ADRENOCORTICAL REGULATION OF PROTEIN METABOLISM DURING PROLONGED PHYSICAL EXERTION

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Experiments on male Wistar rats revealed inhibition of incorporation of labeled amino acids into tissue proteins during swimming. If prolonged swimming was accompanied by increased adrenocortical activity, the blocking of protein synthesis in the liver disappeared. Adrenalectomy prevented activation of alanine aminotransferase and the fall in the free amino acid level in the liver during physical exertion, whereas injection of corticosterone into adrenalectomized animals restored these changes.

KEY WORDS: protein synthesis; muscular work; corticosterone; alanine aminotransferase; adrenalectomy.

The role of glucocorticoids in the induction of synthesis of enzyme proteins and in the supplying of amino acids for this process [3, 4, 7] highlights a channel in their action on protein metabolism through which corticosteroids control adaptive processes.

In this investigation the role of glucocorticoids was studied in the regulation of protein metabolism during muscular work.

EXPERIMENTAL METHOD

Male Wistar rats weighing 170-210 g were used. The animals were made to undergo physical exertion, in the form of swimming in water at a temperature of 33°C, for 1.5 h without a load, for 1.5 h with a load (6% of body weight), and for 6 h or 12 h without a load. The rats in the experiments involving swimming for 3 h were adrenalectomized. The concentrations of free amino acids in the liver, myocardium, skeletal muscle, and blood plasma were determined with the Hitachi KLA33B analyzer. Activity of alanine aminotransferase in the liver [10] and the intensity of incorporation of ^{14}C-amino acids into proteins of the liver, heart, and skeletal muscle were determined. Labeled protein digests with a radioactivity of 50 μCi was injected intraperitoneally 1.5 h before the end of physical exertion. The radioactivity of the tissue preparations was determined with the "Protok" apparatus in counts/100 sec/g protein. Protein was determined by Lowry's method [8]. The corticosterone concentration in the blood plasma, determined fluorometrically after thin-layer chromatography, was used as the index of adrenocortical activity.

EXPERIMENTAL RESULTS AND DISCUSSION

During swimming for 1.5 h without a load, the incorporation of amino acids into liver proteins decreased, but into myocardial proteins it increased (Table 1). During swimming while loaded, incorporation of amino acids into proteins of all tissues studied decreased. At the end of swimming for 12 h unloaded, incorporation of amino acids into proteins of skeletal and heart muscles was reduced, whereas into liver proteins it was the same as in the control. It is important to note that these changes occurred against the background of a raised blood corticosterone level. During exertion under other conditions no significant changes in the blood corticosterone concentration were found (Table 2).

The antianabolic changes arising in the tissues during physical exertion [1, 11] can thus be manifested when the blood glucocorticoid concentration is substantially unchanged. However, an increase in adrenocortical

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TABLE 1. Effect of Physical Exertion on Incorporation of Amino Acids into Tissue Proteins (changes in % of control, M ± m)

Test object	Swimming for 1.5 h unloaded	Swimming for 1.5 h loaded	Swimming for 12 h unloaded
Liver	−32,2±1,3 (6)*	−29,2±2,9 (6)*	−10,7±5,6 (10)
Myocardium	+10,1±1,7 (6)*	−31,3±3,2 (6)*	−27,3±5,0 (8)*
Skeletal muscle	−1,1±8,7 (6)	−41,1±5,1 (6)*	−44,4±2,6 (8)*

Legend. Here and in Tables 2 and 3, statistically significant ($P < 0.05$) changes are marked by an asterisk. Number of experimental animals given in parentheses.

TABLE 2. Blood Plasma Corticosterone Concentration (in μg %) after Swimming for 1.5 and 12 h

Test object	Control group	Swimming for 1.5 h loaded	Swimming for 12 h unloaded
I	7,6±0,77 (8)	7,9±0,65 (9)	14,2±1,75 (9)*
II	15,4±0,52 (6)	17,0±0,01 (6)	—
III	20,6±1,59 (6)	—	38,7±3,62 (8)*

