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ATP-induced changes in rat skeletal muscle contractility

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BACKGROUND: Extracellular purine compounds, adenosine triphosphate (ATP) and adenosine, are involved in regulation of many cell functions, engaging in rapid and long-term cellular processes. The nucleotides, including ATP, exert their extracellular effects by influencing membrane P2 receptors. ATP outside of the cell rapidly is metabolized by the ecto-enzyme system to produce adenosine, which acts on separate adenosine (P1) receptors. Since adenosine and ATP often are functional antagonists, ATP degradation not only limits its effect, but also brings new ligand with different, often opposing, properties. Great variety and widespread of P2 and adenosine receptors in the body emphasize the important physiological and pathophysiological significance of these receptors, and make them very attractive as targets for potential drug action.

The existence of several subtypes of P2 and adenosine receptors has been shown in the skeletal muscles. ATP as a co-transmitter is densely packed together with classical neurotransmitters in the presynaptic vesicles of vertebral motor units but until recently ATP was refused to have its own functional role there and was recognized only as a source of adenosine. However, on the eve of the third millennium there appeared data that ATP, released from the nerve ending and acting on presynaptic P2 receptors, suppresses subsequent quantum release of acetylcholine. The final product of its degradation, adenosine, performs a similar inhibitory effect acting on presynaptic adenosine receptors.

Despite the fact that the mechanisms of presynaptic inhibitory action of ATP and other purines were studied earlier, the object of those studies was usually neuromuscular synapse of cold-blooded animals. The few studies, in which experiments were carried out on preparations of warm-blooded animals, described the basic effects of purines. These often were guided by the convenience of preparation of the synapses of the diaphragm. We think that those results cannot be considered as typical effects of ATP and other purines on skeletal muscles and could not be extrapolated to all warm-blooded animals. Furthermore the role of ATP and its derivatives in the accumulation of vertebrate muscular effort has not been investigated.

It is known that in physiological conditions vertebrates may mobilize only up to a third of the maximum muscle force. Why the two-thirds of muscular strength are not used normally but may be used at stress, remains unknown.

It is known that the body's adaptive response to stress is a change in the activity of the endocrine system. The leading role in this is given to catechol amines and glucocorticoids, mobilized in significant quantities in blood under stress.

We have found previously that incubation of frog sartorius muscle with hydrocortisone resulted in a decrease of contraction amplitude. However, when hydrocortisone was used in combination with ATP, its inhibitory effect on contractile responses disappeared. It is interesting that hydrocortisone had

no effect on the inhibitory effect of adenosine. In the following experiments, assessing the effect of hydrocortisone on rat soleus muscle, it was established that hydrocortisone and purines had similar inhibitory effect. When ATP and hydrocortisone were given together the same oppression occurred.

OBJECTIVE: To study the effects of ATP and adenosine on contraction parameters of rat skeletal muscle and assess the impact of the catechol amines on these processes.

METHODS: Contractions of rat soleus muscles were recorded isometrically by mechanical sensor Linton FSG-01 (UK) according to standard procedures. The average of muscle parameters received within 30 seconds (30 responses) was treated as one result. Amplitude and time characteristics of the curve reductions were estimated. During all experiments standard Krebs solution flowed through the bath continuously to which agents were added at necessary concentrations. All experimental animals were maintained and prepared for dissection under the European Convention for the Protection of Vertebrate Animals used in scientific experiments. All agents used in the study were supplied by Sigma Chemical Company Ltd. (UK), Tocris Cookson and Research Biochemicals International (USA).

RESULTS: The concentration of 100 μM for adenosine is close to saturation [1], and for its predecessor ATP this concentration is created after the passage of a pulse through the synapse [2]. We used this concentration of purines to study the mechanism of action of adenosine and ATP on neuromuscular synapse.

The effect of adenosine was partially inhibited in the presence of 100 μM 8-SPT, an antagonist of adenosine receptors. The contraction force of "fast" and "slow" rat skeletal muscles was raised by half in the presence of norepinephrine. In the presence of norepinephrine adenosine exerted its effect fully, but ATP by half reduced its depressor effect on the contraction force of both muscles.

CONCLUSIONS:

1. Norepinephrine increases half times of the reduction of «fast» and «slow» skeletal muscle.
2. In the presence of norepinephrine, inhibitory effect of adenosine on contraction force is maintained.
3. Inhibitory effect of ATP on contraction force of studied skeletal muscles becomes twice less pronounced in the presence of norepinephrine.

We think that reduction of ATP depressive effect on the skeletal muscle by norepinephrine may be an adaptive response to acute stress.

Keywords: Norepinephrine, effect of ATP, rat, skeletal muscle, neuromuscular synapse

References

[1] Ribeiro JA, Walker J. The effects of adenosine triphosphate and adenosine diphosphate on transmission at the rat and frog neuromuscular junctions. Br J Pharmacol. 1975;54(2):213-8. doi:10.1111/j.1476-5381.1975.tb06931.x

[2] Hume RI, Honig MG. Excitatory action of ATP on embryonic chick muscle. J Neurosci. 1986;6(3):681-90. Available from: http://www.jneurosci.org/content/6/3/681.full.pdf