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The influence of melatonin on the functional state of the human body during desynchronosis

In the article the mechanisms of melatonin action in the human body, exploring its impact on circadian rhythms, sleep, the immune system, and overall physiological function were considered. A focal point is the use of melatonin as a pharmacological tool to address dyssynchrony, particularly in students facing new time zones or geographic latitude changes. The study aims to understand melatonin's potential influence on regulating biological rhythms and the general physiological state in such scenarios. It scrutinizes how melatonin affects circadian rhythms, sleep, activity, and overall physiological balance during disruptions in biorhythmic synchronization. Recent studies were analyzed, revealing promising prospects for melatonin in regulating desynchronization and maintaining human health amid altered biological rhythms. Findings indicated that students in the experimental group, who took melatonin, experienced enhanced academic performance, increased work capacity, and improved mood. That underscored melatonin's positive impact on the functional state of the human body, even in the presence of desynchronosis. A study involving 100 students identified changes in circadian rhythms contributing to seasonal depression, with daily melatonin tablets proving effective in alleviating desynchronization symptoms. The article furnishes vital scientific data and practical recommendations, catering to professionals in biomedicine, biology, and pharmacology, as well as individuals keen on understanding human health and biological rhythms.

Keywords: desynchronosis, melatonin, biorhythm, chronotype, dyssomnia.

Introduction

The development of desynchrony in the lives of modern individuals is influenced by both exogenous and endogenous factors. Mostly, desynchrony arises from the use of artificial light sources during the dark phase of the circadian rhythm, leading to the emergence of circadian disruptions and alterations in physiological processes [1, 2].

The functioning of the immune system is closely intertwined with the regulation of homeostasis by various neuroendocrine systems. Therefore, changes in ethological status and immune status in desynchrony can mutually reinforce or weaken allostatic adjustments [3–5]. Many studies on desynchrony focus on nocturnal animals, such as rodents, birds, and hamsters, which differ from humans in their response to light [6].

Desynchrony significantly affects the homeostatic adaptation mechanisms, primarily through the reduction of melatonin production. Melatonin influences the sleep-wake cycle, immune processes, aging, blood circulation, mental state, and thermoregulation [7, 8]. Melatonin receptors, found in various tissues, including neurons in the suprachiasmatic nucleus, and immune-competent cells, demonstrate its direct neurotropic and immunotropic effects [9]. Additionally, melatonin may exert autocrine or paracrine effects.

Melatonin production in the pineal gland follows a circadian rhythm, influenced by the alternation of light and darkness. The synthesis of melatonin begins with the hydroxylation of L-tryptophan to 5-hydroxytryptophan, which is then converted to serotonin before finally forming melatonin [10–13]. The regulation of melatonin synthesis involves the release of norepinephrine during the night, which stimulates adrenergic receptors in the pineal gland, leading to increased melatonin secretion [14]. The metabolism of melatonin in the saliva occurs through three main pathways: classical, alternative, and the kynurenine pathway.

Melatonin acts through two main types of receptors, named MT1 and MT2, also referred to as Mel1a and Mel1b. MT1 receptors are expressed in various tissues, including immune cells, blood vessels, aorta, heart, immune system, adrenal glands, skin, sweat glands, kidneys, renal pelvis, placenta, breast milk, pineal gland, and brain areas such as the hypothalamus, amygdala, hippocampus, and substantia nigra. MT2 receptors are mainly found in the hypothalamus, suprachiasmatic nucleus, eye retina, pituitary gland, blood vessels, adrenal glands, gastrointestinal tract, sweat glands, skin, and immune-competent cells [15].

Materials and Methods

1st-year foreign students aged 19–24 years from the Faculty of Medicine at the International Business University (IBU), registered with the state utility enterprise “City Student Clinic” in Almaty, were selected as the subjects of the research. The total number of volunteers was 100 students, comprising 75 men and 25 women.

In the research, students were divided into three groups depending on the level of health. According to health level I, 23 students had slight changes in the temporal structure of their physiological states. According to health level II, 32 students had physiological desynchronosis. According to health level III, 55 students experienced severe changes in the physiological state of the body in the temporal structures, and this group itself was further divided into two subgroups (group III A and subgroup III B). Additionally, with the permission of the ethical committee, various doses of antioxidants were used in the state utility enterprise with the right of economic management of the “City Student Clinic” to normalize group III suffering from pathological desynchronosis.

