SESSION III

BIOLOGICAL RHYTHMS
SLEEP

Wednesday (September 15, 2021; 15:30 – 17:50)
Thursday (September 16, 2021; 12:25 – 13:00)

Chair:

Dr. hab. Jolanta Orzel-Gryglewska
Department of Animal and Human Physiology, University of Gdansk Poland

DETAILED SESSION III SCHEDULE

Opening lectures (Wednesday, September 15, 2021; 15:45 – 16:55; *virtual stream A*)

S3.L1 SLEEP FOR MENTAL HEALTH. **G. Lipinska[1], R. Lewis[1], L.C. Roden[7,8], K. Scheuermaier[5], F.X. Gomez-Olive[4], D.E. Rae[7], S. Iacovides[5], A. Bentley[2], J.P. Davy[3], C.J. Christie[3], S. Zschernack[3], J. Roche[5], K.G.F. Thomas[1]** ([1]UCT Sleep Sciences and Applied Cognitive Science and Experimental Neuropsychology Team (ACSENT), Department of Psychology, University of Cape Town, Cape Town, South Africa, [2]Department of Family Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, [3]Department of Human Kinetics and Ergonomics, Rhodes University, Grahamstown, Makhanda, South Africa, [4]MRC/Wits Rural Public Health and Health Transitions Research Unit (Agincourt), School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; [5]Brain Function Research Group, School of Physiology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, [7]Division of Exercise Science and Sports Medicine, Department of Human Biology, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa, [8]Faculty Research Centre for Sport, Exercise and Life Sciences, School of Life Sciences, Faculty of Health and Life Sciences, Coventry University, Coventry, United Kingdom).

S3.L2 WHAT DOES THE SLEEPING BRAIN KNOW ABOUT ITS SURROUNDING? **M. Wislowska** University of Salzburg, Centre for Cognitive Neuroscience, Laboratory for Sleep and Consciousness Research, Salzburg, Austria).

Oral presentations (Wednesday, September 15, 2021; 16:55 – 18:05; *virtual stream A*)

S3.L3 REPETITIVE ACTIVATIONS OF POSTERIOR AND/OR PERIFORNICAL HYPOTHALAMIC REGIONS ELEVATE CSF OREXIN-A CONTENT AND FASTEN RECOVERY OF NORMAL SLEEP CYCLE FROM DEEP ANESTHESIA INDUCED ARTIFICIAL SLEEP. **Kh. Bezhanishvili, E. Chkhartishvili, N. Maglakelidze, M. Babilodze, O. Mchedlidze, N. Nachkebia** (I. Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia).

S3.L4 THE CIRCADIAN AND ANNUAL RHYTHM OF OREXIN A SECRETION INTO BLOOD PLASMA IN EWES. **K. Kirsz[1], K. Lukowicz[1], M. Szczesna[1], D. Zieba-Przybylska[1]** ([1]Agricultural University in Krakow, Animal Science Faculty, Department of Animal Nutrition, Biotechnology and Fisheries, Krakow, Poland).

S3.L5 LASTING EFFECTS OF EARLY POSTNATAL DYSFUNCTIONING OF BRAIN MUSCARINIC CHOLINERGIC SYSTEM AND ITS' SUPER-SENSITIVITY IN ADULT AGE – CHARACTER OF SLEEP DISORDERS AND BEHAVIORAL DISTURBANCES. **N. Nachkebia, E. Chkhartishvili, O. Mchedlidze, N. Maglakelidze, M. Babilodze, E. Chijavadze** (I. Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia).

S3.L6 OREXIN-A INJECTED IN LATERAL VENTRICLE AMELIORATES LASTING EFFECTS OF EARLY POSTNATAL DYSFUNCTIONING OF BRAIN MUSCARINIC CHOLINERGIC SYSTEM ON SLEEP-WAKEFULNESS CYCLE. **N. Maglakelidze, O. Mchedlidze, E. Chkhartishvili, M. Babilodze, Kh. Bejanishvili, E. Chijavadze, N. Nachkebia** (I. Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia).

