IRSTI 34.39.53

Ablaikhanova N.T.[1],Turyskeldi Sh.S.[2], Mataeva K.S.[3], Kozhakhanov S.M.[4], Ablaikhanova N.T.[5], Tussupbekova G.A.[6], Kulbaeva M.S.[7], Gumarova L.Zh.[8]

[1]candidate of biological sciences, acting as associate professor, e-mail: Nurzhanat.Ablaihanova@kaznu.kz
[2]master-student, e-mail: smankizi@mail.ru
[3]master-student, e-mail: kary.95@mail.ru
[4]student, e-mail: S.kozhahanov@mail.ru
[5]master of medical sciences, e-mail: nurzat7632@gmail.com
[6]candidate of medical sciences, acting as associate professor, e-mail: Gulmira.Tussipbekova@kaznu.kz
[7]candidate of biological sciences, acting as associate professor, e-mail: Marzhan.Kulbaeva@kaznu.kz
[8]candidate of biological sciences, acting professor, e-mail: Lyazzat.Gumarova@kaznu.kz
Al-Farabi Kazakh National University, Kazakhstan, Almaty

CHANGES IN CIRCADIAN DYNAMICS OF ANIMALS IN RESPONSE TO NOISE

In this paperare considered the changes in circadian dynamics in animals under the influence of stress factors.One of the reasons of such an interest in chronobiological research lays in data gathering, that unquestionably provides evidence of relation between organism's circadian rhythms and arousal of various pathogenic conditions in humans. Noise is a stress-factor. Development of such a condition causes tension of hypothalamus-pineal body-corticoadrenal system. Corticosteroid hormones, cholesterol and glucose concentrations in blood increase and eosinophils concentration falls. Due to these disorders, changes in circadian rhythms of the organism arise. Nevertheless, using such methods in chronomedicine, as amplitude changes in rhythms, change of mesor or period of rhythm independently is sufficiently acceptable and justified in a number of specific cases. Amplitude increase (decrease) of circadian rhythm under influence of stress. The amplitude of circadian rhythms possesses exclusively important significance for assessment of functional state of a human.

Key words: circadian rhythm, noise, circadian dynamics, desynchronosis, chronomedicine.

Аблайханова Н.Т.[1], Тұрыскелды Ш.С.[2], Матаева К.С.[3], Кожаханов С.М.[4], Аблайханова Н.Т.[5], Түсіпбекова Г.А.[6], Кулбаева М.С.[7], Гумарова Л.Ж.[8]

[1]биология ғылымдарының кандидаты, доцент міндетін атқарушы, e-mail: Nurzhanat.Ablaihanova@kaznu.kz
[2,3]магистратура студенті, e-mail: smankizi@mail.ru; kary.95mail.ru
[4]бакалавриат студенті, e-mail: S.kozhahanov@mail.ru
[5]медицина ғылымдарының магистрі, e-mail: nurzat7632@gmail.com
[6]медицина ғылымдарының кандидаты, доцент міндетін атқарушы, e-mail: Gulmira.Tussipbekova@kaznu.kz
[7]биология ғылымдарының кандидаты, доцент міндетін атқарушы, e-mail: Marzhan.Kulbaeva@kaznu.kz
[8]биология ғылымдарының кандидаты, профессор міндетін атқарушы, e-mail: Lyazzat.Gumarova@kaznu.kz
әл-Фараби атындағы Қазақ ұлттық университеті, Қазақстан, Алматы қ.

Шудың әсері кезіндегі жануарлардың циркадианды динамикасының өзгеруі

Бұл мақалада стресс факторларының әсерінен жануарлардың циркадианды динамикасындағы өзгерістер қарастырылған. Хронобиологиялық зерттеулерге деген қызығушылықтың бір себебі – организмдегі циркадианды ырғақтардың бұзылуы мен әртүрлі патологиялық жағдайлардың пайда болуы арасындағы байланыстың айқын дәлелі болып табылатын деректердің жинақталуы. Шу – бұл стресс факторы болып табылады. Шудың әсері кезінде гипоталамус-гипофиздік-кортикоадреналдық жүйенің әлсіреуі байқалады. Қан құрамында кортекостероидтық гормондардың, холестериннің және глюкозаның құрамы артады, ал эозинофилдердің саны азаяды. Осыған байланысты, ағзада циркадиандық ырғақтардың өзгеруі пайда болады. Бұл жүйенің ырғақтарының хроноструктурасының бұзылуы тұтас құбылыс деп санауға болады және ырғақтардың параметрлеріндегі бұзылыстардың болуы шартты болып табылады. Дегенменде, осындай ырғақтардың амплитудасының өзгеруі, ырғақтың периоды мен мезорының өзгеруі сияқты диагностикалық критерийлерді қолдану бірқатар нақты жағдайларда толығымен қолайлы болып табылады. Стресс әсерінен циркадианды ырғақтың амплитудасы жоғарылайды немесе төмендейді. Циркадиандық ырғақтардың амплитудасы адамның функционалдық жағдайын бағалау үшін өте маңызды.

Түйін сөздер: циркадиандық ырғақтар, шу, циркадианды динамика, десинхроноз, хрономедицина.

Аблайханова Н.Т.[1], Турыскелды Ш.С.[2], Матаева К.С.[3],
Кожаханов С.М.[4], Аблайханова Н.Т.[5], Тусупбекова Г.А.[6],
Кулбаева М.С.[7], Гумарова Л.Ж.[8]

[1]кандидат биологических наук, исполняющая обязанности доцента, e-mail: Nurzhanat.Ablaihanova@kaznu.kz
[2,3]студент магистратуры, e-mail: smankizi@mail.ru; kary.95@mail.ru
[4]студент бакалавриата, e-mail: S.kozhahanov@mail.ru
[5]магистр медицинских наук, e-mail: nurzat7632@gmail.com
[6]кандидат медицинских наук, исполняющая обязанности доцента, e-mail: Gulmira.Tussipbekova@kaznu.kz
[7]кандидат биологических наук, исполняющая обязанности доцента, e-mail: Marzhan.Kulbaeva@kaznu.kz
[8]кандидат биологических наук, исполняющая обязанности профессора, e-mail: Lyazzat.Gumarova@kaznu.kz
Казахский национальный университет им. аль-Фараби, Казахстан, г. Алматы

Изменение циркадианной динамики у животных при действии шума

В данной работе рассмотрено изменение циркадианной динамики у животных при действии стрессовых факторов. Одна из причин повышенного интереса к хронобиологическим исследованиям заключается в накоплении данных, неоспоримо свидетельствующих о связи нарушений циркадианной ритмики организма с возникновением различных патологических состояний. Шум является стресс-фактором. Развитие этого состояния вызывает напряжение гипоталамо-гипофизкортикоадреналовой системы. В крови увеличивается содержание кортекостероидных гормонов, холестерина и глюкозы, а количество эозинофилов уменьшается. И соответственно в связи с этими нарушениями в организме появляются изменение циркадианных ритмов. Естественно предположить, что нарушение хроноструктуры ритмов той или иной системы – явление целостное, и проведенное в следующих подразделах деление по различию проявлений нарушений параметоров ритмов условно. Тем не менее, использование таких диагностических критериев в хрономедицине, как амплитудные изменения ритмов, изменения мезора или периода ритма, самостоятельно вполне допустимо и оправдано в ряде конкретных случаев. Под влиянием стресса амплитуды циркадианного ритма увеличивается или уменьшается. Амплитуда циркадианных ритмов имеет исключительно важное значение для оценки функционального состояния человека.

Ключевые слова: циркадианный ритм, шум, циркадианная динамика, десинхроноз, хрономедицина.

Exploring theoretical and practical problems of chronobiology and chronomedicine is a science area of high relevance. One of the reasons of such an interest in chronobiological research lays in data gathering, thatunquestionably provides evidence of relation between organism's circadian rhythms and arousal of various pathogenic conditions in humans. Human body is a complex, self-regulated, hierarchically organized system of oscillators, interrelation of which sustains coherence of various processes in time, characteristic to a healthy organism (Hildebrandt, 2006: 144).

Adaptive physiological rhythms have been developed in the process of evolution as a form of adaptation of organisms to cyclically changing conditions of the environment. The most explored rhythm being circadian, reflects on periodicity of geophysical factors, driven by Earth rotation on its axis. First of all, natural lighting normally changes within 24 hours. Day and night cycle, temperature and humidity of air, intensity of electric and magnetic fields, currents of different cosmic factors that fall on Earth in a specific time cycle are all exposed to daily variations.Evolution of all forms of life on Earth was accomplished under the influence of these factors, fluctuations of these in present times, just like millions of years ago, play a vital role for all Earth's inhabitants, without exception. For instance, sunrise signals daytime animals to start their activities: gathering of food, building of shelter, nursing the offspring, and at nighttime nocturnal animals start to be active. All of the animals "adapt" to this 24-hour rhythm. And those who can not follow this naturally set regime die. In order to survive, any type of organism needs to correlate its own rhythm with the surrounding rhythms. Adapting of a specific organism or species adapting to surrounding conditions in a wide biological understanding is synchronizing of life processes (rhythms) of an organism to a whole population with exterior rhythms, thus, circadian periodicity of life functions is an innate quality.

