

Prophylaxis of cognitive functions disorders progressing with age in women

Iwona Bojar

Institute of Rural Health, Lublin, Poland

Numerous structures of the central nervous system are responsible for cognitive functioning. The cortex is responsible for the accumulation of long-term memory. The hippocampus participates primarily in the formation of short-term episodic memory. The amygdala is involved in the formation of emotional memory. In the shell are collected the recordings of our procedural memory, memory of skills, while the caudate nucleus is responsible for our instinctive behaviour, i.e. the genetic memory. Cognitive functioning depends on the efficient co-functioning of the above-mentioned structures of the encephalon. Studies in the area of neurobiology indicate that the region where there occur the first changes related with ageing is the so-called prefrontal cortex and parietal lobes [1, 2].

There are many theories which attempt to explain the processes and the scope of changes in cognitive functioning related with age [3, 4, 5, 6]. At the same time, it has been confirmed that the speed of processing most significantly decreases with age. Considering the basic differences in speed, the indices of selective attention remain almost unaltered with ageing. However, attention divisibility and capability for shifting attention, i.e. our cognitive plasticity [1, 2].

Several mechanisms are responsible for the ageing of human body cells, including nerve cells. One such mechanism is telomere shortening, the so-called replication old age. Telomeres shorten with age, nevertheless, the pace of their shortening depends, on the one hand, on the genetic susceptibility, and on the other, on the effect of environmental factors and our life style. For example, cigarette smoking accelerates the pace of telomere shortening. The second mechanism mentioned is the mechanism of damaging proteins and cellular organelles by free radicals stimulated by environmental factors. The important mechanisms of cellular ageing is also damage to the mechanism of DNA repair, which leads to the accumulation of mutations in a cell and its early apoptosis, as well as abnormal growth factor signals [7].

Nowadays, Alzheimer's disease is the most serious neurodegenerative disease, its frequency of occurrence increasing with age. At the moment of occurrence of the first symptoms of this disease, most often, the nerve cells are already irreversibly damaged. This is probably due to the reason that there are still no sufficiently effective medicines for this disease. Consequently, the attention of researchers is directed towards the possibilities of prevention or delaying the occurrence of Alzheimer's disease. Females are more frequently afflicted by this disease than males; therefore, women are the population group where prophylaxis should play a special role.

The American Alliance for Aging Research recommends 10 steps to preserve brain fitness until late old age [8]. These steps are:

- 1) Brain diet;
- 2) Intellectual activity;

- 3) Regular physical activity;
- 4) Social contacts.

These first four steps will be discussed in a further section of the study.

Step 5) Sufficient amount of sleep. Scientific studies confirmed that sleep which is too short, less than five hours daily, increases the risk of dementia. Studies on animals demonstrated that shortness of sleep was related with an elevated level of β amyloid in cerebrospinal fluid. A similar mechanism of the effect of sleep deficiency is suspected in humans [9].

Step 6) Stress control. Both an intensive short-term stress and chronic stress may cause damage to nerve cells. According to the results of studies, long-term stress is related with an unfavourable effect of elevated levels of cortisol on the brain, and an increased risk of the development of dementia and Alzheimer's disease [7].

Step 7) Prevention of brain injuries. According to literature, not only large cerebral strokes leading to permanent damage to cerebral structures are the cause of cognitive disorders, but also accumulation of fine injuries over a long period of time may accelerate the development of dementia. It was found that in sportsmen practicing contact sports, changes of the dementia type occur earlier, compared to the population not exposed to micro-injuries of the nervous central system [10].

Step 8) Normal body weight. Obesity positively correlates with a higher risk of development of dementia. Also, diseases accompanying obesity, such as diabetes or hypertension, contribute to this. However, it should be kept in mind that in older people aged over 60 the reduction in body weight may also be a bad prognostic indicator, because it may be the first symptom of developing dementia [11].

