Influence Diet on Cognitive Function and Brain Health

[1]Chen Yuyu and [2]Changhui Zhou
[1,2]Chongqing Medical University, Yuzhong District, Chongqing 400016, P.R.China.
[1]yuyuchen16@160.com, [2]zhou25411@hotmail.com

Correspondence should be addressed to Chen Yuyu : yuyuchen16@160.com.

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Abstract – The functionality of an individual's brain is influenced by the interaction between various environmental factors, including diet, and genetic predispositions. The objective of diet in maintaining optimal brain function may significantly contribute to the treatment and prevention of mental health illness. Experimental models and epidemiological studies have provided evidence demonstrating that both the collective and specific constituents of the human diet exert an influence on brain function. This narrative review examines the five primary dimensions of brain function that have an impact on mental health and performance. The topics of interest include: (1) the development of the brain; (2) the networks and neurotransmitters involved in brain signaling; (3) memory and cognitive processes; (4) symmetry between protein synthesis and breakdown; and (5) the detrimental consequences resulting from persistent inflammatory processes.

Keywords – Central Nervous System, Cognitive Function, Brain Health, Memory and Cognitive Processes, Persistent Inflammatory Processes.

I. INTRODUCTION

The brain is a complex organ that regulates various facets of human existence, encompassing cognitive processes, recollections, affective states, tactile perception, motor abilities, visual acuity, respiratory functions, thermoregulation, appetite, and additional physiological functions. The central nervous system (CNS) integrates the spinal cord and the brain system. The average weight of an adult brain is approximately 3 pounds, with a composition consisting of approximately 60% fat [1]. The remainder is integrated of salts, carbohydrates, and protein. The brain does not consist of muscular tissue. The region in question contains both nerve cells, specifically glial cells and neurons, including blood arteries. The brain can be divided into two distinct components: white matter and gray matter. The outer region of the brain, known as the cortex, exhibits a darker shade, while the inner region, referred to as the white matter, displays a lighter hue. The white matter is situated in the periphery of the spinal cord, whereas the gray matter is situated in its interior (refer to **Fig 1**). The majority of gray matter is composed of neuron somas, which are spherical cell bodies. Conversely, white matter primarily consists of axons, which are long and thin projections that connect neurons to each other. These axons are enveloped in a protective covering called myelin. The presence of diverse neural components contributes to the observable variation in coloration on specific scans.

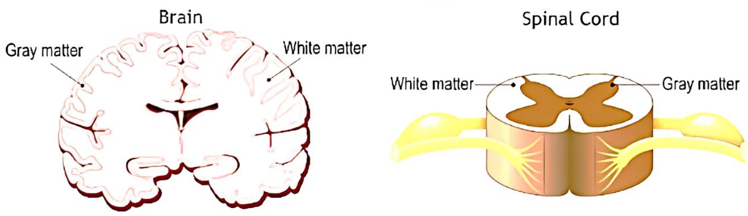

Fig 1. White and gray matter in the spinal cord and the brain

In this scholarly article, we offer a narrative review that focuses on the influence of diet on five key aspects of brain neurophysiology that have implications for mental well-being and cognitive function. Our approach differs from a systematic review that examines the specific findings of nutritional interventions researches pertaining to the development of the brain and the general brain health (refer to **Fig 2**). Various areas of study within neuroscience encompass brain signaling networks and neurotransmitters, cognition and memory, synaptic plasticity, proteostasis, and the detrimental consequences of chronic inflammatory processes, among others. The section pertaining to the increasing comprehension of the influence of nutrition on the epigenetic regulation of brain function draws to a close.

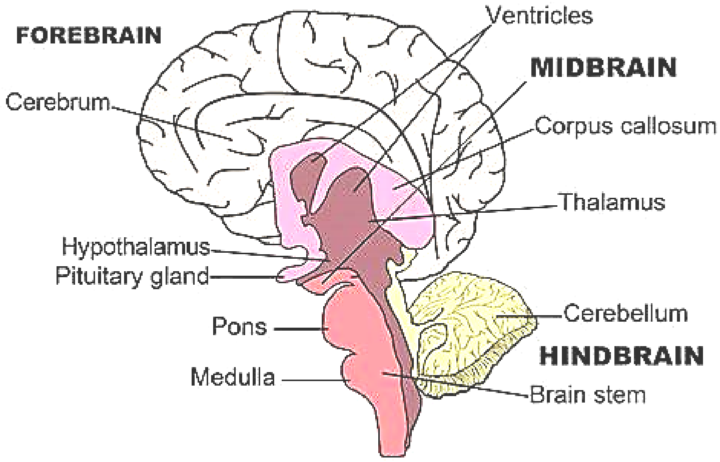

Fig 2. Various aspects of the brain functionality and structure influenced by balanced diet

The implementation of identical measures that contribute to robust and enduring physical well-being will similarly yield advantages for cognitive functioning, thus underscoring the significance of attending to both domains. The consumption of Western-style diet featured by more intake of saturated fats, polished carbohydrates, and foods with high caloric density, coupled with the habit of overeating, has been considered as a risk element for the decline of cognitive function and overall health. The diet type has been observed to have a direct impact on hippocampal volume that is a vital brain part integrated in memory and cognition in humans.

This paper provides a review of the benefit of diet on various aspects of brain development, including brain signaling networks, neurotransmitters, cognition and memory, protein synthesis and degradation balance, as well as the detrimental effects of chronic inflammatory processes on mental health and performance. The subsequent sections of the paper are organized as follows: Section II focusses on a review of neuroprotective benefit of particular diets. Section III discuss the effects of diets on the development of the brain system. Section IV reviews dietary impact on brain signaling networks, while Section V discusses dietary impact on cognition and memory. Section VI reflects on diet in the balance between protein degradation and formation. Section VII provides a conclusion to the article.

II. NEUROPROTECTIVE BENEFIT OF PARTICULAR DIETS: A REVIEW

In the conventional ketogenic diet, the fat to carbohydrate plus protein ratio is typically 3:1 or 4:1. This ratio results in approximately 80-90% of total calorie intake being derived from fats, while carbohydrates contribute around 4% and proteins contribute around 6% of total calories [2]. The implementation of dietary modifications to enhance acceptability and adherence is prevalent; however, it may pose challenges when attempting to directly compare results across different trials. Dietary modifications encompass alterations in the fat-to-carbohydrate ratio, modifications in the composition and amounts of macronutrients, and extension of the duration of the diet. Ketosis, which is marked by elevated concentrations of ketone bodies in the bloodstream, is the desired outcome of both conventional and modified ketogenic diets.

Ketone bodies refer to a collection of chemically interconnected, water-soluble compounds that are generated through the beta-oxidation of fatty acids as part of regular physiological metabolism. The most widely recognized ketone molecules are acetone, acetoacetate, and beta-hydroxybutyrate (BHB). The typical range for ketone bodies in the bloodstream is observed to be within the interval of 100 to 250 M. However, in instances of nutritional or physiological ketosis, it is not uncommon for these concentrations to elevate to a range of 0.5 to 5 mM. On the other hand, in the context of pathological ketoacidosis, it is observed that the levels of ketone bodies in the bloodstream can potentially rise to a range of 15-25 mM. Blood and urine ketone levels are frequently employed as a means of assessing adherence to a specific dietary regimen. Nevertheless, it is important to note that elevated ketone levels do not necessarily correlate with improved outcomes.

