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Brain food: how nutrition alters our mood and behaviour

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review

Summary

Studies have been showing the food we eat affects chemical composition of our brain and alters our mood. Nutrition affects cognitive possibilities, including alertness and the production or release of neurotransmitters, the chemical messengers that carry information from one nerve cell to another. Foods are made up of more than one nutrient, and their interaction is going to affect the production and release of neurotransmitters. Neural impulses are largely resulting from sodium-potassium exchange, but numerous others such as complex carbohydrates, amino acids (tryptophan and tyrosine), fatty acids, particularly omega-3 fatty acids, affect permeability of cell membrane, neurotransmitter metabolism and glial cells. The delicate brain chemical balance is somewhat controlled by the blood – brain barrier. Still, brain remains highly susceptible to changes in body chemistry resulting from nutrient intake and deficiency. The direct connection between nutrition, brain function and behaviour exists, without any doubt. It can be seen through brain's capability of receiving, storing and integrating sensory information, while initiating and controlling motor responses. These functions correspond to mental activities and form the basis for our behaviour. Constant rise in number of evidence from epigenetic studies confirms that specific nutrients alter our brain development and susceptibility to diseases. Still, specific combination of foods can be extrapolated to a dietary regime, like the Mediterranean diet which has shown its positive impact on maintaining brain function and lower incidence of neurodegenerative diseases. This is of special importance since elderly population (people of 65 years and older) is on the rise all over the world, and the quality of life becomes a priority.

Keywords: nutrition, food composition, neurotransmitters, mood, behaviour

Nutrition and cognitive performance

All that we experience affects synapses (junctions of neurons), and these changes are responsible for memory and other mental abilities. According to Thurston primary mental abilities are (set in 1938): verbal fluency (eloquence), verbal comprehension, visual and spatial (physical) abilities, memory, numerical ability, perceptual speed spotting, inductive reasoning (from individual to general) and deductive reasoning (from general to specific). Practically, when something that we are going to remember happens electric signal occurs, causing chemical and structural changes in the neurons. These changes are possible due to a series of reactions involving various molecules, including calcium, some enzymes and neurotrophins, aiming for synapses activation. Healthier brain produces more neurotrophins, which reinforce links between neurons in the part of the brain responsible for learning and memory. Parts of the brain where specific memory is stored have been discovered. For semantic memory, which concerns facts are responsible multiple cortical areas, while procedural memory involved in motor learning depends on the other parts of the brain, including basal ganglia (Fig. 1). Nutrition in the first years of life can have a significant impact on development; the ability to learn, communication, analytical thinking, successful socialization and adaptation to new situations (Isaacs and Oates, 2008; Budson and Price, 2005).

Proper nutrition and health are closely interrelated throughout life, but probably the highest importance is expressed in the first years of life. Inadequate nutrition causes lower cognitive development, reduced attention and concentration and reduces performance in later life. Also, foetal programming in utero should not be neglected, for its proven influence on the later development of a child (Langley-Evans, 2008). As nicely illustrated by Vanhees et al. (2014) we are what we eat, and so are our children. Their extensive review on epigenetic studies clearly illustrates the importance of balanced diet of both, mother and father. Besides macronutrient composition of the diet (high-fat diets, protein restricted diet, diet high in carbohydrates), intake of specific micronutrients, especially those involved in one-carbon metabolism (folic acid, vitamin B_2, B_6 and B_{12}) day by day shows more potential in programming offspring's epigenome (Vanhees et al., 2014).

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At birth, the brain reaches 70 % size and 25 % weight of an adult brain. In the subsequent period, are created new nerve cells (neurons) that travel to their final destination. Brain changes throughout life. It normally makes fiftieth part of human body weight (average weighs between 1000-1500 grams), in adolescence reaches its definite size (Benton, 2008). Brain is a very dynamic organ, showing high plasticity. Due to this characteristic, altering our diet in terms of having a balanced nutrition without any deficiency or over-nutrition can preserve our brain from deterioration. For example, one study showed that high-dose supplementation with folic acid during early pregnancy shows association with increased neurodevelopment, resulting in enhanced vocabulary development, communicational skills and verbal comprehension at 18 months of age (Chatzi et al., 2012). Similar findings have been shown for boosting cognitive performance and intake of iron (after correcting iron deficiency anaemia) (McCann and Ames, 2007; Black et al., 2011; Goergieff, 2011).

