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Changes to Some Hormones and Glucose in the Blood of Rabbits Subjected to Physical Exertion and Regimes of Darkness and Light, and Subfetal Hypoxia of Ontogenesis

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Abstract

As the main purpose of this article, we set the task of studying the mechanism of changes in the parameters of melatonin, insulin, adrenaline and glucose in the blood of rabbits that had undergone prefetal hypoxia of prenatal ontogenesis and been subjected to physical exertion and light conditions in the postnatal period of development. The article presents our research and its results. The purpose is to study the effect of long-term "on" and "off" functions of the epiphysis on various stressors, such as hypoxia and physical activity, and on physiological changes in the performance of the pancreas and adrenal glands in rabbits. Based on the results of the experiments, it was found that in physiologically epiphysectomized animals of different ages contained in the light and dark regimes, melatonin levels fall with increased insulin and rise with reduced insulin, and adrenaline levels fall from the norm under the action of physical exercise and photoperiodic action, but rise as a stress hormone during exercise with a reduction of melatonin. As numerous experiments show, the results of our research confirm an inverse relationship between melatonin and insulin, as well as between melatonin and adrenaline. However, the results obtained during the light mode differ from those taken during the dark mode, an increase in the level of melatonin is observed during physical activity in the dark mode, and a decrease in the light mode. It was found that with exercise and the photoperiodic factor in 30-day-old animals, in the circadian rhythm during exercise and under illumination hormone levels increase at first and then decrease in accordance with artificially created stress reactions.

Keywords: hypoxia; melatonin; insulin; adrenaline; glucose; ELISA

Introduction

Melatonin, one of the oldest evolutionary biochemical substances, was discovered by American dermatologist A. Lerner and isolated from bovine epiphyses in 1958. Melatonin from L-tryptophan is formed from serotonin by the agency of arylalkylamine-N acetyltransferase (AA-NAT; a key regulator). This substance is already present in single-celled organisms and in plants, and therefore in ordinary plant food, but in insignificant, 'homeopathic' concentrations that have no effect on the mammalian organism. In vertebrate animals, the main source of melatonin is the pineal gland. Neurologist O. Marburg suggested that the epiphysis - the upper appendage of the brain, releases a substance that inhibits the functions of the hypothalamus (the most important structure at the base of the brain that controls the lower appendage, the pituitary gland) and, as a result, the development of the reproductive system. At about the same time, it was established that the epiphysis contains a substance that causes depigmentation (blanching) of the skin in tadpoles. 40 years later, this fact played a decisive role in the discovery of melatonin. Interestingly, Lerner, the discoverer of melatonin, first described its sedative (sedative) effect when administered to humans (Anisimov *et al.,* 2002; Anisimov *et al.,* 2003; Anisimov *et al.,* 2006; Anisimov *et al.,* 2000; Anisimov *et al.,* 2000).

Melatonin is involved in regulating the functions of the central and autonomic nervous systems, the endocrine organs, the immune system and their daily rhythmic activity. Hypoxia causes a complex restructuring of the functioning of various body systems to ensure the delivery of the required amount of oxygen to tissue. Adaptation to hypoxia has a significant effect on the central nervous system, central haemodynamics, microcirculation in various organs, oxygen metabolism, free radical lipid oxidation, the main enzymes in detoxification systems and immunity. The mechanisms that influence adaptation to hypoxia in the brain are considered. It has been established that improving cerebral circulation is one of the important protective effects of adaptation to hypoxia (Arushanyan, 2005; Arushanyan, 2005; Aliyev & Mammadova, 2017; Aliyev *et al.,* 2018; Aliyev & Mammadova, 2016; Aliyeva & Aliyev, 2017; Aliyev *et al.,* 2017; Aliyev *et al.,* 2009; Aliyeva & Aliyev, 2015; Aliyev *et al.,* 2003).

