

## VITAMIN D IN THE DIET AND ITS EFFECTS ON THE NERVOUS SYSTEM

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## ВИТАМИН Д У ИСХРАНИ И ЊЕГОВА ДЕЈСТВА НА НЕРВНИ СИСТЕМ

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### ABSTRACT

Vitamin D is a liposoluble organic compound that, in addition to calcium metabolism and its effect on the skeletal system, also has numerous other effects on other organ systems, such as the cardiovascular, endocrine, skeletal and immune, but also on the central nervous system. The primary source of vitamin D is food of animal origin; however, vitamin D is synthesized in the skin upon its exposure to sunlight. In this paper, we will also present the studies corroborating the theory that numerous neurological and psychiatric manifestations are due to deficiency of vitamin D.

**Key words:** vitamin D; vitamin D deficiency; nervous system diseases.

### САЖЕТАК

Витамин Д је липосолубилно органско једињење, које, осим што учествује у регулацији метаболизма калцијума и утиче на скелетни систем, има и бројне друге ефекте на друге органске системе, као што су кардио-васкуларни, ендокрини, коштани, имунски, али и централни нервни систем. Примарни извор витамина Д је храна животињског порекла. Међутим, витамин Д се синтетише у кожи након излагања сунчевој светлости. У овом раду представимо студије које поткрепљују теорију да су бројне неуролошке и психијатријске манифестације последица недостатка витамина Д.

**Кључне речи:** витамин Д; недостатак витамина Д; болести нервног система.

### INTRODUCTION

The most significant source of vitamin D for people is exposure to sunlight. Ultraviolet (UV) radiation provides the synthesis of 2/3 of the necessary concentrations of vitamin D. Food intake provides the remaining one-third of the vitamin D (1). Taking into account and the content of vitamin D in 100 grams of foods, research shows that the largest source of vitamin D is cod liver oil (2, 3). This oil contains, on average, 210-250 µg (2, 3). A smaller, but certainly significant, source is wild salmon, which contains from 5.9 to 24.7 µg/1 (2-4). Vitamin D can also be found in the meat of cod (5.7-15.4 µg) (5), hake (8 µg) (2), mackerel (8.8-16.1 µg) (2, 3), canned sardines (4.6 µg) (2), tuna (6.7 µg) (3), and anchovies (2.6 µg) (2). Vitamin D-rich mushrooms are wild, edible *Cantharellus tubaeformis* mushrooms that contain 13.6-29.8 µg (5,6) as well as *Agaricus bisporus* mushrooms with 0.2 µg (3). Among dairy products, vitamin D is present in unfortified whole milk and yoghurt at a concentration of 0.1 µg (3), and in cheddar cheese that can have 0.3-0.6 µg (2,3). Among animal products, turkey meat is the most important source of vitamin D, 100 g of this meat contains 2.2 µg of vitamin (2). Slightly lower concentrations are present in pork bacon (1.6 µg) and beef liver (1.2 µg) (3), while of chicken contains only 0.1 µg (3). Higher concentrations of vitamin D are present in butter (1.5 µg) (3) and raw, whole egg (1.8 to 2.05 µg) (2, 3).

Research conducted around the world has shown that the dominant source of vitamin D varies from country to country. In Norway, the largest source of this vitamin is fish and fats (7). While in Finland it is milk and milk products (8). In the United Kingdom (UK), fish oil, meat and meat products, cereals and their products make the most significant contribution to maintaining adequate daily intake of vitamin D in the adult population (9). In Spain, fish is responsible for 65% of the daily intake of vitamin D (10). In contrast, fortified milk provides 39% - 58% of daily needs in the United States (11). In Japan, the most significant source of vitamin D is fish and eggs, while in Ireland it is meat, fish and spreads (12).

Apart from its natural form, vitamin D can be introduced into the organism through fortified foods. Foods that are enriched with vitamin D also vary among countries around the world. In practice, milk, margarine, mushrooms and cereals are most commonly enriched food. Enrichment can be made in several ways. One of them is the increased exposure of mushrooms to UV radiation. Concentrations of vitamins that are synthesized depend on the length of exposure and the dose of radiation delivered. The synthesized concentrations of vitamin D in mushrooms remain durable even after its treatment (drying, cooking, baking). In products of animal origin, an increase in the concentration of vitamin D is achieved by the rise in the concentration of vitamins in foods used in animal feeding (13).

