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THE CHRONORHYTHMICAL INDICES OF ION-REGULATING RENAL FUNCTION AT MELATONIN ADMINISTRATION ON THE BACKGROUND OF PINEAL GLAND HYPERFUNCTION

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The chronorhythms of main renal functions in conditions of pineal gland hyperfunction are still unwell examined. The use of exogenous melatonin is one of the major non-light factors that can entrain the renal circadian rhythm, but results in clinical samples have been mixed. This is not surprising because there can be great individual variability in endogenous melatonin production, such as light and behavior can also change melatonin levels.

So, the main purpose of our work was to determine the changes in indices of ion-regulating renal function in conditions of pineal gland hyperfunction and melatonin administration.

Experiments were conducted on 45 pubertal nonlinear male albino rats at conditions of 7 days constant darkness. Animals were divided into three groups – the first – control group, the second group's animals were hold under constant darkness, the third one – obtained only melatonin on the background of hyperfunction of pineal gland.

The indices of ion-regulating renal function were characterized by hypernatremia in the second examined group. We also registered increase of sodium ions concentration in urine and its excretion which exceeded data of animals that were hold in constant darkness condition. Mezor of the rhythm of sodium ions concentration in urine was 1,2±0,01 mmol/l with amplitude – 5,7±1,68%. Sodium-potassium coefficient increased on 30% during 24 hours darkness if compare with control group. The increase of sodium ions concentration in the blood plasma caused the growth of its filtration charge. The absolute reabsorption of ions was changed also – it was twice less than in case of control group of animals.

Administration of melatonin (2,5 mg/kg) on the background of hyperfunction of pineal gland led to decrease of sodium ions proximal transport for 47% if compare with control group of animals. Acrophase was registered at midnight, bathyphase – at 8.00 a.m. and midday. An average level for a day was 1,0±0,09 mmol/2 hours/100 g, the amplitude of the rhythm – 26,5±3,07%.

Distal sodium ions transport after melatonin administration (0,5 mg/kg) has changed in the same manner. Rhythm structure also changed, the highest level was registered at 24.00, the lowest – at 8.00 a.m. that coincides with the rhythm of secretion of endogenous melatonin. Mezor of the rhythm was 88,9±3,86 mkmol/2 hours/100 g, amplitude – 12,1±3,62%. This index is 34% less than in control group, and only 2% less than in animals, which did not have indole, mentioned above.

We came to the conclusion that melatonin partially prevents disturbances of renal functions, caused by the conditions of pineal gland hyperfunction.

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MOLECULAR MECHANISMS OF CIRCADIAN RHYTHMS

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A circadian rhythm is a roughly 24 h cycle in the physiological processes of living beings, including plants, animals, fungi and cyanobacteria. In a strict sense, circadian rhythms are endogenously generated, although they can be modulated by external cues such as sunlight and temperature. Circadian rhythms are important in determining the sleeping and feeding patterns of human beings. There are clear patterns of brain wave activity, hormone production, cell regeneration and other biological activities linked to this daily cycle.

Animal research determined that the molecular machinery behind the circadian rhythm exists in each cell of the suprachiasmatic nucleus (SCN) in the hypothalamus, a small group of neurons in the brain. Studies in which SCN maintained in cell cultures still generated a twenty-four hour rhythm provide further evidence for this fact, though outside light is necessary for the resetting of the rhythm to keep the organism in sync with the solar day. In the studies of circadian rhythms in *Drosophila melanogaster* it was discovered the protein that is encoded by period gene located on the X chromosome, which appeared to build up during the night and degrade during the day on a circadian rhythm. Oscillations in levels of both per transcript and its corresponding protein PER have a period of approximately 24 hours and together play a central role in the molecular mechanism of the *Drosophila* biological clock driving circadian rhythms in eclosion and locomotor activity. In *Drosophila*, per mRNA levels oscillate with a period of approximately 24 h, peaking during the early subjective night. The PER product also oscillates with a nearly 24-hour period, peaking about six hours after per mRNA levels during the middle subjective night. When PER levels increase, the inhibition of per transcription increases, lowering the protein levels. However, because PER protein cannot directly bind to DNA, it does not directly influence its own transcription; alternatively, it inhibits its own activators. After PER is produced from per mRNA, it dimerizes with Timeless (TIM) and the complex goes into the nucleus and inhibits the transcription factors of per and tim, the CLOCK/CYCLE heterodimer.

Other physiological changes that occur according to a circadian rhythm include heart rate and many cellular processes (oxidative stress, cell metabolism, immune and inflammatory responses, epigenetic modification, hypoxia, hyperoxia response pathways, endoplasmic reticular stress, autophagy and regulation of the stem cell environment).