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Review report

MODERN POSSIBILITIES OF CORRECTION OF CIRCADIAN RHYTHM DISORDERS

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Abstract. *The aim of the study is* to systematize data on modern opportunities for correction of circadian rhythm disorders.
Materials and research methods. The domestic and foreign literature on the prevention and treatment of desynchronosis was analyzed. The search was performed using electronic databases MEDLINE, Embase, Scopus, Web of Science, and eLIBRARY for 2012-2021. The keywords "desynchronosis", "treatment", "prevention" and their combinations were used for the search.
Research results and their analysis. The results of the research showed that the following methods of correction of circadian rhythm disturbances are currently available: diet, taking melatonin, changing sleep regime, changing physical activity schedule. It was noted that when forming an optimal training schedule, it is important to take into account the chronotype of the athlete. Exogenous melatonin can be used to normalize sleep, but turning off artificial light 1.5-2 hours before sleep and not eating at night is considered a better option. This approach will allow the athlete to maximize his/her potential, to achieve better athletic performance and to prevent desynchronosis.

Key words: *athletes, chronotype, circadian rhythms, correction, desynchronosis*

Conflict of interest. The authors declare no conflict of interest

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Обзорная статья

СОВРЕМЕННЫЕ ВОЗМОЖНОСТИ КОРРЕКЦИИ НАРУШЕНИЙ ЦИРКАДНЫХ РИТМОВ

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Резюме. *Цель исследования* – систематизация данных о современных возможностях коррекции нарушений циркадных ритмов.
Материалы и методы исследования. Проанализированы данные отечественной и зарубежной литературы о профилактике и лечении десинхронозов. Поиск проводился с использованием электронных баз данных MEDLINE, Embase, Scopus, Web of Science, eLIBRARY за 2012–2021 гг. Для поиска использовались ключевые слова «десинхроноз», «лечение», «профилактика» и их сочетания.
Результаты исследования и их анализ. Результаты исследования показали, что в настоящее время существуют следующие методы коррекции нарушений циркадных ритмов: диета, прием мелатонина, изменение режима сна, изменение графика физической активности. Отмечено, что при формировании оптимального тренировочного графика важно учитывать хронотип спортсмена. Для нормализации сна допустимо применять экзогенный мелатонин, но более оптимальным вариантом считается выключение искусственного освещения за 1,5–2 ч до сна и отказ от приема пищи в ночное время. Данный подход позволит спортсмену максимально эффективно использовать свой потенциал, добиться более высоких спортивных результатов и предотвратит развитие у него десинхроноза.

Ключевые слова: *десинхроноз, коррекция, спортсмены, хронотип, циркадные ритмы*

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Circadian rhythms (from the Latin words circa, "about, around" and dies, "day") are systematically repeated changes in various biological processes in the human body associated with the changing times of the day. Many circadian rhythms have been identified, including the rhythms of internal body temperature, rhythms of cortisol and melatonin secretion, sleep and wakefulness cycles [1]. In all mammals, the part of the nervous system responsible for the organization of circadian behavior is located in a paired structure in the hypothalamus known as the suprachiasmatic nuclei (SCN). The suprachiasmatic nuclei are considered to be the main regulator coordinating circadian rhythms. Information about daylight hours is transmitted from the subcortical center via the retinohypothalamic pathway directly to the SCN [2]. The received information is integrated by the brain, which changes the activity of its neurons and forms neural and humoral signals for the whole organism. Thus, SCNs influence other body systems like a clockwork mechanism [3].

Nowadays, especially in an urban environment, humans are subjected to a chaotic life rhythm, which leads to a deterioration in the quality of sleep and daytime activity. In people who work at night or frequently travel in different time zones, disturbances in the rhythm of sleep and wakefulness lead to a conflict between the circadian system and the signals received from the environment [4, 5]. At the same time, a balanced circadian organization is necessary to prepare the body for daytime activity and requires a well-coordinated synchronization with the day-night cycle. Epidemiological and experimental studies show that constant exposure to factors that cause circadian rhythm disruption increases the risk of metabolic, cardiovascular and cancer diseases [5].

Thus, the influence of desynchronosis on the human organism is exclusively negative. At the same time, it can be argued that in the future, the deleterious effects of circadian rhythm disturbances caused by frequent time zone changes and unbalanced lifestyle will become more widespread. Therefore, it is currently very relevant to consider the need for pharmacological and non-pharmacological correction of circadian rhythm disturbances. This issue is particularly relevant for athletes, because the state of desynchronosis can reduce the effectiveness of training and ultimately affect athletic performance.