Session summary

Poster session (September 16, 2021; 12:25 – 13:00; *virtual stream C, interactive*)

S3.P1 THE SLOW OSCILLATION (<1 HZ) BEFORE SLEEP IN THALAMO-CORTICAL NEURONS. **V. Tsomaia, N. Nachkebia** (Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia).

S3.P2 ANTIBACTERIAL ACTIVITY OF ANTIDEPRESSANTS, INHIBITORS OF MONOAMINE'S REUPTAKE, DEPENDS FROM THEIR ANTIDEPRESSIVE EFICACY ON SLEEP DISORDERS. **N. Rogava[1,2], Z. Lomtatidze[2], N. Maglakelidze[1], Kh. Bejanishvili[1], N. Nachkebia[1]** ([1]I. Beritashvili Center of Experimental Biomedicine,[2]Sokhumi State University, Tbilisi, Georgia).

S3.P3 BLOOD LEUKOCYTES IN YOUNG AND OLD RATS UNDER DESYNCHRONOSIS INITIATION ON THE BACKGROUND OF WHOLE BODY CRYOSTIMULATION. **V.V. Lomako, O.V. Shylo** (Institute for Problems of Cryobiology and Cryomedicine of National Academy of Sciences of Ukraine, Department of Cryophysiology, Kharkiv, Ukraine).

S3.P4 PITUITARY-THYROID SYSTEM IN YOUNG AND OLD RATS UNDER PREVENTIVE WHOLE-BODY CRYOSTIMULATION AND CIRCADIAN DISRUPTION. **O. Shylo[1], V. Lomako[1], D. Lutsenko[1], L. Samokhina[2]** ([1]Institute for Problems of Cryobiology and Cryomedicine, NAS of Ukraine, Kharkiv, Ukraine, [2]G.D. L.T. Malaya National Institute of Therapy of National Academy of Medical Sciences of Ukraine, Kharkiv, Ukraine).

S3.L1

SLEEP FOR MENTAL HEALTH

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Sleep is critical physiological state that has emerged as an important regulator of multiple biological systems. For decades, researchers have understood that sleep difficulties are pervasively reported in individuals with psychiatric disturbances, but more recently findings have described how sleep disturbance may help drive psychopathology or interact with other biological and psychological states to exacerbate symptoms. For example, findings from our own laboratory show that sleep difficulties are related to the presence of cognitive disturbances in individuals diagnosed with posttraumatic stress disorder. Another study we conducted showed that emotional dysregulation characteristic of depressive and posttraumatic symptoms had an influence on symptom severity, but primarily *via* sleep disturbance. We showed *via* structural equation modeling that individuals who tended to struggle with emotion regulation strategies had poor sleep quality and these sleep disturbances were strongly predictive of increased depressive and posttraumatic symptom severity, with little direct influence of emotion regulation strategies on symptoms. In a recent study conducted during the COVID pandemic we broadened our understanding of how sleep interacts with lifestyle factors such as exercise and sedentary behaviour including time spent on screens. We showed that spending more time on screens and sitting, and less time being active, increased insomnia symptoms and in turn depressive and anxiety-related symptoms. These findings highlight the importance of sleep, not as an isolated physiological function, but nested in a greater biological and psychological milieu.

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S3.L2

WHAT DOES THE SLEEPING BRAIN KNOW ABOUT ITS SURROUNDING?