Functioning of many organs and systems of a human is implemented through a special circadian program, in which the driver seat of the biological rhythm is occupied by suprachiasmatic nucleus (SCN) of hypothalamus. Through it, adaptation of an organism's internal world to the changing surroundings of the outside happens. Factors that affect rhythms of the processes in a live organism are called synchronizers. The most important synchronizers are light and darkness sequence, durations of the light period (Anisimov, 2007: 40).

Information about light is obtained by ganglia of retina in the eye, which contain melanopsinphotopigment. Circadian information passes from retina to SCN of hypothalamus through retina-hypothalamus tract, then – to superior cervical ganglion and then into pineal gland. Nerve endings of superior cervical ganglion inject noradrenalin into pineal body tissue, this initiates synthesis of melatonin in the pineal body. Rhythm of melatonin production possesses circadian characteristics. Light oppresses production and secretion of melatonin, therefore maximal level of this hormone in blood is observed during night and the minimal – in the mornings and during daytime.With help of melatonin circling with blood, the main rhythm maker controls and synchronizes rhythms of all peripheral organs and tissues. Along with rapid development of genetics, molecular structure of biological clocks has been established, it presents a group of circadian genes and their protein products. Within the 24-hour period circadian protein content in a cell changes naturally, reflecting on various phases of the 24-hour cycle. In mammals key circadian genes are Clock, Bmall, Period (Per1, Per2, Per3) and Cryptochrome (Cry1, Cry2). Circadian genes are organised in a transcription-translation loop, regulation here is carried out through feedback principle. Activator proteins BMAL1 and CLOCK link with the regulatory part of DNA (Ebox), along with this clock genes Per and Cry (Cryptochrome) start working. This happens in the early morning hours. Within 2 hours after clock genes are activated in a cell, the highest level of concentration of related mRNA's is observed, and by midday the largest amount of PER and CRY proteins can be observed. These protein molecules are first stored in cell cytoplasm, and at night time they gradually get back into nucleus and supress the activity of BMAL1 and CLOCK proteins, forming a strong complex with them, which leads to blocking of Per and Cry genes. Then, PER and CRY proteins slowly break down, and BMAL1 and CLOCK molecules are released to start the new 24-hour cycle in the cell. Total duration of such a cyclic process accounts for approximately 24 hours. This transcription-translation loop aids to sustain clear manifestation of circadian rhythmics in mammals (Zaslavskaya, 2011: 2).

A wide spectrum of biological processes is regulated by circadian clocks, including the sleep and wake cycle, body temperature, energy exchange, cell cycle, hormone secretion and else. Biological importance of natural day and night fluctuations of physiological functions is defined by sustaining high activity rates, stamina and productivity during day and respectively, rest and recovery during night. However, it is important to closely care for break downs of circadian clocks, which lead to irregulations in circadian rhythms (CR), which is in fact a serious problem that refers to the major functions of live organisms. Directions of chronobiological research are numerous and include research in fields such as comparative anatomy, physiology, genetics, molecular biology and biology of organisms' behaviour. In healthy state, time organisation of human's organism is characterised by phase synchronisation in field of long-wave rhythms; on the other hand, it is distinguishable through ordered activity of autonomous rhythms in medium and short-wave range of the spectrum (frequency and phase coordination). External and internal failures of CR synchronisation with displacement of phases and a deviated from 24-hour cycle periodicity can be observed during various diseases, such as, depression, oncological conditions, cardio-vascular pathologies. Break down of frequency and phase coordination of autonomous rhythms in medium-wave range is characterised by rejections of normal reaction readiness of vegetative functions and disorders of regulation economy (Pelesa, 2009: 91-100).

Circadian fluctuations are usually observed in more organised uni-cell organisms and in isolated tissues of multicellularorganisms, nevertheless, in both, vertebrates and invertebrates a part of nervous system plays the role of circadian rhythm maker for the whole organism. Micheal Menaker and his colleagues illustrated that in some birds this function is carried out by pineal gland, which rhythmically produces melatonin hormone in the brain. Pineal gland activity is regulated by light that enters through vertex in the scull. It is even possible to displace a phase of circadian rhythm in sparrows, by implanting a pineal body from a bird that inhabits a different time zone.

In rodents, melatonin is secreted rhythmically too, but under control of two clusters of neurosecreting cells – suprachiasmic nuclei that are located to the left and to the right in hypothalamus, above the crossing of visual nerve. Information about light and darkness comes from eyes. Daily portions of melatonin synchronize circadian fluctuations. In apes, such a role is played by suprachiasmic nuclei. In humans with trauma in this part of hypothalamus disorders of rhythm functions are observed, this allows us to assume a similar role of suprachiasmic nuclei in humans. Phase of rhythms of these nuclei can be moved through eyesight, by an electric stimulus, brain injections of analogous neuromediators that cause natural discharge of neurons, and by melatonin. Secretion of melatonin by pineal body is stimulated by psychomimetics (LSD, mescalin, cocaine) and supressed by drugs used for psychic diseases.

Dynamics of day and night physiological rhythms in humans and higher animals is determined not only by innate mechanisms but also by an adapted 24-hour stereotype of activity. Existent data concerning the possibility of desynchronisation by frequency of specific circadian rhythms presents an opportunity to assume existence of a number of relatively independent oscillators, every one of which regulates a rhythm of a specific, widely branched functional system (Pelesa, 2010: 23).

In numerous organisms, central regulators do not cause fluctuations in peripheral tissues, but only synchronise the circadian rhythms, innate to every organism cell by frequency and phase.

Regulation of physiological rhythms in higher animals and humans is mostly maintained through hypothalamus-pineal body system.

The circadian mechanism is not universal. It differs in relation to biological species and even to types of cells in one organism. It is assumed that the circadian mechanism is specifically closed on a cellular level, for instance, in comparison to menstrual cycle that includes nervous and endocrine interrelations of many tissues. Cellular mechanisms can be explored through methods of biochemistry and genetic engineering. It is possible to alter the routine of circadian clock by numerous biochemical methods. Initially, mostly light impulses were used. Thus, for drosophila, constant lighting – even on the level of lighting of a non full moon – is sufficient to stop the clock from working. The light in this case acts indirectly, it does not hit the molecules of the fluctuation mechanism (Shishko, 2010: 4).

In most circadian rhythms the period is nearly independent from temperature levels, given it remains in range of physiologically acceptable norms. Moreover, compared to genuine independent systems (from temperature), circadian clocks are not immune to temperature changes: the smallest differences in temperature are capable to displace their phase. Other than light and temperature change, many chemical substances affect the periodicity, these influence permeability of membranes and break down protein synthesis. Injecting these for a short period of time leads to phase displacement. However, the processes involved are numerous and various and it is not clear how exactly they influence the clock. Supposedly, not ATP itself, neither process of its synthesis and break down are details of the mechanism of the clock. The same can be said about protein synthesis.

Furthermore, disruption of CR in short time measurements is followed by disorders in 24-hour activities, tiredness, insomnia and disorientation. Such diseases as manic-depressive psychosisand also numerous disorders of sleep are associated with pathological dysfunctions of CR. Prolonged impairements of CR can lead to impaired conditions of internal tissues and organs (Ulaschik, 1999: 9-13).

Cyclic nature of biological functions on all levels is one of the requirements of survival of live organisms and is observed as one of the essential features of living matter, its vital quality, worked out through evolution. In biosystems of any level of complexity oxidation-reduction processes flow rhythmically and in correspondence to physical and cosmic rhythms. In relation to this, livelihoods of organisms, functioning of organs and systems, exchange of substances, energy and information in living systems obey the lawsbiologically-structural-timely discreteness. Thus, understanding of periodicity in living nature is key. Rhythms are present in the organism from the very birth to death, acquiring specific features during lifetime. Biological rhythms imply physiological processes that are repeated after equivalent amounts of time, differing in intensity and complexity of the involved structures (periodically repeating changes of character and intensity of biological processes and phenomenas, characteristic to living matter on all levels of its organisation- from molecular to subcellular). Depending on origin of inducing agent biological rhythms are distinguished as exogenic, those caused by periodical influence from outside, and endogenic, autonomous, the ones caused by active processes within the organism. In most of the cases in clinical practice doctors seldom think about this issue. In truth, the issue is fundamental, as biorhythmology is a fundamental science, chronomedicine being its vital component (Makarov, 2000: 24-27).

