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THE ROLE OF MELATONIN IN DISORDERS OF THE PSYCHO-EMOTIONAL SPHERE

An analysis of the works of domestic and foreign literature devoted to the study of the effect of melatonin on the psycho-emotional state of the organism was carried out. According to most researchers, the trend towards an increase in the prevalence of depressive disorders continues. Currently, there is a search for new approaches in the treatment of depression. The relationship between melatonin and the occurrence of depressive disorders requires further study.

Keywords: melatonin, depression, circadian rhythm, neuroinflammation, nervous system, chronotype.

Introduction. According to the World Health Organization (WHO), the June 2022 World Mental Health Report noted that 1 billion people in the world suffer from mental disorders, including 15% of working age. During the coronavirus pandemic, the prevalence of depression increased by 25%. Depression remains a major problem in the modern world. Despite research on depressive disorders and their treatment with antidepressants, about 80% of inpatients with depression and 70% of outpatients complain of sleep disturbances. Currently, there are several available hypotheses for the occurrence of depressive disorders. Among them are neurotransmitter dysfunction hypotheses and chronobiological concepts, i.e. altered circadian rhythms mediated by melatonin. Melatonin is a universal biological regulator of vital rhythms for all living organisms, as evidenced by its secretion in all animals, starting with unicellular [1,2].

The history of the discovery of melatonin (MT) is associated with the name of Aaron Lerner, a professor of dermatology at Yale University, who studied the nature of vitiligo. Having reviewed the publication of C. McCord and F. Allen (1917), who found that the use of an extract of the pineal glands of cows led to a lightening of the cover of tadpoles by compressing the dark epidermal melanophores. Professor A. Lerner came to the conclusion that a substance responsible for pigmentation and destruction of pigments is formed in the pineal gland, and thought that this substance would help in the treatment of skin diseases. In the early 1950s a group of scientists led by Lerner succeeded in isolating an extract from cow pineal glands that brightens the skin of frogs. The experiment was delayed, so it was decided to complete work on it, but shortly before the end of the term, scientists managed to isolate and determine the structure of the main substance - it turned out to be N-acetyl-5-methoxytryptamine, which was named melatonin. The resulting discovery was described by Lerner in an article published in 1958 in the Journal of the American Chemical Society [17].

Melatonin performs important antioxidant and chronobiotic functions for the body, but also affects carbohydrate metabolism, secretion of insulin, leptin, adiponectin, adipocyte proliferation, and eating behavior. The mechanism of action of melatonin lies in its amphiphilicity, which allows it to penetrate through cell and nuclear membranes and directly interact with intracellular organelles. The antioxidant function of MT can be distinguished, and it consists in the inhibition of the formation of hydroxyl radicals, the protection of lipids, proteins and DNA, and cellular apoptosis. Melatonin also has the ability to limit oxidative stress and regulate energy metabolism. Including body weight, insulin sensitivity and glucose tolerance. The effects of MT are realized at the stages of energy consumption (nutrition), redistribution of energy reserves and energy consumption. Synchronization of human eating behavior with metabolic processes also occurs with the participation of melatonin.

It has been found that melatonin is synthesized in the human body in the cells of the bone marrow, intestines, on the skin and in the retina of the eye. According to the first assumptions, melatonin was considered a hormone involved in the regulation of circadian rhythm mechanisms in living beings, but later it was found that, in addition to this hormonal function, MT is involved in the regulation of seasonal and lunar cycles in animals and humans. The level of melatonin in human blood fluctuates during the day: during daylight hours

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it does not exceed 10 pg/ml, at night its concentration rises, reaching a maximum at 2-4 am to 200 pg/ml or more. It is known that in breast milk the level of tryptophan, the precursor of MT, also has a circadian rhythm, which determines the rhythm of sleep and wakefulness of the newborn. Recently, studies have shown that enterochromaffin cells of the intestinal mucosa are the source of melatonin. Moreover, most of them are in the duodenum and rectum. The transport function of melatonin in the blood is carried by the protein albumin. At night, the concentration of melatonin rises in the fluid of the spinal cord, ovarian follicles, seminal fluid and fluid of the anterior chamber of the eye. After being released from the bond with albumin, melatonin binds to specific receptors on target cells and penetrates into the cell nucleus. The main metabolite of melatonin in urine is 6-hydroxymelatonin sulfate, the level of excretion of which in the urine corresponds to the concentration of melatonin in serum [45].

Depressive disorders currently occupy the fourth place among morbidity in the world population, and according to WHO data, by 2023 they will be in second place, second only to pathologies of the cardiovascular system. According to available data, up to 10% of the world's population suffer from depression, and up to 45% of people have experienced a depressive episode at least once in their lives [1].