Step 9) Avoidance of unhealthy habits (cigarette smoking, alcohol abuse, use of stimulants or narcotics). It has been unequivocally confirmed in reliable scientific studies that cigarette smoking increases the risk of development of dementia. Also alcohol abuse, even sporadically, more rarely than once a month, accelerates the development of dementia by approximately three years. However, it is an interesting fact that the consumption of small amounts of alcohol, especially red wine, is conducive for our cognitive functions. With respect to stimulants and narcotics, according to the currently applicable knowledge, they increase the risk of development of neurodegenerative changes in the brain, despite the publication of single reports concerning the possibility of application of cannabis plasters in the treatment of Alzheimer's disease [12].

Step 10) Genes. To-date, the $\epsilon 4$ allele of the apolipoprotein E (APOE) gene carrier status is the only proven risk factor of late revealed Alzheimer's disease. The carrier state of one $\epsilon 4$ allele of the apolipoprotein E (APOE) gene increases the risk three times, whereas the carrier status of two such alleles is related with a 10-fold higher risk of Alzheimer's disease [13].



Referring back to Step 1, according to many studies, the most favourable diet for our brain is the Mediterranean diet [14]. This diet is rich in fishes, olive oil, garlic, and many other vegetables with strong anti-oxidant properties. It contributes to the regulation of glycaemia, improves lipid profile, decreases the level of cholesterol, and improves the condition of blood vessels. For example, olive oil contains a substance called oleocanthal, which prevents the accumulation of β amyloid in the brain and inhibits the formation of tau tangles, basic pathologies in Alzheimer's disease. It was found that regular use of the Mediterranean diet decreases the risk of cognitive disorders developing with age by 28%, and adhering to the Mediterranean diet reduces the risk of transition from mild cognitive disorders to dementia by approximately 50%.

The content of antioxidants in the diet is important for the maintenance of normal cognitive functioning. The products containing high amounts of antioxidants are vegetables, especially greens, such as lettuce, spinach, and cruciferous vegetables such as cabbage, Brussels sprouts, or broccoli. According to scientific reports, a diet rich in vegetables with strong antioxidant properties may decrease the risk of dementia by approximately 30% [15].

Also, various kinds of fruits have strong antioxidant properties, especially bilberries, blueberries, or blackberries, which contain large amounts of polyphenols and anthocyanins [16]. Nuts and almonds are very favourable in the everyday diet which, apart from substances with strong antioxidative and antiinflammatory properties, stimulate the secretion of acetylcholine in the central nervous system – a neurotransmitter participating in cognitive processes acting against the accumulation of β amyloid in the brain [17].

A diet containing food products with a low glycaemic index is also beneficial for cognition. It has been confirmed that post-meal glucose excursions are related with the accelerated development of neurodegenerative changes [18].

A low-calorie diet rich in Omega-3 polyunsaturated fatty acids and free from saturated fat, Omega-6 fat, and trans fats is also important for the brain. Scientific studies show that high consumption of saturated fat and trans fats increases the risk of dementia four times. A high-calorie diet, through its effect on insulin resistance, may contribute to an increased accumulation of β amyloid in the brain [17, 19].

The consumption of cacao, which contains flavanols with strong antioxidative and anti-inflammatory properties, is very beneficial for efficient cognitive functioning. It was also confirmed that high consumption of cacao stimulates cerebral circulation and contributes to the regeneration of neurons and stimulation of neurogenesis [20, 21].

Also caffeine, apart from antioxidative and anti-inflammatory properties, contributes to the removal of toxins from the brain, and may limit the accumulation of β amyloid. Epidemiological studies demonstrated that coffee, which apart from caffeine, contains other substances with antioxidative properties, is one of the main sources of antioxidants in the diet of women from Western countries [22]. Similarly beneficial is the consumption of tea, containing epigallocatechin-gallate which, apart from antioxidative properties, neutralizes the toxic effect of β amyloid and chelates iron ions in the brain.

