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ANALYSIS OF THE ORGANISM'S ADAPTATION MECHANISMS TO THE FUNCTIONAL LOAD OF SWIMMING BASED ON CHANGES IN HEMATOLOGICAL PARAMETERS

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An experimental study of the adaptation mechanisms to the physical load of swimming was performed by analyzing the changes in the hematological parameters of rats` peripheral blood. Integrative markers of cellular immune inflammation were calculated based on the ratios between formed blood elements. At the beginning of the research, the resistance of rats to hypoxic hypoxia was determined. Medium-resistant animals were selected for the experiment. Then they were trained by swimming for 10 days using an additional load. At the end of the experiment, an increase in the resistance of these animals to hypoxic hypoxia was noted. An increase in the concentration of hemoglobin and erythrocyte indices was found during the analysis of red blood parameters. A decrease in segmented neutrophils, an increase in lymphocytes, and a decrease in thrombocytes were registered. In our analysis of the integrative markers related to cellular immune inflammation, we observed significant changes in all indicators reflecting the anti-inflammatory effects of the physical exercises we applied. Notably, there were no signs of overtraining and overload. The use of such markers is highly practical, as they provide an adequate, effective and available means of evaluating the organism`s adaptive potential when performing functional loads of various intensity and duration.

Key words: adaptation, functional load of swimming, resistance to hypoxic hypoxia, markers of cellular immune inflammation.

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АНАЛІЗ МЕХАНІЗМІВ СТАНОВЛЕННЯ АДАПТАЦІЇ ОРГАНІЗМУ ДО ФУНКЦІОНАЛЬНОГО НАВАНТАЖЕННЯ ПЛАВАННЯМ НА ОСНОВІ ЗМІН ГЕМАТОЛОГІЧНИХ ПОКАЗНИКІВ

Було проведено експериментальне дослідження механізмів адаптації до фізичного навантаження плаванням шляхом аналізу змін гематологічних показників периферичної крові щурів. Обчислювали інтегративні маркери клітинного імунного запалення за співвідношеннями між окремими форменими елементами крові. На початку досліджень визначали резистентність щурів до гіпоксичної гіпоксії. Для експерименту відбирали середньорезистентних тварин. Далі їх тренували плаванням упродовж 10 днів з використанням додаткового вантажу. В кінці експерименту було відмічено підвищення резистентності цих тварин до гіпоксичної гіпоксії. При аналізі показників червоної крові було встановлено підвищення концентрації гемоглобіну та еритроцитарних індексів. Реєстрували зниження сегментоядерних нейтрофілів, підвищення лімфоцитів, зменшення тромбоцитів. При аналізі обчислених нами інтегративних маркерів клітинного імунного запалення у дослідних тварин були виявлені показові зміни усіх показників, що відображають протизапальні ефекти застосованих нами фізичних навантажень, з відсутністю ознак перетренування та перевантаження. Застосування таких маркерів має важливе практичне значення, оскільки є адекватним, ефективним та доступним способом оцінки адаптивного потенціалу організму при реалізації функціональних навантажень різної інтенсивності та тривалості.

Ключові слова: адаптація, функціональне навантаження плаванням, резистентність до гіпоксичної гіпоксії, маркери клітинного імунного запалення.

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The development of adaptive reactions of the organism when subjected to functional loads is determined primarily by the nature and intensity of the active factor, as well as the individual`s physical qualities. When such exposure effectively mobilizes compensatory mechanisms and builds resistance, it becomes important to analyze the specific mechanisms that facilitate these processes in detail. In particular, it is known that the physical load of swimming has a complex pronounced effect on the functional systems of the organism [6]. Among the significant effects, the impact on the physiological properties of the blood system can be distinguished [11, 12]. This type of load also induces thermogenic modulations at the level of skeletal muscles, white and brown adipose tissues [3]. It is known that swimming is effective in the treatment of metabolic syndrome, reducing insulin resistance [3]. Aerobic swimming training stimulates angiogenesis by activating the migration and proliferation of endothelial progenitor cells in healthy individuals and individuals with metabolic syndrome, congestive heart failure, coronary heart disease, and prediabetes [8]. Research has indicated that some animals can develop resistance to specific types of stress and exhibit inflammatory reactions when adapting to physical loads [5]. Swimming is a natural behavioral model for some animals, providing the benefit of minimal mechanical stress. This characteristic enhances the effectiveness of using swimming as a functional load model under experimental research conditions.