The study employed the following methods:

1. Chronobiological Assessment: First of all, students were briefed about the chronobiological assessment and instructed to comply with certain guidelines to ensure accurate measurements. They were advised to avoid strenuous physical activity, caffeine consumption, and alcohol intake during the assessment period. Each student participated in the measurement sessions conducted over three consecutive days. At predetermined time points (7:00, 10:00, 13:00, 16:00, 19:00, 22:00, 1:00), students were brought to the assessment area where trained personnel measured their systolic and diastolic pressure, as well as pulse rate.

Calibrated instruments were used to obtain accurate readings of cardiovascular parameters. Measurements were taken in a controlled environment to minimize external influences on the results.

Data collected from each student's measurements were meticulously recorded, including the time of measurement and corresponding cardiovascular parameters. This information served as the basis for subsequent analysis using the “Rhythm” computer program.

2. Chronotype Assessment: Questionnaire Administration: The Ostberg and Horn questionnaire was distributed to each student along with clear instructions on how to complete it. Students were encouraged to respond honestly and accurately to the questions based on their personal preferences and habits regarding sleep and daily activities. Students completed the questionnaire individually in a quiet and private setting to ensure confidentiality and minimize external distractions.

Assessment of patients' chronotype by O. Ostberg and D. Horn questionnaire. The Ostberg questionnaire consists of 19 questions. The questions were mainly based on the preferences of the person who participated in the survey (which time to choose for waking up, going to bed, doing physical activity, etc.). After filling out the questionnaire, it is analyzed and the chronotype of the subject is determined based on the sum of the points. According to the results of the survey, the subjects are divided into five chronotypes: clearly indicated morning, weakly indicated morning, indifferent (individual) type, weakly indicated evening, clearly indicated evening chronotype is determined. Upon completion, researchers analyzed the responses to determine each student's chronotype. This involved summing the points assigned to each question according to the questionnaire's scoring system.

3. “WAM” (well-being, activity, mood) questionnaire. Each student received the “WAM” questionnaire along with instructions for completion. They were asked to evaluate their well-being, activity levels, and mood based on the provided pairs of opposite characteristics.

The questionnaire consists of 30 pairs of opposite characteristics, according to which the subject is asked to evaluate his situation. Each pair represents a scale in which the subject notes the degree to which one or another description of his situation is relevant. Subjects are asked to associate their condition with a number of symptoms on a multi-point scale. The scale consists of indices (3 2 1 0 1 2 3). Students rated each pair of characteristics on a multi-point scale ranging from -3 to +3, indicating the degree to which each description reflected their current situation. Students completed the questionnaire independently, ensuring that their responses accurately reflected their subjective experiences. Responses from all students were compiled and analyzed to identify patterns and trends in well-being, activity levels, and mood among the study participants.

Results and Discussion

The possibility of melatonin correction for pathological desynchronosis developing in students studying in the Republic of Kazakhstan from abroad during educational activities was investigated.

Using the Ostberg questionnaire, five different chronotypes were identified in the study participants. Differences were found between groups with clearly expressed morning chronotype (12.7 %), weakly expressed morning chronotype (16.9 %), indifferent chronotype (43.4 %), weakly expressed evening chronotype (11.4 %), and clearly expressed evening chronotype (15.5 %) (Fig. 1).

By determining the chronotype, the diurnal typology of foreign students, or individual differences in activity and alertness in the morning and evening, was established. Knowing their chronotypes helps them understand how their internal body clock works during their learning process, adapting to a new place, and how to synchronize it with their daily activities and tasks to make the most of their time. Identifying and understanding how your chronotype affects your sleep and wake times can help you to improve your productivity, gain insight into your health, and learn new ways to improve your sleep quality.