Particularly, an initiating moment for this article to be written was arousal of serious reservations amongst Russian population in relation to so called summer and winter time, in fact, in relation to correct organisation of season and 24-hour lifestyle of people. Understanding of importance of the present problem has led to creation of Problem Committee of Russian Academy of Medical Sciences (RAMS) “Chronobiology and chronomedicine” in 1981, under supervision of a soviet academic F.I. Komarov, who has managed the organisation for 15 years. Further it was confirmed that such a decision was vital. It is important to say that by that moment Worldwide and European organisations of chronobiologistshad already been created. Without stopping to look at well-known facts that particularly indicate existence of various types of biorhythms (seasonal, 24-hour, circadian, hourly and so on) it is desired to underline the importance of exploring and implementing of principles of chronomedicine. Practically, this concerns all areas of our lives. Recently a heated debate about summer and winter time zones has arised yet again, the debate has been on for more than 20 years. Seemingly simple technical problem: moving the clock for one hour before arrival of summer or winter. Meanwhile, the deceiving simplicity withholds an alarmingly important biological problem – rebuilding of rhythms. Biorhythmology has introduced a principally new term in clinical means – “desynchronosis”, which practically had not been used in clinical practices, despite the understanding of the states of a living organism that this term carries. Only through this term can we explain the ongoing changes in the organism that desynchronosis causes, these can be pre-diagnosed and predicted. Desynchronosis is an unhealthy state of an organism, pathological syndrome that accompanies desynchronisation (misalignment) of rhythms. There are external and internal types of desynchronosis, it is also distinguished by levels of manifestation – initial, moderate and highly-expressed. The most common reason for desynchronosis is restructuring of the familiar given time that causes conflicts with circadian rhythms, their rebuilding (for instance, trans-meridian flights, shift and night works and so on). Desynchronosis can also arise as impairment of adaptation during various pathologies or ageing. According to mechanism of developmentdesynchronosis is stress (Gabinsky, 1998:23- 25). Circadian rhythm is set genetically and is oriented to change of day and night. Clinically, disorders in circadian manifest through tiredness, malaise, impairment of sleep, often worsening of the existed condition or even developing a new one. For illustrative purposes a practical example of the arising desynchronosis can be the state that is followed by long-distance flights where changing of time zones is involved, so called JetLag. People, who are obliged to make trans-meridian transfers (businessmen, tourists, military men, sportsmen, pilots, railmen) are well aware of this disorder, levels of manifestation of which can often become a serious obstacle for successful implementation of their professional obligations. Another example of misalignment of biorhythms that is no less seldom but even more relevant is so called “social jet lag”. Contemporary authors refer a number of symptoms to this term, these also arise during disorders of familiar sleep and wake cycle (similar to jet lag mentioned earlier), in this case not caused by long-distance transfers but by other reasons of social character: prolonged holidays, long weekends (well-known “Monday syndrome”), student examination period, vacation, school breaks – at times when 24-hour sleep and wake regime is dislocated by more than 2 hours.In addition, it is fair to say that a factor sharply impairing desynchronosis (sometimes the main factor causing it) is often times the accompanying intake of alcohol – a psychoactive substance that possesses numerous disregulating effects (negative impact on sleep and wake cycle – functioning of gastro-intestinal tract, cardio-vascular system and others). In present times, it is accepted that even a single intake of ethanol leads to disorders in physiological rhythms, that might be characterized as typical failure of “biological clocks”, meaning desynchronosis. To maintain circadian rhythmics of an organism – the most ancient adaptation system – exists a system in the organism that is composed of retina (light, darkness), suprachiasmic nuclei, hypothalamus and pineal body. In fact, this system determines the 24-hour and respectively seasonal rhythms of the organism. Namely, these are the fundamental factors that determine functioning of an organism and arousal of desynchronosis. Melatonin is a hormone of pineal body and it plays a role of a signal molecule that specifically initiates processes of hourly rhythm of synthesis of the protein, which is an intrinsic part of circadian rhythm.

According to data from B.Y. Brodskii and colleagues, melatonin is a marker of direct intercellular communications. Desynchronosis is subdivided into acute and chronical. Acute desynchronosis arises as a result of sudden misalignment of rhythms of time detectors and the organism. For example, after transcontinental flights on modern airplanes, which, in a short period of time cross multiple time zones, an acute disorder of relation between phases of rhythm of sleep and wake cycle arises. In situations when the impact of such a factor is prolonged, chronic desynchronosis is developed. Chronic desynchronosis is a pathological condition underlined by permanent desynchronisation of organism's functions. Desynchronosis can be caused by a number of external reasons, social and natural. Social causes include for example: biotropic factors of anthropogenic origin, such as 1) toxic substances. 2) total social stress in large industrial cities, related to hard work or driving, abundance of information and so on; prolonged misalignment of sleep and wake rhythm. 3) misalignment between 24-hour stereotype of an organism and discrete time. 4) desynchronosis caused by orbital and inter-planet space travel. Desynchronosis caused by external natural factors are, for instance, desynchronosis related to: 5) extreme natural conditions, 6) changes in rhythms of the operating gelio-geophysical time sensors, such as cycles of sun activity, 24-hour and seasonal variations of climate, change of climate, 7) rhythms of geomagnetic fields of Earth, caused by Sun rotation, 8) a-periodical changes in gelio-geophysical factors that arise during solar flares and geomagnetic storms. Such an ordering of reasons that cause desynchronosis is conditional, as always when considering any type of multi-factor system of disorder of chronostructure of circadian rhythms (Zhang, 2009: 818-820).

It is logical to assume that disordering of chronostructure of rhythms of one or another system is a coherent phenomenon, and the following subdivision by different manifestations of impairments of rhythm parameters is conditional. Nevertheless, using such methods in chronomedicine, as amplitude changes in rhythms, change of mesor or period of rhythm independently is sufficiently acceptable and justified in a number of specific cases. Amplitude Increase (decrease) of circadian rhythm under influence of stress. The amplitude of circadian rhythms possesses exclusively important significance for assessment of functional state of a human. Despite the fact that amplitude variations are most often combined with other manifestations of desynchronosis, it is necessary to note that registration of amplitude change can serve as a fine test during prenosological diagnostics. Thus, for example, during a chronobiological observation of a group of sportsmen doing academic rowing it was established that one of the first symptoms of exhaustion is disturbance of rhythm chronostructure of hemodynamics recordings, which manifested through a decrease in amplitude of their circadian rhythms. Characteristically, that after a 3-hour flight, passengers experience a decrease in amplitude of 24-hour fluctuations of physiological indicators, while decrease of rhythm amplitude is the most-pronounced during a flight in eastwards direction. V.A. Matykhin and others note that the higher the speed of transfer is, the lower the amplitude of 24-hour fluctuations recordings are. While estimating various periods of presence of workers on shift during trans-longitude flights in conditions of polar regions N.M. Fateyeva recognized that apart from significant fluctuations of average 24-hour level of blood clotting, there are sufficiently sustainable changes in intrasystemic synchronisation of regulated parameters. The main manifestations of such changes are: vanishing of statistically significant 24-hour rhythm, a highly expressed dislocation of acrophases, emerging of statistically significant 12-hour rhythms; this is especially characteristic in the initial period of the flight. Relative stabilisation of temporary organisation of homeostasis readings is recorded on 30-35th day of the shift, and it reaches a sufficiently stable state by the 45th day of work. It is appropriate to remind that changes in circadian rhythm amplitude of cardiovascular system readings is observed not only when desynchronosis is caused by external factors but also when it is caused internally(Agarwal,2010: 51-58).

Synchronisation of rhythm- is a vital process of functioning of mammals' organs, an indicator of direct intercellular communications. Disorders of intercellular communications leads to activation of cellular death mechanisms. The role of melatonin in an organism is very unique. It determines the rhythmical activity, such that, in fact is a universal adaptogene, which "calibrates" functions (internal clock) of the organism to the constantly changing conditions of the surroundings. This factor is key in the issue of an organism's survivability, effectiveness of its functioning independent from its level of organisation. Besides, antioxidant properties of melatonin determine its protective abilities during free radicals attacks on DNA, lipids and proteins. Melatonin can affect processes of free radicals in any cell of the organism. Immune-modulating properties of melatonin are not of less importance, these are determined by production of immune-competent cells and secretion of cytokines by these cells. It has been proven that melatonin is not only a messenger of the main endogenic rhythm, but also its corrector in relation to the environment. Due to this, any change in melatonin production going beyond natural physiological fluctuations can lead to misalignment of biological rhythms of both the organism amongst itself (internal desynchronosis) and with the rhythms of the environment (external desynchronosis). Specifically, disorder of melatonin production is a reason of sudden disease syndrome, idiopathic intestinal cramps in new-borns, seasonal affective disorders. As mentioned, any disease is accompanied by desynchronosis, and the harder the disease, the more manifested is the dysfunction. It was illustrated through the example of ischaemic heart disease patients, hypertonic disease, ulcer and other disorders (Aronow, 2003a: 1354-1355). Quantity and rhythm of melatonin daily production serve as markers for severity of desynchronosis. It has been established that the harder the disease passes or the more frequent worsening of the disorder is, the less is melatonin production, and the less apparent the difference between its night and day production is. In some difficult cases, the day and night melatonin production rates become almost identical. In periods of remission the curve of melatonin production returns to the one that had been before worsening. Nevertheless, it will not be normal, which supports our opinion that patients with chronic disease will always be in more or less unstable state of balance. Works of recent years have shown that melatonin plays a distinguishable role in desynchronosis elimination and its prevention. These days there is a medication form of melatonin – melaxen, which allows to successfully treat the diseases and prevent them. Moreover, while treating patients with various diseases it has become apparent that combining "profile" medications with melaxen is significantly more effective than traditional therapy. Apart from this, some unexpected effects have been observed. Thus, during treatment of a worsened ulcer disease with presence of *Helicobacter pylori* and no use of standart therapy with antibiotics, implementing only melatonin remission of the disease has been achieved, the microorganisms have vanished. A research that illustrated progressive decrease in pineal body production of melatonin with age appeared to be very important, the decreased production has led to a fall in difference of the hormones' abundance during night and day(Aronow, 2003b: 1357-1358).