The purpose of the study was to research the mechanisms of adaptation to the functional load of swimming by analyzing changes in the hematological parameters of the rats` peripheral blood.

Materials and methods. To ensure sample homogeneity and eliminate the confounding effects of the estrous cycle on metabolic and cardiorespiratory responses, the research was conducted exclusively on sexually mature male rats weighing 180–200 g. This retrospective study presents a secondary analysis of data collected between May and June 2012. The investigation was carried out at the Department of Normal Physiology of Danylo Halytsky Lviv National Medical University. By applying recent analytical approaches, the study re-evaluates existing findings to align them with the current scientific discourse. The experiments were conducted in accordance with the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes (Strasbourg, 1986).

At the beginning of the research, before 48 h, the resistance of rats to hypoxic hypoxia was determined. This assessment was conducted in an inlet exhaust hypobaric chamber at a simulated altitude of 11,000 m (by Berezovsky VA) [1]. The resistance criterion was the time from the moment of ascent (speed 180 m/s) to the appearance of the second agonal breath. Animals whose endurance time to hypoxic hypoxia was between 7 and 12 min were considered medium resistant to hypoxia.

To ensure a homogeneous sample, only animals with medium resistance to hypoxia were selected for further investigation and divided into 6 groups with a total of 138 individuals. The remaining 69 rats with high and low resistance, accounting for 33.3% of the initial population (207 animals), were excluded from the experiment during the pre-screening phase.

At the end of the experiment, 24 hours after the 10th day of swimming, the resistance of the rats to hypoxia was determined for the second time.

The rats were divided into groups (n = 23): Group 1 – experimental, which were trained by swimming for 10 days using additional load, and then a blood sample was taken; Group 2 – experimental, which were trained by swimming for 10 days using additional load, and then resistance to hypoxia was assessed; Group 3 – control, which swam for 10 days without using additional load, and then a blood sample was taken; Group 4 – control, which swam for 10 days without using additional load, and then determination of resistance to hypoxia was carried out (by Berezovsky VA) [1]; Group 5 – a group of intact animals, whose blood sample was taken; Group 6 – a group of animals that swam once without using an additional load before the appearance of signs of fatigue.

The number of animals per group did not change by the end of the experiment.

The animals were trained by swimming once daily for 10 days. For this, a cylinder with water, 55 cm in diameter and 80 cm in height, was used. The water temperature was maintained within 24–26 °C. Each animal was trained separately. Additional swimming load was provided by attaching calibration weights (10% of the animal's body mass) to the base of the tail using soft bands. Fatigue was observed after the first three underwater dives. Following this, the rats were quickly removed from the water and dried with a towel. To prevent complete fatigue, we interrupted the swimming by allowing the rats to sink to the bottom of the cylinder.

Control group rats swam without a load every day, once, for 10 days. Each session lasted 0.9–1 min, corresponding to the average duration of swimming of the experimental animals during the study.

Blood sampling from the tail vein was carried out 24 hours after 10 days of swimming. Hematological parameters were determined using the COULTER-T840 analyzer.

At the end of this experimental stage, the animals were not euthanized (decapitated) because they were allocated to further investigations.

We calculated the integrative cellular immune inflammation markers, as a simple ratio between the neutrophil and lymphocyte counts, the platelet and lymphocyte counts, the lymphocyte and monocyte counts measured in peripheral blood: Segmented neutrophil-to-lymphocyte ratio (NLR, Neutrophil-to-lymphocyte ratio), Platelet-to-lymphocyte ratio (PLR), Lymphocyte-to-monocyte ratio (LMR) and Systemic immune-inflammation index (SII=NLR×platelets).

The results were tested for normality of distribution using the Shapiro-Wilk test. The data were normally distributed, so the difference between groups was assessed using Student's t test. Data are presented as means (M) and standard deviations (SD). The significance level of $p<0.05$ was assumed. Statistical evaluation was conducted using Microsoft Excel software (Microsoft Excel for Office 365) and OriginPro (version 2019b, OriginLab Corporation, USA).