M. WISLOWSKA

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During sleep, the brain turns "inward", and engages in processes like regeneration or memory consolidation. At the same, it needs to continue monitoring the environment for potential threats. If a lion appears in the vicinity, arousal and awareness need to be fully regained at once, to allow the organism to undertake an appropriate action. Nowadays, we rarely expect to find a lion in our bedroom - nevertheless, we take an advantage of the sleeping brain's watchfulness, when for example setting up our alarm clocks. However, if one of the main functions of sleep is to consolidate new memories, these processes should be protected from unnecessary interference. It would therefore make sense to filter out all of the environmental noise, like sounds for example, and prevent them from reaching the sleeping brain. Nevertheless, our own experience, along with the scientific evidence, shows that this is not the case. How does the sleeping brain achieve the balance between internal processing and external monitoring, is not a trivial question. During this lecture, we will look into the results of recent empirical studies investigating information processing during sleep. Presentation of (usually acoustic) stimuli to sleeping participants induces patterns of the brain activity that can be very similar to, or very different from those observed during wakefulness, depending on the sleep stage, stimulus material, or even analytical strategy. After the lecture, we shall be left with an impression, that the sleeping brain is complex, magnificent, and anything but trivial. It holds the key to our wellbeing, success in university exams, and even our survival.

Acknowledgements: M.Wislowska is supported by the Austrian Science Fund (FWF, W1233-B).

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S3.L3

REPETITIVE ACTIVATIONS OF POSTERIOR AND/OR PERIFORNICAL HYPOTHALAMIC REGIONS ELEVATE CEREBROSPINAL FLUID (CSF) OREXIN-A CONTENT AND FASTEN RECOVERY OF NORMAL SLEEP CYCLE FROM DEEP ANESTHESIA INDUCED ARTIFICIAL SLEEP

KH. BEZHANISHVILI, E. CHKHARTISHVILI, N. MAGLAKELIDZE, M. BABILODZE, O. MCHEDLIDZE., N. NACHKEBIA

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Consideration of the hypothalamic orexinergic system as the neurophysiological substrate or cellular target necessary for the acceleration of coming out from barbiturate anesthesia-induced artificial sleep is the main goal of the present investigation. For this aim the effects of repetitive electrical stimulations of posterior (PH) and perifornical hypothalamus (PfH) on the recovery of normal sleep-wakefulness cycle from barbiturate anesthesia-induced artificial sleep was studied by us for the first time. For the assessment whether this methodical approach can indeed elevate the level of endogenous orexins in cerebrospinal fluid (CSF), we have also studied for the first time the changes in the level of CSF orexin-A in different stages of barbiturate anesthesia, under the impact of repetitive electrical stimulations of PH and PfH orexin-producing neuronal regions. In white wild rats (n = 9), after surgical implantation of recording/stimulating electrodes and postoperative recovery, deep anesthesia was induced by intraperitoneal injection of different doses of sodium ethaminal. EEG registration was started immediately and lasted continuously for 48 hours (control, group I). In experimental rats, 10 min after anesthesia to be started, electrical stimulations (8–12v, 200c/s, 0.1 ms) of PH (group II) and PfH (group III) were begun. Stimulations lasted for 1 hour with 5 min intervals between subsequent ones. CSF orexin-content was measured by ELISA. It appears that repetitive activations of PH and PfH orexin neurons significantly accelerate (by 30–40%) wakefulness recovery from anesthesia-induced sleep. The first fragments of wakefulness were soon followed by normal deep slow wave sleep (DSWS) episodes. Normal DSWS recovery was accelerated in post-stimulation period by 1.5 h then during spontaneous recovery in un-stimulated controls. The latency of the first episode of REM sleep decreased significantly, from 23–24 h in un-stimulated controls to 11–12 h in experimental animals. REM sleep latency diminished much more, to 10 ± 0.5 h, after repetitive electrical stimulation of PfH orexin-producing neurons. Significant elevation of CSF orexinA content was noted in stimulated animals from both experiments. Therefore elevation of the content of endogenous orexin-A in CSF, in response to the repetitive electrical stimulations of PH and PfH orexin-producing neuronal regions, significantly shortens anesthesia time and accelerate coming out from barbiturate anesthesia-induced artificial sleep, through the acceleration of normal sleep-wakefulness cycle recovery.