Seasonal worsening of internal organs diseases pose a special interest. During periods of biological spring and autumn, parameters of organism's circadian rhythms are in a process of either increasing or decreasing of their amplitude, thus in a counter phase. In our opinion, this moment is one of the decisive in pathogenesis of seasonal worsening of disease, because it leads to a condition that can be called a seasonal physiological desynchronosis. Seasonal impairments of internal organs diseases do exist. They constitute a complex process that is based on a fundamental law, and the role of "major violin" is played by melatonin. Research dedicated to melatonin has opened a new direction not only in biology but in medicine, in treatment and prevention of disease impairment, including the seasonal ones. Increasing of physiological functions that provide organism's physical activity (frequencies of heart contractions, minute blood volume, arterial pressure, body temperature, oxygen consumption, blood sugar levels, physical and mental productivity and else) during day and their decrease at night is characteristic to human body. Specific correlations between phases of different 24-hour rhythms are observed in normal conditions. Maintaining consistency of these correlations provides alignment of bodily functions in time, identified as internal alignment. Besides, under influence of changing with 24-hour periodicity environmental factors (synchronizers, or time sensors) external alignment of circadian rhythms takes place. There are primary (carrying major significance) and secondary (less significant) synchronizers. In animals and plants, primary synchronizer is, as a rule – sunlight, in humans it can also be social factors. Presence of circadian rhythmics of arterial and venous pressure in humans is evident of melatonin participation in regulatory functions of cardio-vascular system. Existence of melatonin receptors in intermuscular layer and endothelium of vessels is yet another piece of evidence. In most animal research in terms of improved arterial vessels tone in vitro and in vivo it has been demonstrated that physiological, as well as pharmacological doses of melatonin exert a vasodilating effect, however melatonin effect on vessel tone is not unambiguous and depends not only on state of the vessels. Mechanisms through which melatonin affects vessel tone include binding of melatonin with own receptors of smooth muscle cells and endothelium of vessels, by influencing adrenergic and peptidergic (vasointestinal peptide, substance P) endings of perivascular nerves and secondary messengers in adrenergic stimulation chain of muscle contraction, as well as inhibition of serotonin secretion by structures of CNS, vasopressin, hypothalamus and noradrenaline by adrenal gland. Without hesitation, impairing melatonin production may play a major role in pathogenic mechanisms of coronary pathology. This is demonstrated by effects of melatonin itself and clinical studies, which show reduction of night melatonin production in patients with IHD, as well as in patients with acute angina. Melatonin is capable of exerting influence on sizes of impact sites, reduce frequency of ventricular arrhythmia and decrease mortality (Shin, 2007: 656-662).

According to our research data, an increased concentration of melatonin in patients with neurocirculatory dystonia is an evidence that on functional disorders stage, melatonin production can increase and then if the disease progresses depletion of reserve possibilities starts at the stage of forming of a somatic disorder. As severity of cardio-vascular pathology progresses not only does production in total decrease but also rhythmics of melatonin production are impaired and significant differences in day and night production are no more distinguishable. These results allowed inclusion of melatonin into traditional therapy of hypertonic disease (HD) and IHD. During comparison of therapy results of these groups of patients, receiving melatonin, reduction of headaches was noted in 35%, of them, 15% have reported reduction of dizziness, photopsia- 25%, noise in ears – 15%. In group of patients receiving traditional therapy, these symptoms were less obvious – 25, 5, 10 and 10%, respectively (Blagonravov, 2010: 559-561).

Based on fact that alcoholism induces sharp decrease or complete stoppage of melatonin synthesis by pineal body, domestic researchers, in hospital conditions carried out a series of experiments pointed at implementation of melatonin as replacement therapy in order to treat some manifestations of alcoholic withdrawal syndrome of medium severity. These works have proven that patients in this condition show signs of internal desynchronosis, as evidence, absence of reliable circadian rhythmic of systolic and diastolic arterial pressure and biorhythm of axillary temperature during withdrawal was present. Positive results were gathered when melatonin (melaxen) was prescribed in doses ranging from 6-9 to 12 mg/24-h in an acute period of alcohol withdrawal. Thus, dynamics of improvement in a group of patients that received melaxen as a mono-hypnotic (6mg at 10p.m. In duration of 2-4 days of staying in hospital), had better characteristics in comparison to patients who received benzodiazepines. Advantages of melatonin became easiness of falling asleep and prolonged duration of night sleep. An absolute absence of adverse effects (characteristic during prescription of sedative substances-irreplaceable part of standard therapy) was also observed when melaxen therapy was carried out, even in high doses. This allowed to officially recommend such medication during combined therapy of such a disease. While examining mechanisms of action of magnetic storms on patients with HD and IHD, an important role of pineal body melatonin secretion has been determined. Received data allowed to work out a prevention mechanisms for impairments during magnetic storms if melaxen is included in the therapy (3mg, 2-3 days before the storm). Daily and seasonal periodicity of clinical manifestations during worsening of ulcer disease, has found an explanation in misalignment of genetically determined rhythms of melatonin production with rhythms of the the environment (desynchronosis). As our clinical observations demonstrated, when melatonin is included in the plan of therapy for duodenum ulcer patients, the effect significantly exceedes the one of standard therapy, morphological state of stomach's mucous membrane was clearly improved according to results of electro-microscopic and immunohistochemical observations, which hinted at a deeper remission in similar amounts of time. Melatonin's role in aging cancerogenesis, sleep impairments and a number of diseases is vitally important. It is not less important in organization of labour and rest. Therefore, whatever field of human life is concerned, be it labour, leisure, illness, age, therapy, e.t.c.- the key role in everything is played by human's rhythmical organisation; it is the fundamental base. Going back to the issue of seasonal time change, even just one hour change, we, to a certain degree cause desynchronosis with all of the after-effects that were stated previously. If the difference in time change is significantly greater than that, all of the disadaptation mechanisms start taking place. Winter 2011-2012 demonstrated how uncomfortable the population was feeling after changing of "winter" time to "summer". In a 24-hour period, dark time was dominating over light time, apart from discomfort, this can be followed by development of depression-a fact, well-known in northern countries (Sweden, Norway) (Yamazaki, 2005: 241-249). In any case, in our country the time change was accompanied by an apparent emotional outburst and a reaction of the population that went as far as an intercession with the Government. This is a bright example but we need to take into account that many other circumstances can also cause desynchronosis. For instance, shift work, night lifestyle, excessive TV watching and so on. It was demonstrated that daily and seasonal rhythms of life of healthy and sick people is mainly dependent on maintaining genetically laid foundations of life. An understanding that disorders of these rhythms lead to desynchronosis and the after-effects has arisen. It is obvious that practically implementing principles of chronobiology and chronomedicine is vitally important (Imai, 1996: 172-185).

Understanding of necessity of daily monitoring the readings of arterial blood pressure, pH, stomach juice, with the aid of which approach to therapy is determined (chronotherapy) serves as another evidence. Now it is hard to imagine examining the oatients without this data. There are specialized journals: "Vladikavkaz med-biological informant", "Railway medicine – professional biorhythmicity". "Chronobiology and chronomedicine guidelines", a monograph "Melatonin: perspectives of implementing in clinics" were published in 2012, in previous years several monographs dedicated to melatonin were published.

Such principal issues as necessity of exploring biorhythmicity in med schools in frames of theoretical (biology, pharmacology) and clinical disciplines were raised.In a natural habitat organisms are always influenced by a complicated dynamic complex of factors, on top of this actions of some factors change (enhance, inhibit, deform) actions of others, which creates problems for determining their role in biotropy extent. Impairments of temporary organism structure arise when its internal rhythms are subject to orderly structure misalignments, causes of such misalignments can vary – external and internal. Impairments of natural flow of biological rhythms, their mutual alignment, meaning desynchronosis, is an essential component of total adaptation syndrome and in this, connection of biological rhythms problem with adaptation problems can be seen (Viskin,1999: 1429-1434).

Failures of CR in short time periods leads to a failure in 24-hour activity, tiredness, insomnia and disorientation. Such diseases as manic-depressive psychosis and various problems with sleep are associated with pathologic dysfunction of CR. Prolonged failures of CR can be followed by deterioration of internal tissues' and organs' condition, for instance, cardio-vascular disease (CVD). Chronomedicine was most largely introduced into cardiology practices. First of all, this is linked with an important role of cardio-vascular system (CVS) in organism's livelihood, as well as high incidence of cardio-vascular pathologies that lead to disabilities and death. Besides, the main parameters of cardiac activity can be easily registered and monitored, which is essential when assessing chronobiological indicators. The most important parameters of cardiac activity – frequency of heart contractions (FHC), arterial pressure (AP), variability of heart rhythm (VHR) – all possess their precise biological rhythms, synchronized in time in relation to sleep and wake period.