Results of the study. During the experiment, the duration of swimming of experimental rats (with an additional load) before the appearance of fatigue had a phase character. The shortest duration was recorded on day 5 and the longest on day 10 (Fig. 1).

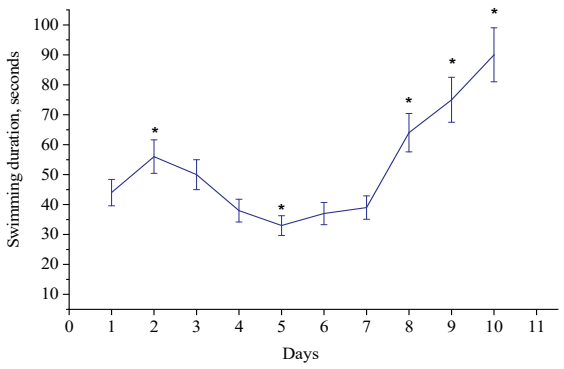

Fig. 1. Duration of swimming with load of rats within the 10-day swimming course.

Note: * the difference from the measurement of first day was statistically significant $p<0.05$.

At the end of the experiment, on the 10th day, experimental rats showed signs of complete fatigue after the first two underwater dives, so further training was stopped.

Rats were tested separately for their ability to swim without a load for the first three underwater dives. The duration of swimming was 45±5 minutes.

When analyzing blood parameters in the control group of animals, no statistically significant changes were found compared to intact ones.

In the group of experimental animals after swimming, there was a little increase in hemoglobin concentration (142.05±5.72 g/l vs 128.81±4.30 g/l, $p<0.05$). Additionally, improvements were observed in the erythrocyte indices: mean corpuscular haemoglobin (MCH) increased from 17.45±0.51 pg to 19.31±0.70 pg ($p<0.05$), and mean corpuscular haemoglobin concentration (MCHC) rose from 32.26±1.17 g/dl to 35.40±1.54 g/dl ($p<0.05$), as shown in Table 1.

Table 1

Blood indicators of intact rats, of control group and group after swimming with load

Parameters	Intact	Control	After swimming with load
	mean±SD	mean±SD	mean±SD
Erythrocytes [10^{12}/l]	6.55±0.42	7.03±0.35	6.73±0.39
Haemoglobin [g/l]	127.52±7.11	128.81±4.30	142.05±5.72 *
Haematocrit [%]	40.03±3.12	39.96±2.91	38.53±2.71
MCV [fl]	57.21±2.91	54.75±3.43	58.02±4.12
MCH [pg]	16.73±0.82	17.45±0.51	19.31±0.70 *
MCHC [g/dl]	31.57±1.53	32.26±1.17	35.40±1.54 *
Leukocytes [10^9/l]	12.3±0.99	11.3±1.29	12.0±0.97
Band Neutrophils [%]	2.93±0.61	3.04±0.55	3.21±0.43
Segmented Neutrophils [%]	26.03±1.74	25.12±1.42	19.04±2.31 *
Lymphocytes [%]	59.87±4.99	64.53±5.64	81.10±6.53 *
Eosinophils [%]	2.18±0.21	2.54±0.17	2.33±0.19
Monocytes [%]	3.79±0.43	4.31±0.54	4.04±0.32
Platelets [10^9/l]	732.43±53.07	716.43±45.11	625.33±35.34 *

Abbreviations: MCV = mean corpuscular volume; MCH = mean corpuscular haemoglobin; MCHC = mean corpuscular haemoglobin concentration.

Notes: * difference from the control group statistically significant $p<0.05$.

As for white blood cell parameters, the experimental animals demonstrated a decrease in the relative concentration of segmented neutrophils by 24 % (19.04±2.31 % vs 25.12±1.42 %, $p<0.05$), an increase in the relative lymphocyte concentration by 26 % (81.10±6.53 % vs 64.53±5.64 %, $p<0.05$), compared to the control group. A little decrease in the concentration of platelets was registered (625.33±35.34 10^9/l vs 716.43±45.11 10^9/l, $p<0.05$), compared to the control group.

When analyzing the integrative markers of cellular immune inflammation calculated by us in experimental animals, significant changes in all parameters were revealed (Table 2).