Stress such as hypoxia, various physical activities and exposure to light are one of the most pressing problems of modern medicine and biology (Anisimov *et al.,* 2002; Anisimov *et al.,* 2003; Anisimov *et al.,* 2006; Anisimov *et al.,* 2000). It is known that acute or chronic effects of stressors on the mammalian organism often lead to various forms of metabolic disorder (Aliyev *et al.,* 2017; Aliyev *et al.,* 2009; Aliyeva & Aliyev, 2015; Aliyev *et al.,* 2003). In particular, stress (hypoxia, physical exercise and photoperiodism) is accompanied by changes in the

production of insulin and glucagon, the synthesis of glucose and melatonin, and as a result, change in adrenaline (Anisimov *et al.,* 2006; Arushanyan, 2005). Scientific references on stress, hypoxia and related diseases revealed pronounced differences in subjects' individual sensitivities to the development of pathological effects of stress loads (Anisimov *et al.,* 2006; Anisimov *et al.,* 2000). A reliable prognostic criterion for resistance to stress by rats is their behavioural activity in the open field test. It has been established, in particular, that active animals are prognostically more resistant to similar effects of stress than passive individuals (Anisimov *et al.,* 2006; Aliyev & Mammadova, 2017).

To protect the body from the negative effects of emotional stress, the leading task is to increase individual resistance to stress. Scientific data, as well as the results of our previous experiments, indicate that the epiphyseal neurohormone melatonin is one of the natural anti-stress substances produced in mammals (Anisimov *et al.,* 2006; Broedel *et al.,* 2003; Lazarev *et al.,* 1976). In experimental studies on rats, it was demonstrated that under acute stress loads, melatonin prevents changes in organs that mark stress (the thymus and adrenal glands) and prevents a reduction in the content of glycosaminoglycans, the main components of the skin's connective tissue. It was found that melatonin's involvement in the body's response to emotional stressors is associated with changes in the biochemical and neurochemical processes in brain structures. Melatonin's specific participation in the maintenance of physiological functions in animals of different individually typological characteristics was established (Kvetnaya & Knyazkin, 2003; Komarov *et al.,* 2004; Levin *et al.,* 2005; Malinovskaya & Komarov, 2006; Musina *et al.,* 2005).

In recent years, along with other neurotransmitter systems, the melatonergic system (Pishchak, 2004; Tunez *et al.,* 2003; Vinogradov & Pogorelov, 1987; Zamorsky & Pischak, 2000; Zamorsky, 2003), which is an integral component of the body's chronoperiodic system (Rom-Bugoslavskaya *et al.,* 1993; Chazov & Isachenkov, 1974; Pishchak, 2004; Tunez *et al.,* 2003; Vinogradov & Pogorelov, 1987; Zamorsky & Pischak, 2000; Zamorsky, 2003), has been isolated. Characteristic features of the melatonergic system are thought to be (Chazov & Isachenkov; Magner, 1990; Sapronov & Fedotova, 2002; Fedotova & Sapronov, 2005; Klieverik *et al.,* 2005; Pishchak, 2004): 1) photosensitivity, 2) daily (or circadian) rhythm (with the highest levels of melatonin production at night, in the dark), 3) an age-related chronic progressive weakening of its activity. An involvement of the melatonergic system in the pathogenesis of certain diseases is considered possible (Musina, 2005; Sapronov & Fedotova, 2002). It may be assumed that the components of the melatoninergic system can be used by the body to adapt to the action of not only photoperiodically-dependent adverse environmental effects, but

also to non-periodic hazardous effects, for example, during hypoxia and exposure to the photoperiodic factor (Broedel *et al.,* 2003; Kvetnaya & Knyazkin, 2003; Komarov *et al.,* 2004; Lazarev *et al.,* Lazarev; Levin *et al.,* 2005; Vinogradov & Pogorelov, 1987; Zamorsky, 2003). Living organisms can exist in changing environmental conditions only due to the presence of innate programmes of adaptation to rhythmic changes in the environment and the corrective mechanisms of those programmes in accordance with external periodicals (Broedel *et al.,* 2003; Rodriges *et al.,* 2004; Rokitsky, 1961; Rowe & Kennaway, 2002). The role of the correcting factor in the body's chronoperiodic system is performed by the photoperiod, or the length of daily illumination. In the photoperiodic system of the brain (Simonneaux & Ribelayga, 2003; Shorokhova *et al.,* 2015), the length of the photoperiod becomes a change in the circulating level of melatonin - the main pineal hormone (Tunez *et al.,* 2003; Vinogradov & Pogorelov, 1987; Zamorsky, 2003). At the same time, melatonin synchronizes the rhythms of peripheral tissues, provides anti-stress and antioxidant protection of the body, modulates the activity of the brain's neurotransmitter systems and the whole neuroendocrine system. This ensures adaptation of the organism to dangerous effects of the external environment, particularly under conditions of total illumination and darkness (Malinovskaya *et al.,* 2006; Fedotova & Sapronov, 2005; Klieverik *et al.,* 2005; Raykhlin & Kvetnoy, 1992).