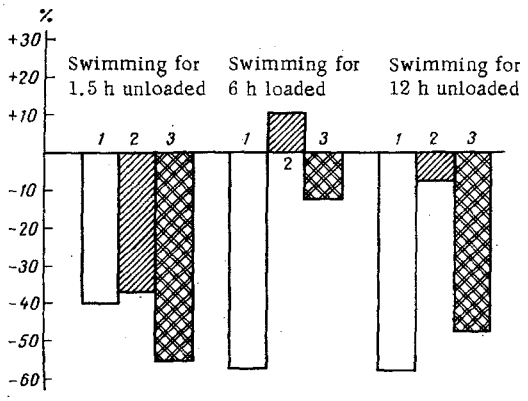

Fig. 1

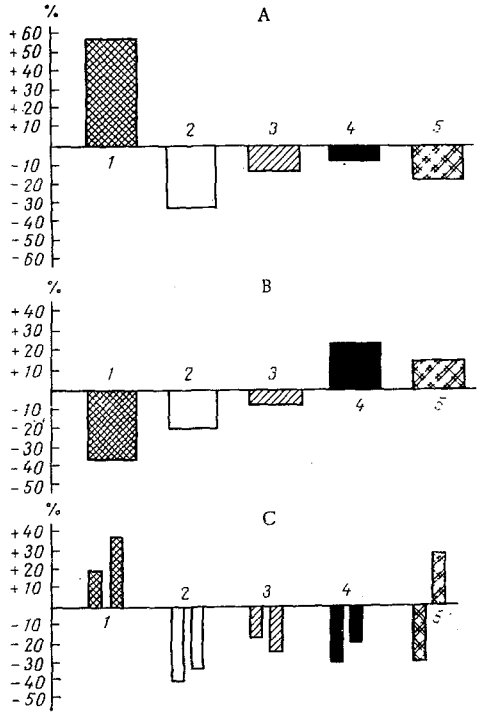

Fig. 2

Fig. 1. Content of free amino acids (in % of control) in liver (1), myocardium (2), and skeletal muscle (3) of rats after swimming with different loads.

Fig. 2. Content (in % of control) of corticosterone in blood plasma (1) and of free amino acids in liver (2), myocardium (3), skeletal muscle (4), and blood plasma (5) during swimming for 3 h by rats undergoing mock adrenalectomy (A), adrenalectomized rats (B), and adrenalectomized rats receiving corticosterone (C).

activity may be an important condition for restoration of protein synthesis in the liver during prolonged expenditure of energy.

The concentration of free amino acids fell during swimming for 1.5 h loaded in all tissues, during swimming for 6 h it fell only in the liver, and during swimming for 12 h it fell both in the liver and in skeletal muscle (Fig. 1). The main contribution to the free amino acids in the liver was made by asparagine, threonine, serine, glutamine, glycine, and alanine; in the myocardium by asparagine, threonine, and glutamine; in skeletal muscle by lysine, histidine, threonine, serine, glutamine, glycine, and alanine. Under the influence of exertion the concentrations of these amino acids varied in the same direction as their total content.

The experiments on adrenalectomized rats showed that the decrease in concentration of amino acids in the liver was connected with the action of glucocorticoids. For instance, in rats undergoing the mock operation

TABLE 3. Blood Plasma Corticosterone Concentration and Liver Alanine Aminotransferase Activity of Adrenalectomized Rats and of Rats Undergoing Mock Operation

Index studied	Corticosterone, μg%		Adrenalectomized		Adrenalectomized + corticosterone
	control	after exertion	control	after exertion	after exertion
Corticosterone, μg%	18,1±3,92 (7)	29,0±4,56 (6)*	9,3±0,87 (6)	7,8±0,43 (4)	22,6, 25,6
Alanine aminotransferase activity, conventional units/mg protein	2,17±0,05 (6)	2,50±0,13 (5)*	1,83±0,12 (7)	1,65±0,15 (6)	2,26, 2,41

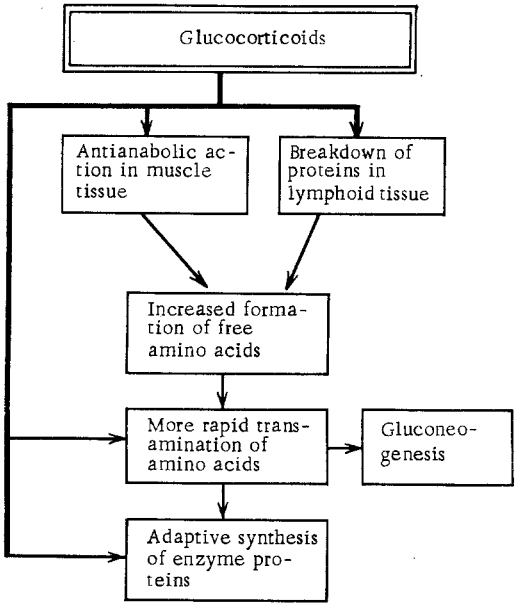

Fig. 3. Scheme representing effect of glucocorticoids on protein metabolism.

and made to swim for 3 h, the blood plasma corticosterone concentration rose but the content of free amino acids in the liver fell (Fig. 2). In skeletal and heart muscles and blood plasma it was substantially unchanged. Of the adrenalectomized rats kept on a diet with salt, those which were in a good condition 7-8 days after the operation were used in the experiments; the reason why they were in this good condition was evidently the development of accessory adrenocortical tissue. Evidence of this was given by their very high blood corticosterone concentration (9.3 ± 0.87 μg%), which fell after swimming for 3 h. Swimming caused no significant decrease in the liver amino acid level of these animals. However, in two adrenalectomized rats which received 125 μg corticosterone by intramuscular injection before swimming, the exercise led to a decrease in the liver amino acid content.