Misalignment of various CVS parameters' biorhythms can be followed by development of pathological conditions with the following structural changes in information, energy and exchange. Therefore, it is vital to perform biorhythmic research in even those patients who are having initial manifestations of one or another cardio-vascular pathology. Impairments of AP and FHC also pose an importance in development of worsening of CVD. This is confirmed by a plethora of science papers, authors of which explore mechanisms responsible for circadian fluctuations of these parameters. Thus, Leary A, et al. revealed a tight positive connection between increasing morning activity upon awaking and "spikes" in AP and FHC in their works. In relation to this, patients having arterial hypertension (AH) and IHD were recommended to withdraw from energy-demanding physical exercise right after awaking. However, this issue remains disputable. It is necessary to point out that misalignment of biological rhythms and impairment of their natural flow is not solely an indicator of pathology development but it can also be a result of an already existing disease. This, in turn, becomes more disadvantageous as CR impairments can lead to a number of condition worsening factors. Failure of daily AP rhythm is associated with a greater frequency of target organs' damage and with an extended risk of cardio-vascular events, related to overload of pressure. Complex studies of physical activity, vegetative functions and sensitivity to sodium allow us to explain in detail the physiology of AP circadian changes and pathophysiology of 24-hour rhythmsin various conditions and during different diseases. In healthy patients, normal daily profile of AP is characterised by a night decrease of 10-20% as compared to day levels. In healthy patients, this daily Ap profile is determined by various psycho-behavioural factors and is accompanied by changes in neurohumoral factors, including tone of vegetative nervous system's sympathetic region and renin-angiotensin-aldosteron system (RAAS) (Dunlap,1999: 271-290).Those who do not show signs of AP decrease at night >10% compared to daytime belong to a group of patients with impaired AP circadian dynamics ("non-dippers"). In this patients the impaired CR is associated with kidney diseases and cardio-vascular events- heart attacks and strokes. In a series of experiments, levels of night time DAP and impairments of CR by "non-dipper" type were important predictors of chronic heart failure (CHF) development in patients who had no myocardial infarction (MI). Associated with other cardio-vascular risk factors, failure of daily AP fluctuations is an important predictor of mortality from all reasons. In some researchchange of daily AP rhythm was connected to the risk of heart failure development. The researchers have verified whether the changed daily AP rhythm is connected to disadvantageous outcome (death or hospitalisation due to CHF worsening) in patients with CHF. It was determined that an impaired daily AP rhythm, when added to other standard predictors, is in fact, an essential prognostic factor during CHF. An increased night time AP and high readings of plasma BNP right before discharging the patients from hospital were determined to be significant predictors of stroke in patients with CHF.

Congestive heart failure is associated with changes in sympathetic and parasympathetic nervous systems, weakening of baroreflective function, which affects daily AP rhythm directly. Thus, if normally cardio-vascular CR parameters are bimodal (two phased), with lowest readings at night sleep period, when its progressing normal circadian AP and FHC rhythmicity change and bimodality of CR fades. During CVD profile of FHC changes. Daily FHC rhythm is characterised by a special indicator – circadian index (CI). While studying CI in various groups of patients with CVD (dilated cardiomyopathy, ID, idiopathic arrhythmia, AH and else), that survived and unexpectedly died because of it, as the condition developed, an increase in heart daily rhythm rigidity was detected. Flattening of circadian FHC profile reflects on depletion of cardiac rhythm adaptive reserves and is clinically associated with poor diagnostics and high risk of arrhythmogenic syncope conditions and sudden death in patients from risk groups. The leading role in organism's cyclic processes coordination is played by circadian fluctuations of nervous system's functional activity. Vegetative nervous system's daily fluctuationsare closely linked to light-darkness and sleep-wake cycles. VNS's sympathetic region's tone prevails during day time activities, parasympathetic – during night sleep. Apart from this, along with VNS, physical activity, location of body in space and baroreflexes are responsible for daily circadian rhythm changes in healthy humans. In patients with cardiovascular pathologies, changes of CR parameters of heart rhythm variability were noted. For instance, in patients with AH and AH with paroxysms ofatrial fibrillation, break downs of daily CRV parameters' rhythms, characterised by temporary misalignment of SDNN rhythm, as well as decreasing of mesor value and amplitude of CRV parameters' CR that reflect on sympathetic and parasympathetic influences. In patients with CHF daily CRV and variability of QT intervals can also be modified due to neuro-humoral activation, functional and structural remodelling of the heart. 121 patients with stable CHF were observed during one of the research works. With aid of cosine analysis, readings of CRV CR parameters and QT-intervals were determined. In addition to an expected increase in FHC and prolonging of QT-interval, a decrease in QT-interval's circadian variability and a dislocation of RR interval's maximum towards later hours in those who have died in comparison to those who survived have been detected.These 2 parameters happened to become independent predictors of cardiac arrest when performing multidimensional Cox regression analysis. While studying the 24-hour regime of RR interval's variability in patients with CHF a decrease in all indicators has been revealed during the period, as well as presence of pathological CR for frequency parameters of RR intervals. In a study with simultaneous Holter ECG analysis during physical activity it was shown that sympathetic-vagal balance is dislocated towards sympathetic tone in patients with heart failure. Along with this, physical activity is a subject of organism's homeostasis ultradian dynamics(Hasting, 1998: 425-445).

Circadian dynamics were noted in cardio-vascular events. Knowing the daily disease risk rhythmic along with pharmacological and pharmacodynamical properties of drugs provides success in treating a series of pathologies. Chronotherapy is especially relevant for diseases, that present a clear risk CR for their appearance or appearance of their symptoms, such as allergic rhinitis, arthritis, asthma, heart attacks, cardiac failure, stroke, ulcer. Appearance of cardio-vascular events has obvious seasonal fluctuations and a higher predisposition of episodes in spring and winter periods. High incidence of acute heart attacks, angina, acute heart failure, hypertonic crisis and sudden death was observed in spring and winter as well as during changing of seasons, namely in January, February, March, April, October, November and December. Daily rhythm for cardio-vascular events was characterized by a morning peak that lasted until midday. During extended observations of patients with AH, Kario K. et al. have revealed a positive correlation between brain strokes frequencies and extent of morning increase in AP, while the extent of increase of morning pressure did not depend on average daily levels of pressure and a series of other indicators. According to the authors, this indicator is an independent and prognostically significant factor in development of brain adversities. It is assumed that effective control of AP with aid of antihypertension substances can possibly improve prognosis of those with AH, by decreasing the frequency of brain strokes development. Viskin S. et al. was one of the first wide-scale research works on circadian variations of newly emerged paraxisms of atrial fibrillations (PAF). The research has identified that emerging of PAF is characterised by emerging of two peaks with a significant increase in episode frequencies in morning and evening periods. During a week significantly smaller amounts of emerged PAF's were recorded on Saturdays. And the greatest number of arrhythmias was observed on last months of each year. The most studied issue remains chronopathology of heart attacks – daily dispersion of its emerging, scale of myocardium damage and lethal outcome. There are guidelines on dependence of repeated heart attack from time of the day. The maximal number of cases was registered for late morning hours (8-11.59 a.m.), which are rightfully considered as "high-risk" hours in relation to emerging of repeated necrosis. In time period from 4pm to 7:59pm only 9.8% of heart attack incidence occurs. These hours can be considered as hours of "relative wellness". Apart from this, a number of studies have determined that starting of heart attacks between 0-12 hours led to a significantly larger scale of necrosis in respect to other periods of time of heart attack emergence. An increased frequency of cardio-vascular disasters in morning hours is mostly determined by an enhancement of sympathetic-adrenal system activity at this time period. Sympathetic nervous system enhances catecholamine production, blood's clotting activity increases, heart rate goes up, shortening of heart cycle duration, which leads to an increase in myocardium oxygen demand. These changes are especially apparent in patients with blood circulation pathologies. Each one of these factors can serve as a trigger to develop adversities of CVD (Kamory, 2008: 289-294).

Life-threatening break downs of rhythm that impair flow of myocardial infarction are also characterized by presence of circadian. A research on bunnies has looked at emergence of ventricular fibrillation (VF) in relation to time of acute coronary failure emergence. Indiction of coronary failure in a period from 3:30pm to 6pm has led to emergence of VF and death of animals in 100% of cases. Modelling of heart failure from 11am to 3pm did not induce VF in 89% of cases. CR CRwas noted in emergence of sudden heart death in patients with innate or adaptive heart pathology. Total mechanism, laid in the foundation of ventricular arrhythmias presents a break down in duration and form of myocardium repolarisation process.

It was shown in an experiment with mice that expression of ion channels and duration of QT-interval also have daily rhythms and are controlled by an endogen-dependant oscillator – Klf15. Klf15 transcriptionally controls rhythmical expression of Kv channel-bound protein 2 (KChIP2) – critical subunit, essential for creation of outwards K^+ flow. Deficit or excess of Klf15 leads to a loss in rhythmicity of QT-intervals, breaking of repolarisation and increases predisposition to ventricular arrhythmias. In one of prospective studies CR was identified in number of deaths per hour and in patients with stagnant heart failure after a heart attack. Major peak- between 6 and 12am, 202 of 517 deaths (39%) happened during this 6-hour period. The highest frequency of ambulance calls for patients with CHF in relation to worsening of the disease is at winter months, on Mondays, from 8am to 3pm, which points out at rhythmicity of emergence of adversities for the pathology. Daily rhythm of QT dispersion was shown in patients with CHF, which can also be potentially significant for therapy and prevention of sudden heart death in patients of this group. The fact that break downs of organism's temporary coordination function are one of the first evidences for development of a pathological process, makes research in the field of biorhythm changes important in assessment of pre-pathological conditions, disease diagnosis, organisation of preventing activities, and also in prognosis of flow and outcome of the pathology, development of their adversities and adequate therapy of already existing pathologies with use of chronotherapy principles. Thus, taking into account the high incidence of cardiological pathologies, chronobiological research in this area is quite relevant. While problems of chronobiology and chronotherapy of AH are sufficiently studied, there is too little information about features of cardiac activity CR in patients with CHF. Meanwhile, namely with progress of heart failure AP, FHC and CRV circadian rhythms can significantly vary, hence directly or indirectly affecting emergence of a series of adversities of CVD. Therefore, fundamental research in this area, including establishing norms of daily dynamics of FHC, AP, CRV are vitally important for their following implementation in practical activity. Because, based on features of chronostructure of cardiac activity parameters in patients with CHF it will be possible to adjust therapy, including improvements of diagnostic methods based on main principles of chronotherapy, and possibly prevent some adversities during the pathology.