Materials and methods

1-month-old rabbits of the *Chinchilla* breed were used in the study; they were obtained from adult rabbits that had undergone conditions of several hypoxia at different stages of the pregnancy germinal 1-10, pre-pubertal 10-20 and fetal 20-30 periods of development. In this paper, we have shown results from the pre-pubertal 10-20 hypoxia.

The hypoxia model nitrogen (N2) 93% and oxygen (O2) 7%, proposed by B. P. Khvatov and Ye.M. Khvatova (Rokitsky, 1961; Shorokhova *et al.,* 2015), was chosen for the hypoxia of pregnant individuals. B.P. Khvatov is an outstanding embryologist who gradually studied the development of the embryo. Using his methodology, our department has been working with prenatal hypoxia for a long time, exposing pregnant rabbits to embryonic, prefetal and fetal hypoxia of prenatal development of embryogenesis. The animals were kept in a pressure chamber with mixtures of these gases (mix of oxygen and nitrogen) for 20 minutes. After normal prenatal hypoxia, which normally grew and grew, blood was taken from the marginal ear vein and centrifuged for 20 minutes at a speed of 1500 rpm to obtain

plasma. An EDTA preservative was added to the plasma samples to maintain the molecular integrity of the hormones melatonin and insulin. Their quantities were determined by enzyme immunoassay using a Cusabio reagent-kit according to the manufacturer's protocol (ELISA - enzyme linked immune sorbent assay). Quantitative measurement was performed on a StatFax + 303 analyzer manufactured in the USA (Awareness Technologies Inc.) using light filters with a wavelength of 450 or 630 nm for the hormones. Further, the rabbits were subjected to 5-, 20- and 40-minutes of physical exertion - running on a treadmill, after which blood was taken and the hormone content determined: melatonin, insulin and adrenaline. Illumination conditions were arranged as follows: a group of 30-day-old rabbits was divided into 2 groups: one group in conditions of complete illumination, and one in conditions of complete darkness, for 10 days each.

The data obtained were processed by statistical methods, using the standard Excel and Student data packages. All the data obtained were processed by methods of variation statistics with an assessment of reliability using the bases of variation statistics for biologists, Rokitsky P.F. (Rokitsky, 1961; Shorokhova *et al.*, 2015).

The studies were carried out on the Chinchilla breed of rabbit and were planned in 4 series:

The first series of experiments is the study of changes in some hormones and glucose in the blood of 30-day-old rabbits subjected to physical exertion and a photoperiodic factor in normal conditions.

The second series of the experiment is the study of changes in certain hormones and blood glucose in 30-day-old rabbits, subjected to physical exertion and a photoperiodic factor in conditions of germinal hypoxia.

The third series of the experiment is the study of changes in some hormones and blood glucose in 30-day-old rabbits, subjected to physical exertion and a photoperiodic factor in conditions of pre-feminine pre-fetal hypoxia.

The fourth series of experiment is the study of changes in some hormones and blood glucose in 30-day-old rabbits, subjected to physical exertion and a photoperiodic factor in conditions of fetal hypoxia.

Animals were divided into two groups: control and experimental. For the study, we took for each series 72 control and 216 experimental rabbits, with each series consisting of a norm (no PE, no FF), a norm (5 min PE, no FF), a norm (20 min PE, no FF), norm (40min PE, no FF), norms (no PE, light FF), norms (5min PE, light FF), norms (20min PE, light FF), norms (40min PE, light FF), norms (no PE,

darkness FF), norms (5min PE, darkness FF), norms (20 min PE, darkness FF), norms (40min PE, darkness FF).

For the experiment, blood is taken from the outer marginal vein of the rabbit's ear to a tube with the anticoagulant K_2EDTA (potassium ethylenediaminetetraacetate). The tube of blood is then centrifuged to obtain plasma. Next, the plasma's hormone level is determined by the ELISA method using the Cusabio kit. The experiment is conducted according to the manufacturer's protocol. The hormone results (ELISA - enzyme linked immunosorbent assay), are quantified on a StatFax + 303 US analyzer (Awareness Technologies Inc) using light filters with a wavelength of 450 or 630 nm to quantify hormones in plasma.