Table 2

The integrative cellular immune inflammation markers of intact rats, of control group and group after swimming with load

Parameters	Intact	Control	After swimming with load
	mean±SD	mean±SD	mean±SD
NLR [AU]	0.43±0.05	0.39±0.04	0.23±0.03 *
PLR [AU]	99.31±6.95	98.28±7.01	64.27±5.43 *
LMR [AU]	14.87±1.33	15.07±1.43	20.25±1.81 *
SII [AU]	258.7±26.21	279.4±23.72	143.83±15.11 *

Abbreviations: NLR, Neutrophil-to-lymphocyte ratio (Segmented neutrophil-to-lymphocyte ratio); LMR, Lymphocyte-to-monocyte ratio; PLR, Platelet-to-lymphocyte ratio; SII, Systemic immune-infammation index (SII=NLR×platelets); AU, Arbitrary unit.

Note: * difference from the control group statistically significant $p<0.05$.

The ratio of segmented neutrophils to lymphocytes (NLR) (0.23±0.03 AU vs 0.39±0.04 AU, $p<0.05$), platelets to lymphocytes (PLR) (64.27±5.43 AU vs 98.28±7.01 AU, $p<0.05$) and systemic immune inflammation index (SII) (143.83±15.11 AU vs 279.4±23.72 AU, $p<0.05$) decreased, however, the ratio of lymphocytes to monocytes (LMR) increased (20.25±1.81 AU vs 15.07±1.43 AU, $p<0.05$), compared to the control group (Fig. 2).

After testing resistance to hypoxic hypoxia, it was found that the endurance time in the animals of the control group remained unchanged, lasting between 7 to 12 min, similar to that of medium-resistant rats. In contrast, the endurance time for the rats in the experimental group increased to 20–30 min. According to the established classification, these rats were categorized as highly resistant.

Based on the research results, we analyzed the changes in hematological parameters to determine the peculiarities of the development of the organism's adaptation mechanisms at the level of the blood system in response to a relatively short-term and intense functional stress (since the experimental animals were subjected to an additional load).

At the end of the experiment, it was noted that although the concentration of erythrocytes did not differ from the control group, the erythrocyte indices

and hemoglobin concentration slightly increased. The activation of the reserves of these formed blood elements is important for ensuring an adequate response of the organism to stress, caused, among other things, by increased oxygen demand of organs and tissues during physical exertion.

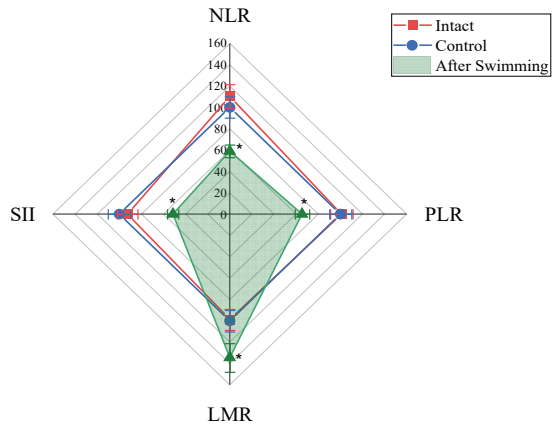

Fig. 2. Analysis of cellular immune inflammation markers neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR) and systemic immune-inflammation index (SII) of intact rats, of control group and group after swimming with load. Values are presented relative to the control group of rats (100 %).

Note: * difference from the control group statistically significant $p<0.05$.

At the same time, after the swimming course, a significant decrease in platelet concentration was recorded in the animals of the experimental group. Probably, this was a consequence of their mobilization and involvement in the relevant physiological processes under these conditions. It is well known that physical activity of varying intensity significantly impacts the structural and functional state of the walls of blood vessels. In turn, platelets, among others, perform an essential angiotrophic function, ensuring normal permeability and resistance of vascular walls. Their role in the primary hemostasis is well known. Under certain conditions, they can exhibit pro-inflammatory properties.

At the end of the training, while the concentration of platelets and neutrophils decreased, an increase in lymphocytes, components of the adaptive immune system, was recorded in experimental animals.

Discussion. Exercise-induced lymphocytosis is thought to occur in proportion to the intensity and duration of this exposure [2]. Key mechanisms involved in this process include the effect of catecholamines and increased shear stress resulting from elevated blood flow during exercise.