Chronotypes

Because many people have a certain similarity and regularity in the functioning of biorhythms, several so-called chronotypes have been identified. A discrepancy between training timetable and an athlete's chronotype can lead to a chronic state of desynchronosis. In this case a decrease in performance, poor well-being, headache and bad mood can be observed. In this connection, it is important to consider the issue of circadian typology.

A chronotype is an expression of circadian activity in a person. Three categories of chronotypes have been defined: the morning type (M-type), the evening type (E-type), and the intermediate type (N-type), which does not belong to the first two. While the M-type shows a peak of activity of a person's psychophysiological parameters mainly in the morning hours, the E-type is characterized by a peak of activity in the evening, the N-type is something in between the M and E-types [6]. Thus, a chronotype is a characteristic predisposition of a person to morning or evening activity, usually assessed with the help of questionnaires. The most commonly used questionnaire is the Morningness-Eveningness Questionnaire — MEQ [7].

Studies have shown that exogenous, endogenous and psychobiological (lifestyle) factors simultaneously influence fluctuations in daily performance. Body temperature is considered to be an endogenous indicator of the human circadian rhythm. There is a connection between body temperature and sports performance: increased body temperature contributes to more intensive use of carbohydrates and facilitates muscle fiber contraction mechanism during physical activity, which in its turn increases an athlete's performance [8]. An important endogenous indicator of circadian rhythm is also cortisol, whose peak concentration is observed in the early morning hours. This substance is considered a marker of psychophysiological stress and is associated with a decrease in athletic performance [9].

In different chronotypes, the time of reaching the maximum values of oral temperature and cortisol levels differs. E-types were found to have a maximum serum cortisol concentration on average 55 min later, and maximum body temperature values 2 h later than M-types. In addition, M-types show an increase in serum melatonin concentration about 3 h earlier than E-types. Consequently, M-types tend to wake up and to go to bed earlier than other chronotypes. It is important to note here that age and gender have a significant effect on chronotype: women and the elderly demonstrate a strong predisposition to morning type activity compared to young people [10]. There is also evidence that M-type athletes feel better when they perform submaximal exercise in the morning, while E-type athletes expend more effort to achieve the same results in the morning hours [11,12].

Based on the above, it should be emphasized that the determination of an athlete's chronotype can be crucial for the design of effective training programs and the prevention of desynchronosis. It is necessary to take into account the activity features of each type: M-types are most active in the morning; E-types in the evening; N-types in the middle of the day.

Nutrition and desynchronosis

In addition to preparing the body for daytime activity, the circadian system regulates eating behavior. The rate of peristalsis and motility of the human gastrointestinal (GI) tract peaks in the morning hours. Experimental studies have shown that during wakefulness a certain type of bile acid and protein transporter secretion optimizes digestive functions [5].

It has also been found that diurnal rhythms of the human gut microbiota improve energy metabolism during the active phase of wakefulness and promote detoxification during the sleep phase [5, 13]. Thus, eating during daylight hours is most optimal. However, with the proliferation of artificial light, people have deviated from the original eating regimen only during daylight hours. It has been shown that food intake that does not coincide with natural circadian rhythms negatively affects human health. In particular, disruption of the normal sleep-wake cycle and eating at night have been associated with an increased risk of obesity and metabolic syndrome [5].

Based on the data on the variability of the functional state of the gastrointestinal tract during the day and the influence of meal timing on circadian rhythms, diets potentially effective for the treatment of desynchronosis have been proposed. In particular, a study was conducted on the Argonne diet, which can be used when traveling to another time zone and is based on a diet based on the principle: PIR — fasting — PIR — fasting [14]. Four days before the day of arrival at the destination, the diet begins according to the following pattern. The first day is PIR: on this day breakfast and lunch should be rich and high in protein, and dinner should be high in carbohydrates. The second day is a FAST, light meals, low-carbohydrate foods. The third day is FAST again. The fourth day is a FAST, which continues until breakfast at the destination. All four days alcohol intake is prohibited. High-protein breakfasts and lunches stimulate an active physical waking cycle, providing a burst of strength and energy, while high-carbohydrate dinners induce sleep [15]. Light unloading days of "fasting" help restore the biological digestive clock, adapting it to the conditions of the new environment even before arriving in the new time zone.