Ketogenesis: HMG-CoA synthase 2 (HMGCS2) catalyzes 2 acetyl-CoA molecule condensation, resulting in the formation of beta-hydroxy-methylglutaryl-CoA (HMG-CoA). Subsequently, HMG-CoA is metabolized into acetyl-CoA and acetoacetyl-CoA (ACA) via HMG-CoA lyase actions. The enzyme known as hydroxybutyrate dehydrogenase (BDH) facilitates the conversion of ACA to BHB, while acetone is generated through a spontaneous decarboxylation process (sp). The liver employs monocarboxylate transporters (MCT) to facilitate the entry of ACA and BHB into the bloodstream. The process of ketogenesis involves the cellular uptake of acetyl-CoA (ACA) and beta-hydroxybutyrate (BHB) via MCT transporters. Subsequently, these compounds undergo reconversion into acetyl-CoA within the mitochondria. The resulting acetyl-CoA molecules are then utilized in the Krebs cycle to produce GTP and ATP. Furthermore, BHB has the capacity to be converted into acetoacetate through BDG actions, adding to its roles in generating NADH for the electron transport chain.

When the body's supply of glucose becomes depleted, it undergoes a metabolic adaptation known as ketogenesis, wherein it utilizes ketone bodies as an alternative source of fuel. Glycolysis may be hindered by fasting, intense physical activity, or a diet characterized by a significant reduction in carbohydrate intake, such as a very low-carbohydrate diet (KD), resulting in the initiation of ketogenesis. Limited information is available regarding the comparative significance of extrahepatic ketogenesis, a metabolic process that takes place in the mitochondria of different neuronal cell types and the retinal pigment epithelium, in addition to liver hepatocytes. Dietary fatty acids undergo the process of beta-oxidation to generate acetyl-CoA, which subsequently undergoes enzymatic and cofactor-mediated transformations to form ketone bodies (as depicted in **Fig 3**).

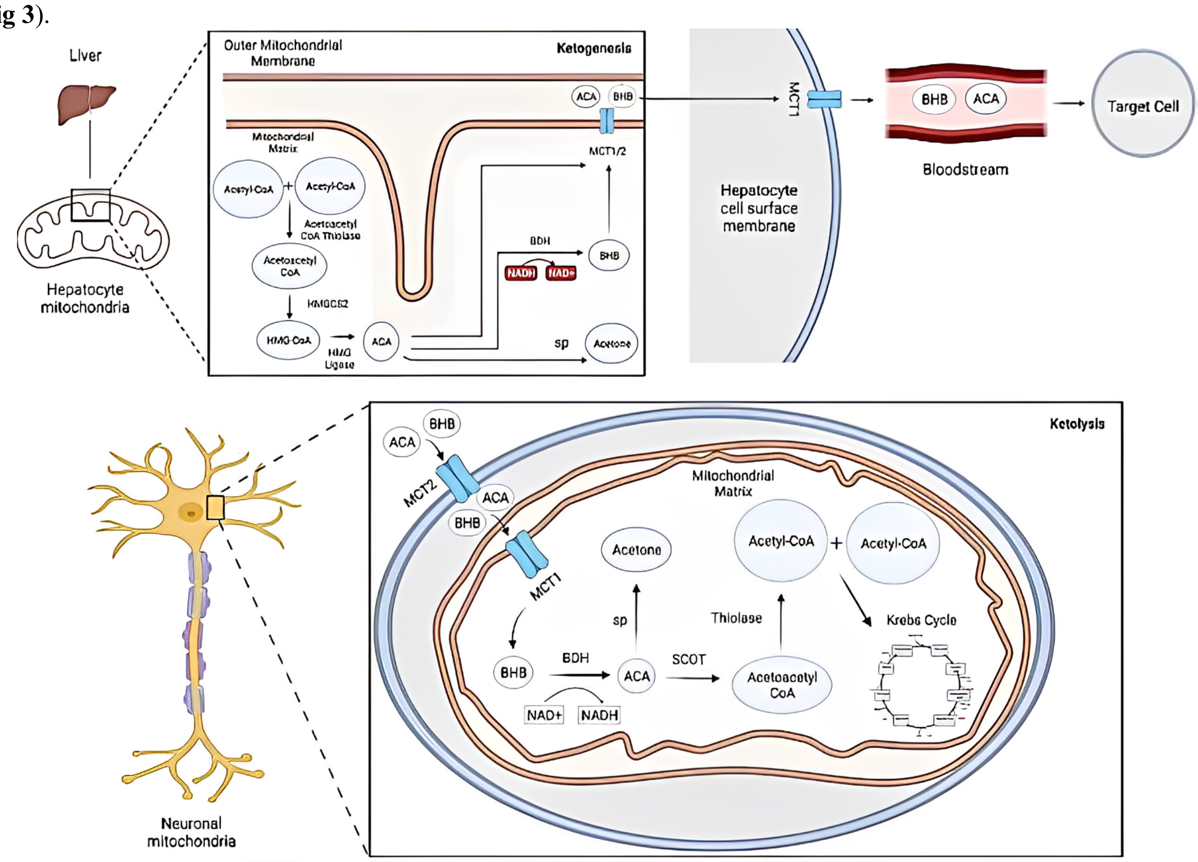

Fig 3. Metabolic pathways of ketone bodies

The enzyme HMG-CoA synthase 2 (HMGCS2) is a significant regulator of the rate of a biochemical reaction. It catalyzes the conversion of acetoacetyl-CoA, which is derived from two molecules of acetyl-CoA, into beta-hydroxy-methylglutaryl-CoA (HMG-CoA) by reacting with an additional molecule of acetyl-CoA. The enzymatic process facilitated by HMG-CoA lyase involves the conversion of HMG-CoA into acetyl-CoA and ACA. In a reversible manner, the conversion of ACA to BHB is facilitated by the combined action of -hydroxybutyrate dehydrogenase, which catalyzes NADH oxidation, or through spontaneous decarboxylation. In order to provide energy to the brain and other organs during the process of ketolysis, the liver transports acetoacetate (ACA) and beta-hydroxybutyrate (BHB) into the bloodstream through the utilization of monocarboxylate transporters (MCT).

