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## **The impact of diet on neurodegenerative diseases**

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**Abstract**

**Background:** Nowadays the average age of population is increasing, resulting in a growing proportion of older people in society. Diseases typical of older adults pose a major challenge for modern medicine. These include, among others, neurodegenerative diseases.

**Aim:** To provide a general overview of the most common neurodegenerative diseases, with particular emphasis on substances essential for the proper functioning of the nervous system and diets used to prevent and alleviate the symptoms of neurodegenerative diseases.

**Materials and methods:** This article reviews the publicly available literature from recent years on neurodegenerative diseases, diets used in their treatment and substances essential for the proper functioning of the nervous system.

**Results:** Oxidative stress plays a significant role in the development of nervous system damage in neurodegenerative diseases. Therefore, for the proper functioning of the nervous system, it is essential to provide antioxidant substances in the diet, which mitigate the effects of oxidative stress. Vitamins and polyunsaturated fatty acids are also important in the diet. These nutrients are part of a healthy, balanced diet, which includes the Mediterranean diet.

**Conclusions:** Using a well-balanced diet as a part of healthy lifestyle can prevent neurodegenerative diseases, and if they do occur, slow their progression or help improve the quality of life of those affected. Therefore, diet and a healthy lifestyle are extremely important for healthy aging and the prevention of age-related diseases.

**Keywords:** antioxidants; diet; disease prevention; neurodegenerative diseases; vitamins

## **1. Introduction and the aim**

With advances in medicine, improved quality of life, increased education, and the development of health education, the average age of the population is steadily increasing [1],[2],[3]. This results in a growing proportion of older people in society, and with it, new challenges related to diseases specific to this age group arise [3],[4],[5],[6],[7]. With age, the body gradually loses its regenerative capacity, which is associated with a greater risk of aging-related diseases. Cardiovascular diseases are a major problem in society. However, diseases of the nervous system, including neurodegenerative diseases, constitute an important group of diseases associated with high mortality, affecting not only individuals but also the families of patients who are responsible for caring for the affected individual [3],[4],[5],[6],[7],[8],[9]. To date, there is no effective causal treatment for neurodegenerative diseases. Treatment largely involves attempts to control the main symptoms and modify the course of the disease. Due to the nature of neurodegenerative diseases (changes in the nervous system develop slowly, often much earlier than symptoms appear), it turns out that they can be prevented to some extent or further damage can be inhibited at an early stage and their symptoms can be alleviated by following appropriate nutritional recommendations [8]. That is why the aim of our work is to provide a general overview of the most common neurodegenerative diseases, with particular emphasis on substances essential for the proper functioning of the nervous system and diets used to prevent and alleviate the symptoms of neurodegenerative diseases.

## **2. State of knowledge**

### **2.1. Neurodegenerative diseases**

Neurodegenerative diseases are a group of progressive disorders of the nervous system that involve damage and loss of nerve cells. In most cases, the etiology is unknown, but it is usually multifactorial, depending on both genetic and environmental factors [6],[10],[11]. They lead to deterioration of motor function and memory impairment, leading to dementia. Symptoms of neurodegenerative diseases typically appear gradually as a result of long-term changes in the nervous system. Among the most common neurodegenerative diseases that pose a challenge to an aging population are Alzheimer's disease (AD), Parkinson's disease (PD), and amyotrophic lateral sclerosis (ALS), which will be the focus of the remainder of this article [6].

**2.1.1. Alzheimer's disease (AD)** is a degenerative brain disease characterized by the deposition of abnormal proteins – beta-amyloid (extracellularly and in the walls of cerebral vessels) and tau protein (intracellularly). This causes damage and death of nerve cells, and consequently, reduces the production of neurotransmitters essential for proper brain function. The incidence of Alzheimer's disease increases with age and is more common in women [12], [13], [14]. Most cases are sporadic, unrelated to a familial history. Comorbidities such as hypertension, heart failure, and type 2 diabetes contribute to its development, as well as Down syndrome, depression, traumatic brain injury and hearing loss. Additional factors contributing to the development of Alzheimer's disease include low physical activity, lack of social contact, and a high level of education, while not protecting against its onset, delays symptoms and may contribute to a milder course of the disease [12], [13].