Enzyme-linked immunosorbent assay (abbreviated as ELISA) is a laboratory immunological method for the qualitative or quantitative determination of various low-molecular compounds, macromolecules, viruses, etc. based on a specific antigen-antibody reaction. Identification of the resulting complex is carried out by using the enzyme as a label to register a signal. The theoretical basis of ELISA lies in modern immunochemistry and chemical enzymology, knowledge of the physicochemical laws of the antigen-antibody reaction, and in the basic principles of analytical chemistry.

ELISA is one of the most rapidly developing areas of chemical enzymology. This is because in ELISA a unique specificity of the immunochemical reaction (that is, antibodies bind exclusively to certain antigens, and to no other) is combined with highly sensitive detection of the enzyme label (up to 10−21 mol in the sample). The high stability of the reagents, the simplicity of registration methods, the possibility of creating cascade systems to amplify various chemical signals, the relatively low price and many other advantages of the ELISA method have contributed to its widespread adoption in various fields of medicine, agriculture, the microbiological and food industries, environmental protection and scientific studies (Anisimov *et al.*, 2003; Anisimov *et al.*, 2006; Anisimov *et al.*, 2000a; Anisimov *et al.*, 2000).

Results and discussion

The data we obtained are shown in table 1, table 2 and table 3. As can be seen from table 1 (with prefetal hypoxia), indicators for melatonin, insulin, adrenaline and glucose in the blood plasma of 30-day-old rabbits were 26.55 ± 3.87 ** U / ml, 26.95 ± 1.2 ** U / ml, 275.38 ± 24.27 ** U / ml and 90.5 ± 0.97 **, respectively. These parameters after a short 5-minute physical activity were: for melatonin -

36.31 ± 2.26 ** U / ml, for insulin - 15.58 ± 2.34 * U / ml and adrenaline 428 ± 50.09 ** * U / ml, glucose 97.3 ± 2.58 *. These parameters, after a short 20-minute exercise, were: for melatonin - 77.86 ± 3.23 *** U / ml, for insulin - 19.48 ± 1.2 *** U / ml and adrenaline 475.6 ± 24.27 *** U / ml, glucose 151.83 ± 3.84 ***. After 40 minutes of long-term physical exercise, these parameters were: for melatonin - 5.76 ± 0.85 *** U / ml, for insulin - 65.01 ± 2.02 *** U / ml and adrenaline 780.43 ± 50.09 *** U / ml, glucose 68.16 ± 2.58 ***.

The amounts of melatonin, insulin, adrenaline and glucose in the blood were also determined in 30-day-old rabbits subjected to a photoperiodic factor. The photoperiodic factor in our experiment is characterized by conditions of light and darkness.

During prefetal hypoxia of embryogenesis, in 30-day-old rabbits, the concentrations of melatonin, insulin, adrenaline and glucose in the blood plasma of the month-old rabbits, which had a 10-day coverage, were expressed as: 46.36 ± 2.46*** U / ml, 135.43 ± 6.79 *** U / ml, 314.55 ± 16.94 *** U / ml and 89.16 ± 2.34***, respectively. When the content was of rabbits in dark conditions, these parameters were: for melatonin - 119.13 ± 4.36 *** U / ml, for insulin - 96.88 ± 2.2** U / ml, adrenaline 372.58 ± 15, 86 *** U / ml and glucose 66.33 ± 4.55 ***, respectively. During prefetal hypoxia and hypoxia of embryogenesis, 30-day-old rabbits undergoing 10-day lighting were subjected to short-term, 5-minute exercise and the concentrations of melatonin, insulin, adrenaline and glucose in the blood plasma of monthly month old rabbits were expressed: 31.28 ± 1.87 * ** U / ml, 143.16 ± 3.56 *** U / ml, 421.05 ± 6.27 *** U / ml and 48.5 ± 6.33 ***, respectively. During embryonic hypoxia of embryogenesis, 30-day-old rabbits undergoing 10-day coverage were subjected to a short-term, 20-minute exercise and the concentrations of melatonin, insulin and adrenaline in the blood plasma of monthly rabbits were expressed: 24.28 ± 1.7 ** U / ml, 151.58 ± 2.08 ** U / ml, 543.76 ± 35.4 * U / ml and 93.83 ± 4.82 ***, respectively. During prefetal hypoxia of embryogenesis, 30-day-old rabbits undergoing 10-day coverage lighting were subjected to long-term 40-minute exercise and the concentration of melatonin, insulin, adrenaline and glucose in the blood plasma of monthly rabbits were expressed: 12.91 ± 2.13 ** * U / ml, 163.25 ± 3.67 **** U / ml, 743 ± 35.83 *** U / ml and 70.33 ± 1.69 ***, respectively.