Giacosa, Merlo, Filiberti, Visconti,Hill, and Gerber for the ECP Mediterranean Diet Group [3] conducted an analysis of futuristic cohort researches, which reviewed the effects of Mediterranean diet adherence on various health outcomes, such as stroke and impairment of mild cognition. The findings of this analysis revealed a vital linkage between Mediterranean diet adherence and minimizes cognitive decline risks. The diet is distinguished by its emphasis on consuming substantial amounts of monounsaturated fat, predominantly found in olive oil, as well as vegetables, fruits, whole grains, fish, and plant proteins. Conversely, it involves a comparatively limited consumption of sweets, refined grains, and red meat. The activation of the gut-brain axis could potentially be facilitated by adherence to the Mediterranean diet, thereby demonstrating its potential efficacy as an antidepressant. The Dietary Approaches to Stop Hypertension (DASH) diet is a dietary regimen characterized by reduced sodium intake, with a primary focus on consuming a diverse range of fresh fruits and vegetables, whole grains, and beneficial fats such as olive oil, canola oil, and avocados. According to Manta et al. [4], individuals who adhered to the DASH diet over an extended period of time exhibited enhanced overall cognitive performance.

In a study conducted by Filippou et al. [5], the researchers assessed the effects of the Mediterranean-DASH Interventions for MIND (Neurodegenerative Delays) diets on neurodegenerative interval. The diet score employed in the study incorporated particular diet elements, which have earlier been indicated to have neuroprotective properties. The study revealed a negative correlation between the dietary score and the rate of decline in overall cognitive ability. The rate of decline in cognitive function for individuals in the highest tertile of MIND diet scores was found to be equivalent to that of individuals who were 7.5 years younger than those in the bottom tertile. In their study, Coelho-Júnior, Trichopoulou, and Panza [6] performed a cross-sectional analysis to examine the interlinkage between the MIND diet, Mediterranean diet, and the cognitive functionality in representative elderly populations of the United States. A comprehensive evaluation of global cognitive performance was conducted utilizing a standardized measure of test performance. This study found that a strong commitment to following the MIND diets and Mediterranean diets were interlinked with advanced cognitive functionality and a minimized probability of cognitive impairments in a sizable and representative group of elderly individuals.

Research conducted on animals has demonstrated that the implementation of calorie restriction has been associated with enhancements in cognitive performance. A recent study on human intervention revealed that implementing a calorie-restricted diet, resulting in weight loss, yielded improvements in recognition memory and was accompanied by an increase in gray-matter volume among obese women. These findings were compared to a control group that did not undergo any dietary modifications. The ketogenic diet, also referred to as a low carbohydrate diet, has garnered significant attention as a strategy for achieving short-term and rapid weight loss. A recent review of data derived from both animal and human subjects has substantiated the cognitive advantages associated with these dietary regimens.

III. EFFECT OF DIETS ON BRAIN DEVELOPMENT

In the earlier phase of brain development, precursor cells give rise to both neuronal and glial cells, which are crucial for proper brain functioning. These cells undergo a process of migration to reach their respective mature locations within the brain. During the period spanning from one to two years of age, there is a significant proliferation of neurons in the brain, accompanied by the attainment of the highest level of synapse development. Microglia are involved in a phenomenon known as synaptic pruning, wherein they eliminate superfluous synapses and cells. The production of the myelin sheath represents the final stage in the maturation process of the embryonic brain. The presence of this insulating layer facilitates efficient and expedited transmission of signals. The ongoing functionality of stem cell in the CNS persists into adulthood, as they differentiate in glial or neural cells and reposition to the grey or white matter regions of the brain.

The process of neurulation commences on approximately the 22nd day of embryonic development, wherein the neural plate undergoes invagination, resulting in the establishment of neural tubes that will definitely produce the spinal cord and the brain. The enhancement of the neural plate and neural tube is subject to the influence of various nutrients, such as folic acid, copper, and vitamin A. Consequently, it is of utmost importance to maintain a nutritious diet from the earliest stages of development. Around the seventh week of development, the neural tube undergoes division, resulting in the formation of nerve cells, also known as neurons, as well as glial cells, which are responsible for supporting and assisting neurons. After the formation of a neuron, it undergoes migration to its appropriate position within the brain and subsequently initiates the process of cellular extension through the growth of axons and dendrites. Synapses are the anatomical structures formed by the branching projections of neurons, which establish connections with other cells. These specialized junctions play a vital role in facilitating the transmission of nerve impulses.

The process of brain development encompasses the period from conception to infancy. Neurons collaborate in order to form networks, and these networks can be refined through the deliberate elimination of cells and their synaptic connections. During the early stages of infancy and adolescence, it has been observed that a significant proportion of newly generated cells in the brain undergo a process of elimination, resulting in a reduction of nearly 50% in their overall population. The phenomenon of excessive synapse production is concomitant with the process of selectively eliminating synapses. The environmental context in which a child is situated contributes to the acquisition of essential stimuli that facilitate the maturation of intricate neural connections within the brain. The maintenance and strengthening of activated cells and connections is prioritized, while dormant ones undergo pruning. Neurogenesis is a fundamental mechanism by which the brain exhibits plasticity, enabling it to undergo modifications and recover from injuries, thereby facilitating adaptation to the environment.

The significance of lips for brain function and structure

Lipids within the human body perform pivotal functions in numerous biological processes, encompassing the generation of vesicles, ion fluxes regulation, creation of critical microenvironment for cell communication, and signaling feedback and pathways initiation. Docosahexaenoic acid (DHA; 22:6n-3) [7] and Arachidonic acid (20:4n-6) [8] constitute approximately 50% of the composition of fatty acid within the brain. The administration of 42 DHA has been shown to promote neuronal differentiation and influence gene expression in the brain. Additionally, it plays a regulatory role in the functioning of glutamatergic synapses, which are associated with plasticity and cognitive capacity.

While astrocytes have the capacity to synthesize a certain amount of arachidonic acid and DHA from n-6 and n-3 precursors, it is important to note that the brain primarily relies on dietary sources for the majority of fatty acids. Maternal consumption of PUFA (polyunsaturated fatty acids) has an impact on the proliferation of hippocampal cells in fetuses and infants. The composition of brain lipids may serve as an indicator of the lipid profile in food and plasma, as evidenced by

McNamara, Able, Jandacek, Rider, and Tso [9] conducted on a sample size of 48 individuals, including both humans and animals. A polar lipid (Phosphatidylserine) is available in the neuronal membrane and serves a vital function in the transmission and reception of neural impulses. Phosphatidylserine is a dietary supplement that has been suggested to potentially enhance cognitive function and improve memory retention.

Gangliosides, a specific class of glycosphingolipids, are present in substantial quantities in that location. Gangliosides play a crucial role in facilitating the recognition of cell-to-cell, cell motility, cell adhesion, and cell proliferation. The concentrations of gangliosides higher in colostrum and slowly diminish as milk progresses to more mature stages in both human and bovine lactation. Infants who receive supplementary intricate milk lipids demonstrate enhanced brain development and synaptic plasticity. Gangliosides encompass sialic acid, an indispensable structural constituent of the brain that exerts influence on cognitive processes such as learning and memory. The administration of human milk oligosaccharides as a prebiotic during infancy has the potential to facilitate the development of beneficial gut microbiota. This, in turn, has been suggested to have a positive impact on cognitive maturation.