The first changes (prodromal phase) occur long (up to 20 years) before symptoms appear. The disease manifests itself through progressive cognitive functions and memory impairment. Initially, a decline in mental function and personality changes are observed, followed by increasing behavioral disturbances (including sudden outbursts of anger and aggression). The patient begins to require assistance with daily activities. In the final stage, movement disorders develop, and the lifestyle becomes increasingly sedentary, and in the terminal stage, bedridden. The patients require constant care, stop communicating with others, do not recognize close relatives or themselves, and lose control over their own body [5], [12], [13].

Current treatment is symptomatic, and the only period in which causal treatment can be applied is the prodromal phase of the disease. In addition to pharmacological treatment, psychological support, cognitive, reminiscence and environmental therapies as well as management of comorbidities are important. This approach can attempt to slow the progression of cognitive and functional impairments even in the initial stages of the disease. Therefore, constant intellectual stimulation, physical and social activity, and a proper diet are important. Treatment should be continued for the rest of the patient's life [5], [12], [13],[15].

**2.1.2. Parkinson's disease (PD)** is a degenerative brain disorder characterized by the loss of dopaminergic cells in the substantia nigra, leading to dopamine deficiency in the striatum. The etiology is unknown, but it is largely multifactorial, resulting from the interaction of both genetic and environmental factors. It more commonly affects men [16],[17].

Symptoms correlate with neuropathological changes. Initially, nonspecific symptoms such as olfactory disorders, constipation, sleep disturbances, or depression may occur even years before the disease manifests. Later, motor symptoms appear, such as bradykinesia (slowed movement), muscle stiffness, hand tremors, shoulder pain, handwriting changes (micrographia), loss of balance in the upper limb while walking, and catching the lower limb on uneven surfaces. Initially, these symptoms can be controlled with medication, but as the disease progresses, treatment becomes less effective, with balance disorders resulting in falls and non-motor symptoms appearing, most often neuropsychiatric – depression, dementia, anxiety, apathy, and psychotic disorders. Over time, the disease causes severe disability and complete dependence on the help of others. It is worth noting that Parkinson's disease begins asymmetrically. Even in the advanced stages of the disease, when symptoms are bilateral, the asymmetry is noticeable [\[16\]](#),[\[17\]](#).

Pharmacological treatment is primarily symptomatic but extremely effective. Patients often respond well, although it is associated with numerous side effects. Therefore, the principle of using the lowest effective dose (especially dopaminergic drugs) is particularly important in the treatment of this disease. Despite the side effects, such treatment helps significantly slow the progression of the disease and extends the period of functional capacity by up to 7-10 years. In addition to pharmacological treatment, rehabilitation therapy is important to extend the period of independent functioning. Invasive treatment in the form of stereotactic surgery or deep brain stimulation may be considered. Although there is no special diet for Parkinson's disease, appropriate nutritional recommendations are essential for proper digestive function and drug absorption [\[16\]](#),[\[17\]](#).

**2.1.3. Amyotrophic lateral sclerosis (ALS)** is a degenerative disease of the nervous system that causes progressive damage to peripheral and central motor neurons. The etiology is unknown in most cases, but genetic factors are important – 10-15% of cases run in families, but the majority are sporadic [\[18\]](#),[\[19\]](#),[\[20\]](#).

The disease initially manifests as muscle weakness and then atrophy – most often beginning with involvement of the limb muscles (limb onset) or speech and swallowing disorders (bulbar onset), but without sensory impairment. Patients gradually experience increasing difficulty with daily activities, movement, and eating. Some patients require percutaneous endoscopic gastrostomy (PEG). Over time, all striated muscles are affected, most often sparing the

extraocular muscles. Weakness of the respiratory muscles leads to respiratory failure and death. Respiratory support can be achieved by using non-invasive ventilation, which will improve the patient's quality of life, or even artificial ventilation with a ventilator, which can extend life by up to several years. However, it should be remembered that the patient will remain completely paralyzed. Therefore, prior discussion and detailed treatment plans are essential before the patient is no longer able to communicate effectively on their own. Furthermore, approximately 50% of patients experience behavioral or cognitive impairment [\[18\]](#),[\[19\]](#),[\[20\]](#).

