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Influence of the Experience of Health-Improving Jogging on the Level of Functional Activity of Platelets in Men of the Second Mature Age

Medvedev Ilya Nikolaevich[1*], Gusev Alexey Vitalievich[2], Malyshev Andrey Valentinovich[3], Mikhailova Olga Dmitrievna[4], Garina Evgeniya Vladimirovna[5], Petina Elmira Shamilevna[6], Tagirova Naida Dzhamaldinovna[6]

[1] Department of Adaptive Physical Culture and Recreation, Russian State Social University, 129226, Moscow, Russia
[2] Department of Physical Education and Fundamentals of Life Safety, Moscow State University of Psychology and Education (MSUPE), 127051, Moscow, Russia
[3] Department of Service and Food Industry, Sochi State University, 354000, Sochi, Russia
[4] Department of Physical Education, Moscow City Pedagogical University, Institute of Natural Sciences and Sports Technology, 129226, Moscow, Russia
[5] Department of Physical Education, Sechenov First Moscow State Medical University, 119435, Moscow, Russia
[6] Department of Physical Education, Astrakhan State Medical University, 414000, Astrakhan, Russia

***Corresponding author: Medvedev Ilya Nikolaevich**, Department of Adaptive Physical Culture and Recreation, Russian State Social University, st. V.Pika, 4, Moscow, 129226, Russia
E-mail: ilmedv1@yandex.ru

ABSTRACT

Modern science is paying more and more attention to the study of the effect of regular physical activity on platelet activity. The study involved 102 clinically healthy men of the second mature age, which made up 4 groups: the control group - physically untrained (23 people) and 3 observation groups who did daily jogging for 30 minutes a day. Observation group 1 (26 people) trained for 1 year. Observation group 2 (28 people) trained for 3 years. Observation group 3 (25 people) had 5 years of daily running experience. The average volume of platelets, their aggregation activity in response to 2.5, 5, and 10 μM ADP and the content of GP IIb-IIIa and GP Ib on their surface were evaluated. With increasing experience of regular physical training, athletes found a decrease in platelet aggregation in response to all tested ADP concentrations, a decrease in the average platelet size and a decrease in the expression of GP IIb-IIIa and GP Ib. The found significant correlation between the average volume of platelets, on the one hand, and the activity of their aggregation and the number of GP IIb-IIIa and GP Ib receptors on their surface, on the other hand, was more pronounced in athletes. Functionally beneficial changes in the morphological and functional properties of platelets, increasing with the increase in the length of regular jogging in the second adulthood, are another confirmation of the need for a massive increase in physical activity in the second half of ontogenesis.

Keywords: Platelets, Average platelet volume, Platelet aggregation, Glycoprotein IIb-IIIa, Glycoprotein Ib, Regular physical activity, Running.

Correspondence:
Medvedev Ilya Nikolaevich
Department of Adaptive Physical Culture and Recreation
Russian State Social University, st. V.Pika, 4, Moscow, 129226, Russia
Tel.: +79102732263
E-mail: ilmedv1@yandex.ru

INTRODUCTION

Platelets are the smallest blood cells, the main function of which is considered to be participation in hemostasis processes[1,2]. Its platelets are realized by adhesion, aggregation and secretion[3]. Strengthening of these platelet processes very often leads to the formation of thrombophilia and the risk of thrombotic episodes[4,5]. For this reason, recently, many researchers are actively studying the mechanisms of the participation of platelets in hemostasis and their response to various influences[6,7]. At the same time, special attention is paid to the intensity of aggregation and the average volume of platelets, considering them as indicators indicating the level of their general activity[8,9].

Serious importance for platelet aggregation is now attached to the number of receptor molecules located on their surface, which varies in a wide range - the level of GP IIb-IIIa is 2 times[10,11], GP VI is 5 times[12,13] and is capable of changing platelet activity when the general physiological status of a person changes. A clear relationship was found between the level of GP IIb-IIIa[14], GP VI [15,16] molecules on platelets and platelet activity. For this reason, the amount of these proteins is often considered as a marker of the total platelet activity[17,18]. Previously, the relationship between the level of adhesive molecules on platelets and their size, that is, with their surface area, on which these proteins are located, was traced. It has been proven that the larger the platelets, the stronger they aggregate, have more large granules capable of secretion and containing more thrombogenically active substances [19]. For this reason, an increase in the area of platelets is inevitably accompanied by the formation of a tendency of platelets to hyperfunction [20,21].

