his life after feeding him with important functional elements and vitamins. It is noted that with the development and increase of processed and refined food items that have recently entered the human body, there has been a significant increase and acceleration in the incidence of Alzheimer's disease at alarming and frightening rates. It has become worth reconsidering what we eat and focusing on the right food and its goal as one of the factors affecting the health of brain cells. Therefore, nutritional awareness has become essential and nutritional supplementation is essential for a certain age as a fighter and as a preventer before contracting the disease.

Keywords: Brain; Memory; Alzheimer's disease; Therapeutic nutrition

Introduction

As it is known that the brain is the collector of all the qualities that characterize our humanity. It is the most complex part of the human body and the source of intelligence, the interpreter of the senses, the initiator of body movement, and the observer of behavior. Research in neuroscience and behavioral sciences and the development of new research techniques have helped understand how a healthy brain works [1-3], how to maintain its health, and what happens when the brain is diseased or dysfunctional [4,5]. As we know that food has an important role in the development of brain development since childhood, but with the spread of brain diseases and memory deficiency with age, research continues to this day in search of an approach to combating the disease of the century; Alzheimer's Disease (AD). The storm that engulfs the nerve cells in the brain, the death of their tissues, which leads to personality changes and severe deterioration in memory and mental abilities, gradually increases until one becomes completely unable to perform the simplest daily tasks with age [6,7]. Since the brain is the control center of the body, responsible for maintaining the heartbeat, breathing of the lungs, and allowing the body to move, feel and think, it is important to keep the mind elevated. The foods we eat play a big role in maintaining brain health from birth, and can improve some mental tasks, such as memory, focus, language, etc. Thus, brain development continues gradually with age and in improving its performance. What we see today from a wide range of processed foods invading homes, shops and cafes, including sweets, creams, processed and refined starches is far from the foods that are required that boost the immunity

of the human body, brain development, and that which is required to build a strong body and strong mind [8]. It has been observed in recent years the prevalence of deterioration and atrophy of the brain with age, which leads to cell death in a group of people but not others. Unfortunately, there is no definitive cure for this cerebral deterioration to this day [9].

Given that the nature of food has a fundamental and important role in the formation of nerves, brain growth, strengthening its work, developing its skills in different life stages, activating memory, and certainly preventing dementia and Alzheimer's at an advanced age [10,11]. Therefore, the role of food and therapeutic nutrition with its accompanying habits in activating memory and brain functions is an important topic, worthy of research in eliminating diseases and deficiencies in the brain in general and Alzheimer's disease in particular.

Thus, when talking about brain foods, foods rich in omega-3 fatty acids are often at the top of the list, including fatty fish. Studies reveal that eating fish protects the brain from air pollution [12]. About 60% of the human brain is made of fat, and half of these fats are made of omega-3 fatty acids [13]. The brain uses omega-3 to build brain and nerve cells. It is known that these fats are necessary for learning and memory [14]. On the other hand, not getting enough omega-3 is linked to poor learning, as well as depression, so fatty fish is an excellent choice for brain health [15,16]. A rich source of omega-3 fatty acids is a major building block for the brain. It plays a role in sharpening memory and improving mood, as well as protecting your brain from cognitive decline [17].

Caffeine has a number of positive effects on the brain, including increasing alertness. Caffeine keeps the mind alert by blocking adenosine, a chemical that makes individuals feel sleepy. Caffeine also plays a role in improving mood, by boosting certain neurotransmitters, such as dopamine [18]. It was also found that caffeine consumption led to short-term improvements in attention and alertness in participants who completed a cognition test [19]. A long-term coffee drinking is also associated with a reduced risk of neurodegenerative diseases, such as Parkinson's disease and Alzheimer's disease [20,21]. Green tea, also a source of caffeine, boosts brain function, improving alertness, performance, memory and focus, but green tea also contains other ingredients that make it a brain-healthy drink [22]. One such ingredient is L-theanine, an amino acid that can cross the blood-brain barrier and increase the activity of the neurotransmitter GABA, which helps reduce anxiety and makes one feel more relaxed [23,24]. L-theanine also increases the frequency of alpha waves in the brain, helping to relax without feeling tired [25]. Green tea is rich in polyphenols and antioxidants that can protect the brain from mental decline and reduce the risk of Alzheimer's disease and Parkinson's disease. Some studies have shown that green tea helps improve memory [26].