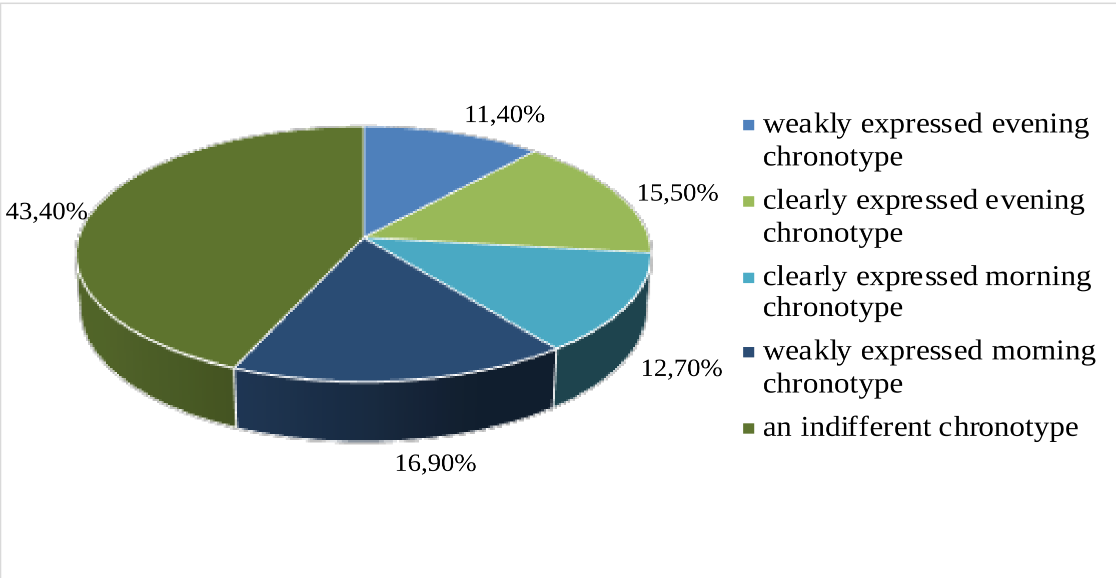

Figure 1. Classification of foreign students by chronotype

Based on the results of autorhythmometry, students of the Faculty of Medicine were divided into 3 groups depending on their health status. The first group included 23 people with a consistent intertemporal structure of physiological functions: most rhythms (65–75 %) are reliable, among them (60–70 %) circadian frequencies prevail; the rhythms of conjugate systems are in phase, mesors, amplitude and characteristics of acrophases are within normal oscillation limits, acrophases correspond to the chronotype of the subjects, and it was determined that their movement zone along the time axis is within 2–4 hours. The results of the analysis in this group show a successful adaptation (health level I). The second group included 32 people with physiological desynchronosis. A decrease in the share of reliable rhythms by up to 50 %, mainly due to a decrease in circadian frequencies, an increase in the share of ultradian rhythms by 5–10 %, a violation of synphasic rhythms, depending on the organism, an increase in the amplitudes and areas of the cyclic acrophases of rhythms from 4 to 6 hours is shown. It was determined that the described rhythm shifts allow to maintain adaptation and rhythm mesors within normal limits (II level of health). The third group included 55 people with obvious disturbances in the intertemporal organization of physiological functions, in which the share of unreliable rhythms was high (>50 %), the share of daily frequencies in the spectrum of reliable rhythms decreased. 38.5 %, the share of ultradian rhythms increased to 45.2 %, amplitudes of rhythms decreased, acrophases of rhythms did not correspond to the chronotype of the subjects, their walking area. Students complain of decreased work capacity, decreased memory, attention, sleep disorders, decreased appetite, increased fatigue, and headaches. These symptoms indicate unsatisfactory adaptation, excessive stress of adaptation mechanisms, and preclinical health disorders were assessed as a state of pathological desynchronization (health level III).

In the group of students with pathological desynchronosis, 30 % of students had a well-defined evening chronotype, 27.4 % had a clear morning chronotype, and 12.3 % had a weak morning chronotype, 24.1 % were indifferent, and 6.2 % had a weakly defined evening chronotype (Fig. 2). A high percentage of pathological desynchronosis in medical students with an evening chronotype may be associated with the early start of classes and mental loads during the first half of the day, that is, they showed a low level of work ability.