During prefetal hypoxia of embryogenesis, in 30-day-old rabbits, undergoing a 10-day condition of darkness were subjected to short-term 5-minute exercise and the concentration of melatonin, insulin, adrenaline and glucose in the blood plasma of monthly rabbits were expressed: 69.56 ± 2.89 * ** U / ml, 119.6 ± 2.48 * U / ml, 458.41 ± 1.85 *** U / ml and 88.66 ± 4.18 *****, respectively. During prefetal

hypoxia of embryogenesis, in 30-day old rabbits, undergoing a 10-day condition of darkness were subjected to short-term 20-minute exercise and the concentration of melatonin, insulin, adrenaline and glucose in the blood plasma of monthly rabbits were expressed: 59.63 ± 3,93 $^{* **}$ U / ml, 111.06 ± 1.95 ** U / ml, 632.17 ± 23.11 *** U / ml and 147.8 ± 6.78 ***, respectively. During embryonic hypoxia of embryogenesis, in 30-day-old rabbits, undergoing a 10-day condition of darkness were subjected to long-term 40 minute exercise and the concentrations of melatonin, insulin, adrenaline and glucose in the blood plasma of monthly rabbits were expressed: 94.43 ± 4.01 $^{* **}$ U / ml, 138.1 ± 3.35 ***** U / ml, 825.23 ± 23.97 *** U / ml and 70.16 ± 3.87 ***, respectively.

Table 1. The concentration of melatonin, insulin, adrenaline and glucose in the blood plasma of one-month-old rabbits after physical exercise (PE). Parameters to be determined: subfetal hypoxia + PE

Determine hormones	Subfetal hypoxia+PE			
	NORM	5 min	20 min	40 min
Melatonin	26.55±3.87**	36.31±2.26**	77.86±3.23***	5.76±0.85***
Insulin	26.95±1.2**	15.58±2.34***	19.48±1.2***	65.01±2.02****
Adrenaline	275.38±24,27**	428±50.09***	475.6±21.24***	780.43±50.09***
Glucose	90.5±0.97**	97.3±2.58*	151.83±384***	68.16±2.58***

P> 0.01* ; P <0.05** ; P <0.001*** ; P<0.02**** ; P> 0.5*****.

Table 2: Concentration of melatonin, insulin, adrenaline and glucose in the blood plasma of 1 month old baby rabbits after the influence of a photoperiodic factor (light) + physical exercise (PE).

Determine hormones	Subfetal hypoxia+FF(light)+ PE			
	NORM (light)	5 min	20 min	40 min
Melatonin	46.36±2.46***	31.28±1.87***	24.28±1.7***	12.91±2.13***
Insulin	135.43±6.79***	143.16±3.56***	151.58±2.08**	163.25±3.67****
Adrenaline	314.55±16.94***	421.05±6.29***	543.76±35.83***	743±35.83***
Glucose	89.16±2.34***	118.5±6.33***	93.83±4.82***	70.33±1.63***

P> 0.01* ; P <0.05** ; P <0.001*** ; P<0.02**** ; P> 0.5*****.

Table 3: Concentration of melatonin, insulin, adrenaline and glucose in the blood plasma of 1 month old baby rabbits after the influence of a photoperiodic factor (dark) + physical exercise (PE).

Determine hormones	Subfetal hypoxia+FF(dark)+PE			
	NORM (dark)	5 min	20 min	40 min
Melatonin	119.13±4.36***	69.56±2.89***	59.63±03.93***	94.43±4.01***
Insulin	96.88±2.2**	119.6±2.48*	111.06±1.95**	138,1±3.35****
Adrenaline	372.58±15.86***	458.41±1.85***	632.17±23.11***	825.23±23.97***
Glucose	66.33±4.55***	88.66±4.18*****	147.8±6.78***	70.16±3.87***

P> 0.01* ; P <0.05** ; P <0.001*** ; P<0.02**** ; P> 0.5*****.