Antioxidants work against both oxidative stress and inflammation, conditions that can contribute to brain aging and neurodegenerative diseases [27]. Berries offer anthocyanins, a group of plant compounds with anti-inflammatory and antioxidant effects. Studies have found that some of the antioxidants in

blueberries build up in the brain and help improve communication between its cells [28,29]. Powerful plant compounds, including antioxidants like leafy green and broccoli are packed with a very high amount of vitamin K, this fat-soluble vitamin is necessary for the formation of sphingolipids, a type of fat found densely in brain cells [30]. Some studies in older adults have also linked a higher intake of vitamin K to improved memory and cognitive status [31]. Broccoli also contains a number of compounds that give it anti-inflammatory and antioxidant effects, which may help protect the brain from damage [32].

Foods rich in many micronutrients are important for brain function, including copper, iron, magnesium and zinc. Zinc is an important element for nerve signals [33]. Its deficiency has been linked to several neurological conditions, including Alzheimer's disease, depression and Parkinson's disease [33]. Magnesium is also essential for learning and memory [34]. Low magnesium levels are linked to many neurological diseases, including migraines, depression and epilepsy [34]. In addition, the brain uses copper to help control nerve signals [35]. When copper levels are out of control, there is a greater risk of developing neurodegenerative disorders, such as Alzheimer's disease [35]. Iron deficiency is often characterized by brain fog and impaired brain function [36]. Flavonoids may help protect the brain. Studies have indicated that eating chocolate, especially dark chocolate, can enhance memory and mood because it contains flavonoids [37]. Research has shown that eating nuts can improve heart health indicators, and that having a healthy heart is linked to brain health [38]. Studies have found that regular consumption of nuts can be linked to a lower risk of cognitive decline in older adults [39]. Several nutrients found in nuts, such as healthy fats, antioxidants and vitamin E, may explain their beneficial effects on brain health. Vitamin E protects cells from free radical damage and help to slow mental decline [40]. While all nuts are good for the brain, walnuts may have an added advantage, as they also provide anti-inflammatory omega-3 fatty acids.

Having vitamins in food is essential. As vitamin C is a powerful antioxidant that helps fight free radicals that can damage brain cells. Additionally, vitamin C supports brain health with age and may protect against conditions such as depressive disorder, anxiety, schizophrenia, and Alzheimer's disease [41]. Folic acid and vitamin B12 deficiency have been linked to depression. Folic acid deficiency is common in older adults with dementia, and studies have shown that folic acid supplementation can help reduce age-related mental decline [42]. Vitamin B12 is also involved in the manufacture of chemicals in the brain and the regulation of sugar levels in the brain [42]. Choline is an important micronutrient that the body uses to produce acetylcholine, a neurotransmitter that helps regulate mood and memory [43]. Curcumin, the active ingredient in turmeric, has been shown to cross the blood-brain barrier, which means it can enter directly into the brain and benefit cells [44]. It is a powerful antioxidant and anti-inflammatory compound. Curcumin may help improve memory in people with Alzheimer's disease [45]. It may also help remove amyloid plaques that are the hallmark of this disease [46]. Curcumin boosts serotonin and dopamine, both of which improve mood. Studies found that curcumin can improve

symptoms of depression and anxiety [47]. Curcumin also helps new brain cells grow and Boosts Brain Derived Neurotrophic Factor (BDNF) [48]. It may help delay age-related mental decline. Notably, most studies use highly concentrated curcumin supplements at doses ranging from 500-2000mg per day, which is far more curcumin than most people consume when using turmeric as a spice [49]. This is because turmeric only consists of about 3-6% curcumin. So, while adding turmeric to food may be beneficial, supplementing with curcumin is necessary.