## THE EFFECT ON THE NERVOUS SYSTEM

Vitamin D in the nervous system works by activating receptors on neurons located in regions responsible for behavioural control. This vitamin stimulates neurotrophin release and protects the brain by preventing antioxidant and anti-inflammatory damage to the blood vessels. The mechanism by which vitamin D exerts its effect on the nervous system and affects mental status has not yet been fully elucidated. It is thought to primarily exert its influence through VDRs located in the hypothalamus, which subsequently exerts a neuroendocrine effect (14). Calcitriol has been shown to induce the expression of tryptophan hydroxylase 2, an enzyme that participates in serotonin biosynthesis (15).

### *Neurological and psychiatric disorders and vitamin D deficiency*

One of the mechanisms that explain the impact of vitamin D deficiency on the onset of depression is a disturbance in calcium metabolism and a decrease in calcium receptors, which inhibits the function of numerous signaling pathways in the brain. Also, the decreased concentration of vitamin D leads to reduced synthesis of serotonin (15).

Vitamin D deficiency is linked to the onset of depression, schizophrenia, bipolar disorder, seasonal affective disorder, and impairment of cognitive function. Numerous studies show that vitamin D deficiency is associated with the onset of depression and that people with adequate vitamin D concentrations have a significantly lower risk of developing the disease. There is a risk of depression in people with hypovitaminosis D both in adolescents and in older adults (16).

In addition to depression, vitamin D deficiency has also been shown to affect anxiety (17). The exact mechanism of occurrence is not yet fully known. Animal studies have shown that defects in vitamin D receptors (VDR), as well as vitamin D deficiency, affect anxiety expression (18). Vitamin D has also shown to play a role in modulating the immune response and secretion of the cytokine TNF- $\alpha$  and C reactive protein (19). More recent evidence suggests that these proteins play a role in the onset of anxiety by affecting the modulation of neurotransmitter metabolism (dopamine, serotonin) (20). It should also be emphasized that 400 IU per day may be enough for healthy people to get Vitamin D regularly through food, sunlight or supplements. However, it should not be overlooked that the doses of vitamin D for therapeutic purposes are significantly higher (21). Vitamin D has a protective effect on certain dementias. Some studies have also shown that this vitamin prevents cognitive degradation (22). Some randomized studies have shown that high-dose vitamin D can reduce the severity of Parkinson's disease symptoms (23). An

increasing number of studies show that vitamin D is one of the most responsible factors for the development of multiple sclerosis, as well as for the degree of expression of the symptoms of this disease (24). Also, recent studies show that some genes responsible for multiple sclerosis are close to genes responsible for creating enzymes that affect vitamin D and various enzymatic processes (25). It is undeniable that vitamin D deficiency plays a role in the development of multiple sclerosis (26). In the case of stroke, some studies have shown a correlation suggesting that people with vitamin D deficiency are more prone to stroke (27).

### *Headache and vitamin D*

Vitamin D deficiency is associated with the development of chronic pain as well as several other neurological disorders (28). Although the way of occurrence has not yet been fully explained, it is noted that people with vitamin D deficiency have frequent and severe headaches (29). The role of vitamin D in the onset of pathogenesis involves the stimulation of painful sensations and the development of inflammation and immune dysfunction (30). At the molecular level, it has been recorded that polymorphism of a gene encoding VDR may increase the risk of migraine without aura. As people with migraines avoid sunlight due to photophobia and are less physically active and spend a lot of time indoors, the risk of deficiency is higher (31).

## CONCLUSION

In addition to having effects on the above-mentioned organ systems, recent research emphasizes the role of vitamin D in the activation of certain receptors in the nervous tissue, causing neurological and psychiatric disorders unless it is present in optimal amounts. These studies show the extent to which vitamin D is present in this public health problem. Special attention should be paid to the primary sources of vitamin D.

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