Acknowledgements: Supported by SRNSFG, Grant #11/04

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S3.L4

THE CIRCADIAN AND ANNUAL RHYTHM OF OREXIN-A SECRETION INTO BLOOD PLASMA IN EWES

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Orexin-A (OXA) is a hypothalamic neuropeptide, which has been mainly recognized as a regulator of sleep/arousal state, energy homeostasis and feeding behaviour. In our earlier studies on seasonally breeding sheep, we demonstrated involvement of OXA in the regulation of annual rhythm of secretory activity of the pineal and the pituitary glands. Studies mostly on nocturnal and nonseasonal rodents have shown that extracellular levels of orexin vary in a circadian pattern, with high levels during the waking period. However, it is difficult to relate this results directly to diurnal, seasonal sheep, in which OXA activity occurs in an annual cycle. Therefore, the purpose of this study was to investigate the circadian and annual rhythm of OXA secretion into blood plasma in ewes. Experiments were conducted separately for June (non-breeding, long-day season, LD) and December (breeding, short-day season, SD). During the LD, ewes were anovulatory and expressed no signs of estrus (progesterone concentration was 0.41 ± 0.03 ng/ ml). Whereas during the SD, estrous cycles of ewes were synchronized by the Chronogest® CR (Merck Animal Health, Boxmeer, The Netherlands). Experiments were performed when ewes were in the midluteal phase (days 8–10) of the estrous cycle. In the morning on the day of each experiment, 5 ewes were fitted with jugular catheters (Careflow, Argon, Billmed Sp. z o.o., Warsaw, Poland) for intensive blood sampling for 24 hours. Blood samples (3 ml) were collected at 15-min intervals beginning 2 hours after fitting catheters. The plasma was separated by centrifugation at 3000×g at 4°C for 10 min and stored at –80°C until the measurement of OXA by enzyme-linked immunosorbent assay (Sheep ELISA kit, Phoenix Pharmaceuticals, Inc., USA). The mean concentrations of OXA was higher ($P < 0.01$) during the LD compared to the SD. In both seasons, we observed the day-night differences in OXA secretion. In the LD, OXA circulating concentrations increased ($P < 0.05$) during the night compare with day. The mean concentration of OXA during the dark phase was 0.92 ± 0.14 ng/ml and during the light phase it was 0.6 ± 0.06 ng/ml. In contrast, OXA secretion decreased ($P < 0.05$) in the dark phase compare to the light phase during the SD. The mean concentration of OXA in the night was 0.7 ± 0.03 ng/ml and in the day it was 0.6 ± 0.05 ng/ml. Our results indicate that there are differences in OXA circulating concentrations depending on the season and the phase of the day in sheep.

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S3.L5

LASTING EFFECTS OF EARLY POSTNATAL DYSFUNCTIONING OF BRAIN MUSCARINIC CHOLINERGIC SYSTEM AND ITS' SUPER-SENSITIVITY IN ADULT AGE - CHARACTER OF SLEEP DISORDERS AND BEHAVIORAL DISTURBANCES

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The question about the involvement of brain muscarinic cholinergic system (MChS) in the mood disorders, and in the major depressive disorder (MDD) among them, has a long history. However, the effects of early postnatal dysfunctioning of this system were not studied at all. We decided to investigate lasting effects of this procedure on the sleep-wakefulness cycle, open field behavior, forced swim test, sucrose preference and the density of M2/M4 muscarinic cholinoreceptors in neocortex and hippocampus. We performed a comparative analysis of the results, obtained by us, with the disorders of the same parameters during MDD for the aim of revealing possible linkage between them and early postnatal dysfunctioning of MChS. Rat pups received subcutaneously atropine (Atr, n=10) and/or scopolamine (Scop, n=10) 30 mg/kg two times daily from postnatal day 7 (P7) until P28. Afterwards rat pups were maintained in home cages under special care. Control rat pups (n=10) receiving distilled water with the same volume and procedure. Surgery and implantation of stainless screws was made in adult age 8–12 weeks after drugs discontinuation. EEG registration of sleep-wakefulness cycle was started 5–7 days after surgery and continued for 10 h daily during 7 consecutive days, in control and experimental animals. Density of M2/M4 muscarinic cholinoreceptors in hippocampus and neocortex was measured by Western blotting by means of specific antibodies. Statistical processing was made by Students' t-test. Adult rats exposed postnatally to anticholinergic drugs showed motor retardation in open field, increased immobilization and "behavioral despair" in forced swim condition, signs of anhedonia assessed by sucrose preference. Incidence of delta waves at the frequencies of 1–1.5 c/s became very low. Slow wave sleep became fragmented and superficial; number of awakenings was raised considerably. REM latency appeared three times shorter, REM incidence was significantly frequent and REM total time increased for two times. Adult hippocampal neurogenesis was significantly reduced. The density of M2/M4 muscarinic cholinoreceptors appeared significantly higher in neocortical and hippocampal plasma membranes. These disturbances are very similar to the disorders characteristic for MDD. We can conclude, that early postnatal dysfunctioning of MChS can be the one of factors contributing depression-like state in adult age.