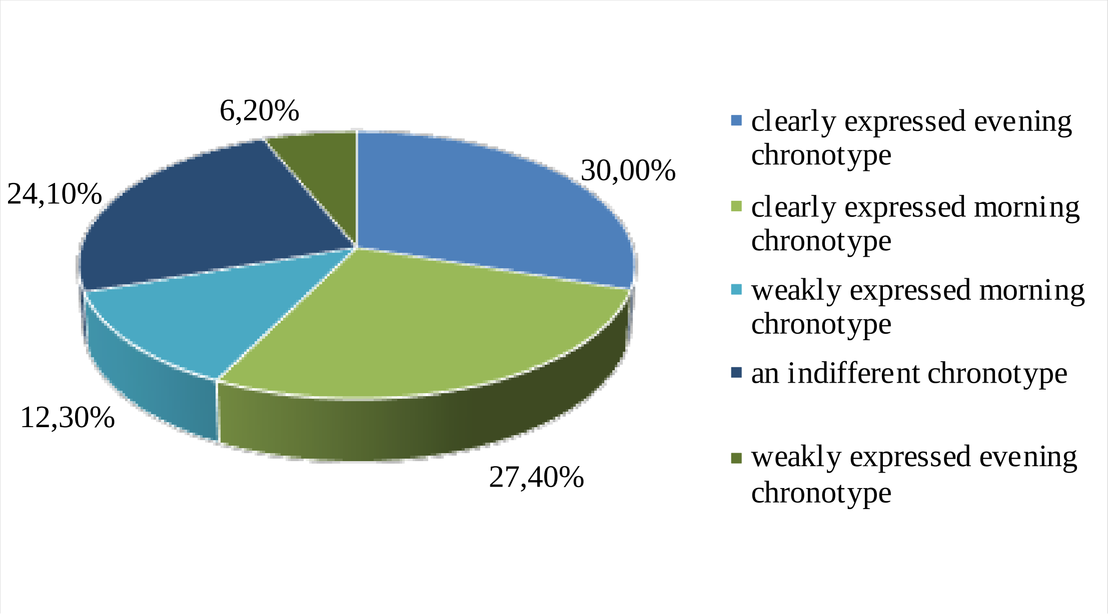

Figure 2. Classification of students with pathological desynchronosis by chronotype

As mentioned above, we classified the experimental group with pathological desynchronosis into two subgroups (group III A, subgroup III B) according to the degree of desynchronosis. Students with obvious disturbances in the architecture of biological rhythms in subgroup III A — 24 students received 0.75 mg of melatonin for 10 days, 30 minutes to 1 hour before bedtime. Students with complaints of obvious disturbances of indicators of biological rhythms in group III B, experiencing dyssomnia, increased fatigue, reduced work capacity, headache, loss of appetite — 31 students, took 3 mg of melatonin for 10 days, 30 minutes to 1 hour before bedtime. After the chronocorrection course, medical students with pathological desynchronosis were examined again.

After chronocorrection of 0.75 mg of melatonin in students with pathological desynchronosis, in the group analysis of the general spectrum of biological rhythms of physiological functions, due to the increase in circadian frequency, the proportion of reliable rhythms increased by 57 % (1.4 times), and by 55.5 % (1.4 times), the share of ultradian rhythms decreased to 26 % (1.7 times).

In the group of students receiving 3 mg melatonin, the percentage of reliable rhythms increased to 57 % (1.4 times), the percentage of diurnal frequency in the spectrum of reliable rhythms increased to 55 % (1.3 times), the percentage of ultradian rhythms decreased to 28.5 % (1.6 times) (Table 1). It is known in scientific literature reviews that melatonin interacts with receptors localized in the suprachiasmatic nuclei of the hypothalamus, synchronizes free-flowing circadian rhythms, corrects endogenous rhythms in relation to exogenous rhythms of the environment, thus increasing the body's adaptation capabilities.

Table 1

Biorhythm spectrum of physiological functions in foreign students with pathological dyssynchrony before and after correction with melatonin

Sinusoidal rhythms: SAP, DAP on the right and left hand, pulse, body temperature, “individual minute”, “individual decimeter” with open and closed eyes	Reliable rhythms % (abs.)				Unreliable rhythms % (abs.)
	Total	Ultradian	Circadian	Infradian	
III A group before chronocorrection n=143	42 (60)	44 (26)	40,5 (24)	16 (8)	59 (85)
III A group before taking 0,75 mg melatonin n=143	57 (85)	26 (22)	55,5 (47)	18,2 (14)	43 (60)
III B group before chronocorrection n=200	40,2 (82)	46,4 (35)	40,5 (32)	13,1 (10)	60 (123)
III B group after taking 3 mg melatonin n=200	57 (115)	28,5 (34)	55 (63)	16,5 (18)	43 (85)
Note – n-the number of analyzed sinusoids; SAP-systolic arterial pressure; DAP-diastolic arterial pressure					