As good foods have benefits for strengthening the brain, there are foods that negatively affect brain health and lead to a deterioration, even in the presence of beneficial foods. Similar to the negative effect of processed foods, sugary drinks can cause weight gain without providing essential nutrients and beneficial calories. Excess sugar can damage memory and brain functions [50,51]. In fact, sugary drinks are also linked to Alzheimer's disease and dementia [52]. Sugary drinks such as soda, energy drinks, and fruit juices should be avoided to enhance memory and keep the brain healthy [53]. Many processed foods, including potato chips, some types of meat and sweets, should be listed as harmful food products that fill the stomach without benefiting the body and potentially harming organs. Consuming a lot of processed foods can lead to weight gain as well as damage to brain tissue. Therefore, eating a lot of foods that are full of salt and sodium can impede blood flow to the brain, affecting skills and memory. High salt intake can also lead to an electrolyte imbalance and dehydration, which is not beneficial for many brain functions [54]. According to several studies, it has been proven that saturated fats and foods rich in sugar can have a negative impact on cognitive skills and verbal memory [55].

It is well known that the brain is one of the most energy-consuming organs in the body, as glucose is the main source of this energy [56]. It was indicated that glucose metabolism provides the energy needed for its functions. The physiological process of the brain is through the production of Adenosine Triphosphate (ATP) compound, which is the main compound that maintains nerve and non-neuronal cells, in addition to the production of neurotransmitters [57]. Its metabolism in the body is critical to brain physiology, as the disorder of glucose metabolism in the brain includes many diseases that may affect the brain itself, and the rest of the body's organs [57]. It is worth noting that glucose is widely available in complex carbohydrates, which are one of its best sources, due to its contribution to slowly releasing energy, and helping the brain to work in a stable manner, this type of carbohydrate is found in starchy foods and whole meal or whole grains [58]. Some research suggests that high sugar consumption causes inflammation in the brain that leads to memory difficulties [58]. When the brain is exposed to an excessive amount of sugar in the daily diet, addiction-like effects occur in the human brain, leading to overeating and weight gain and elicit more intense feelings of hunger compared to foods low in sugar [56-58].

Studies in long-term diabetics have shown that repeated exposure to high levels of glucose reduces mental ability, leading to deficits in learning, memory, speed of movement, and other cognitive

functions. On the other hand, people without diabetes, higher sugar consumption is associated with lower scores on tests of cognitive function [59]. These effects are believed to be due to a combination of high blood sugar, high blood pressure, insulin resistance, and high cholesterol. Research shows that a diet rich in added sugar reduces the production of Brain-Derived Neurotrophic Factor (BDNF), a type of growth hormone that helps brain cells grow [60]. It is an essential chemical for new memory formation and learning [60,61]. Low levels of BDNF are also linked to dementia and Alzheimer's disease. As changes in BDNF expression are associated with both normal and pathological aging and also psychiatric disease [62]. BDNF interferes in brain structures that are important for memory processes such as the hippocampus and para-hippocampal areas [63]. In addition, BDNF promotes cell survival [64] and lead to great variability in BDNF levels in healthy subjects [65]. Accordingly, BDNF is considered as a dynamically regulated player in synaptic plasticity and memory [65]. BDNF also promotes neuronal survival and enhanced nerve transmission via long-term potentiation, this combination of neurogenesis and optimized neuronal functioning significantly improves cognitive performance and protects against neurodegenerative phenomena [66]. From the foregoing, it has become necessary to boost and stimulate BDNF with a catalyst it [67]. Things that can boost BDNF such as plants that are rich in polyphenols and other antioxidants are beneficial for raising BDNF levels [68]. Coffee and coffee berry supplements [68], vitamin D, consume a high-protein diet [69] and restrict carbohydrate intake [70]. Since a very-low-carb diet or ketogenic diet for some appears to increase brain BDNF levels [70]. Moreover, intermittent fasting or prolonged fast periods are a better choice for boosting BDNF which may be due to ketone production [71].

Lack of blood sugar control may increase the risk of Alzheimer's disease. Both amyloid- β (A β) protein toxicity processing and A β clearance are attributable to impaired insulin signaling. Insulin resistance mediates malfunction of bioenergetics and the progression to AD [72,73]. This strong relationship makes some researchers consider Alzheimer's disease or "brain diabetes" or so-called "type 3 diabetes"[74]. Therapeutic strategies related to insulin may succeed in developing Alzheimer's treatments in the future [74]. Evidence also supporting the hypothesis of an increased incidence of type 3 Diabetes Mellitus in the future [75].