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S3.L6

OREXIN-A INJECTED IN LATERAL VENTRICLE AMELIORATES LASTING EFFECTS OF EARLY POSTNATAL DYSFUNCTIONING OF BRAIN MUSCARINIC CHOLINERGIC SYSTEM ON SLEEP-WAKEFULNESS CYCLE

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Orexin/hypocretin-producing neurons are involved in the consolidation of arousal/wakefulness that becomes unstable if orexins are deficient in the brain. On the other hand, suppression of wakefulness can be of the main reasons for the development of sleep disorders and depression. Therefore, it is believed that the hypothalamic orexinergic system may also be involved in the pathophysiology of depression. The aim of the present investigation was to study the effects of intravenously (icv) administered orexin-A on sleep disturbances produced by early postnatal exposure of rat pups to the dysfunction of muscarinic cholinergic system (MChS). Dysfunctioning of MChS was produced by subcutaneous injection of scopolamine (30 mg/kg) in rat pups (n=10), twice daily, from postnatal days 7 to 28. Control rat pups (n=5) received the same volume of saline. Experiments were started 2–3 months after discontinuation of the drug. Implantations of stainless steel screws, for epidural EEG registration, and microinjection cannulas (plastics ones) were made under general anesthesia. Two doses of orexin-A (10 µg/µl and/or 25µg/µl) were injected in lateral ventricle. Experiments with EEG registration of the sleep-wakefulness cycle lasted continuously for 5 hours daily for three consecutive days on each animal, have been started immediately after icv microinjection of orexin-A, after the post-surgery recovery period. It was found that animals exposed in the early postnatal period to the MChS dysfunctioning were characterized in adult age by significant disturbances of the sleep-wakefulness cycle. These changes were very similar to sleep disorders, characteristic of major depressive disorder. ICV microinjection of orexin-A dose-dependently ameliorated disturbances in sleep-wakefulness stages. The elevation of the level of orexin-A in cerebrospinal fluid has an anti-depressive effect in animals subjected in early ontogenesis to the dysfunctioning of muscarinic cholinergic system. It was manifested in the enhancement and stabilization of wakefulness, in an increase of the latency of REM sleep, which was sharply reduced in these animals, and decrease in the incidence of REM sleep that develops as frequently as during depression and requires to be partially deprived.