Brain Development and Micronutrients

The impact of inadequate nutrition on a person's long-term mental well-being and cognitive development is significant and often irreversible during the crucial stages of early life. In this discourse, we examine the latest pre-clinical and human proof pertaining to the influence of dietary factors on neurocognitive developments in typically developing children and infants within the age range of 0 to 59 months. Our focus is particularly directed towards the exploration of emerging nutrients.

During the fourth week of gestation, the process of neural tube closure occurs, accompanied by the initiation of neuron growth within the germinal layers that surround the ventricles. This marks the commencement of human brain development. The subsequent stage involves the neurons migration to its destination and commencing the process of differentiation into distinct neuronal subtypes. During the period of late gestation to early postnatal life, neurons undergo a crucial biological process referred to as neuronal differentiation. This process encompasses various intricate steps, including the creation of axons and dendrites, neurotransmitters synthesis, the creation of intracellular signaling system and synapses, the establishment of complex neural membranes. While the process of synapse formation continues until late adulthood, the synthesis of neurotransmitters initiates prior to birth and reaches its highest point during the third year of life. Concurrently, the initiation of glial cell creation starts in the 2^{nd} gestation trimester, specifically at 32 weeks. Glial cells serve the purpose of enveloping axons with membranous myelin sheath, a procedure known as axonal myelination. This particular developmental process primarily happens during the 2^{nd} gestation trimester and extends into the initial year of life. The process of myelination lingers throughout the lifespan, although it begins to diminish during early adulthood and definitely stops at age 40.

The process of brain structure formation encompasses distinct stages. The transient cerebral structure responsible for regulating behavior during the prenatal and neonatal stages undergoes a transition to the cortical plate at approximately 3-4 months of age. Goal-oriented motor behaviors, such as reaching, have superseded the previously observed aimless general motions. The development of the hippocampus, which plays a vital role in spatial memory, initiates at 32 weeks of gestation and undergoes further growth for a minimum duration of 18 months after birth. During the initial half-year of an individual's life, there is rapid development observed in the prefrontal cortex, a region responsible for intricate cognitive functions such as attention and multitasking. It is important to note that the maturation process of the prefrontal cortex extends into the 3^{rd} life decade. The process of axon and synaptic pruning, which enhances brain functionality, typically initiates during the period spanning from adolescence to early adulthood.

Numerous factors, encompassing pregnancy age during delivery, nutrition, social environment, exert influence on the developmental trajectory of a child's brain. The essential PUFAs linoleic acids, arachidonic acids and docosahexanoic acids are of vital significant in enhancing the development of the brain and the myelination of neurons in infants. The influence of long-chain polyunsaturated fatty acids (LCPUFAs) on neurotransmitter synthesis has been demonstrated by Rifkin et al. [10]. Specifically, LCPUFAs have been found to have an impact on the synthesis of GABA (gamma-aminobutyric acid) ergic, cholinergic and monoaminergic systems. The development of the prefrontal cortex, responsible for attention, inhibition, and impulsivity, is notably reliant on docosahexaenoic acid (DHA).

Maintaining an optimal balance between LA and ALA is crucial for overall health, alongside ensuring an adequate intake of both through dietary sources or supplementation. The study conducted by Kim, Kim, Lee, Kim, Ha, and Chang [11] integrated 960 pregnant women and examined the relationship between the ALA/LA ratio during gestation, and the Psychomotor Developmental Index (PDI) and the Mental Developmental Index (MDI) scores of offspring at 6 months of age. The findings of the study revealed negative correlations between the LA/ALA ratio and the MDI and PDI scores in the offspring. In general, the ALA/LA ratio observed in this group was 11.10 to 6.9.

IV. DIETARY IMPACT ON BRAIN SIGNALING NETWORKS

Depression, sleep, anxiety, arousal, pain perception, and wakefulness are among the various mental and emotional states that have been linked to specific brain functional networks. The interaction between axons and dendrites results in the production of neurotransmitters (NTs), which play a significant role in modulating neuronal communication. The brain contains a diverse array of neurotransmitters (NTs) as well as other signaling elements. These integrate amino acids such as γ-aminobutyric acid, glycine, and glutamate. Catecholamines such as norepinephrine, and dopamine, including monoamines such as acetylcholine and serotonin, are also present. Additionally, biogenic amines like histamine, tryptamine, and tyramine, along with various peptides, purines like adenosine, and nitric oxide contribute to the signaling repertoire in the brain. Restoring a healthy equilibrium between neurotransmitter synthesis, uptake, and regeneration is a key objective in the treatment of neuropsychiatric disorders.

The production and impact of neurotransmitters (NTs) can be influenced by various dietary factors. The production of serotonin is extracted from amino acid tryptophan, therefore ensuring an adequate dietary intake of tryptophan may have an impact on serotonin levels. Both dopamine and norepinephrine share tyrosine as a precursor amino acid. Research studies have demonstrated that the administration of tyrosine supplements can enhance cognitive function, particularly in high-stress situations. Histamine and tyramine are biogenic amines that are present in fermented or preserved foods. These compounds function as active neurotransmitters by selectively binding to particular brain receptors.

Depression and diet

Currently, the most prevalent mental illnesses globally are obsessive-compulsive disorder (OCD), schizophrenia, bipolar disorder, and depression. The food consumption patterns of individuals in numerous American and Asian nations indicate a prevalent deficiency in various essential nutrients, such as vital vitamins, minerals, and omega-3 fatty acids, within the general population. Individuals suffering from mental health disorders frequently exhibit pronounced inadequacies in these essential nutrients, thereby constituting a noteworthy facet of their dietary requirements. Barrea et al. [12] have demonstrated the potential utility of daily supplementation of essential nutrients in reducing symptoms among patients.

According to [13], there have been reports suggesting that amino acid supplements can have potential therapeutic effects in the depression treatment and other mental health disorders due to their conversion into neurotransmitters. There is an increasing body of evidence suggesting that the utilization of dietary supplementation and therapy may serve as a valuable therapeutic intervention. These interventions possess the capacity to be beneficial in the management and potential prevention of various conditions, such as depression, bipolar disorder, schizophrenia, bulimia, panic attacks, attention deficit hyperactivity disorder/attention deficit disorder (ADHD/ADD), autism, and substance abuse. Antidepressants, which are widely prescribed medications, represent a single category of prescription drugs that may potentially elicit adverse effects.

Consequently, patients frequently neglect to adhere to their prescribed medication regimen. Psychologists and psychiatrists frequently encounter significant opposition towards therapeutic interventions. It is imperative to consider that individuals with mental health conditions who exhibit resistance towards adhering to treatment protocols face an elevated risk of experiencing suicide or involuntary admission to psychiatric facilities. The patient's life may be at risk due to drug toxicity, which can occur as a result of prolonged or escalated dosing. The comprehension of alternative and complementary nutritional therapy has the potential to assist psychiatrists in addressing patients' reluctance towards conventional treatment. Psychiatrists have the ability to suggest appropriate doses of dietary supplements by drawing upon established and contemporary studies that have demonstrated their effectiveness. Subsequently, these doses can be modified based on careful monitoring of the patient's response. However, further research is required to ascertain the optimal recommended doses for various nutritional supplements, particularly in relation to specific nutrients. A noteworthy observation regarding the dietary habits of individuals experiencing depression is that their nutritional intake is significantly insufficient.