What should also necessarily be mentioned regarding the problem of the world in 2020-2022 is the relationship of brain activity to human infections with the emerging virus "Covid-19". The crisis of the new Corona epidemic that has infected the whole world has forced the recruitment of researchers to decipher the mystery of this epidemic and its relationship to other diseases, as countries of the world are racing to contain it. Since most people infected with this virus are elderly, it has become necessary to search for the genetic or genetic link between Alzheimer's disease and the dangerous development of the Corona virus. More than a year after the outbreak of the Corona epidemic, the virus still surprised scientists, as new studies confirmed that there is a frightening similarity between encephalitis caused by Covid-19

and inflammation caused by Alzheimer's disease. Scientists have discovered that corona causes brain fog, memory loss, difficulty concentrating, hallucinations and headaches.

Although, the researchers found little evidence that the virus targets the brain directly, they discovered close network relationships between the virus and the genes/proteins associated with many neurodegenerative diseases, most notably Alzheimer's disease [76]. There are pathways in which "Covid-19" can lead to dementia-like diseases, such as Alzheimer's. There is a predisposition of Alzheimer's patients to infection, progression to severe Covid-19, and death from the viral disease. A recent study conducted showed that people with dementia, especially Alzheimer's disease, are at many more times to the risk of dying as a result of infection with the virus [77]. It identified mechanisms by which Covid-19 can lead to Alzheimer's disease-like dementia [78]. By an overlap between Covid-19 and brain changes common in Alzheimer's, which may inform risk management and therapeutic strategies for Covid-19-associated cognitive impairment. Surprisingly, brain scan most recently has shown brain damage linked to Covid-19 months after infection, and brain decline equivalent to the effect of up to a decade of normal aging [77]. As the changes were associated with cognitive decline as well [77]. The results are stark evidence of the virus' impact on the central nervous system. More research will be needed to understand whether the evidence reflects that coronavirus will exacerbate the global burden of dementia.

Summary

Regardless of age, the health of the human body has a significant impact on human mental abilities, mood, and overall brain health. Therefore, it is necessary to consider awareness of good nutrition as an urgent matter to overcome diseases, especially those that do not have a cure, and diseases related to the brain, a complex organ of the body. Fighting Alzheimer's disease is a major problem and an ongoing challenge for research. Despite the efforts, the challenge remains until treatment is reached. It is clear that the severity of the disease is related to age, chronic diseases, and the strength of the body's immunity. Thus, staying away from processed and refined foods that contain dyes and sweeteners, harmful substances that are not necessary for building the body or brain is important. It has also become necessary to pay attention to health, especially with the environmental changes and the spread of viruses that have infected the world today and killed millions of people. Determining how Covid-19 relates to neurological problems will be critical in developing effective preventive and therapeutic strategies to address the sudden rise in neurocognitive impairments that are expected to be seen in the near future. This confirms that more prevention as possible and raising the body's immunity is better than treatment. Food plays a key role in maintaining a healthy brain and can help improve brain function, which includes memory and focus, both short and long term. According to the above information, omega-3 fatty acids, vitamin B12, vitamin B6 and vitamin K are beneficial for the brain. The human body also needs antioxidants to protect brain cells from harmful free radicals. Important nutrients such as

omega-3 fatty acids, flavonoids and vitamin E & C are considered beneficial for brain health. The mentioned food substances also offer many additional benefits to the brain, they may slow age-related mental decline and help ward off Alzheimer's disease. There are still many natural and unprocessed foods which have not been mentioned in this review that helps prevent and fight diseases and strengthens the body's immunity without harming it. Aging, stress and uncontrolled diet lower BDNF levels, but brain health could be preserved by managing stress, exercising, and forming close relationships. Intensive education regarding carbohydrate and calorie counting and meal planning can be useful for individuals with an active lifestyle to effectively improve body glycemic control. Moreover, a healthy meal planning approach, emphasizing portion control and healthful food choices may be more suitable for older individuals with cognitive impairment or learning difficulties. Thus, our nutritional requirements vary at different stages of our life, and we need to adjust our nutritional intake according to our nutritional needs, age stage and stages of growth. This review comes as one of the efforts that urge and emphasize the need to fight Alzheimer's disease early and before symptoms appear by continuous attention to the quality and not the quantity of food at different stages of life.