In recent decades, a number of studies have been carried out in which it has been shown that melatonin secretion is impaired in depressive disorders. It has been found that people with depression have a decrease in plasma melatonin at night. Scientists believe that low levels of melatonin in people with depression are a sign of a decrease in the concentration of norepinephrine and serotonin in the brain. This fact shows that a low value of melatonin can serve. as a marker of the balance of neurotransmitters in the brain. As a result of a detailed study of melatonin secretion in disorders associated with the nervous system, the concept of "low melatonin syndrome" has been described. According to this concept, low secretion of melatonin may be a biological marker of predisposition to depressive disorders [5].

In recent decades, a number of studies have been carried out in which it has been shown that melatonin secretion is impaired in depressive disorders. It has been found that people with depression have a decrease in plasma melatonin at night. Scientists believe that low levels of melatonin in people with depression are a sign of a decrease in the concentration of norepinephrine and serotonin in the brain. This fact shows that a low level of melatonin can serve as a marker of the balance of neurotransmitters in the brain. As a result of a detailed study of melatonin secretion in disorders associated with the nervous system, the concept of "low melatonin syndrome" has been described. According to this concept, low secretion of melatonin may be a biological marker of predisposition to depressive disorders [5].

The works of foreign researchers have shown that in people with manifestations of depression, melatonin secretion depends on the time of day, according to some results, the level of melatonin increases at night [4], according to others, an increase was noted regardless of the time of day, both in the daytime and at night [2]. A study by Szymanska A. [12] showed that the level of daytime melatonin depends on the severity of depressive manifestations (according to the Hamilton Depression Scale) and is higher in people with severe depression, however, the level of night melatonin was increased in all groups with both severe and severe depression. and with mild depression.

A number of studies have shown that people with a late chronotype are more at risk of developing disturbances in the psycho-emotional state, sleep patterns, and seasonal mood swings [34]. Rosenthal N. B co-authors revealed the relationship of seasonal depressive disorders with the violation of biological rhythms [43]. The increase in the risk of depressive disorders in the winter is due to low light during the daytime, which leads to sleep disturbance and is associated with factors such as daytime fatigue and hypersomnia. The etiology of any depression has the same characteristics such as: impaired cognitive functions (ability to concentrate, memory), mood, relationship between sleep, physiological cycles.

In addition, in depressive disorders, a decrease in the range of fluctuations of some rhythms was revealed. It was found that some patients have a shift in the phase of the circadian rhythm to an earlier time (early awakening and activation of the secretory rhythms of melatonin, rapid falling asleep, cortisol and norepinephrine in the early morning hours), while the rest of the individuals have a phase delay (late falling asleep and awakening). This leads to a decrease in the release of melatonin, cortisol, serotonin and thyroid-stimulating hormone, as well as fluctuations in the number of heartbeats and body temperature [3].

Thus, the early signs of depression should not be ignored, it is necessary to consult a specialist and undergo treatment.

The effect of melatonin on the human body in depressive disorders. Melatonin acts on various proteins, cellular and molecular pathways involved in depression [22, 6]. One of the most important mechanisms of action of melatonin in depression is to reduce oxidative stress. Oxidative stress is known to play a role in the pathophysiology of depression [39, 46]. Oxidative stress caused by overproduction of reactive oxygen species (ROS) and/or a defective antioxidant triggers a series of oxidative damage [47]. Oxidative stress easily induces neuronal apoptosis, neurological deficits, and neurotoxicity, thereby accelerating the onset and development of neuropsychiatric disorders, such as depression, Alzheimer's and Parkinson's diseases [44]. It has been proven that the antioxidant function of melatonin is associated with its ability to prevent excessive formation of ROS and with an increase in the level of antioxidants [35]. Melatonin has the function of removing free radicals and an indirect antioxidant effect, and also increases the activity of antioxidant enzymes [23, 41]. Melatonin also regulates the levels of glutathione peroxidase (GP), catalase (CAT), and superoxide dismutase (SOD), antioxidant enzymes that prevent ROS-induced damage [24, 48]. Melatonin upregulates SOD and Cat levels in rats with copper-induced oxidative stress, along with alleviation of depressive-like behavior [25]. In addition, melatonin suppresses serum ROS levels and alters redox signaling molecules in the brain in lipopolysaccharide-treated mice [26]. Recent studies have shown that melatonin greatly increases the activity of SOD, GP and Cat, and reduces the level of malondialdehyde (MDA) [36]. Melatonin improves Cat activity and SOD enzymes and subsequently inhibits lipid peroxidation damage to hippocampal neurons [27]. Melatonin also neutralizes the effect of oxidative stress and restores the activity of SOD, GP, and Cat [28]. Therefore, melatonin exhibits neuroprotective and antidepressant effects through stimulation of the antioxidant system and suppression of intracellular oxidative stress.