ALS is a progressive and incurable disease that leads to death relatively quickly (2-4 years from diagnosis). There is no effective method to halt the disease or restore mobility; symptomatic treatment is used. Rehabilitation, especially breathing exercises, is crucial. The only medication recommended for all patients to slow the progression of the disease is riluzole, but it only prolongs life by 2-3 months. Psychological support (often anxiety disorders and depression due to the disease) and speech therapy may also be helpful – it allows for maintaining the ability to communicate verbally and swallow for a longer period of time [\[18\]](#),[\[19\]](#),[\[20\]](#).

## **2.2. Substances necessary for the proper functioning of the nervous system**

To understand the importance of a proper diet for neurodegenerative diseases, it's worth first understanding which substances are essential for proper body function, with particular emphasis on the nervous system. Proper growth and maintenance of vital functions are supported by adequate nutritional requirements [\[21\]](#). An inappropriate diet causes oxidative stress, an imbalance in redox reactions that disrupts cellular signaling and causes molecular damage, manifesting as disorders in key brain regions [\[22\]](#),[\[23\]](#),[\[24\]](#),[\[25\]](#). Oxidative stress is considered a key factor in the pathophysiology of neurodegenerative diseases [\[26\]](#),[\[27\]](#). It has been shown that supplementation with antioxidant micronutrients can have a positive impact on the aging body by reducing inflammation and antioxidant activity, thus limiting the occurrence of DNA damage. This reduces the risk and incidence of age-related diseases such as neurodegenerative diseases [\[21\]](#), [\[25\]](#). Antioxidants exert their activity in three ways: they prevent the formation of free radicals and their derivatives, interrupt the oxidation reaction of free radicals, and inactivate the products of free radical reactions. There are endogenous antioxidants, which are primarily enzymes produced by the body, and exogenous antioxidants derived from the diet, such as vitamins, polyphenols, flavonoids, bioflavonoids, and carotenoids, which have in vivo activity [\[6\]](#),[\[24\]](#),[\[28\]](#). Most antioxidants are found in fruits (apples, berries

– blueberry anthocyanins are the most powerful antioxidants found in nature) and vegetables (spinach, olives, including olive oil) [24], [29], [30], [31], [32]. They can also be found in processed products such as wine, coffee (a coffee beverage made from coffee beans), and tea (fresh extracts from tea leaves) [24],[33],[34],[35]. It turns out that beans, cereals (whole grains, corn) and dairy products (milk, yogurt and others) are also important sources of antioxidants [24]. Antioxidant vitamins include vitamins A, C, E, and K2 [3],[7],[36],[37],[38]. Although some studies and articles dispute this, B vitamins are essential for the proper functioning of the nervous system and maintaining normal cognitive function, especially in individuals with their deficiencies [7],[39],[40],[41],[42]. Another key vitamin that demonstrates protective effects against neurodegenerative diseases and influences the development and maturation of neurons is vitamin D3 [7],[43],[44],[45],[46],[47]. Polyunsaturated fatty acids (PUFAs), especially omega-3 and omega-6 fatty acids, are also important substances for the nervous system. However, they do not, like antioxidants and some vitamins, regulate chemical reactions and oxidative stress, but are integral to the composition and functionality of neuronal membranes. Excellent sources of fatty acids include fatty cold-water fish, egg yolks, and vegetable oils. However, further research is needed on their effects on the nervous system, as excessive amounts have been shown to have pro-inflammatory properties [9],[48],[49],[50],[51],[52],[53]. These substances are essential for the proper development and functioning of the nervous system, and therefore must be included in appropriate amounts in the diet of both healthy individuals as a preventative measure and those suffering from neurodegenerative diseases to alleviate their symptoms.

