NUTRITIONAL IMPACT ON BRAIN FUNCTION: FOOD FOR THOUGHT, EMOTIONS AND WELLBEING

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Abstract: *The rate of cognitive and emotional dysfunction is increasing in the modern society, therefore nutritional impact on the brain functioning is receiving higher attention in science and practice. In order to summarize the latest scientific knowledge concerning nutritional impact on the nervous system and particularly on the brain functioning we performed literature search and analysis. Increasing number of scientific data show that macronutrients and micronutrients (vitamins and minerals) affect multiple brain processes through control of diverse mechanisms as: synaptic transmission, neurotransmitter pathways, signal-transduction pathways, membrane fluidity, epigenetic changes, etc. Impact of specific macronutrients and micronutrients in brain functioning and their food source is presented in details. We believe that these data might be of interest to wide spectrum of professionals as: physicians, nutritionists, psychologists, neuroscientists etc.*

Keywords: *brain, nervous system, nutrients, food, cognition.*

1. INTRODUCTION

Human brain, as a part of the nervous system, is quite demanding organ concerning energy metabolism and nutrition. Brain energy metabolism is dependent on a continuous cardiovascular supply of two key molecules, glucose as a fuel and oxygen as a molecule used to burn the fuel. Neurons and glia, two types of cells that build the brain, do not own possibility to store glucose and oxygen, regardless they are totally dependent on them. The brain requires a constant supply of energy in the form of adenosine triphosphate (ATP), molecule that also cannot be stored in the brain cells. This molecule is mainly made from glucose through process of oxidative phosphorylation in mitochondria, complemented by aerobic glycolysis in the cytoplasm. It is estimated for the average human adult person in an inactive state, that this organ consumes about 20 % of the total body's energy [1].
Besides energy, the brain needs ingredients of dietary origin called nutrients to build and sustain its own structure, to maintain optimal metabolic functioning, and to fight neurodegeneration and evade premature ageing. Suitable nutrition is essential for physiologically normal brain development especially throughout periods of pregnancy and infancy, critical stages for the brain formation and development. Foundation for the development of cognitive, socio-emotional and motor skills are traced during these stages, thus approving the importance of nutrition for the brain development [2]. Importantly, diverse neuronal cells require different and diverse types of nutrients to perform their specific physiological roles. These nutrients could be classified in to three main classes: macronutrients as carbohydrates, fat and proteins; various vitamins; and assorted minerals. From the point of nutrition and energy metabolism the brain has certain priority in supplies comparing to the rest of the organs. Moreover, it is quite expected that nutritional status and energy metabolism status of the nervous system will strongly affect human cognition and behavior.
For a long period of time, it has been presumed that the relative abundance of definite nutrients might impact cognitive processes, emotions and general wellbeing of a human organism. Since the rate of cognitive and emotional dysfunctions is increasing in the modern society nutritional impact on brain functioning is receiving higher attention. In this paper we will summarize the latest scientific knowledge concerning nutritional impact on the nervous system and particularly on the brain functioning.

2. PHYSIOLOGICAL BASIS OF THE EFFECT OF NUTRIENTS ON COGNITION

Nowadays we are totally aware that nutrition is not significant only for general physiology, motor movement and body composition, but in addition we accept the fact that what we eat have substantial impact on our thought, emotions and wellbeing. There is increasing number of scientific data showing that macronutrients and micronutrients (vitamins and minerals) can affect multiple brain processes through control of diverse mechanisms as: synaptic transmission, neurotransmitter pathways, signal-transduction pathways, membrane fluidity, epigenetic changes, etc.

The effect of visceral signals, such as vagal nerve stimulation (VNS) and gut hormones, on cognitive function has been known and respected for long time [3]. Therefore, through the application of different types of diets and exercises visceral signals have been successfully used in the treatments of depression and other psychological and psychiatric disorders. Scientific investigations demonstrated that vagal nerve stimulation elevates mRNAs for brain-derived neurotrophic factor (BDNF) and fibroblast growth factor 2 (FGF2) in the hippocampus and cerebral cortex of rats, but also the amount of noradrenaline in the prefrontal cortex. Hence, BDNF and noradrenaline have been related with the effects of antidepressant treatments, we may conclude that visceral signal that originate from the gut affects the mood [3,4]. Even more, it has been discovered that gut hormones, such as leptin, ghrelin, glucagon-like peptide 1 and insulin, influence emotions and cognitive processes via mechanisms of neuroplasticity.