Starting from the second adulthood in the body, especially in men, the general pathological burden associated with the progression of subclinical atherosclerosis, increased episodes of destabilization of blood pressure or the formation of arterial hypertension increases and contributes to an increase in the overall activity of platelets [22,23]. This situation is very dangerous, as it creates the risk of thrombosis, threatened with death or disability [24,25].

In this regard, the problem of finding means of "mild" physiological weakening of platelet functions in people belonging to different risk groups is of increased interest in modern medical science [26,27]. As preventive measures against the development of thrombophilia in clinically still healthy people, priority is given to non-drug effects [28].

It is believed that regular feasible physical activity is very effective in terms of preventing thrombophilia from among non-drug means [29]. It has been proven that they have a positive effect on the heart and lungs, which are organs of particular importance for maintaining general vitality and general resistance [30]. Regular physical training also has a very positive effect on blood, which plays a huge role in humoral regulation and in providing tissue trophism [31]. At the same time, the dynamics of the state of its formed elements and especially platelets against the background of regular physical activity has not been studied to the same extent as changes in the functional characteristics of the cardiorespiratory system [32].

Previous studies have shown that increased muscle activity in adolescence and first adulthood can lower the level of platelet activity [33]. The influence of regular feasible physical activity on platelets in people of the second mature age, who are experienced and able-bodied, and often have significant pathology in the body with a high risk of thrombotic manifestations, remains unclear. Until now, the possibilities of regular feasible physical training in the second adulthood have not been clarified in relation to platelet activity and the state of the main mechanisms that determine it. In this age group, the response to regular aerobic exercise of the severity of platelet aggregation, which is realized in the course of their interaction with each other and with other cells through the GP IIb-IIIa and GP Ib receptor molecules, remains unclear.

Purpose of the work: to find out the effect of the experience of regular physical activity on the morphological and functional parameters of platelets in persons of the second mature age.

METHOD

Examination included 102 clinically healthy second mature age males (mean age 43.6 ± 2.4 years), who had no bad habits. Taking into account their attitude to regular physical activity, they were divided into 4 groups. The control group was represented by 23 persons who avoided regular physical activity during their life. Observation group 1 consisted of 26 athletes who did daily jogging in free mode for at least 30 minutes a day for at least 1 year and no more than 1 year and 3 months. Observation group 2 included 28 athletes who jogged every day in a free mode for at least 30 minutes a day for at least 3 years and no more than 3 years and 3 months. Observation group 3 was recruited from 25 athletes who had experience of daily jogging for at least 5 years and no more than 5 years and 3 months for at least 30 minutes a day.

All subjects did not take any medication for 2 weeks before taking them into the study. All subjects gave written voluntary informed consent to their participation in the study. Its conduct was approved by the local ethics committee of the Russian State Social University (protocol No. 2 dated 02.22.2017).

All the examined patients underwent blood sampling from a vein in a 3.8% sodium citrate solution with a final ratio of blood and anticoagulant of 9: 1. Platelet-rich plasma was obtained by centrifuging blood at 180 g for 10 minutes at room temperature. Plasma containing a low number of platelets was obtained from platelet-rich plasma during its further centrifugation under 1500 g for 15 minutes at room temperature. The mean platelet volume, the level of their aggregation, and the number of platelet GP IIb-IIIa and GP Ib were assessed in all examined subjects, recording these parameters in the first hour after blood collection.

The mean platelet volume and platelet count in platelet-rich plasma were determined using an Abacus Junior B hematological analyzer (Diatron Ltd, Austria).

In the work, the platelet aggregation was determined, which was induced in the study by adding ADP to platelet-rich plasma. For this, the standard turbidimetric method was used with the registration of the dynamics of light transmission of platelet suspension (T%). For this purpose, we used an aggregation analyzer of the BIOLA brand (BIOLA, Russia), which allows maintaining 37° C in the plasma sample and stirring it at a speed of 800 rpm. The study used ADP at final concentrations of 2.5 μM, 5 μM and 10 μM. The inducer was added to platelet-rich plasma 30 s after the start of the light transmission assessment and was recorded within 4.5 minutes after the inducer was added to the plasma. During the evaluation of platelet aggregation curves, the highest aggregation level (T% maximum) was taken into account.