Melatonin can improve neuronal survival and neurogenesis [13]. Melatonin promotes neuronal differentiation [14] and exhibits high antioxidant and antiapoptotic properties [29]. Agomelatine increases cell proliferation and neurogenesis in the ventral dentate gyrus and improves

the survival of newly formed cells in both the dorsal and ventral dentate gyrus [7]. As is known, in some neuropsychiatric disorders, such as depression, the hippocampus is severely weakened during neurogenesis [30]. Depression is also associated with induced stress, where there is a decrease in dentate gyrus neurogenesis [8]. Thus, melatonin may exert antidepressant effects by facilitating neurogenesis and preventing apoptosis in the hippocampus.

Melatonin reduces neuroinflammation by reducing IL-1β and TNFα, which contributes to a positive effect on depression [48]. Neuroinflammation is involved in the pathophysiology of depression [37]. Dysfunction of the immune system, showing pro-inflammatory conditions, in patients with severe depressive disorders [21, 40].

It is important to note that studies of patients with depression have demonstrated changes in the structure and function of brain regions during pro-inflammatory processes [20]. Previous studies have shown increased levels of pro-inflammatory cytokines such as IL-1β, IL-6 and TNF-α in depression [10, 31]. With an increase in the concentration of IL-6, there is a decrease in the volume of the hippocampus in patients with depression. Plasma IL-1, IL-6, IL-2 receptors, IL-6 receptors, and acute phase protein concentrations are increased in patients with major depressive disorders [49].

Recent clinical and preclinical evidence suggests that neuroinflammation is a key factor interacting with three neurobiological correlates of depressive disorder: serotonin depletion in the brain, dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, and disruption of the continuous production of sex hormone-forming neurons in dentate gyrus of the hippocampus [21].

Depression also increases levels of inflammatory markers, including TNF-α, IL-1β, IL-2, and IL-6 [19]. It has been shown that melatonin, through anti-inflammatory processes, contributes to the reduction of free radical damage [16]. Melatonin reduces the levels of TNF-α, IL-1β, and oxidative stress mediators in various parts of the rat brain after intracerebroventricular administration of lipopolysaccharides [9].

Melatonin also reduces the lipopolysaccharide-induced increase in TNF-α in maternal serum and fetal brain [15]. In addition, chronic administration of agomelatine suppresses pro-inflammatory cytokines such as IL-6 and IL-1β both in the periphery and in the brain of LPS-exposed rats [32]. Chronic treatment with agomelatine also attenuates depression and suppresses inflammatory signals in epileptic rats. [42]. In mice exposed to lipopolysaccharide, melatonin induces an antidepressant effect by reducing the levels of TNFα, IL-1β, and IL-6, as well as weakening autophagy [26]. Melatonin reduces oxidative stress, NF-κB activation, and depressive behavior after lipopolysaccharide administration to mice [11]. Previous studies have shown that lipopolysaccharide-induced depressive behavior is significantly associated with elevated TNF-α levels, while melatonin administration prevents this mechanism [33]. On the other hand, pro-inflammatory cytokines suppress the release of melatonin. The introduction of recombinant IL-1β reduces the level of melatonin in the blood serum of rats [38]. In addition, suppression of nocturnal melatonin in mothers with mastitis is significantly associated with an increase in TNF-α production [18]. Thus, the antidepressant effect of melatonin may be associated with the suppression of neuroinflammation.

Thus, the analysis of the literature indicates that melatonin has multifunctional biological properties, has a multifaceted beneficial effect on the human body, and its effectiveness and safety in the treatment of symptoms of depression and jet lag is beyond doubt. Currently, any quick search on the biomedical research search engine Pubmed reveals that there are 1948 articles on melatonin and depression. Such a number of articles for the development of the study of melatonin is not enough in our time, so this direction requires further study.

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POINT OF VIEW

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CHARACTERISTICS OF PSYCHO-EMOTIONAL STATE OF PATIENTS REQUIRING PLASTIC SURGERY

The results of psychoemotional state assessment of patients who consulted a plastic surgeon con-cerning aesthetic operations in the maxillofacial region (MF) (ear, nose, blepharoplasty, facelift, etc.) are presented. The work evaluated their personality characteristics, which influence the deci-sion-making for aesthetic operation.

The **aim** of the research is to identify the characteristics of psychoemotional tension in patients who applied to a plastic surgeon for aesthetic operations.

Materials and methods. 145 patients who consulted a plastic surgeon for aesthetic surgery of the face and neck were surveyed. The research was done at Chita State Medical Academy Clinic of the Ministry of Health of the Russian Federation.

Results. The article presents the data concerning the peculiarities of such patients' appearance perception, estimation and pretensions level. The main directions of their psychological support before the aesthetic surgery with the purpose of increasing the efficiency of the performed cos-metic intervention are considered. Meanwhile, inflammatory and oncological diseases of the face cause the highest situational and personal anxiety, while the general level of anxiety is the lowest among the patients dissatisfied with their appearance. At the same time, a close connection of emotional, characterological and behavioral reactions with a person's appearance caused by con-genital and acquired facial defects and deformations was determined.

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