Depression is typified by a pervasive reduction in motivation towards previously pleasurable activities, accompanied by escalating feelings of sadness and anxiety. The potential consequences of this condition may exhibit variability and could necessitate timely therapeutic intervention. Antidepressant medications and psychotherapy are frequently employed as therapeutic interventions for individuals diagnosed with depression, owing to the elevated susceptibility to suicidal ideation associated with this condition. Depressive disorders have been linked to serotonin deficiencies, gamma-aminobutyric acid (GABA), noradrenaline, and dopamine. Uneyama, Kobayashi, and Tonouchi [14] have demonstrated the potential efficacy of particular amino acids such as methionine, phenylalanine, tyrosine, and tryptophan, in the treatment of various mood disorders, such as depression. The conversion of tryptophan to serotonin typically occurs when it is ingested in isolation and on an empty stomach, as evidenced by Roth, Zadeh, Vekariya, Ge, and Mohamadzadeh [15]. Tryptophan has been suggested to potentially facilitate relaxation and promote sleep onset. This proposition implies that the amelioration of depression resulting from low serotonin levels may be achieved through the augmentation of serotonin levels. Dopamine and norepinephrine are produced from precursor amino acid tyrosine, in exceptional instances, phenylalanine.

Phenylalanine and tyrosine, constituents of various dietary supplements, have been recognized for their capacity to enhance cognitive and physical vigilance. The synthesis of S-adenosylmethionine (SAM) occurs through the enzymatic combination of methionine and adenosine triphosphate (ATP) within the brain. Further investigation is required to elucidate the optimal daily dosages of neurochemicals, which may have been taken to stimulate antidepressant impacts, considering the existing paradigm. There has been an observed increase in the incidence of severe depression, which researchers attribute, at least in part, to a reduction in omega-3 fatty acid consumption from fish as well as other dietary sources. The antidepressant effects of both docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) that are both fish oil omega-3 fatty acids, have been demonstrated in human studies.

Multiple theoretical frameworks have been proposed to elucidate the mechanisms underlying this process, with a significant proportion of these models incorporating the involvement of neurotransmitters. For example, it has been observed that EPA has the potential to undergo bioconversion, resulting in the production of leukotrienes, prostaglandins, and various other brain chemicals that are essential for eliciting antidepressant effects. Certain researchers posit that the impact of EPA and DHA on neuronal signal transduction is mediated through the modulation of calcium, sodium, and potassium ion channels, as well as peroxisome proliferator-activated receptors (PPAR) activation. Irrespective of the circumstances, empirical data derived from epidemiological and clinical trials consistently boost the effectiveness of omega-3 fatty acid as a therapeutic intervention for depression.

Daily consumption of supplements of omega-3 fatty acid, specifically those containing 1.5-2 g of eicosapentaenoic acid (EPA), has been shown to have a positive impact on the emotional well-being of individuals experiencing depression, leading to an improvement in mood. There is currently insufficient proof to effectively boost the effectiveness of omega-3 fatty acid doses exceeding 3 grams (g) compared to a placebo. Moreover, in specific circumstances, such as concurrent use with anti-clotting medications, higher doses of omega-3 fatty acids may potentially yield adverse effects. There is evidence suggesting that deficiencies in vitamin B (folate), magnesium, and omega-3 fatty acids, are associated with an elevated susceptibility to depression.

Wakefulness and sleep

Sleep plays a critical role physiological process of restoration due to the brain's continuous processing of novel information. In order to sustain typical cerebral functioning, it is imperative for gamma-aminobutyric acid (GABA) to effectively modulate the equilibrium between inhibitory and excitatory neurotransmission, particularly in relation to the excitatory neurotransmitter glutamate. Melatonin, scientifically referred to as N-acetyl-5-methoxytryptamine, plays a crucial role in modulating the body's circadian rhythms, encompassing the regulation of sleep and wakefulness. Upon the descent of the sun, the human body initiates the secretion of melatonin, a hormone that induces drowsiness and facilitates a decrease in body temperature. Various types of food, including animal-based products such as milk, eggs, fish and meat, as well as plant-centered foods such as vegetables, fruits, and cereals, contain melatonin or its precursor, tryptophan. This observation implies that an individual's dietary choices could potentially influence the levels of melatonin in their brain.

Vitamins B and C have been associated with enhanced sleep quality, as evidenced by scientific research. The potential benefits of Vitamin B12 on sleep quality, the role of Vitamin B3 (niacin) in promoting the conversion of tryptophan to serotonin and melatonin, and the essentiality of Vitamin B6 in the conversion of tryptophan to serotonin have been reported. The regulation of the circadian rhythm, which governs the body's 24-hour clock, may potentially be influenced by vitamin D, thereby impacting gene expression. The sedative properties of Valerian (Valeriana officinalis) have been recognized since the 18^{th} century, rendering it the prevailing herbal remedy for insomnia. The anxiolytic and sedative properties of chamomile (Matricaria chamomilla) are attributed to its ability to modulate GABAA receptors in the central nervous system, resembling the pharmacological action of benzodiazepines. Consequently, chamomile has gained significant popularity as a therapeutic option for individuals suffering from anxiety and sleep disorders. Additional herbs that exhibit comparable effects on both the physiological and cognitive aspects of the human body include Passiflora incarnate (passionflower) and Melissa officinalis (lemon balm).

Narcolepsy (sleep disorder) is characterized by a deficiency in the neuropeptides orexin A and B, which are synthesized in the hypothalamic region responsible for regulating feeding. The potential influence of the composition of amino acid of food on the activation of orexin signaling is worth considering. Histamine, a biogenic amine present in numerous food sources, is considered to have a vital role to play in regulating sleep-wake cycles. Adenosine, a metabolite resulting from the degradation of adenosine triphosphate (ATP) and adenosine diphosphate (ADP), serves as an indicator of energy depletion through its interaction with specific receptors. The brain produces it continuously during the course of the day, and its increasing levels induce drowsiness by inhibiting the transmission of acetylcholine. Theophylline and caffeine function as antagonists of adenosine receptors. The indirect influence of caffeine on dopamine additionally enhances attention and increases activity. Nevertheless, previous research has indicated that the consumption of caffeine leads to vasoconstriction, resulting in a decrease in cerebral blood flow and the availability of oxygen to the brain.

Dopamine and norepinephrine are recognized as neurotransmitters (NTs) within the human body. It has been suggested that consuming foods capable of inhibiting the enzyme catechol-O-methyl transferase could potentially enhance one's state of alertness. Mangiferin, which is present in mangoes (Mangifera indica), serves as an illustrative instance.