### **2.3. Diet and neurodegenerative diseases**

A fast-paced lifestyle, inattention to dietary choices, vitamin and mineral deficiencies, environmental pollutants, and food quality all have an impact on the human body [22],[54],[55],[56],[57]. First we will begin describe appropriate dietary recommendations for the neurodegenerative diseases discussed above. We will then demonstrate general dietary recommendations for healthy individuals that favorably impact the maintenance of aging body functions and highlight what to avoid. As we already know, the first changes in brain structure can occur even many years before cognitive decline and the onset of full-blown diseases. Diet is a key modifiable risk factor for diseases, not just those affecting the nervous system. Since there is no effective causal treatment for neurodegenerative diseases, dietary interventions, as adjunctive therapy to pharmacological treatment, may be a key strategy in alleviating their symptoms. A significant problem in people affected by neurodegenerative diseases is altered appetite and difficulty swallowing, which can ultimately lead to significant weight loss and

malnutrition [21],[60],[61]. Nevertheless, it is noteworthy that in each of the neurodegenerative diseases described at the beginning, diet has a different therapeutic impact [12], [13], [14],[15],[16],[17],[18],[19],[20],[23],[59],[60].

**2.3.1. Diet in Alzheimer's disease (AD)** – its main goal is to prevent the progression of cognitive impairment [26],[62],[63],[64]. Many studies indicate that the Mediterranean diet is ideal for achieving this goal. It is characterized by increased consumption of vegetables and fruits, nuts, seeds, and whole grains. When it comes to fats, vegetable oils, particularly olive oil, play a key role. Saturated fat intake should remain low. The diet is also supplemented by regular consumption of fish and other seafood (at least twice a week) with limited red meat and confectionery [8],[26],[62],[64],[65]. This diet is rich in the previously mentioned antioxidants, vitamins, and fatty acids essential for the proper functioning of the nervous system [26],[60],[63],[65]. The Nordic diet has similar properties. Comparably to the Mediterranean diet, it is characterized by a higher consumption of fruits, vegetables, fish, and whole grains. The use of rapeseed oil plays an important role here, as it has higher levels of essential fatty acids than olive oil. Blueberries are an equally important component of this diet, with anti-inflammatory properties [62]. Another effective diet for Alzheimer's disease may be the ketogenic diet, although its use may be controversial. In this diet, the ratio of a fat to carbohydrates and protein is 4:1 or 3:1, whereas in a traditional diet, carbohydrates provide the main energy source. It consists primarily of meat, oily fish, eggs, butter, cream, cheese, oils, seeds, nuts, avocados, and non-starchy vegetables. At the same time, alcohol and all grains should be avoided, which is associated with low fiber intake, ultimately leading to digestive issues. Currently, there are no calorie recommendations or recommendations regarding the types of fats used in this diet, so if the wrong products are chosen, the ketogenic diet can be detrimental to health and cause digestive complications, liver dysfunction, metabolic disorders, and micronutrient deficiencies. However, when properly managed, it can increase the production of anti-inflammatory proteins and reduce systemic inflammation in the body. An important aspect of Alzheimer's disease is that it leads to impaired glucose metabolism in the brain, and ketone bodies produced as a result of a ketogenic diet can serve as an alternative energy source [22],[26],[66],[67]. A general diet, the so-called anti-inflammatory diet, rich in fruits, vegetables, whole grains, and lean proteins, is also beneficial for the course of AD [68]. The above-mentioned diets used in the supportive treatment of Alzheimer's disease demonstrate neuroprotective effects, delay the progression of cognitive impairment, help alleviate its symptoms, and are associated with lower mortality due to comorbidities associated with AD.

Moreover, combining different types of diets may be beneficial, e.g. the MIND diet, combining the features of the Mediterranean diet and the DASH diet, characterized by the consumption of fruit, vegetables, low-fat dairy products, reduced intake of sodium, saturated fats and cholesterol, used to prevent and support the treatment of cardiovascular diseases [\[26\]](#),[\[62\]](#),[\[64\]](#),[\[65\]](#),[\[68\]](#),[\[69\]](#).