Evidences for the relation between transformation of metabolic energy from foods to neurons on one side, and mental processes on the other side, have also been reported. Not surprisingly this association is bidirectional. The metabolism of energy in neurons can affect synaptic function and consequently affects cognition, while in opposite direction mental processes impact somatic function at the molecular level via signaling molecules as brain-derived neurotrophic factor [3]. Brain regions related with regulation of cognitive and metabolic processes, such as hippocampus and the hypothalamus, are most abundant with BDNF. Elevation in the level of brain-derived neurotrophic factor is detected during stages of learning and memorizing, but also during metabolism of glucose, insulin, lipids and appetite suppression [3]. As a consequence, disorders in energy homeostasis have been related to the pathophysiology of numerous mental illnesses.

Interestingly, extra calories may negatively impact synaptic plasticity and support production of free-radicals which cause neuron cells to become vulnerable to damage and subsequently to cell death [5]. Therefore, diets turn out to be a one of the approaches to cure psychiatric disorders. These diets encompass the control of biochemical basis of nutrients that compose food, but also caloric restriction. Since the brain is an organ highly susceptible to oxygen damage control of nutrients that produce free radical is important step in designment of a diet. Moreover, the diet should also favorize increase intake of antioxidant nutrients. These two steps are part of the strategy used to develop different anti-oxidant diets.

What mostly surprise is the possibility that the impacts of diet on general health and especially on cognitive function can be forwarded across generations through epigenetic changes. These changes include non-genetic events, such as DNA methylation and acetylation, transcriptional activation, translational control and posttranslational modifications. The molecular mechanisms for the impact of nutrients on epigenetic changes are unidentified till today, Although, it is recognized that the BDNF system demonstrates predisposition to epigenetic modifications that can influence brain function [6].

3. IMPACTS OF MACRONUTRIENTS ON NERVOUS SYSTEM

Macronutrients (macros) are crucial nutrients that an organism require in huge quantities to provide with energy and building material in order to function properly. Three main types of macronutrients are: proteins that are made from amino acids; fats that are made from fatty acids; and carbohydrates of different types as monosaccharides, oligosaccharides, and polysaccharides. Macronutrients are present in numerous food sources. The main problem in determination of different diets is the right quantity of macronutrients that should be consumed. Importantly, their effect on cognition depends not only on their quantity, but primarily on their biochemical composition. The Table 1. present main macromolecules linked with brain function, effects they make due to deprivation and optimal intake, and their food source.

Brain cognitive functions are strictly related to the glucose level (Table 1.). Generally, energy deficiency causes poor cognitive functioning, i.e., when glucose levels are low as during state of hypoglycemia. On the other hand, high glucose level over a continued period, as during diabetes, cause effects of brain's functional connectivity and decrease of brain volume. More precisely, glucose affects memorization and attention, while low level of glucose is linked to development of neurodegenerative diseases [7].

The brain needs a numeral amino acid found in food proteins. They are used by the brain for the synthesis of several neurotransmitters and neuromodulators, but also for neuroproliferative and neuroregenerative processes. In general, the presence of certain amino acids in food is linked with improvement in cognition and mood (Table 1.).

Feasting omega-3 fatty acids, especially the most abundant docosahexaenoic acid (DHA), is probably the best-studied interaction between food and brain function. This omega-3 fatty acids are present in neuron cell membranes and are

essential for normal brain function. Nevertheless, human organism is not efficient at synthesizing DHA, therefore, humans are principally dependent on DHA intake by food. It is recognized that food rich in omega-3 fatty acids is essential for normal cognitive development, while diet high in saturated fats has reverse effects (Table 1). Shortage of omega-3 fatty acids in humans has been linked with enlarged risk of numerous mental disorders [7,8].

