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CYCLIC AMP SYSTEM IN MUSCLE TISSUE DURING PROLONGED HYPOKINESIA

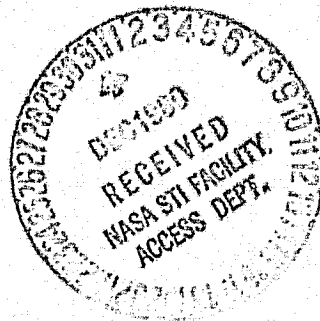
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16. Abstract Components of the cyclic AMP system in the muscle tissue of white rats were studied during 70-75 days of hypokinesia, created by placing the animals in small booths which restricted their movements, and during the readaptation period. In the initial period, cyclic AMP levels and the activities of phosphodiesterase and adenylate cyclase in muscle tissue were increased. The values for these indices were roughly equal for controls and experimental animals during the adaptation period, but on the 70th day of the experiment cAMP levels dropped, phosphodiesterase activity increased, and the stimulative effect of epinephrine on the activity of adenylate cyclase decreased. The indices under study normalized during the readaptation period. (cAMP = Adenosine-3',5'-cyclic-3',5'-monophosphate)		
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CYCLIC AMP SYSTEM IN MUSCLE TISSUE DURING PROLONGED HYPOKINESIA

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Components of the cyclic AMP/^(cAMP)system in the muscle tissue of white 765* rats were studied during protracted hypokinesia (70-75 days) and during the readaptation period. It was ascertained that the level of cAMP and activities of adenylyl cyclase and phosphodiesterase in muscle tissue were elevated during the initial period of motion restriction (particularly on the 5th day). Cyclic AMP content and the activities of both enzymes during the so-called adaptation period (24th to 37th days) did not materially differ from the controls. On the 70th day of the experiment, a sharp drop in cAMP level, increase in phosphodiesterase activity, 766 and decrease in the stimulative effect of epinephrine on the activity of adenylyl cyclase were noted. Appreciable normalization of the indices under study occurred in the readaptation period.

The harmful effects of hypokinesia (restricted motion) on the human and animal body have been familiar to clinicians and biologists for quite some time. Protracted motor activity limitation causes decreased body mass, which, obviously, is associated to a large extent with decreased overall skeletal muscle mass. Dystrophy of parts of muscle fibers occurs, enzyme activities and the fractional makeup of muscle proteins are altered, and shifts in carbohydrate metabolism are noted [1, 2, 5]. Hence, a protracted hypokinetic state is accompanied by serious disturbances in muscle tissue metabolic processes. It has been distinctly shown in recent years that components of the cAMP system play an important role in the regulation of cell metabolism [6]. There are, however, virtually no data in the literature dealing with cAMP content and the activities of adenylyl cyclase and phosphodiesterase in muscle tissue during hypokinesia. In this connection, we set out to study the status of the cAMP system in the skeletal musculature of white rats during various periods of hypokinesia and during the readaptation period.

*Numbers in the margin indicate pagination in the foreign text.

Methodology

The experiments were conducted using non-purebred white rats. Hypokinesia was created by placing the animals in special booths which restricted their movements. Muscle tissue (m. gastrocnemius) was studied during the various periods of hypokinesia (2, 5, 24, 37, and 70 days) and on the 7th day of readaptation. White rats kept under normal vivarium conditions served as the controls. Content of cAMP was determined immunoradiologically using a prepared reagent kit from the "Amersham" company (England), and the activities of adenylyl cyclase and phosphodiesterase were studied using ^3H -ATP and ^3H -cAMP isotopes, respectively, as substrates [4, 7].

Results and Discussion

1767

Determinations of cAMP system components in the muscle tissue of white rats during protracted hypokinesia and in the readaptation period are presented in the table.