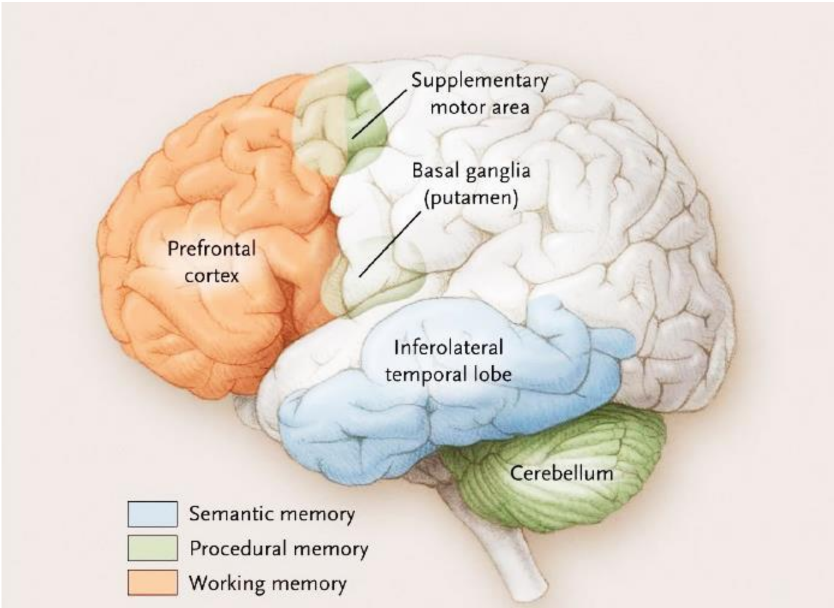

Fig. 1. Memory systems and parts of the brain (Budson and Price, 2005)

Food and neurotransmitters

Neurotransmitters are produced in our brain from numerous nutrients originating from our diet by means of a many-step process. First, nutrients (marked as 1 in Fig. 2), such as amino acids, carbohydrates, fats, and peptides, are extracted and absorbed from the food we eat and transported out of the arterial blood supply to the brain. They are actively carried through the blood-brain barrier and transported into neurons. Enzymes (2) convert these nutrients into different neurotransmitters. Neurotransmitter molecules are actively transported into synaptic vesicles (3). The arrival of an action potential (4) at an end of the axon induces entry of calcium ions, which initiate release of neurotransmitters (5) into synaptic cleft. The neurotransmitter molecule briefly interacts or binds with a protein, i.e. receptor (6), on the neuron surface on the other side of the synapse. Consequence of this binding action is that some ions, such as calcium or sodium, move into the downstream neuron to induce secondary biochemical processes (7), which may have long-term consequences on the neuron's behaviour. Meanwhile, after interacting with the receptor, neurotransmitter's actions must be terminated by reabsorption (8) back into the neuron that originally released it, which is called reuptake. A secondary method of neurotransmitter inactivation is by enzymatic conversion (9) into a chemical that can no longer interact with brain. Once inactivated by enzyme, neurotransmitter is removed from the brain into the bloodstream (10). Such byproducts can be easily monitored in body fluids, and used to determine whether our brain functions normally. Nutritional composition of our diet can interact with any of these previously described processes and impair, or even enhance, the production of neurotransmitters, as well as impair their storage into synaptic vesicles, alter their release from neurons, modify their interaction with receptor proteins (11), slow their reuptake, and possibly even stop their enzymatic inactivation (Wenk, 2010).

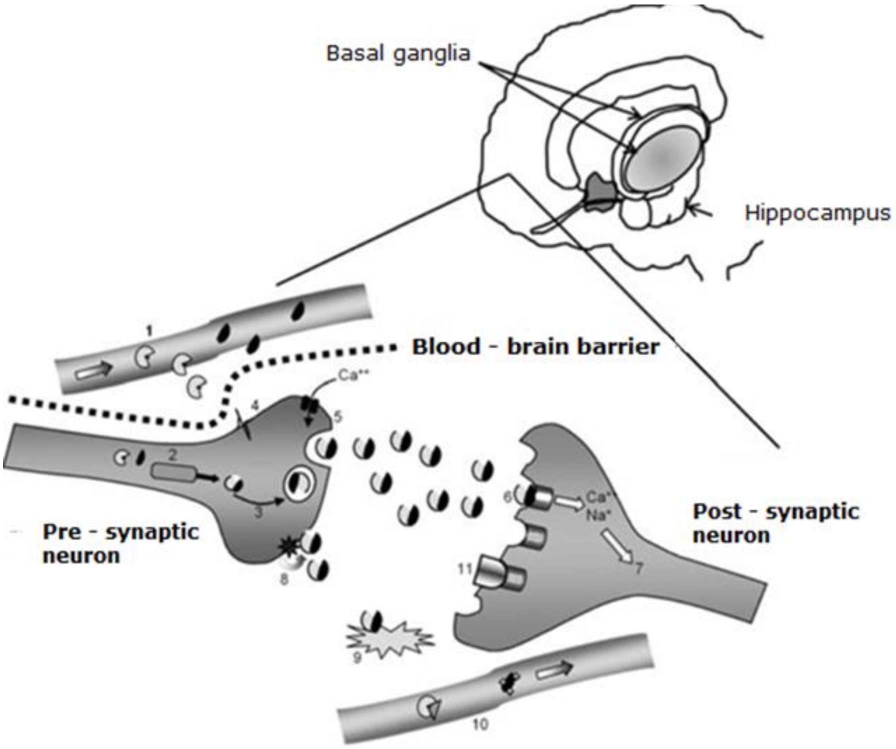

Fig. 2. The absorption of nutrients and their effect on neurotransmitters (Wenk, 2010)

Carbohydrates and the brain

Brain needs two times more energy than other cells in our body, and glucose is the only fuel that can be used directly by the brain (Coimbra, 2014). Neurons are always in a state of metabolic activity and have constant demand for energy, even during sleep. Most of the neuron's energy demand goes on bioelectric signals responsible for communication of neurons; they consume one-half of the brain's energy which is nearly 10 % of total human energy requirements (Coimbra, 2014). Because neurons cannot store glucose, they depend on the bloodstream to deliver a constant supply of this primary fuel. Different sugars have different effects on the brain. While glucose has an impact on regions like insula and ventral striatum, controlling appetite, motivation and reward processing, fructose does not (Page, 2013; Purnell and Fair, 2013).