As a result of our experiments, it was found that the absence of photoperiodism with constant illumination has a modulating effect on the study of indicators, depending on what period of ontogenesis the effect began - in our case it lasted for 10 days, starting on the 30th day of the rabbit's life. Also, the effect of prenatal hypoxia for 10 days in the embryonic period of development, at the time of formation of the internal organs and body systems, inhibits the synthetic function of the epiphysis from the moment of birth. And physical activity leads to a unidirectional change in the activity of antioxidant enzymes, although their expression is different and we see changes in the results. The suppression of the synthesis of melatonin, an antioxidant that can directly interact with other hormones, is also reflected in changes in insulin and adrenaline. According to the literature, exposure to light is a desynchronizing factor that causes significant changes in various body systems, including the immune system (Arushanyan, 2005; Aliyev & Mammadova, 2017; Aliyev *et al.,* 2018; Aliyev & Mammadova, 2016).

Suppressing the function of the pineal gland, achieved by epiphysectomy or having content under constant light (physiological epiphysectomy) leads to synchronization of the circadian rhythms of many physiological functions: accelerated aging of a number of functional systems, development of a number of age-related pathological processes, including malignant neoplasms and, ultimately, shortening the life of the individual (Brizzi *et al.,* 1997; Broedel *et al.,* 2003; Kvetnaya & Knyazkin, 2003; Komarov *et al.,* 2004; Lazarev *et al.,* 1976; Reiter, 1995; Reppert *et al.,* 1989; Rodriges *et al.,* 2004). Light deprivation, which stimulates the function of the pineal gland, has the opposite effect, a geroprotective effect (Lazarev *et al.,* 1976; Rokitsky, 1961). The presence of animals during prenatal development in a condition of short-term hypoxia and with constant

illumination and darkness from the moment of birth for 10 days, affects change in the indices of melatonin, insulin and adrenaline.

The use of the epiphyseal hormone melatonin inhibits the carcinogenesis of animals in both normal lighting mode and with constant light, it prevents the development of pathology associated with age and increases animals' life expectancy. Using melatonin to prevent cancer can be very effective, especially in northern regions, where there are "white nights" in the summer, and electric light shines on for a long polar night (Aliyev *et al.,* 2017; Aliyev *et al.,* 2009; Aliyev *et al.,* 2015; Aliyev *et al.,* 2003; Brizzi *et al.,* 1997; Broedel *et al.,* 2003; Kvetnaya & Knyazkin, 2003; Komarov *et al.,* 2004; Lazarev *et al.,* 2005; Levin *et al.,* 2005; Malinovskaya *et al.,* 2006).

So from plentiful data in the literature (Anisimov *et al.,* 2003; Anisimov *et al.,* 2006; Aliyev & Mammadova, 2017; Aliyev *et al.,* 2018; Aliyev & Mammadova, 2016; Aliyeva & Aliyev, 2017; Aliyev *et al.,* 2017; Aliyev *et al.,* 2009) it is known that the pineal gland hormone - melatonin - is mainly synthesized in the dark phase, while in the light phase this is insignificant. Therefore, disturbances in the normal rhythm of light and darkness in 30-day-old rabbits, laboratory rats and quails cause changes in the circadian rhythm and disturbances in metabolic processes (Anisimov *et al.,* 2006; Anisimov *et al.,* 2000, Aliyeva & Agayev, 2015; Brizzi *et al.,* 1997). From the data obtained it can be noted that, depending on the age of the animals, before and after exercise and the photoperiodic factor, neuro-hormonal regulation of the blood changes during the day. The effect of constant darkness, in contrast to constant illumination, enhances the work of the epiphysis and leads to an increase in melatonin synthesis by this gland (Reiter, 1995; Simonneaux & Ribelayga, 2003; Tunez *et al.,* 2003). This is what we observed in our series of experiments on the dark phase of the photoperiodic factor.