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S3.P1

THE SLOW OSCILLATION (<1 HZ) BEFORE SLEEP IN THALAMO-CORTICAL NEURONS

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The slow oscillation (<1 Hz) is an EEG hallmark of the resting state. The thalamus is involved in several types of oscillatory activity including slow (<1 Hz) rhythms that are considered as the forerunner of the deeper stages of sleep during the transition from wakefulness to sleep as well as the faster activity that occurs during awakening. In order to examine the involvement of muscarinic acetylcholine receptors in slow oscillatory activities, it was interesting for us to investigate the effects of muscarinic combined agonist, carbochol, on the extracellular unitary and field activities and intracellular discharges in brain slice preparations of the rat and cat lateral geniculate nucleus and ventrobasal thalamus. We suggest that the presence of an low-threshold Ca^{2+} potential (LTCP)-mediated burst at the commencement of each UP state may be a mechanism whereby the thalamus is sending a specific priming signal to the cortex that the 'activated' or 'processing' phase of the slow oscillation is about to begin. Of course, the idea that the LTCP-mediated bursts of the slow oscillation signal the upcoming transmission of high-priority information is essentially equivalent to that which has been suggested for the role of LTCP-mediated bursts in TC neurons during wakefulness. Indeed, we have recently postulated that similar cellular mechanisms may underlie both the slow oscillation and the ability to generate LTCP-mediated bursts from depolarized membrane potentials during the wake state. Thus these results suggest that whilst moderate activation of muscarinic acetylcholine receptors on thalamo-cortical neurons mediates a natural change from sleep to wake-related electrical activity.

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S3.P2

ANTIBACTERIAL ACTIVITY OF ANTIDEPRESSANTS, INHIBITORS OF MONOAMINE'S REUPTAKE, DEPENDS FROM THEIR ANTIDEPRESSIVE EFICACY ON SLEEP DISORDERS

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Unlimited uses of antimicrobial agents, frequently applied arbitrarily, contributed to the development of „antibiotic resistance" and new infectious diseases. Therefore searching for non-antibiotic agents with antimicrobial activity, antidepressants among them, is very topical. No less important is the question of whether the antimicrobial activity of antidepressants can be dependent on their effectiveness in restoring sleep disturbances in animal models of depression. Problem is important because antidepressants are supposed to restore disturbances characteristic for major depressive disorder (MDD) - sleep disorders among them, and effective drugs mustn't additionally worsen sleep and general condition of depressive patients. Study was aimed to investigate the antibacterial action of tricyclic, non-selective (melipramin, Group I) and selective (fluoxetine, Group II), antidepressants and the possible dependence of antimicrobial activity on their anti-depressive efficacy to sleep disturbances in animal models of depression. Wild white rat pups (n=5 in each group) received a subcutaneous injection of antidepressants, 30 mg/kg, two times daily, from postnatal day 7 to 28. Control rat pups received saline. Sleep EEG registration have been started 8–12 weeks after the drug discontinuation. Continuous sleep registration in each control rat was made for three consecutive days, 10.00 a.m. – 20.00 p.m. In experimental groups, EEG registration of sleep-wake cycling (SWC), with the same duration, was started after intraperitoneal injection of melipramin and /or fluoxetine (10 mg/kg and/or 15 mg/kg). *Escherichia coli*, *Bacillus subtilis*, *Staphylococcus aureus* and *Mycobacterium phlei* were used as test cultures. Melipramin, (0.01, 0.1 and 1 g/L) and fluoxetine (0.01, 0.1 and 1 g/L) were used for the studying of antibacterial spectrum. In adult rats, with postnatal exposure to melipramin and/or fluoxetine, sleep was disturbed significantly. Single-dose of melipramin produced worsening of sleep quality and whole inhibition of REM sleep during 4–5 h after drug injection. Sleep disorders like depression were developed in the recovery period (24 h after drug injection) - sleep quality becomes deteriorated, sleep interruptions increases, REM sleep latency diminishes, but its incidence rise. The influence of fluoxetine on SWC was relatively weaker and short-term indicating to higher anti-depressive efficacy of the drug. Antimicrobial activity of melipramin and/or fluoxetine on growth-development of *Escherichia coli*, *Bacillus subtilis*, *Staphylococcus aureus* and *Mycobacterium phlei* was dependent on their anti-depressive efficacy on sleep disturbances which has been only revealed by the selective inhibitor of serotonin reuptake, fluoxetine.