Changes in amplitude of daily rhythms is one of the important diagnostic criteria in chronomedicine of not only internal but also external desynchronosis. Changing of rhythm periodicity under stress. As studies of internal desynchronosis suggest, stress, related to pathology presence is accompanied also by changing of circadian rhythm period. Clinical laboratory studies, under maintenance of N.A. Aslanyan allowed to formulate a new term “neorhythmostasis”, hence establishing a relative stationarity of rhythm parameters on a new level that is under stress, namely, switch of circadian rhythmostasis to ultradian infradianneorhythmostasis. For example, while performing of the 261strhythmological research of extracting urine and electrolytes in patients suffering from neurocirculatory dystonia, is was identified that in 168 cases (64%) they exhibit accurate rhythms, however their periods significantly differ from rhythm periods of healthy individuals. Given that in healthy people, amongst statistically clear rhythms, 24-hour rhythm constituted 92%, in patients with neuro-circulatory dystonia only 31% was detected, for infradian – 54%, ultradian rhythms – 15%. In the same time, mesors and urine and electrolyte excretion rhythms amplitude in this group of patients did not sustainably differ from similar indicators of healthy people. L.A. Babayan et al. have illustrated in their work that intact animals under influence of external stress experience dislocation of circadian rhythm period into infradian area. Usually, statistically reliably indicated rhythms of corticosterone and blood minerals in these animals account for 80%, rhythms of mineral extraction with urine – 74%. With this, amongst reliable rhythms in intact animals in calm conditions rhythms of circadian scale dominate (75 and 91% for blood and urine, respectively). It is possible to conclude that most intact animals possess circadian rhythms of water-mineral homeostasis of internal synchronisation by rhythm periods of specific indicators established by a specific value of mesors and amplitudes. Under influence of extended external stress factors (for example alcohol injection) animals’ water-mineral system reorganized its temporary structure. This manifested through circadian rhythm transformation into non-periodic fluctuations or in formation of mainly infradian rhythmicity: for blood and urine indicators circadian rhythms constituted only – 21%, 27%, while infradian rhythms – 56, 54% and ultradian rhythms – 23,19% respectively. It is important to underline that most indictors go through not only change of period but also through significant change in values of some mesors and amplitudes. For instance, reliable rhythms of corticosterone in 100% of cases were located in infradian scale, however, their mesorsand amplitudes statistically reliably ($P<0.01$) exceeded the respective indiators of intact animals in conditions of stress. Quite notably, plasm minerals’ and erythrocytes’ rhythm mesors did not considerably change under stress, hence remained a relative constancy of cellular and non-cellular mineral concentration (Shishelova, 2009: 6).

Cycles of life processes differ by their parameters – period duration, amplitude, phase. In cases when adaptation process flows calmly, without notable damage to organism, when stress levels do not exceed norm levels, their effects on circadian rhythms are low. If the adaptation process flows violently, with apparent and quickly developing changes in the organism, which can be determined by a strong stimuli.

Noise – is a combination of sounds of various frequency and intensity that disorderly blending and travelling in time. Any type of noise is characterised by a specific frequency content, or, as they say spectrum. Noise arises in result of fluctuations of solid and flexible bodies. . Fluctuations of any solid body, liquid or gas is characterised by:

– Amplitude (value of deviation from balance point);

– Frequency (frequency of fluctuations determines tone height, the greater the frequency, the higher the tone of the sound)

– Speed of frequency wave movement in physical or biological surroundings.

Sensibility of the hearing apparatus in domestic animals varies, it depends on the sounds height. Dogs are capable of registering fluctuations of 38 – 80000 Hz, sheep – 20 – 20000 Hz, horse – 30 – 1025 Hz.

The minimal sound energy that can be absorbed by human ear is called hearing threshold. It is 10^{-12} Вт/м^2 (for 1000hz tone). Sound pressure corresponding to this equals 2×10^{-5} Н/м^2. Level of sound loudness (noise) is measured in bels (B) or decibels (dB). Depending on spectrum all noises are divided into three classes: low frequency – up to 350Hz; medium frequency – 350-800hz; high frequency – more than 800Hz (Nekipelov, 2005: 9).

By dispersion of sound life in time noise is subdivided into constant (stable) and intermittent (not constant). Level of sound should not exceed 65-70 dB for domestic animals. Impact of sound depends on its loudness, determined by a special content (frequency of its sounds) and by power of noise.

Organism’s reaction to noise level of more than 70 dB is a complex of symptoms of functional and organic changes that arise parallel to changes of hearing organ’s functions. It is essential to mention dysfunctions of vegetative nervous system. Prolonged effects of noise causes changes in breathing rhythms and rhythms of heart contractions, hypertonia develops. Motor functions of gastro-intestinal tract change, hypersecretion of some internal glands emerges.

Noise absorption can be achieved by growing plants around buildings where animals are kept. Noise-meters are used to measure levels of noise (Sh-3M, IShV-1, Sh-63 and others). For example, Sh-3M measures noises of 25-130dB in a scale of 40-10000Hz (Nekipelov, 2004:2).

Every organism perceives noise in its own way. A lot depends on age, temperament, health state, surrounding conditions. Human hearing organ is capable of adapting to some constant and intermittent noises (hearing adaptation). But this adaptability is not capable of protection from a pathological process – losing sense of hearing, it only temporarily helps. In conditions of city noise a constant tension of the hearing analyser takes place. This causes increase in hearing threshold by 10-25 dB. Noise impairs understanding of speech, especially when it is louder than 70 dB. Damage that strong noise exerts to the ear depends on spectrum of sound fluctuations and character of their change. First of all, a person starts to hear less of high sounds, then medium and low. Danger of losing hearing due to noise largely depends on individual characteristics. Some lose the sense of hearing after a short effect of noise of a relative intensity, others can work with strong noise almost all life without notably damaging their hearing abilities. Gradual impact of strong noise does not only negatively affect hearing but also lead other adversities- ringing in ears, dizziness, headaches, increasing of tiredness (Izmerov,2005: 384).

Excessive noise can be a reason of nervous depletion, psychic oppression, vegetative neurosis, ulcer, disorders of endocrine and cardio-vascular systems. Noise distracts people from work and rest, decreases productivity of work. The most noise-sensitive people are those of older age. At ages before 27 only 46.3% react to noise, at ages 28-37 – 57%, 38-57 – 62.4% and at 58 and older – 72%. Large amount of complaints from people of older age is obviously linked to age properties and state of central nervous system of this age group.

There is a correlation between number of complaints and character of the work. Polling data shows that disturbing effect of noise is a larger concern for those doing analytical work than those who labour physically (60.2 and 55% respectively). As criteria of unhealthy effect of noise, indicators of damage and recovery period of hearing sensitivity, bioelectric activity of brain matter, latent period of conditional-reflex reaction to light and noise, analytical productivity, arterial pressure, frequency of heart contractions, specific readings of ECG.

Other serious changes can be observed under influence of noise: slowing down of heart contractions, decrease in saliva and stomach glands production, disorder of thymus functions and adrenal glands, change in electric brain activity. Noise that exceeds 80-90dB affects excretion of most pineal gland hormones that control excretion of many other hormones. Thus, secretion of cortisone hormone by the adrenal glands can be increased. Cortisone possesses an ability to weaken liver possibilities to withstand toxic substances, including those causing cancer. Under influence of noise of 85dB A rebuilding of energy exchange in muscle tissues was observed, direction of the rebuilding depended on time of influence. Increase of interaction between oxidation and phosphorylation after a two-week impact of noise is an evidence that these process is capable of ATP generation. Indeed, as a result of intensification of oxidative phosphorylation in mitochondria starts a tendency to increase ATP content in muscle homogenate with similar duration of impact. Noise inhibits new formations of energy rich phosphate bonds that depends on state oxidative-phosphorylation processes(Van Dijk,291-309).

Noise of industrial character during timely influence on rats causes inhibition of the main part of developing energy in a cell – oxidative phosphorylation in mitochondria. This fact points at a possibility of using this indicator as a biological criteria of unhealthy effect of noise on the organism. Impairment of energy metabolism processes – a significant factor of unhealthy effect of noise, in turn, may become a reason for breaking balance of a series of biochemical processes in an organism.

Impairment of muscle energetics can be observed as those received in a relative rest state, since some movement excitementin rats was not edonly during the first days of the experiment. Thus, the mainroute of energy generationin form of ATPin a relativerest state of ananimal underprolongednoise exposureisimpaired. Itisknown that duringmus cleactivity energy expenditure of the organis mexpands and a muscleactivelyuses ATP when doingme chanical work.

Pathomorphologicalstudieshaverevealed signs of irritating effects of noise: some activation of brain matter nervous cells of large hemispheres, lipoid depletion of adrenal glands, increase in number of plasma cells in spleen, evident of some increase in immune reactions (Maksimova, 1998: 124-132).