Thus, the levels of melatonin, insulin and adrenaline in intact animals, depending on the circadian rhythm after exercise, vary by decreasing, then increasing, i.e. with a decrease in melatonin, insulin and adrenaline increase , and with an increase in melatonin, insulin and adrenaline decrease. And the amount of adrenaline as a stress hormone increases accordingly. The reason for the decrease or increase of hormones in the blood of intact and animals kept in dark and light conditions and both before and after exercise, is associated with the activation or inhibition of function in the epithalamic-hypothalamic-pituitary-adrenal systems (Anisimov *et al.,* 2006; Anisimov *et al.,* 2000a; Anisimov *et al.,* 2000; Arushanyan, 2005a; Arushanyan, 2005; Aliyev & Mammadova, 2017). The epiphysis acts as an endogenous synchronizer of circadian and seasonal rhythms. The revelation that melatonin does not stand out under bright light has served to revive phototherapy

and now light therapy in the west is widely used by chronobiologists for the treatment of desynchronosis (Anisimov & Zabezhinsky, 2000a; Anisimov *et al.*, 2005; Aliyev & Mammadova, 2016). The data we obtained in the light and dark regimes can also be used by chronophysiologists for the prevention and treatment of diabetes. Based on the above, we can conclude that circadian rhythms affect changes in the level of hormones in the blood of healthy people and mammals; The level of melatonin in the blood of a little rabbit falls in daylight and rises in the dark (Arushanyan, 2005; Aliyeva & Aliyev, 2017). The levels of insulin and adrenaline, on the contrary, rise in daylight, and fall in the dark. This is reflected in the dynamics of all processes and functions that are affected by the epiphysis and depending on a light or dark phase, thereby connecting the body to the general chronometric and biorhythmic regulation embedded in phylogenesis and ontogenesis during exercise and lighting conditions (Anisimov *et al.*, 2003; Anisimov *et al.*, 2000a; Arushanyan, 2005; Aliyev *et al.*, 2018; Aliyev *et al.*, 2009; Zamorsky, 2003).

The effects of constant illumination and constant darkness on the physiological parameters revealed here may be associated with changes in melatonin synthesis by the pineal gland. This hormone plays a significant role in the regulation of puberty, reproductive cycles, stress response and immune response (Reiter, 1995; Reppert *et al.*, 1989; Rodriges *et al.*, 2004; Rowe & Kennaway, 2002; Simonneaux & Ribelayga, 2003; Tunez *et al.*, 2003).

Conclusion

It is interesting to note that the secretion of certain hormones with distinct circadian fluctuations is regulated primarily by circadian clocks (for example, cortisol, melatonin), while the secretion of other hormones is largely dependent on sleep (for example, prolactin, growth hormone), and the secretion of a third group of hormones is simultaneously related to endogenous circadian factors and to sleep (for example, thyroid stimulating hormone, insulin, adrenaline). Being independent of sleep and relatively independent of external masking effects, melatonin secretion is an ideal indicator for the study of circadian factors that can be associated with effective disorders. In recent years, fundamentally new data on the role of melatonin in the regulation of insulin secretion and the pathophysiology of carbohydrate metabolism disorders have been obtained, and the prospects for melatonin use in treatment are discussed. Perhaps this is due to the fact that hormones of the pineal gland, pancreas and adrenal glands in rabbits have a

significant protective effect on the substance of the brain under conditions of ischaemia, hypoxia and stress reaction (physical activity and photoperiodic factor).

The melatoninergic system is significant in the system of antihypoxic protection of the body, carrying this out dependent on the duration of the photoperiod. In an organism adapted to hypoxia, a restructuring of the sympathoadrenal system occurs, and is characterized by hypertrophy of sympathetic neurons, an increase in catecholamine synthesis and catecholamine reserves in the adrenal glands, as well as an increase in cardiac adrenoreactivity. Thus, there is an increase in the reserve capacity of the sympathetic nervous system. It was shown that a course of interval hypoxic training also led to an increase in the power of the mechanisms of autonomic regulation of heart functions at rest due to an increase in the activity of the parasympathetic autonomic nervous system; it also caused optimizing effects on the degree of shifts in heart rate variability (HRV) during simulated acute hypoxia. Hypoxic preconditioning contributed to an increase in the body's resistance to conditions of simulated acute hypoxia, which was manifested in a less pronounced degree of haemoglobin desaturation and a smaller increase in heart rate. It has been established that the training effects of a course of interval hypoxic training are more pronounced in groups of individuals who initially have low resistance to the hypoxic factor relative to subjects who are resistant to acute hypoxia (48, 102). Thus, adaptation to hypoxia has a significant effect on the central nervous system, central haemodynamics, blood microcirculation in various organs, oxygen metabolism, free radical lipid oxidation, the main enzymes of detoxification systems and immunity.

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