As can be seen in the table, on the 2nd to 5th days of hypokinesia the activity of adenylyl cyclase increased an average of 2.3 times and that of phosphodiesterase an average of 1.2 times, while the cAMP level was elevated an average of 1.9 times relative to the controls. The content of all components under study gradually decreased up to the 24th to 37th day of hypokinesia, reaching practically normal values. On the 70th day of hypokinesia the cAMP levels decreased significantly and the activity of phosphodiesterase -- an enzyme that breaks down cAMP -- increased to a statistically significant extent, while the activity of adenylyl cyclase remained virtually unchanged. During the readaptation period (data on the 7th day are shown in the table) cAMP levels and the activities of adenylyl cyclase and phosphodiesterase were practically normalized.

On analyzing the data obtained, it is quite easy to see that, in the initial period of hypokinesia (particularly on the 5th day), activation of the cAMP system occurs, and then the "adaptation" period (24th to 37th days) begins and cAMP system component contents in muscle tissue

TABLE 1. CAMP CONTENT AND THE ACTIVITIES OF ADENYL CYCLASE AND PHOSPHODIESTERASE IN MUSCLE TISSUE DURING HYPOKINESIA AND IN THE READAPTATION PERIOD

Substance	Hypokinesia						Readaptation							
	Control	n	Day 2	n	Day 5	n	Day 24	n	Day 37	n	Day 70	n	Day 7	n
CAMP pmoles in 1 mg tissue	748.6 ± 38.2	26	489.2 ± 71.4	12	692.8 ± 53.1	15	316.8 ± 53.1	12	333.2 ± 36.2	12	144.0 ± 31.2	15	276.1 ± 12.0	12
			> 0.05		< 0.01		> 0.50		> 0.05		< 0.01		> 0.10	
Adenyl cyclase pmoles per 1 mg protein per min.	7.81 ± 0.55	21	11.61 ± 0.72	12	18.04 ± 2.40	14	9.76 ± 1.92	12	8.74 ± 1.70	10	16.61 ± 1.08	15	9.52 ± 0.95	12
			< 0.01		< 0.01		> 0.10		> 0.30		> 0.05		> 0.05	
Phosphodiesterase pmoles per 1 mg protein per minute	751.2 ± 58.7	15	841.2 ± 46.4	10	651.0 ± 48.5	10	838.7 ± 61.7	10	791.1 ± 62.5	10	800.1 ± 11.2	10	810.2 ± 83.5	10
			> 0.10		< 0.05		> 0.10		> 0.20		< 0.05		> 0.05	

N. B.: P is calculated relative to control.

are within normal limits. On the 70th day of hypokinesia, a period of cAMP system depletion is found (cAMP levels are only 39% of normal). It should be noted that the sharp decrease in muscle tissue cAMP content on the 70th day of hypokinesia was seen upon a background of normal values for the activity of adenyl cyclase -- an enzyme participating in cAMP synthesis.

This fact compelled us to make a study of the so-called stimulated activity of adenyl cyclase during the protracted hypokinesia period. We are familiar with the fact that adenyl cyclase activity normally increases sharply when epinephrine is added to a tissue homogenate [3]. Studies we performed (see figure) showed that addition of epinephrine in concentrations of 3×10^{-4} M to homogenates of muscle tissue from the control rats led to a 2.9-fold increase in adenyl cyclase activity ($P < 0.01$), while the activity of this enzyme in homogenates of muscles from experimental rats increased only 1.4 times ($P < 0.05$) in the presence of epinephrine (70th day of hypokinesia). Consequently, qualitative shifts in the adenyl cyclase complex occur during protracted hypokinesia. There is some basis for assuming that further studies on this subject will make it possible to discover the true mechanisms of

muscle tissue metabolic disruptions
during protracted hypokinesia and
find ways to correct them.

Adenyl cyclase activity
pmoles cAMP in 1 mg
protein per minute

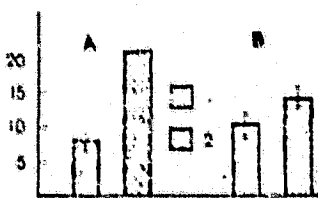


Fig. 1. The effects of epinephrine on the activity of adenyl cyclase in muscle tissue homogenates, normal conditions and during protracted hypokinesia.

- 1 -- without addition of epinephrine.
- 2 -- in the presence of epinephrine (3×10^{-4} M).
- A -- control; B -- hypokinesia (70 days).

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