References

1. Fan L, Li H, Zhuo J, Zhang Y, Wang J, et al. (2016) The human brainnetome atlas: A new brain atlas based on connective architecture. *Cereb Cortex* 26(8): 3508-3526.
2. Zanto TP, Gazzaley A (2019) Aging of the frontal lobe. *Handb Clin Neurol* 163: 369-389.
3. Polanía R, Nitsche MA, Ruff CC (2018) Studying and modifying brain function with non-invasive brain stimulation. *Nat Neurosci* 21(2): 174-187.
4. Conio B, Martino M, Magioncalda P, Escelsior A, Inglese M, et al. (2020) Opposite effects of dopamine and serotonin on resting-state networks: review and implications for psychiatric disorders. *Mol Psychiatry* 25(1): 82-93.
5. Masouleh SK, Plachta A, Hoffstaedter F, Eickhoff S, Genov S (2020) Characterizing the gradients of structural covariance in the human hippocampus. *Neuroimage* 218: 116972.
6. Serý O, Povová J, Míšek I, Pešák L, Janout V (2013) Molecular mechanisms of neuropathological changes in Alzheimer's disease: a review. *Folia Neuropathol* 51(1): 1-9.
7. Zhang H, Zheng Y (2019) [β Amyloid Hypothesis in Alzheimer's disease: pathogenesis, prevention, and management. *Zhongguo Yi Xue Ke Xue Yuan Xue Bao* 41(5): 702-708.
8. Tardy AL, Pouteau E, Marquez D, Yilmaz C, Scholey A (2020) Vitamins and minerals for energy, fatigue and cognition: a narrative review of the biochemical and clinical evidence. *Nutrients* 12(1): 228.
9. Briggs R, Kennelly SP, Neill D (2016) Drug treatments in Alzheimer's disease. *Clin Med (Lond)* 16(3): 247-253.
10. Meeusen R (2014) Exercise, nutrition and the brain. *Sports Med* 44(1): S47-56.
11. Petracci I, Gabbianelli R, Bordoni L (2020) The Role of Nutri(epi)genomics in Achieving the Body's Full Potential in Physical Activity. *Antioxidants (Basel)* 9(6): 498.
12. Chen C, Xun P, Kaufman JD, Hayden KM, Espeland MA, et al. (2020) Erythrocyte omega-3 index, ambient fine particle exposure, and brain aging. *Neurology* 95(8): e995-e1007.