The decrease in content of free amino acids in the liver under the influence of glucocorticoids was evidently connected with induction of the synthesis of enzyme proteins. This was shown by the parallel increase in the blood corticosterone concentration and alanine aminotransferase activity in the liver (Table 3). The original activity of the enzyme in the adrenalectomized animals was significantly lower than in animals undergoing the mock operation. During exertion a tendency was observed for the enzyme activity to diminish further. If, however, corticosterone was injected into the adrenalectomized rats before swimming, their enzyme activity after swimming was the same as in animals undergoing the mock operation.

A scheme reflecting modern views on the influence of glucocorticoids on protein metabolism is given in Fig. 3. The antianabolic action of glucocorticoids, especially in muscle tissue, and the increased breakdown of proteins under their influence in lymphoid tissue [2] lead to increased formation of free amino acids [5], i.e., to the creation of reserves of "building materials" for protein synthesis. Under the influence of glucocorticoids, transamination reactions are also intensified [2, 9], i.e., there is a move toward the preparation of amino acids for protein synthesis and deamination, accompanied by increased production of protein metabolites

[6] and increased glycogen synthesis in the liver at the expense of nonnitrogenous residues of amino acids [9]. The intensification of transcription and translation processes through the influence of glucocorticoids completes the chain of changes in adaptive synthesis of enzyme proteins [3, 4].

The results described above indicate that during prolonged physical exertion glucocorticoids play an important role in the regulation of enzyme synthesis and in the provision of amino acids prepared (transaminated) specially for this process.

LITERATURE CITED

1. A. S. Bazul'ko and V. A. Rogozkin, "Works on physical culture," Uchen. Zapiski Tartu. Univ., 5, No. 311, 43 (1973).
2. R. M. Pakhomovich, in: Textbook of Endocrinology [in Russian], Moscow (1973), p. 231.
3. N. A. Yudaev and T. N. Protasova, Usp. Sovrem. Biol., 72, No. 1, 118 (1971).
4. D. Feldman, J. W. Funder, and J. S. Edelman, Am. J. Med., 53, 545 (1972).
5. H. D. Hoberman, Yale J. Biol. Med., 22, 341 (1950).
6. D. J. Ingle, Ann. N.Y. Acad. Sci., 50, 576 (1949).
7. P. Karlson, Perspect. Biol. Med., 6, 203 (1963).
8. O. H. Lowry, N. J. Rosebrough, A. L. Farr, et al., J. Biol. Chem., 193, 265 (1951).
9. D. Matzett, A. Oriol-Bosch, and K. D. Voigt, Biochem. Z., 335, 485 (1962).
10. S. Reitman and R. Frankel, Am. J. Clin. Pathol., 28, 56 (1957).
11. H. G. Zimmer and E. Gerlach, in: Limiting Factors of Physical Performance (International Symposium) (edited by J. Keul), Stuttgart (1973), p. 102.

EFFECT OF SODIUM SUCCINATE ON SOME INDICES OF CARBOHYDRATE METABOLISM OF THE ISCHEMIC MYOCARDIUM

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The effect of sodium succinate on the concentrations of lactic and pyruvic acids and of glucose in blood draining from the ischemic zone was investigated in experiments on dogs in which the coronary artery was ligated. After intracoronary injection of the compound in doses of 2 and 10 mg/kg the lactic acid concentration was lowered in blood flowing from the ischemic zone: In a dose of 10 mg/kg sodium succinate reduced the assimilation of glucose by the ischemic area of myocardium a little. After intravenous injection of sodium succinate in a dose of 100 mg/kg the lactic acid concentration also fell significantly and the utilization of glucose by the ischemic myocardium was inhibited and its concentration in the arterial blood rose considerably. The reduction in the blood lactic acid concentration may have been due to activation of the Krebs' cycle and increased utilization of oxygen in the ischemic region of the myocardium.

KEY WORDS: myocardial ischemia; succinate; carbohydrate metabolism.

During regional hypoxia of the myocardium succinic acid has many advantages as a source of energy because of the greater rapidity of its oxidation and because of the flavin nature of succinate dehydrogenase [2]. Accumulation of reduced forms of NAD is the factor limiting energy formation in the ischemic myocardium.

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