An experimental group of rats (male and female) under influence of transport noise has given a generation of offspring that was influenced by similar sounds for 3 months. Control group (males, females and offspring) lived in quiet conditions. The groups did not differ in mass and height significantly. Physiologicalresearch on first generation 3-months-old male ratsrevealedthat in experimental group latent time of reflex reactions is shorter by in average 8.6ms, and frequency of heart contractions is 60b/m faster than control group. Therefore, it is possible to assume that in first generation rats, whose mothers before and during pregnancy were exposed to noise a process of excitement in central and vegetative nervous systems prevails. The experiments showed unhealthy effect of transport noise on various organs and organism systems depending on duration of exposure. Influence of noise was established not only on parent organism but also the offspring.

Noise impairs sleep considerably. In developed and more frequently in developing countries, where community is active 24/7, we are in a desperate need to recover correct models of sleep. Our 24-hour sleep rhythm- is the mostly apparent daily rhythm that is observed in people and may animals, but sleep – is something more than just part of circadian system. Sleep- is a very complex state, created by several brain regions, neuromodulating systems and modulators. Due to this level of complexity, sleep is very susceptible to disorders. A recent work has shown that impairments of sleep and circadian rhythm (SCRD) are common for various neurodegenerative and neuropsychiatric diseases during which routes of neuromediatorsare damaged. For instance, SCRD is observed in more than 80% of patients with depression or schizophrenia. Surely, it is uncomfortable to feel sleepy at an appropriate time, but it is only the tip of the iceberg. SCRDisalsoassociatedwith a wide spectrum of interrelated pathologies, such as poor attention and memory, decreasing of mental and physical reactions' speed, reduction of motivation, depression, insomnia, substance exchange impairments, obesity, immune disorders and even higher risk of cancer development. All of these are often observed during psychic and neurodegenerative disabilities. Extremely unfavourable effect is exerted by intermittent, suddenly appearing noises, especially at evening and night hours on the newly fallen asleep person. This is explained by the fact that while falling asleep brain is in a "hypnosis" phase. At this time paradoxical relations with the environment are being developed, hence even weak noise stimuli can exert an unproportioned, strong effect. A sudden noise that appears during sleep (cars, music, etc.) often causes strong fright, especially in sick people and children. Noise reduces duration and deepness of sleep. It has been established that chorological configuration of noises is one of the most important factors, sequence of noises of different intensities. Thus, unstable transport movement breaks sleep more effectively than an intensive and evenly distributed noise (Ablaykhanova, 2013: 239-243). Apparently adaptation to regular and frequent noises happens easier than to irregular and seldom ones. People react to noise during sleep differently. Reaction to noises does not depend on age, gender, and state of health. Thus, during the same intensity of noise, people aged 70 wake up in 72% of cases, whereas children, 7-8 years old – only in 1% of cases. Threshold noise intensity that causes awaking in children is 50 dB A, adults – 30dB a, and older people react to an even smaller value. Women are more easily awakened via noise. This is explained by the fact that women transfer from deep sleep to REM sleep more frequently than men. Noise affects various stages of sleep. Thus, stage of paradoxical sleep, characterised by dreams, fast eye movements and other features, has to take not less than 20% of total sleep; reducing this stage of sleep leads to serious disorders of nervous system and mental activity. Reducing stage of deep sleep leads to hormonal disorders, depression and other psychic pathologies. Under influence of 50 dBA noise, time required to fall asleep extends by an hour or more, sleep becomes superficial, after awaking people feel tiredness, headache and often times increased heartbeat. Absence of normal rest after a day of labour is followed by a state, where naturally developed tiredness does not vanish after work but in fact becomes a chronic exhaustion that facilitates development of a series of diseases, such as break down of central nervous system and hypertonic disease (Ablaikhanova, 2012:4).

Effect of noise on functional state of central nervous and cardio-vascular systems is identified in the process of experimental studies on animals. Fundamental physiological research on determining acceptable levels of noise are the basis of noise hygiene.

Negative results of noise exposure are reduction of total resistance of the organism and reduction in productivity indicators (increase in body mass, milk productivity and else).

Noise is a stress-factor. Development of such a condition causes tension of hypothalamus-pineal body-corticoadrenal system. Corticosteroid hormones, cholesterol and glucose concentrations in blood increase and eosinophils concentration falls. Due to these disorders, changes in circadian rhythms of the organism arise (Ablaikhanova, 2014:251-256).

Литература

Хильдебрандт Г. Хронобиология и хрономедицина. / Г. Хильдебрандт, М.Мозер, М.Леховер. – Пер. с нем. – М.: Арнебия, 2006. – 144 с.

Анисимов В.Н.. Мелатонин: роль в организме, применение в клинике. – СПб.: «Система», 2007. – 40 с.

Заславская И.Н. Отчет о научно-исследовательской работе Проблемной комиссии № 31. «Хронобиология и хрономедицина» за 2011 г. [Электронный ресурс] / Проблемная комиссия РАМН «Хронобиология и хрономедицина». – 2011. – 2 с.

Пелеса Е.С. Особенности хроноструктуры частоты сердечных сокращений и вариабельности сердечного ритма у пациентов с артериальной гипертензией и пароксизмами мерцательной аритмии / Е.С. Пелеса // Кардиология в Беларуси. – 2009. – № 4. – С. 91-100.

Пелеса Е.С. Характеристика циркадных ритмов сердечной деятельности у больных артериальной гипертензией с пароксизмами фибрилляции предсердий: автореф…дис. канд. мед. наук: 14.00.06 / Е.С. Пелеса; УО «БГМУ». – Минск, 2010. – 23 с.

Шишко Е.Д. Суточный ритм, циркадианные гены и злокачественные новообразования / Онкология [Электронный ресурс]. – 2010. – № 4. – С. 23 – 25.

Улащик В.С. Биологические ритмы и хронотерапия // Медицинские новости. – 1999. – № 2. – С. 9-13.

Макаров Л.М. Циркадный индекс как показатель стабильной организации суточного ритма сердца / Л.М. Макаров // Клиническая медицина. – 2000. – № 1. – С. 24-27.

Габинский Я.Л. Хронопатология инфаркта миокарда // Уральский кардиологический журнал. – 1998. – №1. – С. 23- 25.

Zhang X.W. [et al.]. A study on yearly and daily circadian rhythm of cardiovascular events / ZhonghuaNeiKeZaZhi. – 2009. – Vol. 48, No. 10. – P. 818-820.

Agarwal R. Regulation of circadian blood pressure: from mice to astronauts / R. Agarwal // Curr. Opin. Nephrol. Hypertens. – 2010. – Vol. 19, No. 1. – P. 51-58.

Aronow W.S. Circadian variation of death from congestive heart failure after prior myocardial infarction in patients >60 years of age / W.S. Aronow, C. Ahn // Am. J. Cardiol. – 2003. – Vol. 92, No. 11. – P. 1354-1355.

Shin J. [et al.]. Association of diurnal blood pressure pattern with risk of hospitalization or death in men with heart failure // Card. Fail. – 2007. – Vol. 13, No. 8. – P. 656-662.

Blagonravov M.L. [et al.]. Chronobiology of cardiac ventricular fibrillation development in experimental acute coronary failure // Bull. Exp. Biol. Med. – 2010. – Vol. 149. – P. 559-561.

Yamazaki T. [et al.]. Circadian dynamics of heart rate and physical activity in patients with heart failure // Clin. Exp. Hypertens. – 2005. – Vol. 27. – P. 241-249.

Imai Y. [et al.]. Circadian blood pressure variation related to morbidity and mortality from cerebrovascular diseases // Ann. NY Acad. Sci. – 1996. – Vol. 783. – P. 172-185.

Viskin S. [et al.]. Circadian variation of symptomatic paroxysmal atrial fibrillation // European Heart Journal. – 1999. – Vol. 20. – P. 1429-1434.

Dunlap J.C. Molecular bases for circadian clocks / J.C. Dunlap // Cell. – 1999. – Vol. 96. – P. 271-290.

Hasting M.N. [et al.]. Entrainment of the circadian system by nonphotic cues // Chronobiological Int. – 1998. – Vol. 15. – P. 425-445.

Kamory T. [et al.]. Factors associated with incident ischemic stroke in hospitalized heart failure patients: a pilot study // Hypertens Res. – 2008. – Vol. 31, No 1. – P. 289 – 294.

Шишелова Т.И., Малыгина Ю.С., Суан Дат Нгуен. Влияние шума на организм человека // Успехи современного естествознания. 2009. – № 8.- 56 с.

Некипелов О.О., Коповалова А.Н. и др. Влияние шума на оппонентные психофизиологические системы памяти человека // Успехи современного естествознания. 2005. – № 9. – 65 с.

Некипелов О.О., Коповалова А.Н. и др. Шум как экологический фактор среды обитания // Современные наукоемкие технологии. 2004. – № 2.- 56 с.

Измеров. Н.Ф. Человек и шум [Текст] / Н.Ф. Измеров. Г.А. Суворов, Л.П. Прокопенко. – М.: ГЕОТАР – МЕД, 2005. – 384 с.