13. Chang CY, Ke DS, Chen JY (2009) Essential fatty acids and human brain. *Acta Neurol Taiwan* 18(4): 231-241.
14. Fedorova I, Salem N (2006) Omega-3 fatty acids and rodent behavior: Prostaglandins Leukot Essent Fatty Acids 75(4-5): 271-289.
15. Sinclair AJ, Begg D, Mathai M, Weisinger RS (2007) Omega 3 fatty acids and the brain: review of studies in depression. *Asia Pac J Clin Nutr* 16(1): 391-397.
16. Innis SM (2007) Dietary (n-3) fatty acids and brain development. *J Nutr* 137(4): 855-859.
17. Cater RJ, Chua GL, Erramilli SK, Keener JE, Choy BC, et al. (2021) Structural basis of omega-3 fatty acid transport across the blood-brain barrier. *Nature* 595(7866): 315-319.
18. Volkow ND, Wang GJ, Logan J, Alexoff D, Fowler JS, et al. (2015) Caffeine increases striatal dopamine D2/D3 receptor availability in the human brain. *Transl Psychiatry* 5(4): e549.
19. Pasma WJ, Boessen R, Donner Y, Clabbers N, Boorsma A (2017) Effect of caffeine on attention and alertness measured in a home-setting, using web-based cognition tests. *JMIR Res Protoc* 6(9): e169.
20. Cunha RA, Agostinho PM (2010) Chronic caffeine consumption prevents memory disturbance in different animal models of memory decline. *J Alzheimers Dis* 20(1): S95-S116.
21. Eskelinen MH, Ngandu T, Tuomilehto J, Soininen H, Kivipelto M (2009) Midlife coffee and tea drinking and the risk of late-life dementia: a population-based CAIDE study. *J Alzheimers Dis* 16(1): 85-91.
22. Wierzejska R (2017) Can coffee consumption lower the risk of Alzheimer's disease and Parkinson's disease? A literature review. *Arch Med Sci* 13(3): 507-514.
23. Liu Y, Fly AD, Wang Z, Klaunig JE (2018) The Effects of Green Tea Extract on Working Memory in Healthy Women. *J Nutr Health Aging* 22(3): 446-450.
24. Ren T, Zheng P, Zhang K, Liao J, Xiong F, et al. (2021) Effects of GABA on the polyphenol accumulation and antioxidant activities in tea plants (*Camellia sinensis L.*) under heat-stress conditions. *Plant Physiol Biochem* 159: 363-371.
25. Kim S, Jo K, Hong KB, Han SH, Suh HJ (2019) GABA and l-theanine mixture decreases sleep latency and improves NREM sleep. *Pharm Biol* 57(1): 65-73.
26. Hinton T, Johnston GAR (2020) GABA-enriched teas as neuro-nutraceuticals. *Neurochem Int* 141: 104895.
27. felice m, renard j, hudson r, szkudlarek hj, pereira bj, et al. (2021) l-theanine prevents long-term affective and cognitive side effects of adolescent δ -9-tetrahydrocannabinol exposure and blocks associated molecular and neuronal abnormalities in the mesocorticolimbic circuitry. *J Neurosci* 41(4): 739-750.
28. Syamaladevi RM, Andrews PK, Davies NM, Walters T, Sablani SS (2012) Storage effects on anthocyanins, phenolics and antioxidant activity of thermally processed conventional and organic blueberries. *J Sci Food Agric* 92(4): 916-924.
29. Kalt W, Cassidy A, Howard LR, et al. (2020) Recent research on the health benefits of blueberries and their anthocyanins. *Adv Nutr* 11(2): 224-236.
30. Quinville BM, Deschenes NM, Ryckman AE, Walia JS (2021) A comprehensive review: Sphingolipid metabolism and implications of disruption in sphingolipid homeostasis. *Int J Mol Sci* 22(11): 5793.
31. Klomprens EA, Ding Y (2019) The neuroprotective mechanisms and effects of sulforaphane. *Brain Circ* 5(2): 74-83.
32. Chouet J, Ferland G, Féart C, Rolland Y, Presse N, et al. (2015) Dietary vitamin k intake is associated with cognition and behaviour among geriatric patients: The CLIP study. *Nutrients* 7(8): 6739-6750.