Assessment of the level of GP IIb-IIIa and GP Ib on platelet membranes was carried out according to known methods [10, 14] using labeled monoclonal antibodies against these proteins. The number of platelets in platelet-rich plasma was adjusted with autologous plasma to a level of 2.5×10^8 per 1 ml. In the case of a lower number of platelets in plasma, undiluted platelet-rich plasma was used in the study. In order to determine the level of GP IIb-IIIa, specific antibodies CRC64 were used [34]. Antibodies VM16d were used to detect the level of GP Ib [33]. Both types of labeled antibodies were added separately to platelet-rich plasma samples at a final concentration of 10 μg/ml in the absence or in the presence of a 20-fold excess of unlabeled antibodies (to record, respectively, general and non-specific binding). The process of incubation of platelets with antibodies was carried out for 30 minutes at 37° C. At the end of the incubation process, the platelet-bound label and the platelet-free label were separated by centrifugation of platelet-rich plasma using a standard 20% sucrose solution. The specific binding level was determined by subtracting the non-specific binding value from the total binding value. The registered number of glycoproteins was presented as the number of antibody molecules that bound 1 platelet.

Statistical processing was carried out using the "Statistica 10.0 for Windows" program. The study used nonparametric tests: Mann-Whitney U-test and Spearman's rank correlation method.

RESULT

Average platelet volume

The average platelet count in physically untrained volunteers was higher than in those who regularly experienced physical activity. The mean values and variations in the average platelet volume are shown in Table 1. In the control group, the average platelet volume varied from 7.0 to 10.5 fl, while in all physically exercising it ranged from 5.8 to 10.1 fl.

Significant differences were found between the mean values of the mean platelet volume between the control group and the athletes. Moreover, as the experience of physical training increased, an increase in the differences between the average values of this indicator was noted. As a result, these differences were most pronounced in the most long-term physically trained people who made up observation group 3.

Table 1. Average platelet volume in the examined

Considered indicator	Observation group 1, n = 26	Observation group 2, n = 28	Observation group 3, n = 25	Control group, n = 23
Average platelet volume, fl	8.01±0.63* (6.6-10.1)	7.12±0.81** (6.2-10.0)	6.57±0.67** (5.8-9.0)	9.24±0.46 (7.0-10.5)

Note. Significance of differences in indicators of the observation groups compared with the control group: * - p <0.05, ** - p <0.01

Platelet aggregation

In this study, platelet aggregation in the examined subjects was induced by ADP at doses of 2.5 μM, 5 μM, and 10 μM. In all study groups, the mean values of platelet aggregation increased with increasing concentrations of ADP (Table 2).

Table 2. ADP-induced aggregation in the examined

Groups	T, % under the influence of ADP at a dose of 2.5 μM	T, % under the influence of ADP at a dose of 5 μM	T, % under the influence of ADP at a dose of 10 μM
Control group	37.8±1.7	52.6±1.8	63.4±2.4
Observation group 1	35.2±1.2	48.2±1.5	57.1±1.9*
Observation group 2	31.5±0.5**	45.4±1.0*	55.0±1.2*
Observation group 3	28.7±0.7**	41.3±0.8**	50.4±0.9**

Note. Significance of differences in the aggregation index under the influence of a certain concentration of the inducer in the observation group compared with the control group: * - p <0.05, ** - p <0.01.

The highest values of platelet aggregation in response to all concentrations of inducers were observed in the control group, consisting of people who avoided physical exertion. In observation group 1, the activity of the aggregation process was weaker, however, the differences with the control in this group reached the level of reliability only at the maximum concentration of ADP (11.0%). The lower was the platelet aggregation caused by ADP in individuals who jogged for three years. Its parameters were significantly lower than the control at all tested concentrations of the inducer. The values of platelet aggregation in athletes with five years of continuous experience of daily physical training were the least inferior to the control. In observation group 3, at a concentration of ADP of 2.5 μM, the aggregation index was inferior to the control by 31.7%, at a concentration of 5 μM by 27.3%, and at a concentration of 10 μM by 25.8%. At the same time, the reliability of differences with the control of the levels of platelet aggregation caused by all tested concentrations of inducers was maximal in observation group 3.

Platelet aggregation and average platelet volume

In the control group and in the observation groups, moderate correlations were found between the aggregation index and the mean platelet volume (Table 3). In the control group, significant correlations were noted for all applied concentrations of ADP. In the observation groups, who experienced daily jogging regardless of their length of physical training, a correlation was found between the mean platelet volume and the aggregation activity caused by ADP at concentrations of 5 μM and 10 μM. At a dose of the inducer of 2.5 μM, the correlation did not reach the level of reliability.