Therefore, it is important to control the amount of carbohydrate in our diet, as well as the type of food we combine. This is where we get to the glycaemic index (GI) concept. GI is a ranking system categorizing the food according to its impact on blood glucose levels, so GI indicates whether certain foods raise blood sugar levels dramatically, moderately or slightly. The intake of foods made from white flour and white sugar should be limited for the above reasons. Potatoes also have a high GI value (Ek et al., 2012). The best choices are fibre-rich foods. Complex carbohydrates take longer to digest, causing a slower and more gradual release of glucose into bloodstream, leading to a feeling of fullness for longer period of time. A fibre-rich diet, besides its proven effect in the prevention of type 2 diabetes and cardiovascular diseases, probably helps improving memory and cognition (Kendall et al., 2010; Kaczmarczyk et al., 2012). The glycemic response depends on the combination of consumed food. Complex, varied meal that contains complex carbohydrates, proteins and adequate types of fats, rich on dietary fibers will provide a moderate GI and supply the brain for a long time with glucose. Combining foods with high GI and those with a low GI balances the response of the organism (Jenkins et al., 2013).

Fats and the brain

Fatty acids are present in membranes of every cell of our body and make 60 % of the brain’s dry weight, half of which are omega-6 fatty acids, while the other half consists of omega-3 fatty acids. Dietary fats alter the composition of nerve cell membrane and myelin sheath, and that, in turn, influences neuronal function. Fatty acids are involved in the development and growth of the brain, they affect cognitive abilities (attention, reasoning, memory, and learning), vocabulary and intelligence (Gogus and Smith, 2010). Humans cannot synthesize essential fatty acids from simple carbon precursors so they must be acquired through diet. There are two essential fatty acids, both polyunsaturated fatty acids, linoleic acid (LA) which is a precursor of omega-6 fatty acids and alpha-linolenic (ALA), which is a precursor of omega-3 fatty acids. Arachidonic acid (AA) is synthesized from LA, while from ALA eicosapentaenoic (EPA) and docosahexaenoic (DHA) acids are synthesized (Davis and Kris-Etherton, 2003; Vannice and Rasmussen, 2014). Long-chain omega-3 and omega-6 fatty acids compete for the same enzymes cyclooxygenase and lipoxygenase and therefore a diet is considered to be the best way to maintain balance between omega-3 and omega-6 fatty acids. It is believed that this ratio should not be greater than 5:1 in favour of omega-6, and it is known that the Western diet has a ratio of 12:1, or even worse. The importance of this ratio is supported by the fact that inflammatory eicosanoids are formed by the metabolism of omega-6 fatty acids, while EPA and DHA products are thought to be relatively anti-inflammatory (Gogus and Smith, 2010; Vannice and Rasmussen, 2014; Kidd, 2007; Shaikh and Brown, 2013).

Omega-3 fatty acids are critical for foetal and newborn neurodevelopment. During the third trimester of pregnancy, approximately 50-70 mg of DHA per day is delivered to foetus via placental transfer. DHA is accumulated in the central nervous system (CNS) before birth, and therefore considered to play a critical role in the development of cognitive functions (Langley-Evans, 2008; Greenberg et al., 2008; Montgomery et al., 2013). Nutrient deficiencies during development may have long-lasting consequences on neurone outgrowth (Greenberg et al., 2008; Montgomery et al., 2013). A positive correlation has been observed between DHA in red blood cells and visual acuity, as well as other indexes of brain development in newborns (Jensen et al., 2005). Nutritional guidelines during pregnancy recommend an additional intake of omega-3 fatty acids, i.e. 250 mg/day EPA and DHA (Vannice and Rasmussen, 2014; WHO, 2008; EFSA, 2010; FAO, 2010). Essential fatty acids are necessary for the child’s normal growth and development, which is an approved health claim by the European Food Safety Authority. Beneficial effect has been proven by taking 1 % of the total energy of LA and 0.2 % ALA per day (EFSA, 2008). DHA is essential for the growth and functional neurodevelopment of newborns, and required to maintain a normal function of adult brain. Intake of DHA during pregnancy and lactation of at least 200 mg per day, contributes to the normal brain development of foetus and infant (EFSA, 2009). Low brain DHA is associated with age-related cognitive decline, as well as the early development of Alzheimer's disease. On the other hand, increased dietary intake of DHA can result in improved cognitive abilities due to the fact that a lack of essential fatty acids has been linked to deficits in learning and memory (Cunnane et al., 2009; Yurko-Mauro et al., 2010; Cunnane et al., 2013).

