EFFECT OF PHYSICAL ACTIVITY ON BLOOD LIPIDS AND ADRENAL FUNCTION DURING EMOTIONAL STRESS

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It is generally accepted on the basis of several investigations that physical activity has an antiatherogenic effect [3, 7, 10], and that atherosclerosis and myocardial infarction develop less frequently in physically active people [1, 5, 11-13]. Modern man characteristically leads an immobile mode of life and is exposed to a high level of psychoemotional stress, which promotes atherogenesis. However, the effect of physical exertion on the physically untrained and trained subject in a state of emotional stress has not been adequately studied.

The object of this investigation was to study the effect of intensive physical exertion on the indices of lipid metabolism and functional activity of the adrenal cortex in physically trained and untrained animals.

EXPERIMENTAL METHOD

Experiments were carried out on 10 mongrel dogs aged 2 years (five were physically untrained and five were trained). Physical training, consisting of running on a treadmill, was carried out gradually: The duration of running was increased in the course of 15 days from 15 min to 60 min, with the belt moving at a velocity of 7 km/h. Daily training exercises lasting 60 min on the treadmill continued for 90 days, after which emotional

TABLE 1. Effect of Intensive Physical Exertion on Blood Cortisosteroid and Lipid Levels in Dogs after Emotional Stress (first cycle of investigation; M ± m)

Group of animals	Stage of experiment	Corticosteroids, μg %	Triglycerides	Phospholipids	Cholesterol	β-lipoproteins
			mg %			
Untrained	Control (n = 5)	3,91±0,5	106±18,5	188,4±17,1	177±7,0	156±15,0
	Initial level (60th day after stopping hydrocortisone)	2,38±0,2	166,1±19	183,2±13,8	236,2±16,5	289±24,6
	P	<0,02	<0,05	>0,5	<0,01	<0,01
	Stress – 24 h in frame	5,82±1,4	373,8±9,3	442±16,8	506,2±21,2	560±18,2
	P_1	<0,05	<0,001	<0,001	<0,001	<0,001
	Physical exertion	7,16±1,4	526,4±22,1	580±16,7	619,2±28,5	888±13,8
	P_1	<0,001	<0,001	<0,001	<0,001	<0,001
	After resting for 24 h	4,66±1,1	287±13,3	370±17,5	488±20,8	540±18,1
	P_1	<0,05	<0,001	<0,001	<0,001	<0,001
Trained	Control (n = 5)	5,1±0,1	97,6±16,8	184,6±9,6	191,4±3,4	172±11,5
	Initial level (60th day after stopping hydrocortisone)	6,38±0,8	106,3±11,2	161,6±3,1	209,4±9,3	206±13,8
	P	>0,5	>0,5	>0,05	>0,5	>0,5
	Stress – 24 h in frame	9,78±0,7	162±11,1	221±11,7	281,6±19,2	291±13,6
	P_1	<0,02	<0,002	<0,001	<0,001	<0,002
	Physical exertion	10,26±0,6	181,2±13,4	240,4±15,9	301,5±13,4	320±24,5
	P_1	<0,02	<0,001	<0,001	<0,001	<0,001
	After resting for 24 h	8,32±1,08	140,8±15,2	205,1±12,6	265,8±14,2	270±13,6
	P_1	>0,5	>0,5	<0,01	<0,05	<0,002

Legend. Here and in Table 2: P obtained by comparing mean value with control, P_1 by comparing with initial level.

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TABLE 2. Effect of Intensive Physical Exertion on Blood Corticosteroid and Lipid Levels in Dogs after Emotional Stress (4th cycle of investigation; M ± m)

Group of animals	Stage of experiment	Corticosteroids, μg %	Triglycerides	Phospholipids	Cholesterol	β-lipoproteins
			mg %			
Untrained	Control	3,91±0,5	106±18,5	182,4±17,1	177±7,0	156±15,0
	Initial level (end of third cycle)	1,82±0,4	276±18,8	212,4±16,4	310,2±11,5	290±23,1
	P	<0,001	<0,001	>0,5	<0,001	<0,001
	Stress – 24 h in frame	1,58±0,3	341,1±20,8	275,8±5,0	370±28,4	340±13,8
	P_1	>0,5	>0,5	<0,01	>0,5	>0,5
	P	<0,001	<0,001	<0,001	0,001	<0,001
	Physical exertion	1,18±0,1	237,1±13,5	183,4±11,7	275±37,1	268±17,4
	P_1	>0,5	>0,5	>0,5	>0,5	>0,5
	P	<0,001	<0,001	>0,5	<0,05	<0,001
	After resting for 24 h	1,44±0,3	246,3±13,5	192,4±9,4	290,1±24.5	310±14,1
	P_1	>0,5	>0,5	>0,5	>0,5	>0,5
	P	<0,001	<0,001	>0,5	<0,002	<0,001
Trained	Control	5,1±0,1	97,6±16,8	184,6±9,6	191,4±3,4	182±11,5
	Initial level (end of third cycle)	6,34±0,5	105,5±10,3	163,3±3,8	207,1±16,1	210±3,6
	P	>0,5	>0,5	>0,5	>0,5	>0,5
	Stress–24 h in frame	6,98±0,2	118,6±18,9	174,4±11,8	213±13,4	224±7,9
	P_1	>0,5	>0,5	>0,5	>0,5	>0,5
	P	<0,001	>0,5	>0,5	>0,5	<0,05
	Physical exertion	6,48±1,2	108,1±11,1	169,7±13,4	210±14,2	205±18,1
	P_1	>0,5	>0,5	>0,5	>0,5	>0,5
	P	>0,5	>0,5	>0,5	>0,5	>0,5
	After resting for 24 h	6,82±0,7	114,1±15,1	178,6±3,8	211±16,8	212±13,8
	P_1	>0,5	>0,5	>0,5	>0,5	>0,5
	P	<0,001	>0,5	>0,5	>0,5	>0,5