**2.3.2. Diet in Parkinson's disease (PD)** – its goal is, among other things, to support the digestive system, as patients often experience constipation [\[16\]](#),[\[17\]](#). Furthermore, due to the very good response to pharmacological treatment, a properly functioning digestive system has a significant impact on the absorption of medications from the gastrointestinal tract and a favorable therapeutic response. Similar to Alzheimer's disease, a Mediterranean diet is recommended for PD. It may be associated with improved cognitive function, motor skills, and gastrointestinal symptoms [\[8\]](#),[\[61\]](#),[\[68\]](#),[\[69\]](#). Contrary to popular belief, the ketogenic diet has also proven beneficial. Although it exacerbates constipation symptoms in some patients, it correlates with improved cognitive function. Patients can respond to the side effects of this diet by consuming more water, magnesium, salt, and vegetable oils [\[61\]](#),[\[69\]](#),[\[70\]](#),[\[71\]](#). Protein-restricted diets and the MIND diet have also been tried with satisfactory results [\[69\]](#),[\[72\]](#).

**2.3.3. Amyotrophic lateral sclerosis (ALS) diet** is aimed at mitigating neurodegenerative processes and improving nutrition by meeting nutritional needs in malnourished patients with swallowing disorders. Weight loss, metabolic disorders, and nutrient deficiencies common in ALS can accelerate neurodegeneration. Although dietary interventions have limited impact on the course of the disease, attempts are being made to implement diets with neuroprotective and anti-inflammatory effects, such as the Mediterranean diet. Sometimes, gastrostomy intervention is necessary. Such dietary changes can be an effective adjunctive therapy, help improve nutrition, and positively impact the course of the disease [\[18\]](#),[\[19\]](#),[\[20\]](#),[\[73\]](#),[\[74\]](#),[\[75\]](#).

As can be seen from the descriptions of supportive diets used in selected neurodegenerative diseases, a common dietary pattern is based on the consumption of fruits, vegetables, vegetable fats, and whole grains. Such a diet is rich in antioxidants, vitamins, fatty acids, which are necessary for the proper functioning of the nervous system [\[26\]](#),[\[60\]](#),[\[63\]](#),[\[65\]](#),[\[76\]](#).

It turns out that diet can be helpful not only in improving the functioning of sick people but can also be used to prevent neurological diseases. The current challenge is an aging society. Despite

the increase in life expectancy, measures are needed to help people live additional years in good health [77],[78],[79]. Much research is being conducted on individual ingredients and diets that, when used regularly, can support healthy aging and prevent premature mortality from various causes. The importance of the Mediterranean, ketogenic, and MIND diets should be emphasized here again. A significant advantage of these diets is that they not only influence the proper functioning of the nervous system but also contribute to the well-being of the entire body and reduce comorbidities typical of a developing society, such as cardiovascular disease and diabetes [77],[78],[79],[80],[81],[82]. The Mediterranean diet is rich in plants, so it's worth considering vegetarian and vegan diets, which are becoming increasingly popular. Plant-derived compounds can help prevent neurodegenerative diseases. They are rich in phytonutrients and antioxidants, which reduce inflammation and oxidative stress. However, there are concerns that a deficiency in other nutrients important for the nervous system, such as vitamin B12, certain fatty acids, and iron, may be detrimental. Furthermore, they contain a significant amount of antinutritional factors such as phytates and oxalates, which can impair nutrient absorption. Nevertheless, carefully planned and properly supplemented plant-based diets can reduce the risk of neurodegenerative diseases [83],[84],[85],[86].