As well as the separate blood components that respond to exercise, their ratios, calculated as NLR, PLR, LMR, and SII, are also important. They are considered to be diagnostic markers of cellular immune inflammation [4, 9, 13, 15].

Over the last decades, such markers have been studied in a clinical context and are now popular due to their integrative nature [7, 10, 13, 14]. Transferring these markers to exercise physiology is considered very useful and demonstrative.

The sensitivity of markers to the development of inflammation due to acute and chronic physical exertion has been confirmed; therefore, they are considered in the context of assessing the organism's productivity [15, 16]. Changes in these markers can characterize recovery status and periods of overtraining, making them useful for training program design.

It is known that a decrease in the initial values of SII and NLR may reflect the anti-inflammatory effects of exercise [4]. Instead, their increase in response to high-intensity physical activity is a precise characteristic of the inflammation development [13].

A pronounced relationship between physical activity, changes in NLR, PLR, and sleep quality has been established [9]. In particular, moderate physical activity, low values of NLR and PLR markers were correlated with high indicators of sleep quality. Conversely, low physical activity was associated with high values of markers and low sleep quality indicators [9].

The values of these diagnostic markers clearly correlate with functional and metabolic changes in the organism. It is obvious that a low level of physical activity, or its complete absence, has the same adverse effect on the organism as high-intensity physical activity with signs of overloading and overtraining.

It is important that during our experiment, after applying the chosen short-term and intense physical load, we observed a decrease in the NLR, PLR, and SII markers rather than an increase. In contrast, we recorded elevated values of LMR compared to the control group.

It is known that changes in LMR during exercise can reflect modulations of the immune system [4]. Intense physical exercise can cause an increase in both lymphocytes and monocytes, but the magnitude of these changes may vary [2, 15].

Regular and prolonged exercise can lead to adaptation of the immune system. For example, high-level athletes may have even lower LMR values compared to untrained individuals due to changes in lymphocyte subpopulations [4]. In general, LMR values during exercise are associated with the gradual development of adaptation to training.

Therefore, the use of such markers as NLR, PLR, SII, and LMR is of great practical importance, as it is an adequate, effective, and affordable way to assess the adaptive potential of the organism when performing physical exercises of different intensity and duration, as well as when implementing rehabilitation programs.

Conclusion

At the end of the swimming training course, a decrease in integrative markers of cellular immune inflammation was recorded in experimental rats: by 41 % NLR ($p<0.05$), by 35 % PLR ($p<0.05$), and by 49 % SII ($p<0.05$). These results indicate the anti-inflammatory effects of the physical exercises administered under the experimental conditions, in comparison to the control group.

After training, there was a significant increase of 26 % ($p<0.05$) in the relative lymphocyte concentration, which are key components of the adaptive immune system. Additionally, the LMR marker increased by 34 % ($p<0.05$), indicating a progressive adaptation to training.

Following the training course, an analysis of red blood cell parameters revealed a significant increase in hemoglobin concentration, measuring 142.05±5.72 g/l compared to 128.81±4.30 g/l, $p<0.05$ in the control group. Additionally, erythrocyte indices showed increases in MCH (19.31±0.70 pg vs 17.45±0.51 pg, $p<0.05$) and MCHC (35.40±1.54 g/dl vs 32.26±1.17 g/dl, $p<0.05$).

After testing the rats' resistance to hypoxic hypoxia by endurance time, it was found that after the training course, the time increased from 7-12 min to 20-30 min; according to the classification, such rats belonged to highly resistant ones.

When analyzing the integrative markers of cellular immune inflammation, hematological parameters, and the test results for resistance to hypoxic hypoxia, we identified significant changes that demonstrated anti-inflammatory effects of the physical exercises we applied. Additionally, these exercises contributed to an increased resistance in experimental animals to hypoxic hypoxia.

Prospects for further research. Analyzing the specific features of adaptive mechanisms in response to functional loading by calculating integrative markers of cellular immune inflammation is a promising avenue of modern biomedical research. The application of such markers offers an adequate, effective, and accessible method for evaluating the body's adaptive potential, particularly within rehabilitation protocols. Changes in these indicators reflect the body's responses to functional loading (encompassing both acute and chronic adaptation), which opens up prospects for their future implementation across various hypoxic exposure models.

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