Pain

The pain response is primarily triggered by detrimental stimuli, such as tissue damage or inflammation. The regulation of pain is achieved through the counteractive actions of endocannabinoids and endorphins on pain signals. Palmitoylethanolamide and oleoylethanolamide, two additional analgesic agonists, are synthesized endogenously but may also be needed from different sources of diet like egg yolk. Caffeine has the potential to alleviate pain in specific individuals due to its function as a glycine receptor antagonist. The analgesic effects are believed to be modulated by glycine receptor and GABA systems, whereas taurine, a sulfonic α-amino acid, is purportedly present in the majority of animal species. Taurine is primarily obtained through source of diet such as meat and fish, and is consequently stored within the liver due to a decrease in endogenous production as individuals age. Phenylethylamine, a chemical compound present in chocolate, shares similarities with amphetamine and exerts inhibitory effects on the reuptake of the neurotransmitters dopamine, norepinephrine, and serotonin. Consequently, it exhibits notable analgesic properties.

The precursors of endocannabinoids, which are intrinsic compounds that function as ligands for cannabinoid receptors within the human body, consist of arachidonic acid and docosahexaenoic acid. Arachidonic acid has the potential to undergo enzymatic conversion, resulting in the creation of two different endocannabinoids, such as 2-arachidonoyl glycerol and anandamide. The available evidence indicates that endocannabinoids play a significant role in various physiological processes, encompassing motor function, brain development, memory, cognition, and pain regulation. DHA serves as a predecessor to synaptamide, alternatively referred to as N-docosahexaenoyl ethanolamine, and exhibits various noteworthy functions within the brain.

Hemp products derived from Cannabis sativa, commonly referred to as "CBD" products owing to their substantial cannabidiol concentration, are currently experiencing a surge in popularity as dietary supplements. According to reports, these products are purportedly efficacious in alleviating pain, reducing inflammation, and managing neurological disorders. Nevertheless, the legal status of these entities in numerous marketplaces remains indeterminate.

The gut-brain axis

The maintainability of glucose and energy equilibrium necessitates intricate and synchronized interactions between the CNS and the peripheral metabolic organs. The brain's capacity to monitor various physiological processes such as insulin release, food intake, energy utilization, glucose, and lipid metabolism, and hepatic glucose generation enables the achievement of this outcome. The regulation of neurogenesis in the hypothalamus may be influenced by hunger and satiety cues, leading to alterations in hypothalamic functioning. There is increasing evidence to suggest that the gut microbiome, environmental factors, host genetics, psychiatric disorders or mental health in later life unveil significant interactions. The creation of gut-brain axis via gut microbiota is of a vital significance during early development, particularly in preterm newborns.

There are two potential mechanisms through which the microbiota can communicate with the brain through gut-brain axis: direct signaling of the vagus nerve or the activation of receptors that are specifically designed to interact with intestinal and microbial metabolites. The potential association between immune system functioning, psychological stress, and gastrointestinal (GI) disorders such as inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS) can be elucidated by considering the bidirectional interaction between the gut microbiota and the central nervous system. The gut microbiota has a direct effect on the metabolism and availability of numerous neurotransmitters. The microbiota has been associated with mental health situations such as bipolar disorder, schizoaffective disorder, and depression.

Dietary fibers hold significance in relation to brain health due to various factors, one of which is their impact on the gut microbiota. According to a study conducted by Nyaradi, Li, Hickling, Foster, and Oddy [16], there appears to be positive correlations between the cognitive abilities of children and the ingesting of a diet rich in specific types of fiber diet. The creation of short-chain fatty acids butyrate occurs as a result of the fermentation process of fermentable dietary fiber. This particular fatty acid has been found to have advantageous impacts on brain health, either through inducing epigenetic changes within the brain or by considering particular receptors found in the gut. The inclusion of partly hydrolyzed guar gum in the meals of children with autism spectrum disorders has been demonstrated to enhance gut function, reduce serum inflammatory cytokine levels, and alleviate behavioral irritability.

There is a correlation between mood disorders and dietary factors, specifically the interaction between centrally-generated regulators of food arousal and intake, and signals of peripheral metabolism. Gastric inhibitory polypeptide, glucagon-like peptides, peptide YY, ghrelin, and cholecystokinin are a selection of gastrointestinal neuropeptides that exert their effects on the central nervous system. The orexigenic peptide known as galanin has the potential to decrease both dietary fat and alcohol intake. Conditions such as type 2 diabetes (T2D) and obesity have the ability to alter the secretion of peptide hormones. Consequently, these hormonal changes can influence brain function and mood by means of the gut-brain axis.

Proteins can be hydrolyzed through the utilization of chemical and enzymatic processes. Enzymes employed for the hydrolysis of proteins are frequently sourced from animal origins, such as pancreatin and pepsin, or derived from plant sources, including papain from papaya, ficin from fig, and bromelain from pineapple. Proteins undergo digestion through the action of proteolytic enzymes, resulting in the breakdown of these proteins into their individual amino acids and peptides of varying sizes. These enzymes catalyze the hydrolysis of proteins under conditions of optimal temperature and pH, often exhibiting specificity towards specific peptide cleavage bonds. Animal enzymes exhibit a higher degree of substrate selectivity compared to plant enzymes, as the latter possess a broader capacity to degrade a wider array of substrates. Proteolytic enzymes, such as pepsin, frequently target the phenylalanine or leucine bond.

The specificity of papain is relatively broad, as it has the ability to hydrolyze proteins at multiple amino acid residues. Pancreatin has the ability to hydrolyze linkages of tryptophan, arginine, tyrosine, leucine, phenylalanine, and lysine. Hydrolysis through fermentation, involving the production of proteolytic enzymes, takes place when proteins are subjected to incubation with microorganisms. Microbial proteases exhibit diverse enzymatic activities. Bacterial, algal, fungal, and yeast-derived proteases can be easily purified in significant quantities, rendering them highly suitable for utilization in various processing industries.

V. DIETARY INFLUENCE ON COGNITION AND MEMORY

In **Fig 4** illustrates that the cognitive and mnemonic functions of the brain are dependent on sensor receptors and processes that are presently lacking in comprehensive understanding. The phenomenon of long-term potentiation of synaptic activity has the potential to transform specific experiences into enduring memories, whereas long-term depression of synaptic activity can lead to the forgetting of memories. The concept of synaptic plasticity is of paramount importance in comprehending the functioning of the brain. Neurogenesis, the activity-based synaptic connections refinement, and the elimination of unnecessary synapses through pruning are the key mechanisms underlying neuronal plasticity. The arrangement of stimuli exerts an influence on the process of synaptogenesis. This phenomenon is associated with the formation of engrams, which are small-scale neural networks that are unique to individual memories. There exists a strong interconnection between cognitive performance and plasticity. Geng, Chen, Wang, and Wang [17] demonstrated that neuronal plasticity can be induced by various factors, including learning, novelty, dietary modifications, and engagement in aerobic activity.