Van Dijk F.J.H. Non auditory effects of noise in industry. V. A field study in a Shipyard [Текст] / F.J.H. Van Dijk J.H.M. , Verbeek F.F. de Pries // International Archives Occupational and Enviromental Health Perspectives. – Vol.41. – P.291 – 309.

Максимова И.И. Действие импульсного шума с различной частотой следования импульсов на организм человека [Текст] / И.И. Максимова // Шум, вибрация и ультразвук. – М., 1998. – С.124 -126.

Taraktiy E.A., Davydova Yu. A. Seasonal variability of indicators of a blood system of the red-backed mouse (Clethrionomusglareolus) of a different reproductive condition. News of the RAS. Ser. Biology, No 1.- 2007.- pp. 14 – 25.

Аблайханова Н.Т., Тулеуханов С.Т., Кулбаева М.С., Жатканбаева А.Р.Изучение циркадианной динамики электропроводности биоактивных точек кожи животных в норме и при гипоксии в весенний сезон года // Международная конференция Актуальные проблемы физиологии, биофизики и медицины – 2013. – С. 239-243.

Аблайханова Н.Т., Тулеуханов С.Т. и др.Хронофизиологические механизмы устойчивости организма к стрессорным воздействиям Вестник КазНУ. Серия экологическая. – №4. – 2012. – С. 56-57

Аблайханова Н.Т., Төленова Қ.Д., Кулбаева М.С., Төлеуханов С.Т., Еркінбек Ұ.Ы. Шудың ұзақ мерзімді әсерін қояндардың терісіндегі аурикулярлы биоактивті нүктенің биофизикалық қасиеті бойынша зерттеу // Вестник КазНУ. Серия экология, 2014. – №4. – С. 251-256.

References

Ablaikhanova N.T., Tuleukhanov S.T, Kulbaeva M.S, Zhatkanbaeva A.R. (2013) Izucheniye tsirkadiannoy dinamiki elektroprovodnosti bioaktivnykh tochek kozhi zhivotnykh v norme i pri gipoksii v vesenniy sezon goda [Study of circadian dynamics of electrical conductivity of bioactive points of animal skin in norm and hypoxia in the spring season] Mezhdunarodnaya konferentsiya Aktual'nyye problemy fiziologii, biofizikiimeditsiny, pp. 239-243.

Ablaikhanova N.T, Tuleukhanov S.T. and others. (2012) Khronofiziologicheskiye mekhanizmy ustoychivosti organizma k stressornym vozdeystviyam [Chronophysiological mechanisms of the organism's resistance to stressful effects]. Bulletin of KazNU. Ecology series. no 4, pp. 56-57.

Ablaikhanova N.T, Tolenova K.D., Kulbaeva MS, Toleukhanov ST, Erkinbek U.Y. (2014) Shudinuzakmerzimdiaserinkoiandardinterisindegiauriculiarlibioaktivtinukteninbiofizikalikkasietiboyinshazertteu[Investigation of prolonged exposure to noise on the biophysical properties of bioactive auricular points of rabbit skin] // Bulletin KazNU. Ecology series, No 4, pp. 251-256.

Anisimov V.N. (2007) Melatonin: rol' v organizme, primeneniye v klinike [Melatonin: role in the body, use in the clinic] p 40.

Zhang X.W. [et al.]. A study on yearly and daily circadian rhythm of cardiovascular events (2009). ZhonghuaNeiKeZaZhi. vol. 48, pp. 818-820.

Agarwal R. (2010) Regulation of circadian blood pressure: from mice to astronauts. R. Agarwal. Curr. Opin. Nephrol. Hypertens. vol. 19, pp. 51-58.

Aronow W.S. (2003) Circadian variation of death from congestive heart failure after prior myocardial infarction in patients >60 years of age. W.S. Aronow, C. Ahn. Am. J. Cardiol. vol. 92, pp. 1354-1355.

Shin J. [et al.]. Association of diurnal blood pressure pattern with risk of hospitalization or death in men with heart failure (2007). Card. Fail. vol. 13, no 8, pp. 656-662.

Van Dijk F.J.H. Non auditory effects of noise in industry. V. A field study in a Shipyard. F.J.H. Van Dijk, J.H.M. Verbeek, F.F. de Pries. International Archives Occupational and Enviromental Health Perspectives. – vol.41, pp. 291-309.

Gabinsky Ya. L. (1998) Khronopatologiainfarctamiokarda [Chronopathology of myocardial infarction]. Ural Cardiology Journal. no 1, pp. 23- 25.

Dunlap, J.C. (1999) Molecular bases for circadian clocks. J.C. Dunlap. Cell. vol. 96, pp. 271-290.

Hasting M.N. [et al.]. Entrainment of the circadian system by nonphotic cues (1998). Chronobiological Int. vol. 15, pp. 425-445.

Izmerov. N.F. (2005) Chelovekishum [Man and noise]. N.F. Izmerov. G.A., Suvorov L.P., Prokopenko. – Moskva: GEOTAR – MED, p. 384

Maksimova I.I. (1998) Deystviye impul'snogo shuma s razlichnoy chastotoy sledovaniyaim pul'sovna organizm cheloveka [The effect of pulsed noise with a different pulse repetition rate on the human body] / II. Maksimova. Noise, vibration and ultrasound. pp. 124-132.

Makarov L.M. (2000) Tsirkadnyy indeks kak pokazatel' stabil'noy organizatsii sutochnogo ritma serdtsa [Circadian index as an indicator of stable organization of circadian rhythm of heart]. LM. Makarov. Clinical medicine. no 1, pp. 24-27.

Nekipelov O.O., Kopovalova A.N. et al. (2005) Vliyaniye shuma na opponentnyye psikhofiziologicheskiye sistemy pamyati cheloveka [The influence of noise on the opponent's psychophysiological systems of human memory]. Uspekhisovremennogoyestestvoznaniya, no 9, 56 p.

Nekipelov O.O., Kopovalova A.N. (2004) Shum kak ekologicheskiy faktor sredy obitaniya [Noise as ecological factor of the medium of environment]. Sovremennye naukoyemkie tekhnologii, no 2, 65 p.

Zaslavskaya I.N. (2011) Otchet o nauchno-issledovatel'skoy rabote Problemnoy komissii "Khronobiologiya i khronomeditsina" za 2011 g. [Elektronnyy resurs] / Problemnaya komissiya RAMN "Khronobiologiya i khronomeditsina". p 2.

Pelesa E.S. (2009) Osobennosti khronostruktury chastoty serdechnykh sokrashcheniy i variabel'nosti serdechnogo ritma u patsiyentov s arterial'noy gipertenziyey i paroksizmami mertsatel'noy aritmii [Features of the chronostructure of heart rate and heart rate variability in patients with arterial hypertension and paroxysms of atrial fibrillation]. Cardiology in Belarus. no. 4, pp. 91-100.

Pelesa E.S.(2010) Kharakteristika tsirkadnykh ritmov serdechnoy deyatel'nosti u bol'nykh arterial'noy gipertenziyey s paroksizmami fibrillyatsii predserdiy: avtoref. dis. kand. med. nauk: 14.00.06 [Characteristics of circadian rhythms of cardiac activity in patients with arterial hypertension with paroxysms of atrial fibrillation: author's abstract dis. Cand. med.nauk: 14.00.06]. E.S. Peles; UB "BSMU". – Minsk, p. 23

Shishko E.D. (2010) Sutochnyyritm, tsirkadiannyyegenyizlokachestvennyyenovoobrazovaniya [Diurnal rhythm, circadian genes and malignant neoplasms]. Oncology [Electronic resource]. no 4, pp. 23 – 25.

Blagonravov M.L. (2010) Chronobiology of cardiac ventricular fibrillation development in experimental acute coronary failure. Bull. Exp. Biol. Med. vol. 149, pp. 559-561.

Imai Y. [et al.]. (1996) Circadian blood pressure variation related to morbidity and mortality from cerebrovascular diseases. Ann. NY Acad. Sci. vol. 783, pp. 172-185.

Yamazaki T. [et al.]. (2005) Circadian dynamics of heart rate and physical activity in patients with heart failure. Clin. Exp. Hypertens. vol. 27, pp. 241-249.

Viskin S. [et al.]. (1999) Circadian variation of symptomatic paroxysmal atrial fibrillation. European Heart Journal. vol. 20, pp. 1429-1434.

Taraktiy E.A., Davydova Yu.A. (2007) Seasonal variability of indicators of a blood system of the red-backed mouse (Clethrionomusglareolus) of a different reproductive condition. News of the RAS. Ser. Biology, no 1, pp. 14-25.

Ulaschik, V.S. (1999) Biologicheskiyeritmyikhronoterapiya [Biological rhythms and chronotherapy] / B.C. Ulaschik. Medical News, no 2, pp. 9-13.

Kamory T. [et al.]. (2008) Factors associated with incident ischemic stroke in hospitalized heart failure patients: a pilot study. Hypertens Res. vol. 31, pp. 289-294.

Hildebrandt G. (2006) Chronobiologia i chronomeditsyna [Chronobiology and chronomedicine]. H. Hildebrandt, M. Moser, M. Lehover.- Moscow, Arnebia, p. 144.

Shishelova T.I, MalyginaYu.S., SuanDat Nguyen. (2009) Vliyaniye shuma na organizm cheloveka [Influence of the human body's human organism]. Uspekhi sovremennogo yestestvoznaniya. no. 8, p. 6