Table 3. Correlation relationship between platelet aggregation and average platelet volume in the examined

Groups of examined	Correlation coefficients between the mean platelet volume and their aggregation		
	ADP 10 μM	ADP 5 μM	ADP 2,5 μM
Observation group 1, n = 26	0.57*	0.61**	0.31
Observation group 2, n = 28	0.58**	0.58**	0.34
Observation group 3, n = 25	0.59**	0.62**	0.35
Control group, n = 23	0.55*	0.57**	0.37*

Note. Reliability of correlations: * - p <0.05; ** - p 0.01.

Platelet membrane glycoproteins

The amounts of the average content of GP IIb-IIIa and GP Ib on platelets in the examined subjects and variations in their content are presented in Table 4. In physically exercising and physically untrained, there were wide, approximately two-fold and two and a half-fold variation in the content of GP IIb-IIIa and GP Ib on the surface of platelets.

In this work, a decrease in the level of expression of both glycoproteins in physically exercising people was registered as the experience of regular health jogging increased. This ensured the presence of significant differences in the content of both glycoproteins between the control and observation groups 2 and 3, with the greatest experience of physical training.

Table 4. Levels of the considered glycoproteins on the platelet membranes of the examined

Receptor variants	Observation group 1, n = 26	Observation group 2, n = 28	Observation group 3, n = 25	Control group, n = 23
GPIIb-IIIa, 10^3 for 1 platelet	46.2±3.0 (30.0-66.0)	42.5±2.7* (29.0-64.0)	40.2±2.4** (28.0-62.0)	47.9±2.2 (32.0-68.0)
GPIb, 10^3 for 1 platelet	25.0±2.0 (16.0-38.0)	23.1±1.8* (15.0-37.0)	21.2±1.6** (14.0-36.0)	26.7±1.9 (17.0-40.0)

Note. Significance of differences in indicators of observation and control groups: * - p <0.05, ** - p <0.01

The content of GP IIb-IIIa and GP Ib and the average volume of platelets were related to each other in all examined patients. In physically exercising volunteers, regardless of the length of their training and in those who avoided physical exertion, between the content of GP IIb-IIIa and GP Ib and the mean platelet volume, the correlation coefficients (r) were significant and ranged from 0.54 to 0.65 (Table 5). In addition, in all groups, a statistically significant correlation was found between the amount of both glycoproteins on the surface of platelets - g from 0.52 to 0.57 (table 5).

Table 5. Correlations between the level of taken platelet glycoproteins and the average platelet volume

Correlation pairs	Observation group 1, n = 26	Observation group 2, n = 28	Observation group 3, n = 25	Control group, n = 23
	Correlation coefficient values			
GP IIb-IIIa / average platelet volume	0.62**	0.64**	0.65**	0.60**
GPΠ Ib / average platelet volume	0.57*	0.59**	0.54*	0.54*
GP IIb-IIIa / GPIIb	0.54*	0.56*	0.57*	0.52*

Note. Significance of correlations * - p <0.05, ** - p <0.01.

DISCUSSION

In this work, the variations in the mean platelet volume, the severity of platelet aggregation activity and the number of GP IIb-IIIa and GP Ib on platelets were assessed in people of the second mature age who jogged in a free mode for different periods. The observations were carried out in groups of physically trained for one year, three years and five years. The control group was a group of healthy untrained volunteers.

When determining the average volume of platelets and the content of GP IIb-IIIa and GP Ib, some variability of these parameters was found, in the group of physically untrained and in groups of those who exercise for different periods. At the same time, differences in the average platelet volume and the content of GP IIb-IIIa and GP Ib were found between healthy untrained people and those with experience of health jogging. Apparently, this was revealed by a strict selection into groups by gender, age and running experience. The data obtained indicate a clear connection between the state of these indicators in men of the second mature age with the experience of their regular physical activity. Similar results were noted earlier in relation to a consistently low level of expression of GP IIb-IIIa in people leading a healthy lifestyle [35]. At the same time, this work did not take into account the relationship between the expression of this glycoprotein and the level of physical activity.

In the control group, the average platelet volume varied from 7.0 to 10.5 fl, while in all physically trained people it ranged from 5.8 to 10.1 fl. Significant differences were found between the mean values of the mean platelet volume in control and in athletes. Moreover, as the experience of health jogging increased, an increase in differences was revealed between the average values of this indicator. As a result, these differences were most pronounced in the most long-term physically exercising runners who made up observation group 3. The obtained result can be explained by the response of the bone marrow to regular physical activity for a long time [36,37].