Another way to restructure circadian rhythms of nutrition is to use the technique of time-restricted feeding (TRF)[16]. The essence of the method consists in fasting intervals, so-called "food windows" between meals. The duration of a food window is 4-10 hours. The general theory behind TRF is that the diet mimics natural eating patterns based on circadian rhythms. Applying TRF in humans results in eating during daylight hours, when the body is in an active waking state, and not eating at a time when the body is preparing for sleep. The results suggest that the use of this diet reduces the risk of weight gain, increases blood lipoprotein levels, provides optimal glucose homeostasis, and promotes faster adaptation to a new time zone [13]. In contrast, disruption of diet and eating at night have a disruptive effect on circadian synchronicity and alter metabolism [17]. Although the relationship between circadian rhythms and metabolism and nutrition still requires further study, it would not be incorrect to state that there is a close relationship between biorhythms and diet.

Thus, in order to adapt more quickly and adjust circadian rhythms to the new regime, one can use a change of habitual diet. This can be done either in advance of the planned trip, or immediately after the flight. Using a diet accelerates adaptation to a new time zone, prevents circadian desynchronization, and has a favorable effect on the metabolism.

Sleep as a criterion for biorhythm optimization

Sleep is the most important function of the body, providing rest and recovery for the entire body. Athletes often have strict training schedules and business trips with a change of time zones, which against the background of mental stress can have a negative impact on the quality and duration of sleep [18]. Also the frequent use of electronic devices contributes, as many of those devices are capable of increasing nighttime light levels. Some of these devices emit monochromatic blue light (λ max, 460-480 nm), to which light-sensitive retinal ganglion cells are particularly sensitive. Exposure to such light suppresses melatonin production at night [19]. As a result, even low light levels at night delay the onset of sleep, which leads to a worsening of morning well-being in the form of drowsiness and lethargy.

Most adults require 6-8 hours of sleep per night, while athletes may require more. Inadequate sleep in the general population is associated with many negative health outcomes, including neurocognitive, metabolic, immunological, and cardiovascular dysfunction [19]. Sleep disturbance also negatively affects growth hormone and cortisol secretion. It was found that when the circadian rhythm is disturbed and the total duration of sleep is reduced, cortisol levels increase, which leads to the predominance of catabolic processes in the body over anabolic ones [20]. Consequently, athletes who maintained an adequate sleep regimen prior to competition are likely to have an advantage in terms of maximal performance. Increased sleep duration in athletes improves sprint times, accuracy of serve when playing tennis, and increased time spent training with exertion. Cognitive test scores, reaction time, and attention levels also improve [21].

The issue of daytime sleep also deserves attention. If an athlete cannot get a good night's sleep, incorporating daytime sleep into his regimen for the next 24 hours will have a positive effect. This method is worth using when the coach or the athlete himself is aware of the impending disruption of full sleep due to a late return to the place of rest, travel or flight [22].

Melatonin and Sleep

Sleep patterns are mainly regulated by light exposure and melatonin secretion. Melatonin is a derivative of serotonin and is secreted by the pineal gland, which synthesizes and secretes melatonin constantly, but most intensively at night. This process peaks between 2:00 and 4:00 a.m. and is followed by a gradual decrease in secretion. Melatonin has a sedative effect and promotes sleep, which is due to its action on the suprachiasmal nuclei of the hypothalamus. In addition, melatonin causes a hypothermic effect, reducing the temperature of the internal environment of the body, has an antioxidant and immunomodulatory effect [23].

The use of exogenous melatonin has been found to be effective for the prevention and treatment of circadian rhythm disturbances after crossing several time zones. This drug acts as a chronobiotic and can shorten the time needed to restore one's own circadian rhythms after traveling. Melatonin is recommended when crossing 5 or more time zones. In particularly predisposed individuals, it can be used when crossing time zones. Recommended two to four doses are 0.5 to 5 mg. Higher doses have not been shown to be effective in adapting to a new time zone, but have been more effective as a sleeping aid [24].

In addition to melatonin, benzodiazepine-type medications can be used, but there is a high risk of side effects such as daytime lethargy, somnolence, and development of drug dependence [25]. Since these side effects can reduce the effectiveness of the training process and affect the sports results, the use of these drugs in athletes is limited.

Thus, desynchronosis is a rather urgent problem in the modern world. This problem is especially serious for athletes.

In this regard, making an optimal training schedule taking into account your chronotype is the main method of preventing chronic desynchronosis. It is also important to stick to a healthy diet and to get enough sleep. Athletes are allowed to use exogenous melatonin to normalize sleep, but elimination of artificial light 1.5-2 hours before sleep and avoiding meals at night are considered more optimal. The above measures will improve athletic performance, increase training efficiency, and prevent the development of desynchronosis.

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