hyperlipemia was produced in the animals of both groups by subcutaneous injection of hydrocortisone in a dose of 13 mg/kg body weight/day for 5 days. Physical exertion inhibited the development of hydrocortisone hyperlipemia [7]. On the 60th day after stopping hydrocortisone, the lipid level in the physically active dogs was indistinguishable from that in the control, whereas in the untrained animals slight but definite hyperlipemia continued. Against this background emotional stress was induced in both groups of animals by keeping the dogs for 24 h in a special frame, restricting their freedom of movement, after which they ran on the treadmill until complete exhaustion (the dogs lay down on the treadmill belt). The animals were then allowed to rest. The physically trained animals endured the exertion for 1 h 40 min, the untrained dogs for 30 min. Every 5 days the cycle of stress, running until exhaustion, and rest was repeated. Altogether there were four cycles. Blood levels of corticosteroids [6], cholesterol [14], triglycerides [14], phospholipids [9], and β-lipoproteins [2] were determined after stress and running and after one day of rest.

EXPERIMENTAL RESULTS

The results showed that emotional stress in both untrained and physically trained animals was accompanied by an increase in the blood corticosteroid and lipid levels (Table 1). Stress induced more marked hyperlipemia in the untrained dogs: the cholesterol concentration was increased by 114%, triglycerides by 124%, phospholipids by 111%, and β-lipoproteins by 93%. Meanwhile, in physically active animals the cholesterol concentration increased after stress by only 34%, triglycerides by 52%, phospholipids by 32%, and β-lipoproteins by 41% compared with initially. Physical exertion to exhaustion, applied against the background of changes evoked by stress, was accompanied by an even greater increase in the blood lipid and corticosteroid concentration in the physically untrained animals: the cholesterol concentration rose by 162%, triglycerides by 216%, phospholipids by 218%, and β-lipoproteins by 207% compared with initially. Compared with the control, the cholesterol concentration increased by 250% (to 619 mg% compared with 177 mg%; $P < 0.001$). In the group of physically trained dogs the same tendency toward an increase in hyperlipemia was observed after running to exhaustion, but it was less marked. After rest for one day the lipid level in the physically active dogs fell and came close to its initial value. Marked hyperlipemia was preserved in the untrained animals. In the 3rd and 4th cycles of the investigation the blood cholesterol and lipid concentration of the trained dogs returned to normal and remained stable regardless of circumstances. In the 4th cycle on untrained animals the blood cholesterol level fell, but there was no response of the adrenals to stress, evidently because of exhaustion of adrenocortical function. Marked hyperlipemia continued.

It can be concluded from the results of this investigation that intensive physical exertion against the background of stress aggravates disturbances of lipid metabolism due to stress. Particularly sharp disturb-

ances arise in physically untrained animals. Repetition of stress with intensive physical exertion in physically untrained animals is accompanied by exhaustion of the adrenal cortex against the background of persistent and marked hyperlipemia and can be regarded as an atherogenic factor [8]. It will be clear that the use of physical activity as a means of preventing atherosclerosis demands exact criteria of the degree of change of the individual. The use of considerable physical exertion after stress not only restores normal indices of lipid metabolism, but also considerably enhances the hyperlipemia in physically untrained individuals.

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PROTEOLYSIS OF PROTHROMBIN BY β/γ-THROMBIN

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The principal function of the serine proteinase of thrombin is specific cleavage of four bonds between Arg-Gly amino acid residues in the fibrinogen molecule, which triggers the process of fibrin formation. Thrombin also catalyzes proteolysis of various secondary substrates. Prothrombin is hydrolyzed by thrombin at the Arg^{156}-Ser^{157} bond with the formation of prethrombin 1 and fragment I of prothrombin [6, 9, 11]. Prethrombin 1, which has no calcium binding sites, which are located in fragment I, cannot be effectively converted into thrombin and may accumulate in the blood, thus producing self-regulation of thrombin formation [9, 10]. The existence of numerous forms of thrombin, arising through partial proteolysis or autolysis of the enzyme, has recently been demonstrated [2, 5, 8, 11]. Conversion of α-thrombin into the β- and γ-forms is accompanied by loss of coagulating, but preservation of esterase, activity. Inclusion of the γ-form into the stage of fibrin stabilization through activation of factor XIII has been demonstrated [7]. There is no evidence that low-molecular-weight forms of thrombin participate in the regulation of thrombin formation. The object of this investigation was to study the action of β/γ-thrombin on prothrombin, and it was found that proteolytic

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