The highest values of platelet aggregation in response to all concentrations of inducers were observed in the control group, which consisted of people who avoided physical exertion throughout their lives. In observation group 1, the activity of the aggregation process was weaker, however, the differences with the control in this group reached the level of reliability only at the maximum concentration of ADP (11.0%). The lower was the platelet aggregation caused by ADP in individuals who jogged for three years. Its indicators were significantly lower than the control at all tested concentrations of the inducer. The values of platelet aggregation in runners with five years of continuous physical training experience were as inferior to the control as possible. In observation group 3, at an ADP concentration of 2.5 μM, the aggregation index was lower than the control by 31.7%, at a concentration of 5 μM by 27.3%, and at a concentration of 10 μM by 25.8%. At the same time, the reliability of differences with the control of the levels of platelet aggregation caused by all tested concentrations of the inducer was maximal in observation group 3.

In this study, physically exercising individuals were found to have direct correlations between the mean platelet size and the level of their aggregation. In all groups of physically exercising, moderate but significant correlations were found in relation to the doses of ADP 5 and 10 μM. At a dose of 2.5 μM, the tendencies found did not reach a significant level in them and were statistically significant only in the control. Apparently, with an increase in the length of time for health jogging, a gradual physiologically beneficial weakening of the expression of the P2Y12 receptor to ADP occurs in platelets, which serves as the main factor determining the level of ADP-induced aggregation [38].

In this regard, we can say that regular aerobic physical activity is able to lower the average platelet volume and restrain the level of their ADP-induced aggregation. At the same time, the severity of the weakening of platelet aggregation is largely associated with the experience of these trainings, as a result of which, apparently, the amount of GP IIb-IIIa, which is very significant for this process, decreases on platelets. In a previous study [39], direct correlations were found between the expression of this protein and ADP-induced platelet aggregation without taking into account the attitude to physical activity of the subjects.

In this study, it was possible to establish a reliable and strong relationship between the average platelet volume and the content of GP IIb-IIIa on the platelet surface. This was the case for physically untrained and undergoing physical activity for different periods. The data obtained in this work on the relationship between the average platelet volume and the level of GP IIb-IIIa on platelets confirm the results of a previous study [11].

In physically exercising and avoiding physical exertion, a strong relationship was also found between the average platelet volume and the amount of the GP Ib receptor, which is very significant for the implementation of their adhesion. At the same time, as the length of the health jogging experience increased, the level of GP Ib expression weakened, thereby contributing to a decrease in the ability of platelets to adhere.

The results of the study and the work of other authors give grounds to say that the interrelated severity of expression of GP IIb-IIIa and GP Ib and the size of the bulk of platelets depend on the level of human physical activity, an increase in which contributes to their decrease. For example, in athletes, direct correlations were found between the content of GP IIb-IIIa and GP Ib and the average platelet volume, which is quite expected, given the strong dependence of the weakening of the expression of both glycoproteins on the reduction of the platelet surface area during physical exertion. At the same time, it was previously noted that the activity of the expression of collagen receptors on platelets involved in their adhesion with the severity of environmental influences on the body was noted [40,41]. It is becoming clear that an important regulatory mechanism that maintains platelet activity at an optimal level is regular physical activity above daily activity [42]. Apparently, daily physical activity of aerobic nature in the form of jogging contributes to a decrease in the size of platelets circulating in the blood and the redistribution of receptors between their plasma membrane and their internal membranes (the surface of platelet granules and membrane of the tubular system), which leads to a decrease in the activity of platelet participation in hemostasis processes.

CONCLUSION

The variation of the mean platelet volume, the severity of platelet aggregation activity, and the number of GP IIb-IIIa and GP Ib on platelets were assessed in people of the second mature age who jogged in a free mode for different periods. A group of healthy untrained volunteers served as a control. It was found that as the experience of physical aerobic exercise increases, the average volume of platelets decreases, their ability to aggregate decreases, and the amount of GP IIb-IIIa and GP Ib on their surface decreases. As a result of the study, it can be argued that an important regulator of the mechanisms that implement platelet activity is the level of daily regular aerobic physical activity. At the same time, daily jogging in men of the second mature age helps to reduce the size of the bulk of platelets in the blood, redistribute receptors between their plasma membrane and their inner membranes, and weaken their aggregation ability.

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CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

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