33. Cherasse Y, Urade Y (2017) Dietary zinc acts as a sleep modulator. *Int J Mol Sci* 18(11): 2334.
34. Serita T, Miyahara M, Tanimizu T, Takahashi S, Oishi S, et al. (2019) Dietary magnesium deficiency impairs hippocampus-dependent memories without changes in the spine density and morphology of hippocampal neurons in mice. *Brain Res Bull* 144: 149-157.
35. Bagheri S, Squitti R, Haertlé T, Siotto M, Saboury AA (2018) Role of copper in the onset of alzheimer's disease compared to other metals. *Front Aging Neurosci* 9: 446.
36. Carlson ES, Magid R, Petryk A, Georgieff MK (2008) Iron deficiency alters expression of genes implicated in Alzheimer disease pathogenesis. *Brain Res* 1237: 75-83.
37. Nehlig A (2013) The neuroprotective effects of cocoa flavanol and its influence on cognitive performance. *Br J Clin Pharmacol* 75(3): 716-727.
38. Krivanek TJ, Gale SA, McFeeley BM, Nicastrì CM, Daffner KR (2021) Promoting successful cognitive aging: A ten-year update. *J Alzheimers Dis* 81(3): 871-920.
39. Chauhan A, Chauhan V (2020) Beneficial effects of walnuts on cognition and brain health. *Nutrients* 12(2): 550.
40. Fata G, Weber P, Mohajeri MH (2014) Effects of vitamin E on cognitive performance during ageing and in Alzheimer's disease. *Nutrients* 6(12): 5453-5472.
41. Kocot J, Kocot DL, Kiełczykowska M, Musik I, Kurzepa J (2017) Does vitamin c influence neurodegenerative diseases and psychiatric disorders? *Nutrients* 9(7): 659.
42. Ma F, Zhou X, Li Q, Zhao J, Song A, et al. (2019) Effects of folic acid and vitamin B₁₂ alone and in combination on cognitive function and inflammatory factors in the elderly with mild cognitive impairment: a single-blind experimental design. *Curr Alzheimer Res* 16(7): 622-632.
43. Zeisel SH, Costa KA (2009) Choline: an essential nutrient for public health. *Nutr Rev* 67(11): 615-623.
44. Arulseelan, Palanisamy et al. (2016) Role of Antioxidants and Natural Products in Inflammation. *Oxidative Medicine and Cellular Longevity* 2016: 5276130.
45. Aggarwal BB, Harikumar KB (2009) Potential therapeutic effects of curcumin, the anti-inflammatory agent, against neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases. *Int J Biochem Cell Biol* 41(1): 40-59.
46. Münch G, Kuhla B, Lüth HJ, Arendt T, Robinson SR (2003) Anti-AGEing defences against Alzheimer's disease. *Biochem Soc Trans* 31(Pt 6):1397-1399.
47. Tahiana R, Bouazzaoui F, Kaladjian A (2020) Curcumin in depression: Potential mechanisms of action and current evidence-a narrative review. *Frontiers in psychiatry* 11: 572533.
48. Mishra S, Palanivelu K (2008) The effect of curcumin (turmeric) on Alzheimer's disease: An overview. *Ann Indian Acad Neurol* 11(1): 13-19.
49. Amalraj A, Pius A, Gopi S, Gopi S (2016) Biological activities of curcuminoids, other biomolecules from turmeric and their derivatives-A review. *J Tradit Complement Med* 7(2): 205-233.
50. Lennerz BS, Alsop DC, Holsen LM, Stern E, Rojas R, et al. (2013) Effects of dietary glycemic index on brain regions related to reward and craving in men. *Am J Clin Nutr* 98(3): 641-647.
51. Beilharz JE, Maniam J, Morris MJ (2016) Short-term exposure to a diet high in fat and sugar, or liquid sugar, selectively impairs hippocampal-dependent memory, with differential impacts on inflammation. *Behav Brain Res* 306: 1-7.
52. Molteni R, Barnard RJ, Ying Z, Roberts CK, Pinilla GF (2002) A high-fat, refined sugar diet reduces hippocampal brain-derived neurotrophic fac-