After chronocorrection, the acrophases of most of the biorhythms in both subgroups shifted according to the chronotype of the subjects, their walking zones were shortened by 1.5–2 hours, there was a tendency to decrease in mesors of integral indicators (arterial pressure, heart rate, and axillary temperature), and the amplitude of rhythms increased. The change of these indicators shows that the adaptability of foreign students studying at the examined medical faculty has increased.

The duration of “personal minute” and “personal decimeter” in medical students increased in both subgroups after taking melatonin and approached the normal values (Table 2). This showed that spatio-temporal perception improved, adaptation mechanisms and emotional stress decreased.

Table 2

Individual minutes and individual decimeters with open and closed eyes in medical students with pathological dyssynchrony before and after correction with melatonin

A group of students	Indicators			
	“individual minute” when the eyes open	“individual minute” when the eyes closed	“individual decimeter” when the eyes open	“individual decimeter” when the eyes closed
Before correction III A group	52±5,4	50,5±2,3	9,1±0,5	7,8±0,5
III A group after taking 0,75 mg melatonin	58,1±3,3	55,5±3,9	8,9±0,4	8,9±0,2
After correction III B group	54±4,1	51,3±3,2	8,2±0,5	8,2±0,5
III B group after taking 3 mg melatonin	54,7±3,2	55±2,8	9,7±0,1	9,0±0,7

Correction of pathological desynchronosis with 0.75 mg of melatonin resulted in an increase in “well-being, activity, mood” test indicators. After taking 0.75 mg melatonin, there was an improvement of 3.5 % in well-being indicators, 5.5 % in activity, and 10 % in mood. After taking 3 mg of melatonin, there was an improvement of 4.0 % in well-being indicators, 5.8 % in activity, and mood improved by 15.5 % (Table 3). Melatonin had a greater effect on mood indicators and a slower effect on well-being.

It was determined that the effect of melatonin on the mood indicators of the subjects is related to the activity of the psychotropic hormone carried out through serotoninergic mechanisms, the modulation of dopaminergic transmission, and the change in the activity of motivational and cognitive (striatal) mechanisms in people due to the effect on gamma-aminobutyric acid (GABA) neurons.

Melatonin weakens the excitability of the hippocampus and other emotional structures, stabilizes the psycho-emotional sphere by limiting anxiety, anti-stress properties and restoring disorganized vibration processes in the body. It also has a positive effect on seasonal depression. This type of depression is associated with the changing of the seasons and occurs at the same time each year, with symptoms usually appearing in the fall or winter. Because melatonin plays a role in regulating circadian rhythms, melatonin depression is often used at low doses to reduce symptoms. According to a study of 100 people, changes in circadian rhythms contribute to seasonal depression, and taking a daily melatonin pill was effective in reducing symptoms.

Table 3

“WAM” (well-being, activity, mood) test indicators in foreign students with pathological dyssynchrony before and after correction with melatonin

A group of students	Indicators		
	well-being	activity	mood
Before correction III A group	4,95±1,3	4,90±1,3	4,75±1,3
III A group after taking 0,75 mg melatonin	5,15±1,4	5,20±1,4	5,22±1,4
After correction III B group	4,85±1,1	4,80±1,1	4,50±1,0
III B group after taking 3 mg melatonin	5,0±1,2	5,10±1,2	5,15±1,2

After chronocorrection, subjects noted improved sleep. A decrease in the time spent falling asleep and an improvement in well-being upon awakening were observed. The sedative properties of melatonin have been described by many researchers for sleep disorders associated with various pathologies.

Conclusion

The study of medical students who took melatonin reveals positive effects on physiological and psychophysiological functions. Chronoanalysis of individual and group patterns indicates an improvement in the organization and efficiency of the circadian system, overall health levels, and quality. Moreover, melatonin supplementation led to an increase in the sleep quality of students affected by desynchronosis, while those with pathological desynchronosis showed a decrease in their well-being.