Brain diet should also include such spices as cinnamon and curry. Cinnamon decreases insulin resistance and reduces the level of cholesterol and triglycerides and contains methyl hydroxy chalcone polymer, which probably inhibits

the formation of tau tangles, especially important in the prevention of Alzheimer's disease [23]. Curcumin present in curry also shows strong antioxidative and antiinflammatory action. It inhibits the deposition of β amyloid in the brain and accelerates its decomposition and disposal. Frequent consumption of small amounts of spices is more beneficial than large amounts consumed rarely [24].

Interesting scientific reports show that the consumption of apple juice may exert a favourable effect on cognitive functions. Apple juice contains quercetin – a substance with strong antioxidative properties. In addition, it was confirmed that apple juice increases the secretion of acetylcholine in the brain and reduces the accumulation of β amyloid [25].

Considering the high contents of antioxidants, women who consume large amounts of phytoestrogens also benefit with respect to cognitive functions.

Vitamins in the diet are also indispensable for normal cognitive functioning, such as vitamin D, folic acid, niacin and vitamin B12. Folic acid and B-group vitamins in higher doses decrease the level of homocysteine in the brain, which damages nerve cells [26, 27].

Within the last several years, studies have been conducted concerning substances called sirtuins, which are mediators of the effect of caloric restrictions on longevity. Despite the fact that studies of these substances are still continuing, it is known that they promote the expression of a number of genes encoding proteins which increase metabolic activity, decrease apoptosis of cells, stimulate protein folding, and neutralize the hazardous effect of reactive oxygen species. Moreover, sirtuins increase the susceptibility of cells to insulin and accelerate glucose metabolism. They also decrease the accumulation of β amyloid by exerting an effect on an increase in the activity of α -secretase, an enzyme participating in the metabolism of β amyloid. The substance which stimulates the activity of sirtuins is resveratrol contained, among others, in red wine [28, 29, 30].

Another interesting substance, which several years ago was hailed as a longevity substance is carnosine (beta-alanyl-L-histidine). This is the substance showing strong antioxidative properties, its anti-atherosclerotic effect was confirmed, it improves blood vessels elasticity and oxygenation of cells. It also has a detoxifying effect on the body. In addition, from the aspect of cognitive functions, apart the above-mentioned beneficial effects, this substance prevents cell damage by β amyloid and inactivates β amyloid in the brain [31, 32].

Returning to the 10 steps recommended by the Alliance for Aging Research, regular physical effort is necessary to maintain a high psychological condition. Every type of effort related with the practicing of sports, as well as with daily activity, increases the secretion of a brain-derived neurotrophic factor, the secretion of which declines with age. The brain-derived neurotrophic factor enhances the development and survival of new neurons and stimulates synaptogenesis. A higher level of this factor is associated with an observed increase in hippocampal volume [33]. Walking eight kilometres weekly is recommended to protect the brain structures responsible for learning and memorizing for five and up to ten years [34].

Cognitive activity in the form of mental activity (learning new things), occupational activity or active forms of leisure contributes to the increase in our 'cognitive reserve', and therefore, decreases the risk of occurrence of cognitive disorders and dementia. Also, cognitive activity increases secretion of



the brain-derived neurotrophic factor. Studies confirmed that individuals with a high cognitive activity have an increased hippocampal volume. It is an interesting fact that people with a higher level of education have greater cognitive capabilities, despite an identical amount of pathological changes observed in them, typical of Alzheimer's-type dementia [35, 36].

And finally, Step 4 – social contacts/social activity. It has been confirmed that people who have a limited number of social contacts and show low engagement in social life may be more exposed to the development of dementia. Through social activity we also expand our 'cognitive reserve', and in this way we may decrease the risk of cognitive disorders [37].

While evaluating the effect of cognitive components, forms of spending leisure time, social and physical activity, in one of the studies it was found that each component is equally important for protection against the development of dementia [38].

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