- tor, neuronal plasticity, and learning. *Neuroscience* 112(4): 803-814.
53. Knüppel A, Shipley MJ, Llewellyn CH, Brunner EJ (2017) Sugar intake from sweet food and beverages, common mental disorder and depression: prospective findings from the Whitehall II study. *Sci Rep* 7(1): 6287.
54. Lauriola M, Mangiacotti A, Onofrio GD, et al. (2018) Neurocognitive disorders and dehydration in older patients: clinical experience supports the hydro molecular hypothesis of dementia. *Nutrients* 10(5): 562.
55. Alonso AM, Woods SC, Pelchat M, Grigson PS, Stice E, et al. (2015) Food reward system: current perspectives and future research needs. *Nutr Rev* 73(5): 296-307.
56. Poulouse SM, Miller MG, Scott T, Hale B (2017) Nutritional factors affecting adult neurogenesis and cognitive function. *Adv Nutr* 8(6): 804-811.
57. Tran DMD, Westbrook RF (2017) A high-fat high-sugar diet-induced impairment in place-recognition memory is reversible and training-dependent. *Appetite* 110: 61-71.
58. Freeman CR, Zehra A, Ramirez V, Wiers CE, Volkow ND, et al. (2018) Impact of sugar on the body, brain, and behavior. *Front Biosci (Landmark Ed)* 23(12): 2255-2266.
59. Christopher TK, Seaquist ER (2008) Cognitive dysfunction and diabetes mellitus. *Endocrine reviews* 29(4): 494-511.
60. Huang EJ, Reichardt LF (2001) Neurotrophins: roles in neuronal development and function. *Annu Rev Neurosci* 24: 677-736.
61. Kowiański P, Lietzau G, Czuba E, Waśkow M, Steliga A, et al. (2018) BDNF: A key factor with multipotent impact on brain signaling and synaptic plasticity. *Cell Mol Neurobiol* 38(3): 579-593.
62. Ng TKS, Ho CSH, Tam WWS, Kua EH, Ho RC (2019) Decreased Serum Brain-Derived Neurotrophic Factor (BDNF) levels in patients with Alzheimer's Disease (AD): a systematic review and meta-analysis. *Int J Mol Sci* 20(2): 257.
63. Hofer M, Pagliusi SR, Hohn A, Leibrock J, Barde YA (1990) Regional distribution of brain-derived neurotrophic factor mRNA in the adult mouse brain. *EMBO J* 9(8): 2459-2464.
64. Volosin M, Song W, Almeida RD, Kaplan DR, Hempstead BL, et al. (2006) Interaction of survival and death signaling in basal forebrain neurons: roles of neurotrophins and proneurotrophins. *J Neurosci* 26(29): 7756-66.
65. Miranda M, Morici JF, Zononi MB, Bekinschtein P (2019) Brain-derived neurotrophic factor: A key molecule for memory in the healthy and the pathological brain. *Front Cell Neurosci* 13: 363.
66. Numakawa T, Odaka H, Adachi N (2017) Actions of brain-derived neurotrophic factor and glucocorticoid stress in neurogenesis. *Int J Mol Sci* 18(11): 2312.
67. Nagahara A, Tuszynski M (2011) Potential therapeutic uses of BDNF in neurological and psychiatric disorders. *Nat Rev Drug Discov* 10(3): 209-219.
68. Sangiovanni E, Brivio P, Agli MD, Calabrese F (2017) Botanicals as modulators of neuroplasticity: Focus on BDNF. *Neural Plast* 2017: 5965371.
69. Glenn JM, Madero EN, Bott NT (2019) Dietary protein and amino acid intake: links to the maintenance of cognitive health. *Nutrients* 11(6): 1315.
70. Gyorkos, Amy et al. (2019) Carbohydrate-restricted diet and exercise increase brain-derived neurotrophic factor and cognitive function: a randomized crossover trial. *Cureus* 11(9): e5604.
71. Mattson MP, Moehl K, Ghena N, Schmaedick M, Cheng A (2018) Intermittent metabolic switching, neuroplasticity and brain health. *Nat Rev Neurosci* 19(2): 63-80.
72. Nguyen TT, Ta QTH, Nguyen TTD, Le TT, Vo VG (2020) Role of insulin resistance in the Alzheimer's disease progression. *Neurochem Res* 45(7): 1481-1491.
73. Caberlotto L, Nguyen TP, Lauria M, Priami C, Rimondini R, et al. (2019) Cross-disease analysis of Alzheimer's disease and type-2 Diabetes highlights the role of autophagy in the pathophysiology of two highly comorbid diseases. *Sci Rep* 9: 3965.
74. Trang NT, Hoai QT, Nguyen TKO, Nguyen TTD, Giau VV (2020) Type 3 diabetes and its role implications in Alzheimer's disease. *International Journal of Molecular Sciences* 21(9): 3165.
75. Dolata AR, Piwowar A (2019) Neurometabolic evidence supporting the hypothesis of increased incidence of type 3 diabetes mellitus in the 21st Century. *Biomed Res Int* 2019: 1435276.
76. Zhou y, Jielin Xu, Hou Y, Leverenz JB, Kallianpur A, et al. (2021) Network medicine links SARS-CoV-2/COVID-19 infection to brain microvascular injury and neuroinflammation in dementia-like cognitive impairment. *BioRxiv*.
77. Douaud G, Lee S, Almagro FA, Arthofer C, Wang C, et al. (2022) SARS-CoV-2 is associated with changes in brain structure in UK Biobank. *Nature*.
78. Reiken S, Sittenfeld L, Dridi H, Liu Y, Liu X, et al. (2022) Alzheimer's-like signaling in brains of COVID-19 patients. *Alzheimers Dement*.