Interesting results shows a study by Conklin et al. (2007). The study involved fifty-five healthy adults who completed two 24 h dietary recall interviews. Based on an intake of EPA and DHA, the respondents were divided into three groups: low intake (0-20 mg/day, 16 respondents), medium intake (25-70 mg/day; 21 respondents) and high intake of EPA and DHA (80-1600 mg/day, 18 respondents). Magnetic Resonance Imaging (MRI) scans of respondent's brains revealed a positive correlation between increased intake of these two fatty acids and the volume of gray matter in the anterior cingulate cortex, the right hippocampus and the right amygdala. Since mentioned areas are responsible for mood, scientists believe that increased intake of EPA and DHA has a positive effect on mood, but also on memory functions (Conklin et al., 2007).

The best dietary sources of omega-3 fatty acids are oily fish (sardines, mackerel, tuna, anchovies), cold water fish (herring, salmon), algae, zooplankton and seafood as well as seeds and nuts. Nutritional supplements containing purified and concentrated fish oil are also a valuable source of omega-3 fatty acids in the diet of a modern man (Shaikh and Brown, 2013; Bradbury, 2011). The amount of EPA and DHA in fresh fish varies depending on a species. Oily fish is particularly useful for pregnant women, and it is recommended to be consumed once a week. But the special attention is needed with canned tuna for possible intoxication with mercury. Species of fish that are long-lived and high on the food chain tend to have higher levels of methylmercury which has negative impact on the nervous system of a foetus. A total amount of methylmercury in fish remains relatively unchanged after cooking (WHO, 2007; WHO, 2010; Brown, 2010).

Amino acids and neurotransmitters

The most common neurotransmitters are: acetylcholine, glutamate, gamma-aminobutyric acid (GABA), glycine, serotonin, dopamine, norepinephrine, epinephrine and histamine produced by our brain directly from nutritional components of our diet. Activity and levels of these neurotransmitters depend on food intake and change in nutrient intake can significantly affect behaviour, sleep and energy levels (Sommer, 1995; Gustafson, 2008).

Serotonin is produced from the amino acid tryptophan, which is found in protein-rich food, such as chicken, dairy products, eggs and legumes. Ironically, consumption of high-protein foods decreases levels of tryptophan and serotonin in the brain, while the consumption of carbohydrate-rich foods has the opposite effect. After consumption of high-protein foods, tryptophan competes with other amino acids in order to pass the blood-brain barrier, which results in a lower increase in brain serotonin. When large amounts of carbohydrates are eaten, insulin is released, causing the absorption of the majority of amino acids into the bloodstream while giving advantage to tryptophan for brain access, leading to increased level of brain serotonin. The resulting increase in brain serotonin promotes the feeling of calmness, improves sleep, increases pain tolerance and reduces food cravings (Sommer, 1995; Fernstrom, 2013; Parker and Brotchie, 2011).

Dopamine and norepinephrine are synthesized from the amino acid called tyrosine, with the assistance of folic acid, magnesium and vitamin B_{12}. Unlike tryptophan, tyrosine level raises after consuming a protein-rich foods which leads to increased levels of dopamine and norepinephrine, both affecting alertness and mental energy (Sommer, 1995; Fernstrom, 2013; Parker and Brotchie, 2011; Daubner et al., 2011). Acetylcholine is synthesized from choline and unlike other amino acids that have to compete for brain access, choline does not need to. The best source of choline is egg yolk. Acetylcholine is important for memory and general mental ability. Reduced levels of acetylcholine are associated with memory loss, decreased cognitive function and Alzheimer's disease at old age. Choline deficiency induces neuronal death and mental fatigue, a person cannot think clearly, is depressed and forgetful (Sommer, 1995; Holmes et al., 2002; McCann et al., 2006).

Mediterranean diet

When speaking about brain food we must not forget about one specific dietary regime which shows immense potential in maintaining and boosting brain functioning. This is the Mediterranean diet (MD). Despite several differences between Mediterranean regions, they all have something in common. The specific combination of foods make it so simple and yet so complicated at the same time (Banjari et al., 2013). Yet this is exactly the perfect combination of macro and micronutrients, making it a number one choice for health and longevity. Health benefits of the MD go well beyond preventing cardiovascular diseases, lover mortality and morbidity (Banjari et al., 2013), as shown by the Lion Diet Heart Study (De Lorgeril, 2013), study by Trichopoulou et al. (2003) in Greece, or the PREDIMED study conducted in Spain (Estruch et al., 2013). Protective effect of the MD has been determined for number of degenerative diseases, like cancers dementia, and the risk of Alzheimer's disease (Shah, 2013; Lourida et al., 2013; Sofi et al., 2013). Furthermore, Skarupski et al. (2013) showed its potential in reducing depression among people of 65 years and older. Also, rising interest of the non-Mediterranean countries, firstly Scandinavian countries, resulted in vast number of evidence showing the MD potential in protecting from premature death (Hodge et al., 2011; Gardener et al., 2011; Hoevenaar-Blom et al., 2012; Martínez-González et al., 2012; Hoffman and Gerber, 2013; Tognon et al., 2013), and cerebrovascular diseases (Misirli et al., 2012).

Food and mood

We can boost our mood by retaining available neurotransmitters in the gap between nerve cells as long as possible and it seems possible, but yet-to-be-tested, that expressions of foods in art can also serve to improve mood. Regulation of three key neurotransmitters responsible for mood (dopamine, noradrenaline and serotonin) by modulating food intake impacts durability of their stimulation of nerve cells, thus impacts mood and behaviour (Privitera et al., 2013; Hamburg et al., 2014).