Table 1: Impact of macronutrients on nervous system functioning

NUTRIENT	EFFECTS OF DEPRIVATION	EFFECTS OF OPTIMAL INTAKE	SOURCE
Glucose	poor memorization [7]; reduced intellectual capacity [7]; risk of dementia in older [7]; perturbed cerebral glucose metabolism is linked to Alzheimer's disease [9].	good memorization [7]; improves face recognition [7]; improves attention [7]; improves cognitive symptomatology of neurodegenerative diseases [10].	honey, dried fruits, fruit drinks, grapes, sweat corn.
Proteins	impaired functioning of the brain, especially hippocampus and the hypothalamus [7]; altered visual and auditory evoked potentials [7].	formation of cerebral proteins and neurotransmitters leads to improved cognition [7]; improve cognitive status in older [11].	milk and milk products, meat, eggs, peanuts,
Amino acids	tryptophan has effect on mood and depression [7]; serotonin modulate dietary behavior [7]; serotonin deficit can worsen cognitive dysfunction in schizophrenics [7].	tyrosine improves cognitive performance and appetite [7]; ingestion of the 7 essential amino acids led to improved attention, cognitive flexibility and psychosocial functioning [12].	beef, poultry, fish, eggs, dairy, soy, quinoa.
Omega-3 fatty acids	deficiency during perinatal period in Alpha Lipoic Acid induce anomalies in the composition of different types of neurons [7]; decrease in docosahexaenoic acid leads to hypophysis, and decrease in the size of neurons in hippocampus [7]; Alpha Lipoic Acid deficiency affects serotonergic and cholinergic neurotransmission [7]; deficiency in omega-3 fatty acids perturbs hearing and tasting at the level of cerebral response [7]; low consumption of eicosapentaenoic and docosahexaenonic acids, is linked to delayed brain development, increased risk for Alzheimers Disease [13].	omega-3 fatty acids are potent neuroprotectors [7,8]; Alpha Lipoic Acid induce protection against ischemia in the spinal cord preventing necrosis and apoptosis of motor neurons [7]; omega-3 fatty acids improve psychomotor development, quality of sleep and learning performance [7]; supplementation of omega-3 fatty acids during pregnancy and lactation improves IQ of children [7]; supplementation with omega-3 fatty acids improves visual functions [7].	oils from rapeseed, soybean and walnuts fish, and seafood; nuts and seeds (flaxseed, chia seeds, and walnuts); plant oils (flaxseed oil, and canola oil).
Unsaturated and saturated fatty acids	oleic acid has role in nervous system formation during pregnancy and nursing [7]; oleic acid decrease is lined with behavioral disturbances [7]; elevated saturated fatty acids have negative effects on age-related cognitive decline and mild cognitive impairment [14].	Alpha Lipoic Acid improves neurosensory and higher functions such as learning [7].	vegetable oils, fish and nuts. butter, lard, full-fat milk and yogurt, full-fat cheese, high-fat meat.
Phosphatidyl-choline		improves memory, learning, concentration, memorization of words, and mood in elderly subjects with cognitive decline [7]; choline and phosphatidylcholine maintain cognitive performance [15].	eggs, milk, meat, fish and some plant foods and certain beans.

DHA might enhance cognitive functioning by improving synaptic plasticity, increasing synaptic membrane fluidity, via effects on metabolism, and by reducing oxidative stress. In opposite, nourishments with elevated amount of trans and saturated fats negatively affect cognition. Rodent studies based on diets with “junk food” (high amounts of saturated fat and sucrose) demonstrated higher incidence of neurological disorders and worse performance in learning [3].