At this point, it would be appropriate to show the "other side of the coin" and present dietary patterns that negatively impact the functioning of the nervous system. Currently, especially among young people, an unfavorable lifestyle is becoming increasingly common, associated with reduced physical activity, sedentary work, smoking, and an unhealthy diet with excessive food portions. This is a major identified factor contributing to the development of various diseases. Even traditional diets considered healthy, such as the Mediterranean diet, are subject to changes, especially in terms of portion size, proportions of food groups, and the use of industrially produced foods. This is largely due to the spread of western dietary patterns and the globalization of food production, which leads to the standardization of dietary habits [57],[77],[84],[87]. The western diet is characterized by a high content of sugar, salt, unhealthy fats, and refined grains, while the consumption of vegetables and fruits is low. Furthermore, the foods and beverages consumed in the western diet are often highly processed and contain substances that enhance their taste and appearance. Food processing reduces the amount of naturally occurring nutrients, anti-inflammatory and antioxidants and usually involves adding additional fats, sugars and sodium [56],[79],[84],[88]. The result is a diet poor in nutrients and low in fiber. This promotes intestine microbiome disruption and immunological changes, resulting in chronic inflammation [79]. Such a diet is associated with pathological brain aging,

poorer cognitive function, and contributes to the risk of dementia [79],[84],[88]. The characteristically higher sugar and salt intake is itself widely associated with poor health. It correlates with obesity, diabetes, hypertension, neurodegeneration, and vascular dysfunction, thus leading to systemic inflammation, oxidative stress, and ultimately cognitive decline [56],[61],[84]. As we can see, the Western diet, which contains a large amount of pro-inflammatory foods, not only influences the development of neurological diseases but also contributes to obesity, diabetes, heart disease, and circulatory system disease. These diseases impair vascular reactivity and hemodynamic functions, impeding cerebral perfusion and further exacerbating nervous system diseases through multiple mechanisms [56],[79],[84],[88].

Beyond diet itself, it's also important to consider environmental pollutants, which impact the food we consume. Unconscious and unnoticeable to the naked eye, pollution exceeds consumers' ability to choose between healthy and unhealthy products. Human-induced environmental changes lead to the release of chemical compounds into soil, water, and air. These compounds can enter the food chain and bioaccumulate. Of particular importance to food is the contamination and accumulation of heavy metals such as copper, nickel, and mercury, as well as plant protection products used in agriculture (pesticides, which include herbicides and insecticides). These substances affect not only the quality of groundwater and soil, but also the quality of food, through the deposition of contaminants, especially on fresh vegetables and fruits. If consumed by consumers, they can cause neurotoxic effects [57],[89].

Overall, unhealthy diet and environmental pollution contribute to the burden of diseases in various systems of the human body, including neurodegenerative diseases, causing an increase in premature mortality [87],[90].

### **3. Conclusions**

An aging population and the increasing incidence of neurodegenerative diseases pose a challenge for the modern world [1],[2],[3],[4],[5],[6],[7]. Currently, there is no effective causal treatment for neurodegenerative diseases, but it appears that there is a link between dietary habits and the alleviation of these diseases' symptoms and improvement in patients' quality of life [8],[91],[92]. Studies demonstrate a significant impact of diet on cognitive function, memory, and the risk of neurological disorders [60],[91]. A neuroprotective diet rich in antioxidants, vitamins, and unsaturated fatty acids, particularly those found in plant foods, may prove beneficial in the supportive treatment of neurodegenerative diseases [7],[46],[93]. One

such diet is the Mediterranean diet. Furthermore, proper nutrition may be beneficial not only in the treatment of neurodegenerative diseases but also in other human diseases and their prevention. On the other hand, a Western-style diet, containing more pro-inflammatory ingredients, along with environmental pollutants, contributes to the development of chronic diseases and higher mortality [\[57\]](#),[\[84\]](#),[\[90\]](#). To summarize, proper nutrition significantly affects the proper functioning of the human body, which is why diet appears to be one of the most important modifiable factors influencing the onset of disease. Healthy eating habits, along with regular physical and mental activity, effectively reduce the development and symptoms of neurodegenerative diseases. This reduces overall premature mortality and contributes to a longer healthy lifespan. Therefore, targeted actions are needed to promote a healthy lifestyle [\[22\]](#),[\[46\]](#),[\[79\]](#),[\[84\]](#),[\[87\]](#),[\[90\]](#).

### **Authors' contribution**

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