Chocolate and caffeine

A study of 8000 people has shown that people who consume chocolate live longer compared to those who never eat chocolate. Positive effect of a chocolate lies in its flavonoid content. Chocolate flavonoids reduce the amount of low-density lipoprotein (LDL) cholesterol and reduce blood pressure. They also show the potential to slowdown growth of cancer cells (Engler and Engler, 2004; Paoletti et al., 2012). Due to chocolate production processes, it is believed that only dark chocolate products with a cocoa content of approximately 70 % or higher truly offer a significant benefit of flavonoids (Goldoni, 2004; Rawel and Kulling, 2007). Cocoa beans contain 61 % of cocoa butter, tannin, catechin and alkaloids theobromine and caffeine, which have different effects on our brain and emotions. Cocoa beans are also rich in hydrolysis products of polyhydric phenols such as quercetin, caffeic and p-hydroxycinnamic acid (Jalil and Ismail, 2008; Smit et al., 2004; Parker et al., 2006). It is known that chocolate contains over 300 substances, but the key ingredient is phenylethylamine. Most phenylethylamine is metabolized in the body, but some reaches the brain where it leads to dopamine increase. After consumption of chocolate, phenylethylamine is released into the human system producing the arousing effects of an intense emotional stimulus leading to euphoria. Some antidepressants have a similar effect, because they inhibit monoamine oxidase (MAO inhibitors) and prevent the degradation of phenylethylamine. Therefore, chocolate can have antidepressant effect. Chocolate contains anandamide, a substance that is an endogenous cannabinoid and occurs naturally in the brain where stimulates positive feelings. Anandamide targets the same brain structure as tetrahydrocannabinol (THC), the active ingredient in cannabis. Chocolate also contains tryptophan. The release of endorphins is stimulated with chocolate generating feeling of pleasure and promoting a sense of well-being. Alkaloids in chocolate, as well as in wine and beer improve mood (Smit et al., 2004; Parker et al., 2006).

Some researchers believe that women crave chocolate prior to menstruation because it contains high levels of magnesium. Magnesium deficiency increases the intensity of premenstrual syndrome. Even 91 % of women have cravings for chocolate in the second half of their menstrual cycle, with greater desire in the afternoon and early evening, and magnesium intake could significantly improve premenstrual mood changes (Ghalwa et al., 2014).

Another CNS stimulant is caffeine, which shows positive and adverse effects depending on a dose and frequency of administration. Caffeine is a chemical methylxanthine, first isolated from coffee beans, which is the major source of caffeine, but is also found in other drinks such as green and black tea, Guaraní, cocoa and soft drinks, especially Cola and energy drinks (Persad, 2011). The amount of caffeine present in products depends on the type of a product, serving size and preparation method. Chocolate also contains small amounts of caffeine, but for the sake of comparison it can be said that a cup of cocoa contains 20 mg of caffeine, while a cup of tea contains 40 mg on average, and a cup of coffee contains 155 mg of caffeine (Heckman et al., 2010).

Caffeine acts as an antagonist to adenosine receptors. Adenosine is a substance produced in the body as a product of increased metabolism and signals fatigue and the need for rest (Higgins et al., 2010). Caffeine therefore acts as a psychostimulant in the brain: enhances attention, causes alertness, improves memory and increases the ability to process degraded stimuli. At the same time also raises heart rate, increases force of myocardial contraction, secretion of urine and secretion of gastric juice. The most notable behavioural effects of caffeine occur 15 minutes after drinking caffeinated beverage (Persad, 2011).

Due to caffeine effects, including increased alertness, energy, ability to concentrate and wakefulness, it is primarily used as a stimulant in fatigue and somnolence. Consumption of caffeinated coffee in a dose-dependent was found to reduce the incidence of dementia, particularly Parkinson's disease (Fredholm, 2011).

Scientists believe that caffeine consumption is safe up to 200 mg per day and has beneficial effects on the body even in people with hypertension (Cano-Marquinaa et al., 2013).

Ingestion higher than 400 mg of caffeine, especially in caffeine-sensitive individuals, pregnant women and children, may have adverse effects like insomnia, excessive excitement, nervousness, increased heart rate and increased gastric acid secretion (Persad, 2011; Higgins et al., 2010; Nehlig et al., 1992; Snel and Lorist, 2011).

Conclusions

Studies have shown that food can promote proper functioning of the brain. In order to improve our mental abilities, concentration, memory and vigilance, proper nutrition is of great importance. By affecting neurotransmitters, substances that activate different regions of the brain, actively participate in the creation of nerve impulses and thereby regulate our mental abilities, emotions and mood. Cognitive performance and maintenance of mental health, especially among elderly may be improved with proper diet consisting of complex carbohydrates, polyunsaturated fatty acids, especially omega-3 fatty acids, proteins and specific foods containing specific nutrients, like flavonoids. In addition, mood and concentration as well as alertness can be affected by moderate consumption of chocolate and caffeinated beverages. Keeping in mind the risk factors for loss of mental abilities, by proper nutrition we can potentially prevent or delay neurodegenerative changes in the brain including Parkinson's and Alzheimer's disease. The conclusion arising from the compiling evidence elaborated in the text says that in order to improve cognitive performance and maintain brain vitality the Mediterranean diet should be chosen. The Mediterranean diet poses itself as a possible solution via its specific combination of foods which are, if separately analysed for nutrient composition, the ideal combination to maintain and keep proper brain function through old age.