4. IMPACTS OF VITAMINS ON NERVOUS SYSTEM

Evidences from scientific research propose that higher dosage of vitamins may improve brain functions. As first, specific vitamins are fundamentally involved in the cellular and physiological processes related to the brain function. As second, slight proportions of the human population display lack in some vitamins, proposing that larger proportion might have suboptimal micronutrient status, thus challenging their nervous system status. Finally, epidemiological investigations suggest a link amongst specific vitamin dosage and cognitive function and mood [16]. Table 2. presents impact of individual vitamins, as a specific classes of micronutrients, on brain function and their food source.

Table 2: Impact of vitamins on nervous system functioning

VITAMIN	EFFECTS OF DEPRIVATION	EFFECTS OF OPTIMAL INTAKE	SOURCE
Vitamin A	neurobiological alterations and spatial learning impairments [17].	implicated in synaptic plasticity in the regions of the brain involved in learning and memory, such as the hippocampus [17,18]; maintenance neurobiological functions indirectly through glucocorticoid pathway [19].	liver, milk, eggs, fish; green vegetables, carrot, oranges.
Vitamin B1	lassitude, lower intelligence, irritability, cramps; [17]; contributes to the development of Alzheimer disease [20].		sunflower seeds, fish, nuts.
Vitamin B3	may leads to depression [17].	reversed memory loss in AD-like mice [21].	red meat, poultry, fish.
Vitamin B6	deficiency linked with neuropsychiatric disorders (seizures, migraine, chronic pain and depression) [22]; deficiency during gestation and lactation alters neurotransmitter system that play role in learning and memory [23].	combats depression, irritability, premenstrual symptoms and premenstrual depression [17].	milk, ricotta, tuna, salmon, eggs, chicken, liver, carrots, bananas, beef, spinach.
Vitamin B9	major abnormalities during the elaboration of the nervous system in the infant, while in the elderly, deficiency decreases intellectual capacity [17].	improves cognitive function by reducing the levels of peripheral inflammatory cytokines in elderly [24].	eggs, green vegetables, maize, liver, chickpeas.
Vitamin B12	neurological disorders, psychic disturbances (memory loss, pain, and abnormal sensations at limb extremities) [17]; low serum vitamin B12 levels are associated with neurodegenerative disease and cognitive impairment [25].	improves memory performance of middle-aged [17].	food of animal origin: meat, eggs, shellfish, fish; and to a lesser extend, cheese.
Vitamin C	vitamin C deficiency has been proposed to play a role in age-related cognitive decline and in stroke risk and severity [26].	associated with a lower alteration in cognitive performance [17]; plays a role in neuronal differentiation, maturation, myelin formation and modulation of the neurotransmitter systems [27].	citrus, pepper, strawberries, tomatoes, cruciferous vegetables.
Vitamin D	low vitamin D levels are associated with cognitive impairment and Alzheimer's disease [28].	protects neurons of the hippocampus, and modulates transport of glucose to the brain [17].	cod liver oil, salmon, , tuna, sardines, beef .
Vitamin E	alters brain fatty acid profile and induces retinal abnormalities [17].	protect against ageing of the brain [17]; reduces risk of Alzheimer disease [17]; neutralize active and toxic forms of oxygen and scavenge free radicals [17].	vegetable oils, eggs, meat, cereal germs.

There are plenty of evidences that micronutrients as vitamins play role in cerebral functioning [17]. Vitamin A has a role in synaptic plasticity. Vitamin B1 is involved in production of energy from glucose in the brain cells and this process modulates cognitive performance especially in older population. Lack of Vitamin B3 is also related to Alzheimer disease. Vitamin B6 is used to fight depression. Vitamin B9 preserves brain throughout development phase and strength memory during process of ageing. The highest concentrations of vitamin C in the human body are found in the brain. Vitamin D is of interest in the prevention of neurodegenerative or neuroimmune diseases. Vitamin E is known by antioxidant respond to the oxygen species deriving from food and has influence on brain plasticity.