The hippocampus refers to a segment of the brain that exhibits neurogenesis capabilities and is known to have significant involvement in the processes of learning, memory formation, and emotional regulation. Deficiencies in this domain are correlated with heightened manifestations of depression and anxiety, alongside a notable decline in cognitive performance. Glutamate serves as the primary excitatory neurotransmitter in neuronal cognitive networks. Studies have shown that the addition of magnesium ions (Mg2+) can enhance learning and memory. This is achieved by impeding the impacts of N-methyl-D-aspartate (NMDA) glutamate receptors coupled with calcium ion (Ca2+) channels. Consequently, this inhibition reduces neuronal hyperexcitability. Zinc cations (Zn2+) exhibit an affinity for NMDA receptors, leading to the activation of glutamate release. The presence of Zn2+ ions is significantly higher in the hippocampus and other regions of the brain, indicating that Zn2+ plays a vital role in maintaining proper brain functioning.

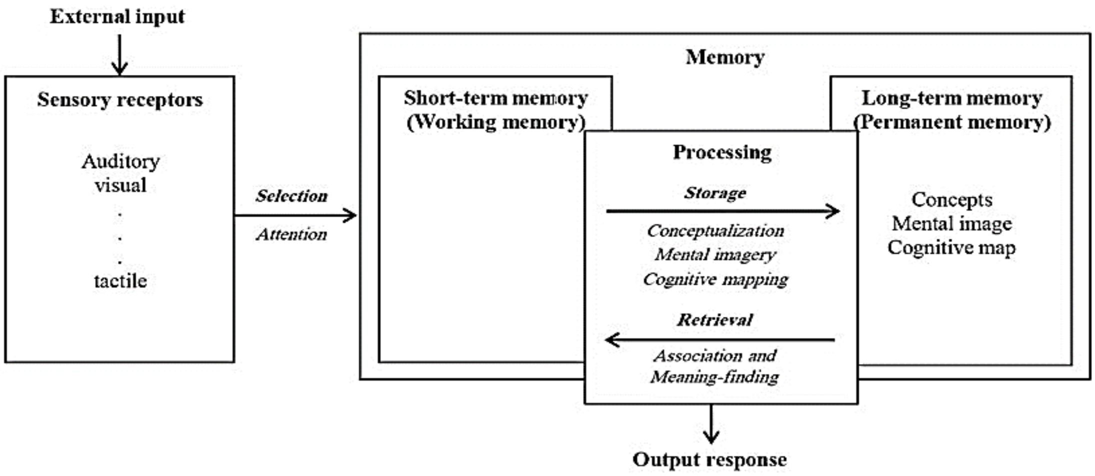

Fig 4. Cognitive memory processes

The blood-brain barriers play a critical role in maintaining a tightly controlled and safeguarded environment that is essential for the intricate signaling processes that take place within the brain. The pathophysiology of the aging brain exhibits suggestions of blood-brain barrier breakdown, as evidenced by the presence of albumin metabolites in the cerebrospinal fluids. Hence, implementing dietary interventions that promote the maintenance of the functional and structural blood-brain barrier integrity could potentially contribute to the preservation of cognitive abilities. Glucose serves as the principal energy substrate for optimal brain functioning. Factors that affect glucose absorption can have an impact on both long-term and short-term memory. The risk of developing dementia is positively correlated with advancing age, and there exists a significant association between various factors including glucose metabolism, mitochondrial function, and energy supply.

Enhancing the malleability of the hippocampus at both structural and functional levels, augmenting the production of neurotrophic factors, preserving synaptic efficacy, and promoting the generation of new neurons in adulthood are all mechanisms through which dietary and lifestyle interventions can potentially decelerate or potentially reverse the initiation of neurodegenerative disorders and the decline of cognitive abilities. Caloric restriction and intermittent fasting have emerged as two dietary interventions that have garnered considerable interest as potential catalysts for brain plasticity. Lifestyle interventions, such as implementing a diet with restricted calorie intake, engaging in weight reduction practices, and increasing levels of physical exercise, have been found to have enduring positive effects on cerebral blood flow.

The potential impact of Alzheimer's disease (AD) can potentially be alleviated through the utilization of specifically designed multicomponent diets, such as Souvenaid (Fortasyn Connect). These diets are specifically formulated to supply the brain with essential nutrients required for facilitating the amalgamation of novel synapses and maintainability of preexisting neural connections. The meal plan incorporates various essential nutrients, such as eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), uridine monophosphate (UMP), folate (folic acid), choline (COH), vitamins B6, C, B12, and E, as well as the phospholipids and minerals selenium. The therapeutic prospective of precursor compounds for prebiotic fibers and membrane phospholipids has been established in a murine framework of PD (Parkinson's disease).

The administration of n-3 PUFA as a supplement has been shown to potentially mitigate cognitive decline in older individuals who do not have dementia. Additionally, it may play a vital role in averting the commencement of age-based dementia and the accumulation of amyloid deposits, although the available evidence is inconclusive. Zhuang et al. [18]

revealed a significant correlation between elevated plasma degrees of docosahexaenoic acid and eicosapentaenoic acid and a reduced rate of cognitive decline among older adults. A 26-week randomized controlled experiment has yielded promising results in the utilization of magnetic resonance imaging. A meta-analysis by Kelaiditis, Gibson, and Dyall [19] yielded results suggesting that n-3 polyunsaturated fatty acids (PUFAs) do not exert an impact on cognitive decline. The association between n-3 PUFAs and fish consumption suggests that the consumption of whole fish may offer additional health advantages attributable to the presence of other advantageous constituents. Parvalbumin, a piscine protein, exhibits the potential to mitigate the synthesis of amyloid--synuclein, thereby potentially conferring protection against Parkinson's disease.

Medium-chain triglycerides (MCTs) are a lipid constituent of notable nutritional importance due to their rapid metabolism into ketones by the body, which can serve as an alternative energy source for the brain. Zhuang, Fujikura, Ohkura, Higo-Yamamoto, Mishima, and Oishi [20] have demonstrated that the administration of medium-chain triglycerides (MCTs) can enhance cognitive function in genetically modified mice specifically bred to develop Alzheimer's disease. A limited body of research has examined the impact of incorporating medium-chain triglycerides as a dietary supplement on cognitive performance.

Retinoic acid, which is a derivative of vitamin A, serves as a possible signaling element in the brain, governing processes like neuronal viability, neurogenesis, and synaptic plasticity. Further investigation is warranted, as current evidence does not substantiate the notion that the consumption of folic acid supplements, either alone or in conjunction with supplementary B vitamins, enhances cognitive function or serves as a preventive measure against dementia or Alzheimer's disease. The meta-analysis conducted on the effects of vitamin B and vitamin B12 elements for homocysteine reduction did not reveal any significant impact on cognitive capacity in the aging population. Al-Kuraishy et al. [21] observed a reduction in brain volume over a span of two years among elderly individuals with hyperhomocysteinemia, a condition associated with dementia. However, the administration of B vitamins, specifically folate and B12, was found to alleviate this brain volume loss.