References

Banjari, I., Bajraktarović-Labović, S., Misir, A. et al. (2013): Mediterranean diet and cardiovascular diseases, *Timočki medicinski glasnik* 38 (4), 188-202.

Benton, D. (2008): The influence of children's diet on their cognition and behaviour, *Eur. J. Nutr.* 47 (3), 25-37.

Black, M.M., Quigg, A.M., Hurley, K.M. et al. (2011): Iron deficiency and iron-deficiency anemia in the first two years of life: strategies to prevent loss of developmental potential, *Nutr. Rev.* 69 (Suppl 1), S64-S70.

Bradbury, J. (2011): Docosahexaenoic Acid (DHA): an ancient nutrient for the modern human brain, *Nutrients* 3, 529-554.

Brown, L.S. (2010): Life cycle nutrition: An evidence-based approach. In: Edelstein S, Sharlin J (ed) Nutritional requirements during pregnancy and lactation. Jones and Bartlett Publishers, London.

Budson, A.E., Price, B.H. (2005): Memory dysfunction, *N. Engl. J. Med.* 352, 692-699.

Cano-Marquinaa, A., Tarínb, J.J., Canoc, A. (2013): The impact of coffee on health, *Maturitas* 75, 7-21.

Chatzi, L., Papadopoulou, E., Koutra, K. et al. (2012): Effect of high doses of folic acid supplementation in early pregnancy on child neurodevelopment at 18 months of age: the mother-child cohort 'Rhea' study in Crete, Greece, *Public Health Nutr.* 15 (9), 1728-1736.

Coimbra, N.C. (2014): Nourish - Carbohydrates Fuel Your Brain. The Franklin Institute Online. http://www.fi.edu/learn/brain/carbs.html. Accessed 15 February 2014.

Conklin, S.M., Gianaros, P.J., Brown, S.M. et al. (2007): Long-chain omega-3 fatty acid intake is associated positively with corticolimbic gray matter volume in healthy adults, *Neurosci Lett.* 421 (3), 209-212.

Cunnane, S.C., Plourde, M., Pifferi, F. et al. (2009): Fish, docosahexanoic acid and Alzheimer's disease, *Prog. Lipid Res.* 48, 239-256.

Cunnane, S.C., Chouinard-Watkins, R., Castellano, C.A. et al. (2013): Docosahexaenoic acid homeostasis, brain aging and Alzheimer's disease: Can we reconcile the evidence?, *Prostaglandins Leukot Essent Fatty Acids* 88, 61-70.

Daubner, S.C., Le, T., Wang, S. (2011): Tyrosine hydroxylase and regulation of dopamine synthesis, *Arch. Biochem. Biophys* 508 (1), 1-12.

Davis, B.C., Kris-Etherton, P.M. (2003): Achieving Optimal Essential Fatty Acid Status in Vegetarians: Current Knowledge and Practical Implications, *Am. J. Clin. Nutr.* 78 (3), 640S-646S.

De Lorgeril, M. (2013): Mediterranean diet and cardiovascular disease: historical perspective and latest evidence, *Curr. Atheroscler Rep.* 15:370. DOI: 10.1007/s11883-013-0370-4.

EFSA, European Food Safety Authority (2008) ALA and LA and growth and development of children, *The EFSA Journal* 783, 1-9.

EFSA, European Food Safety Authority (2009) DHA and support of the cognitive development of the unborn child and breastfed infant, *The EFSA Journal* 1007, 1-14.

EFSA, European Food Safety Authority (2010) Scientific Opinion on Dietary Reference Values for fats, including saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids, *trans* fatty acids, and cholesterol, *EFSA Journal* 8 (3), 1461.

Ek, K.L., Brand-Miller, J., Copeland, L. (2012): Glycemic effect of potatoes, *Food Chem.* 133 (4), 1230-1240.

Engler, M.B., Engler, M.M. (2004): The vasculoprotective effects of flavonoid-rich cocoa and chocolate, *Nutr. Res.* 24 (9), 695-706.

Estruch, R., Ro,s E., Salas-Salvadó, J. et al. (2013) Primary prevention of cardiovascular disease with a Mediterranean diet, *N. Engl. J. Med.* 368 (14), 1279-1290.

FAO, Food and Agriculture Organization of the United Nations (2010) Fats and fatty acids in human nutrition: Report of an expert consultation. FAO, Rome.

Fernstrom, J.D. (2013): Large neutral amino acids: dietary effects on brain neurochemistry and function, *Amino Acids* 45 (3), 419-430.

Fredholm, B.B. (2011): Methylxanthines. Handbook of Experimental Pharmacology 200. Springer, Berlin.

Gardener, H., Wright, C.B., Gu, Y. et al. (2011): Mediterranean-style diet and risk of ischemic stroke, myocardial infarction, and vascular death: the Northern Manhattan Study, *Am. J. Clin. Nutr.* 94 (6), 1458-1464.