5. IMPACTS OF MINERALS ON NERVOUS SYSTEM

Physiological role and significance of trace elements can't be judged only by their concentration in the nervous system structures. Mostly they are present in low and variable amounts. Some minerals have only one main role, while others may play different important roles in various processes and different organs. The passage of trace elements into the brain is rigorously controlled by the brain barrier system, as the blood-brain and blood-cerebrospinal fluid barriers. They mostly assist the function of metalloproteins in neurons and glial cells. Some of the trace elements are present in the presynaptic vesicles and may be released with neurotransmitters into the synaptic cleft [29]. Definitely, their significance for brain structure and function overwhelms the amount in which they are represented. Table 3. presents impact of individual minerals, as a specific classes of micronutrients, on brain function and their food source

Table 3: Impact of minerals on nervous system functioning

MINERAL	EFFECTS OF DEPRIVATION	EFFECTS OF OPTIMAL INTAKE	SOURCE
Iron	iron deficiency leads to anaemia [17]; deficit in iron leads to less efficient supply of oxygen to the brain and decreases brain energy production [17]; iron deficiency during embryogenesis impairs myelination [17]; iron deficiency is observed in children with attention deficit/hyperactivity disorder [17].	iron treatment normalizes cognitive functioning in young women [30].	meat, poultry, and seafood are richest in heme iron, while fortified grains, nuts, seeds and legumes, contain non-heme iron.
Copper	unbalanced metabolism homeostasis could be linked to Alzheimer disease [17,31].		meat, shellfish, fish, grains, nuts, seeds.
Zinc	low zinc level leads to reduced appreciation of taste in older [17]; zinc deficit induces behavioral changes [17]; low maternal intakes of zinc during pregnancy and lactation associated with less focused attention in neonates and decreased motor functions at 6 months of age [32]; dietary zinc deficiency associated with memory impairment[33].	Zinc plays a role in cognitive development and participates in the mechanisms for perception of taste and smell [17].	oysters, some cheeses, steak poultry livers, green vegetables.
Iodine	mental retardation detected in children due to iodine deficiency during pregnancy [17].	iodine supplementation improves cognition in iodine-deficient schoolchildren [34,35].	mussels, oysters, seafish and eggs.
Magnesium	deficiency is usually linked to spasmophilia [17]; plays a role in all the major metabolisms[17,36].	protects cognitive functions and synaptic plasticity in streptozotocin-induced sporadic Alzheimer's model [36,37].	milk, whole grains, dark-green, leafy vegetables
Selenium	reduced amount leads to neurodegenerative diseases [17]; selenium deficiency alters neurological development [17].	selenium mediates exercise-induced adult neurogenesis and reverses learning deficits induced by hippocampal injury and aging [38].	mushrooms, seafood, eggs, mussels, oysters, fish

Disturbance of iron homeostasis in the brain can distress neurophysiological mechanisms, cognition, and social behavior, and contributes to the progression of a various neuro-pathologies. Impairments of homeostatic mechanisms in brain copper metabolism have been associated with neurodegeneration and Alzheimer disease. In the central nervous system zinc is either tightly bound to proteins present in free state in cytoplasm or in presynaptic vesicles [39]. It has been described a role for magnesium in migraine and depression, whereas some data suggest a protective effect of magnesium for chronic pain, anxiety, and stroke [36]. Importance of selenium and seleno-protein for brain function is determined in wide spectrum from antioxidant protection to neuronal signaling [40].

6. CONCLUSION

For a quite long period of time food was remarked as a resource with a single role, to deliver energy and material to a living organism. Recently, capacity of food to prevent and defend towards illness is finally approved and practically used to design appropriate diet and life style. There are plenty of evidences that help us to recognize molecular, cellular and physiological basis of food impact on thought, emotion and mood. These results will help us to determine how best to manipulate diet to intense the resistance of neurons to insults and sustain and promote cognitive fitness.
Is it really necessary for all of us to change our feeding habits drastically in order to live healthier and longer? Our choices of what, when and how much are we eating are definitely influenced by our society, culture, habits, religion, but also by our knowledge, level of education, lifestyle and health policy. The fact that today we have much wider choice of different sources of food that is composed of various macronutrients and micronutrients make whole problem much easier. The task of diet designing is to balance between our habits and pleasure on one side and health and proper brain function on the other side.

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