VI. DIET IN THE BALANCE BETWEEN PROTEIN DEGRADATION AND FORMATION

The acquisition of essential nutrients and energy through the consumption of a balanced and nutritious diet is imperative for achieving and sustaining optimal physical performance, preventing illnesses, maintaining a healthy weight, and promoting mental well-being. Maintaining a healthy diet necessitates the consumption of a diverse array of foods while concurrently limiting the intake of added salt, sugar, and saturated fats. A well-balanced diet requires consideration of various nutritional requirements based on factors such as age, gender, and level of physical activity. It is recommended that each of the five food categories, in the recommended proportions, contribute significantly to the overall dietary intake. These meal options provide a comparable amount of essential micro- and macronutrients, encompassing a variety of food groups. The average composition of a healthy diet typically consists of approximately 50-60% carbohydrates, 12-20% protein, and 30-50% fat. In order to maintain optimal functionality, it is imperative that every organ and tissue within the human body receives the necessary nutrients and calories to sustain a healthy weight. The maintenance of optimal health and well-being in an individual is contingent upon the adoption of sound dietary habits, consistent engagement in physical activity, and the attainment and sustenance of a healthy body mass index.

The optimal composition and quantities of breakfast foods, lunch foods, snacks, and supper foods vary for each age group. Protein is the sole essential nutrient for muscle development and the synthesis of erythrocytes responsible for transporting oxygen and nutrients to muscular tissues. In order to uphold an individual's physical health and overall well-being, it is necessary to adhere to a dietary regimen that is abundant in high-quality carbohydrates, lean sources of protein, essential fats, and an adequate intake of water, alongside regular engagement in physical activity. In addition to weight management, the adoption of a healthy lifestyle offers supplementary advantages such as improved sleep quality and enhanced subjective well-being.

Regular physical exercise has been found to provide significant support for brain-related outcomes and functions. Making adjustments to one's dietary habits, such as augmenting physical activity, has the potential to facilitate rapid and efficient weight loss. Consuming the appropriate types of carbohydrates is of utmost importance. Simple carbohydrates, which are heavily relied upon by a significant portion of the population, are frequently derived from sugary and processed meals. Fruits and vegetables are rich sources of natural fibers, vitamins, minerals, and other essential components that are vital for proper bodily functioning. Moreover, these food items possess minimal caloric content and are devoid of any fat. In addition to serving as a source of energy, unsaturated fats have been found to potentially contribute to the reduction of inflammation.

The maintenance of proteostasis, which refers to the intricate balance between the synthesis, folding, and breakdown of proteins, plays a critical role in ensuring the optimal functioning of nerve cells and may undergo changes as individuals age. Numerous neurodegenerative disorders, like Parkinson's disease, Alzheimer's disease, Pick's disease, Huntington disease, and Lewy body and frontotemporal dementia, have been associated with the unfolded protein response. This response is initiated by the creation of misfolded proteins and aggregates within neuronal cells. The aggregation of proteins, such as the amyloid- precursor, into oligomers and polymers, has been observed to have negative brain function impacts. These proteins, which are known to have significant physiological obligations, such as GABA receptors binding, can impair normal brain function when they form larger structures. The lysosomal autophagy pathway and ubiquitin-proteasome model are conventionally employed for the purpose of effectively eliminating malfunctioning proteins. Chaperones, specifically those involved in the transportation of debris to lysosomes for degradation, are frequently observed to be overexpressed in the cerebral regions of individuals afflicted with mental disorders.

The current understanding is that the process of aging diminishes the cellular capacity to uphold proteostasis, thereby rendering the body more susceptible to degenerative ailments. Given that smaller aggregates and oligomers of misfolded protein have the potential to induce toxicity in nerve cells, the identification of substances capable of impeding oligomer formation or their interactions with cell membranes holds promise for delaying the degenerative impact on nerve cells. It has been suggested that EGCG, a compound present in green tea, exhibits such inhibitory properties. The association between optimal mitochondrial function and sufficient energy supply is closely tied to the maintenance of proteostasis. Insulin-based growth factor-1 plays a vital obligation in the energy brain metabolism. The regulation of mitochondrial metabolic capability is controlled by the insulin-based growth factor 1 (IGF-1) system of signaling. The IGF-1 breakdown product, known as cyclic glycineproline, plays a vital role in maintaining optimal brain function by modulating the signaling of IGF-1. Numerous clinical studies have demonstrated that the administration of black currant anthocyanins extract leads to an elevation in cyclic glycine-proline levels among individuals diagnosed with Parkinson's disease (PD).

Protein aggregates that induce neuronal disruption within the brain can potentially originate from various locations within the human body. Khalid, Petroianu, and Adem [22] have demonstrated that individuals with diabetes exhibit elevated levels of AGE (advanced glycation end-products) and their corresponding receptor, which facilitates the infiltration of amyloid oligomers from the peripheral brain regions. The initial identification of the Alzheimer's disease may be facilitated by observing the limitation of cerebral flow of blood that is influenced by the effect of pericytes amyloid oligomers that encompass cerebral blood vessels. The AMP-stimulated kinase signaling system was recognized as a crucial mechanism, linked to transitions in proteostasis and autophagy, in a systems biology-driven study of the cell regulations of the process, which contribute to dementia and cognitive decline. The utilization of dietary components that activate AMPK may potentially mitigate the risk of cardiovascular disease and type 2 diabetes, as AMPK serves a pivotal role in cellular energy sensing, including within brain cells. Several neurodegenerative disorders, like Huntington's disease and Alzheimer's, Parkinson's, have been allied to malfunction and abnormal activation of AMPK. This suggests that targeting this pathway through dietary interventions may be a potential approach to modulate the initial phases of cognitive decline.

VII. CONCLUSION

The maturation of the brain is impacted by various factors, such as the maternal diet during gestation, the nutritional condition of the infant and toddler, alongside other environmental elements and enduring epigenetic mechanisms. The significance of maintaining a balanced state between synapse and neuron formation, as well as the essential process of synapse pruning during childhood and adolescence, raises uncertainty regarding the potential benefits of unilaterally promoting neuronal growth on brain performance. The composition of one's diet has the potential to modify the quantities and impacts of active neurotransmitters (NTs) or impede the functioning of pertinent receptors. Consequently, this can have an influence on the brain's signaling networks that are linked to mood and behavior, including but not limited to depression, sleep and wakefulness, pain, and other related factors. The brain's cardiovascular health and the efficiency of its mitochondria have a significant impact on cognition and memory due to their reliance on energy. The inhibition of synaptic plasticity, which plays a fundamental obligation of the cognitive process like memory formation and thinking, has been found to have a negative impact on cognitive performance and memory retention. The aforementioned statement remains valid in regards to the capacity of cells to effectively control the generation of misfolded or unfolded proteins, as well as the subsequent breakdown of these proteins through autophagy or proteasomes.

Data Availability

No data was used to support this study.

Conflicts of Interests

The author(s) declare(s) that they have no conflicts of interest.

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There are no competing interests.

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