Georgieff, M.K. (2011): Long-term brain and behavioral consequences of early iron deficiency, *Nutr. Rev.* 69 (Suppl 1), S43-S48.

Ghalwa, N.A., Qedra, R.A., Wahedy, K. (2014): Impact of calcium and magnesium dietary changes on women pain and discomfort from premenstrual syndrome at the Faculty of Pharmacy-Gaza Strip, *WJPPS* 3 (2), 981-1005.

Gogus, U., Smith, C. (2010): n-3 omega fatty acids: a review of current knowledge, *Int. J. Food .Sci. Technol.* 45, 417-436.

Goldoni, L. (2004): Kakao zrna i kakao proizvodi. In: Tehnologija konditorskih proizvoda: Kakao i čokolada. Kugler, Zagreb.

Greenberg, J.A., Bell, S.J., Van Ausdal, W. (2008): Omega-3 fatty acid supplementation during pregnancy, *Rev. Obstet Gynecol* 1 (4), 162-169.

Gustafson, E. (2008)_ Nutrition and mental health. In: Fundukian LJ, Wilson J (ed) Gale encyclopedia of mental health. 2nd ed. Thompson Gale, Detroit.

Hamburg, M.E., Finkenauer, C., Schuengel, C. (2014): Food for love: the role of food offering in empathic emotion regulation, *Front Psychol.* 5:32. DOI: 10.3389/fpsyg.2014.00032.

Heckman, M.A., Weil, J., Gonzalez de Mejia, E. (2010): Caffeine (1, 3, 7-trimethylxanthine) in foods: A comprehensive review on consumption, functionality, safety, and regulatory matters, *J. Food Sci.* 75 (3), R77-R87.

Higgins, J.P., Tuttle, D.T., Higgins, H.L. (2010): Energy beverages: content and safety, *Mayo Clin. Proc.* 85 (11), 1033-1041.

Hodge, A.M., English, D.R., Itsiopoulos, C. et al. (2011): Does a Mediterranean diet reduce the mortality risk associated with diabetes: evidence from the Melbourne Collaborative Cohort Study, *Nutr. Metab. Cardiovasc. Dis.* 21 (9), 733-739.

Hoevenaar-Blom, M.P., Nooyens, A.C., Kromhout, D. et al. (2012): Mediterranean style diet and 12-year incidence of cardiovascular diseases: the EPICNL cohort study, *PLoS One* 7 (9):e45458.

Hoffman, R., Gerber, M. (2013): Evaluating and adapting the Mediterranean diet for non-Mediterranean populations: A critical appraisal, *Nutr. Rev.* 71 (9), 573-584.

Holmes, G.L., Yang, Y., Liu, Z. et al. (2002): Seizure-induced memory impairment is reduced by choline supplementation before or after status epilepticus, *Epilepsy Res.* 48 (1-2), 3-13.

Isaacs, E., Oates, J. (2008): Nutrition and cognition: assessing cognitive abilities in children and young people, *Eur. J. Nutr.* 47 (3), 4-24.

Jalil, A.M.M., Ismail, A. (2008): Polyphenols in cocoa and cocoa products: Is there a link between antioxidant properties and health?, *Molecules* 13, 2190-2219.

Jenkins, D.J.A., Augustin, L.S.A., Malick, A. et al. (2013): Glucose: Chemistry and Dietary Sources. In: Encyclopedia of Human Nutrition. 3th ed. University of Toronto, Toronto.

Jensen, C.L., Voigt, R.G., Prager, T.C. et al. (2005): Effects of docosahexaenoic acid intake on visual function and neurodevelopment in breastfed term infants, *Am. J. Clin. Nutr.* 82 (1). 125-132.

Kaczmarczyk, M.M., Miller, M.J., Freund, G.G. (2012): The health benefits of dietary fiber: Beyond the usual suspects of type 2 diabetes mellitus, cardiovascular disease and colon cancer, *Metab. Clin. Exp.* 61, 1058-1066.

Kendall, C.WC., Esfahani, A., Jenkins, D.J.A. (2010): The link between dietary fiber and human health, *Food Hydrocolloid* 24 (1), 42-48.

Kidd, P.M. (2007): Omega-3 DHA and EPA for cognition, behavior, and mood: clinical findings and structural-functional synergies with cell membrane phospholipids, *Altern. Med. Re.v* 12 (3), 207-27.

Langley-Evans, S.C. (2008): Metabolic programming during pregnancy: Implications for personalized nutrition. In: Kok F, Bouwman L, Desire F (ed) Personalized Nutrition. Principles and Applications. CRC Press, Routledge.

Lourida, I., Soni, M., Thompson-Coon, J. et al. (2013): Mediterranean diet, cognitive function, and dementia: a systematic review, *Epidemiology* 24 (4), 479-489.

Martínez-González, M.A., Guillén-Grima, F., De Irala, J. et al. (2012): The Mediterranean diet is associated with a reduction in premature mortality among middle-aged adults, *J. Nutr.* 142 (9), 1672-1678.

McCann, J.C., Ames, B.N. (2007): An overview of evidence for a causal relation between iron deficiency during development and deficits in cognitive or behavioral function, *Am. J. Clin. Nutr.* 85, 931-945.