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S3.P3

BLOOD LEUKOCYTES IN YOUNG AND OLD RATS UNDER DESYNCHRONOSIS INITIATION ON THE BACKGROUND OF WHOLE BODY CRYOSTIMULATION

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The aim of the work was to study the effect of whole body cryostimulation (WBC) on leukocyte blood parameters in rats of different ages with a model of circadian desynchronosis (CD). The work was carried out on young and old (6 and 18 months) male outbred white rats according to biotic requirements. CD was initiated by single prolongation the light period by 12 h. One WBC (–120°C, 90 s) session was applied the day before CD initiation. Quantitative and qualitative assessment of leukocyte types were performed in blood smears after treated with fixative and stained with hematological dye, and integral leukocyte indices (ILI,), allowing to assess the state of certain links of immune system and body resistance without using special methods, were calculated. CD increased the band neutrophils number as well as cause leukocytosis and leukopenia in young and old rats correspondingly. Segmental neutrophils decreased in young animals and increased in old animals, but the change in lymphocyte number had the opposite direction. Eosinophils decreased only in young animals. Changes in ILI indicate an increase in young neutrophils, activation of cells of specific protection and hypersensitivity of the immediate type, strengthening of humoral immunity, intoxication, lack of inflammation and impaired immunoreactivity, and also increase adaptation ability in young animals. In old rats, immunoreactivity was impaired, inflammation and non-specific defence cells increased. CD initiation on the background of WBC caused to an increase in the total number of leukocytes and monocytes in young animals, and to decrease in old rats; segmental neutrophils, on the contrary. The lymphocytes and eosinophils decreased only in old rats. Band neutrophils increased, more significantly in young animals. ILI revealed a predominance of young neutrophils, macrophages and effector immune system activity, decreased immunoreactivity in young rats. The predominance of cellular immunity, increased intoxication, activation of inflammation and impaired immunoreactivity, predominance of nonspecific defence cells, microphages and allergy reduction were noted in old rats.

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S3.P4

PITUITARY-THYROID SYSTEM IN YOUNG AND OLD RATS UNDER PREVENTIVE WHOLE-BODY CRYOSTIMULATION AND CIRCADIAN DISRUPTION

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Perturbation of fluctuation of the endocrine system that occurs due to chronic circadian disruption (CD), resulted from shift-work, jet lag or irregular sleep-wake cycle, is recognized as the main mechanism of increasing the risk of cardiovascular, autoimmune and metabolic disorders as well as a number of psychological disorders. Thyroid hormones (TH) are necessary for normal differentiation and growth of the body, metabolism and thermoregulation, etc. Their synthesis and secretions from thyroid follicular cells are controlled by the thyroid-stimulating hormone (TSH), which level depends on the TH concentration in the blood. The main circadian pacemaker of the body located in the suprachiasmatic nuclei (SCN) of the anterior hypothalamus affects the TSH level as well, which is manifested in its daily fluctuations in the blood. Moreover, TSH amount is modulated by the sleep-wake cycle, the quality of which is altered to some extent under the whole-body cryostimulation (WBC). We aimed to study the preventive effect of WBC on activity of the pituitary-thyroid system in rats with the model of circadian disruption (CD). In young and old (6 and 18 months) males of white outbred rats, CD was modelled by a 12 h single prolongation of the light period. One WBC session was performed in a cryochamber (at a temperature of –120°C, 90 s) the day before the initiation of CD. The content of total (T4) and free thyroxine (T4f), total (T3) and free triiodothyronine (T3f) as well as TSH in blood serum (BS) was determined by enzyme-linked immunosorbent assay. The data were statistically processed by the Kruskal-Wallis method. Initiation of CD led to a decrease in TSH in BS in both young (5.35 ± 0.66 vs. 1.47 ± 0.07 nM/L, $p < 0.05$) and old rats (3.38 ± 1.42 vs. 0.81 ± 0.01 nM/L, $p < 0.05$). The preventive WBC application before CD initiation helped to maintain the level of TSH in the BS at the level of control values (4.64 ± 1.8 and 1.91 ± 0.11 nM/L, in young and old animals, respectively). No significant differences in the levels of total or free T3 and T4 in BS after CD and preventive WBC application were found (with exception for a decrease in T3f in old rats with WBC). Thus, the preventive WBC application stabilizes the response of the pituitary-thyroid system of young and old rats to the CD initiation.

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