The acquired results suggest that melatonin can be effectively used to regulate and correct physiological functions in students, offering a potential solution for addressing health-related challenges. This research supports the notion that melatonin, administered in suitable doses, could positively influence the academic and exam performance of students, making it a viable option for enhancing their overall well-being.

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Десинхроноз кезінде адам ағзасының функционалдық күйіне мелатониннің әсері

Мақалада адам ағзасындағы мелатониннің әсер ету механизмдері, соның ішінде оның тәуліктік ырғаққа, ұйқыға, иммундық жүйеге және физиологиялық функционалдық күйге әсері қарастырылды. Зерттеулер мен клиникалық бақылаулар негізінде десинхронозды түзету үшін мелатонинді фармакологиялық агент ретінде қолдануға ерекше назар аударылды. Жұмыстың мақсаты — жаңа уақыт белдеуінде орналасқан немесе географиялық ендіктің өзгеруіне байланысты десинхроноздан зардап шегетін студенттердің биологиялық ырғақтарын және жалпы физиологиялық жағдайын реттеуге мелатониннің ықтимал әсерін анықтау. Мелатониннің тәуліктік ырғаққа әсер ету механизмдері, сондай-ақ бұзылған биоритмиялық синхрондау жағдайында оның ұйқыға, белсенділікке және жалпы физиологиялық тепе-теңдікке әсері қарастырылады. Мелатонинді десинхронозды реттеуде және өзгерген биологиялық ырғақтар жағдайында адам денсаулығын сақтауда қолдану перспективаларын ұсына отырып, өзекті зерттеулер талданды. Зерттеу нәтижелері мелатонинді қабылдаған тәжірибелік топтағы студенттердің оқу үлгерімі жақсарып, еңбек қабілеттері артып, көңіл күйлерінде сергектік пайда болғаны анықталды. Яғни десинхроноз кезінде де, адам ағзасында функционалдық күйінің өзгерістеріне мелатониннің оң әсер еткені белгілі болды. 100 адамға жүргізілген зерттеуге сәйкес, тәуліктік ырғақтағы өзгерістер маусымдық депрессияға ықпал ететіні және мелатонин таблеткасын күнделікті қабылдау десинхроноз симптомдарын азайтуда тиімді болды. Мақала авторлары биомедицина, биология және фармакология саласындағы, сондай-ақ адам денсаулығы мен биологиялық ырғақтарға қызығушылық танытатын мамандарға маңызды ғылыми деректер мен практикалық ұсыныстар ұсынады.

Кілт сөздер: десинхроноз, мелатонин, биоырғақ, хронотип, диссомния.

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Влияние мелатонина на функциональное состояние организма человека при десинхронозе

В статье рассмотрены механизмы действия мелатонина в организме человека, в том числе его влияние на циркадные ритмы, сон, иммунную систему и физиологическое функциональное состояние. На основании исследований и клинических наблюдений особое внимание уделено использованию мелатонина в качестве фармакологического средства для коррекции диссинхронии. Цель работы — определить возможное влияние мелатонина на регуляцию биологических ритмов и общее физиологическое состояние студентов, находящихся в новом часовом поясе или страдающих десинхронозом вследствие изменения географической широты. Рассмотрены механизмы влияния мелатонина на циркадные ритмы, а также его влияние на сон, активность и общее физиологическое равновесие при нарушении биоритмической синхронизации. Проанализированы современные исследования, открывающие перспективы использования мелатонина в регуляции десинхронизации и поддержании здоровья человека в условиях измененных биологических ритмов. Результаты исследования показали, что студенты экспериментальной группы, принимавшие мелатонин, улучшили свою успеваемость, повысили трудоспособность и имели более бодрое настроение. То есть было известно, что мелатонин оказывает положительное влияние на изменение функционального состояния организма человека даже при десинхронозе. Согласно исследованию, у 100 студентов были изменения циркадных ритмов, которые способствуют сезонной депрессии, а ежедневные таблетки мелатонина были эффективны в уменьшении симптомов десинхроноза. Авторами статьи представлены важные научные данные и практические рекомендации для специалистов в области биомедицины, биологии и фармакологии, а также для тех, кто интересуется здоровьем человека и биологическими ритмами.

Ключевые слова: десинхроноз, мелатонин, биоритм, хронотип, диссомния.

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