McCann, J.C., Hudes, M., Ames, B.N. (2006): An overview of evidence for a causal relationship between dietary availability of choline during development and cognitive function in offspring, *Neurosci. Biobehav. Rev.* 30, 696-712.

Misirli, G., Benetou, V., Lagiou, P. et al. (2012): Relation of the traditional Mediterranean diet to cerebrovascular disease in a Mediterranean population, *Am. J. Epidemiol.* 176 (12), 1185-1192.

Montgomery, P., Burton, J.R., Sewell, R.P. et al. (2013): Low blood long chain omega-3 fatty acids in UK children are associated with poor cognitive performance and behaviour: A cross-sectional analysis from the DOLAB study, *PLoS ONE* 8 (6):e66697.

Nehlig, A., Daval, J.L., Debry, G. (1992): Caffeine and the central nervous system: mechanisms of action, biochemical, metabolic and psychostimulant effects, *Brain. Res. Rev.* 17 (2), 139-170.

Page, K.A., Chan, O., Arora, J. et al. (2013): Effects of fructose versus glucose on regional cerebral blood flow in brain regions involved with appetite and reward pathways, *JAMA* 309 (1), 63-70.

Parker, G., Brotchie, H. (2011): Mood effects of the amino acids tryptophan and tyrosine, *Acta Psychiatr Scand* 124, 417-426.

Parker, G., Parker, I., Brotchie, H. (2006): Mood state effects of chocolate, *J. Affect Disord.* 92, 149-159.

Paoletti, R., Poli, A., Conti, A. et al. (2012): Chocolate and Health. Springer, Milan.

Persad, L.A.B. (2011): Energy drinks and the neurophysiological impact of caffeine, *Front Neurosci.* 5:116, PMC3198027.

Privitera, G., Moshaty, B., Marzullo, F. et al. (2013): Expressing food through art: evidence for a nutrient-specific effect on mood, *JBBS* 3 (2), 163-167.

Purnell, J.Q., Fair, D.A. (2013): Fructose ingestion and cerebral, metabolic, and satiety responses, *JAMA* 309 (1), 85-86.

Rawel, H.M., Kulling, S.E. (2007): Nutritional contribution of coffee, cacao and tea phenolics to human health, *J. Verbr. Lebensm.* 2, 399-406.

Shah, R. (2013): The role of nutrition and diet in Alzheimer disease: a systematic review, *J. Am. Med. Dir. Assoc.* 14 (6), 398-402.

Shaikh, S.R., Brown, D.A. (2013): Models of plasma membrane organization can be applied to mitochondrial membranes to target human health and disease with polyunsaturated fatty acids, *Prostag Leukotr Ess* 88 (1), 21-25.

Skarupski, K.A., Tangley, C.C., Li, H. et al. (2013): Mediterranean diet and depressive symptoms among older adults over time. The Journal of Nutrition, *Health & Aging* 17 (5), 441-445.

Smit, H.J., Gaffan, E.A., Rogers, P.J. (2004): Methylxanthines are the psycho-pharmacologically active constituents of chocolate, *Psychopharmacology* 176, 412-419.

Snel, J., Lorist, M.M. (2011): Effects of caffeine on sleep and cognition, *Prog. Brain Res.* 190, 105-117.

Sofi, F. Macchi, C., Casini, A. (2013): Mediterranean diet and minimizing neurodegeneration, *Curr. Nutr. Rep.* 2, 75-80.

Sommer, E. (1995): Food and mood. The complete guide to eating well and feeling your best. Henry Holt, New York.

Tognon, G., Lissner, L., Sæbye, D. et al. (2013): The Mediterranean diet in relation to mortality and CVD: a Danish cohort study, *Br. J. Nutr.* 111 (1), 151-159.

Trichopoulou, A., Costacou, T., Bamia, C. et al. (2003): Adherence to a Mediterranean diet and survival in a Greek population, *N. Engl. J. Med.* 348, 2599-608.

Vanhees, K., Vonhögen, I.G.C., van Schooten, F.J. et al. (2014): You are what you eat, and so are your children: the impact of micronutrients on the epigenetic programming of offspring, *Cell Mol. Life Sci.* 71, 271-285.

Vannice, G., Rasmussen, H. (2014): Position of the Academy of Nutrition and Dietetics: Dietary fatty acids for healthy adults, *J. Acad. Nutr. Diet* 114 (1), 136-153.

Wenk, G.L. (2010): Your brain on food. How chemicals control your thoughts and feelings. Oxford University Press, New York.

WHO, World Health Organization (2007): Exposure to mercury: a major public health concern. WHO, Geneva.

WHO, World Health Organization (2008): Interim summary of conclusions and dietary recommendations on total fat and fatty acids: From the Joint FAO/WHO Expert Consultation on fats and fatty acids in human nutrition. WHO, Geneva.

WHO, World Health Organization (2010): Children's exposure to mercury compounds. WHO, Geneva.

Yurko-Mauro, K., McCarthy, D., Rom, D. et al. (2010): Beneficial effects of docosahexaenoic acid on cognition in age-related cognitive decline, *Alzheimers Dement* 6 (6), 456-464.