THE EFFECT OF GLUTAMIC ACID, ASPARAGIN, GLYCOCOLL AND ALANINE ON THE CONTRACTILITY AND SENSITIZATION TO POTASSIUM IONS OF A SKELETAL MUSCLE

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At the end of the last century, substances which acted on skeletal muscles to produce prolonged rhythmic contractile activity were discovered. These substances include guanidine, aminopyridine, tetraethylammonium et al. In addition to the above effect, all these substances can considerably enhance the contractile reaction of a skeletal muscle to potassium ions [2, 7], which play an essential role in the process of muscular contraction. Since they are prevented by curare and by denervation [1, 2, 6], the effects of these substances must be due to acetylcholine, which can be liberated by potassium ions.

Besides the above variant of sensitization to potassium ions, there is another effect by veratrine [5]. Because neither curare nor denervation remove veratrine sensitization to potassium [1, 2, 9], it evidently develops in the muscle itself rather than in the synaptic region.

In previous investigations, we demonstrated the ability of various amino acids, glutamic acid included, to suppress the contractile activity of skeletal muscles induced by guanidine and proserine [3, 4].

This work studies the effect of glutamic acid, asparagin, glycocoll and alanine on skeletal muscle contractions induced by aminopyridine and tetraethylammonium, i.e., by substances which act like guanidine.

The experiments were performed on a frog's isolated rectus abdominis muscle. The muscle was placed in a bath containing a Ringer's solution through which oxygen was bubbled; after 1-2 hours, the muscle was subjected to the action of tetraethylammonium in a concentration of 1:25,000-50,000 or α-aminopyridine in a concentration of 1:50,000. The resulting contractions were recorded for 10-20 min with a kymograph, and then a freshly prepared solution of glutamic acid, asparagin, glycocoll or β-alanine (sodium bicarbonate was used to neutralize the glutamic acid solutions) was added.

In concentrations 1:1000 or higher, all the experimental amino acids showed an inhibitory effect of contractions induced by aminopyridine and tetraethylammonium (Fig. 1). In order to relative strength of effect, the amino acids were as follows: glutamic acid, asparagin, glycocoll, alanine.

It seemed possible to expect the amino acids to influence the other effect of guanidine and similarly acting substances, i.e., sensitization to potassium ions. The second portion of the work investigated this question. The same experimental object was used.

We established the potassium chloride concentration which caused minimal contraction of the muscle at the beginning of each experiment. After the Ringer's solution in the glass had been changed several times, the latter was filled with a Ringer's solution containing guanidine in a concentration of 1:40,000, tetraethylammonium in a concentration of 1:25,000-200,000 or α-aminopyridine in a concentration of 1:200,000 (alone, these concentrations were not sufficient to cause the muscle to contract); the concentration of potassium chloride was determined again after 5-10 min. Then an analogous determination was done in the presence of one of the above amino acids.

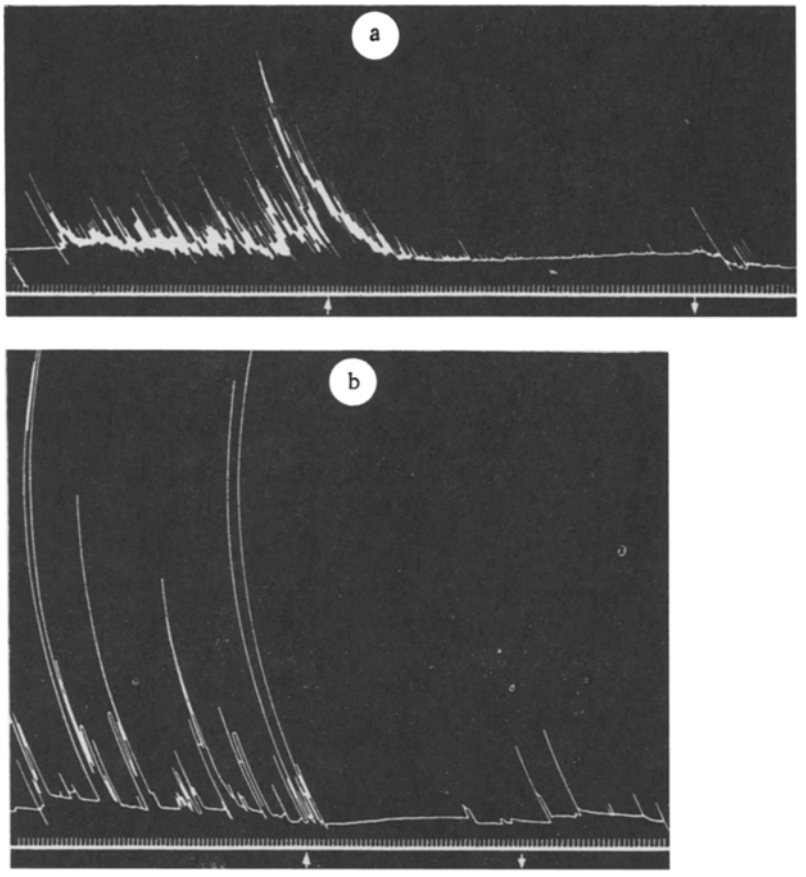

Fig. 1. Contractions of a frog's rectus abdominis muscle effected by aminopyridine in a concentration of 1:100,000 (a) and tetraethylammonium in a concentration of 1:25,000 (b). Up arrows – glutamic acid added in a concentration of 1:500,000; Down arrows–washing out. Time shown in 5-second marks.

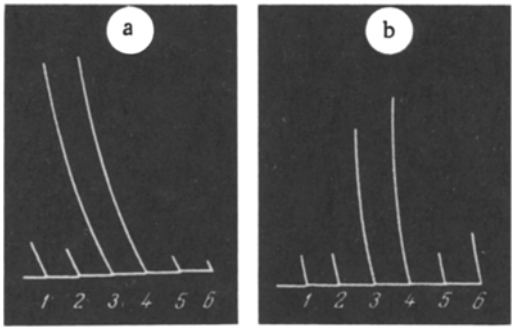

Fig. 2. Contractions of frog's rectus abdominis muscle effected by potassium chloride in a concentration of 1:2,500. a) 1, 2) Before action of tetraethylammonium; 3, 4) after 10-min action of tetraethylammonium in a concentration of 1:200,000; 5, 6) after 10-min action of 1:500 glutamic acid and 1:200,000 tetraethylammonium simultaneously; b) 1, 2) before action of veratrine; 3, 4) after 10-min action of veratrine in a concentration of 1:10,000,000 5, 6) after 10-min action of 1:500 glutamic acid and 1:10,000,000 veratrine simultaneously.

It was established that all the experimental amino acids (glutamic acid, asparagin, glycocoll and alanine) inhibit sensitization of a skeletal muscle to potassium ions by guanidine, tetraethylammonium and aminopyridine. This effect is produced by the same concentrations of the amino acids which were found to inhibit the muscle's rhythmic contractile activity. The strongest effect in this case also was observed with glutamic acid (Fig. 2,a). We were surprised to find that glutamic acid also inhibits the second type of sensitization to potassium, i.e., that induced by veratrine (Fig. 2,b). Asparagin and glycocoll produced a lesser inhibitory effect on veratrine sensitization. We could not obtain this effect in the experiments with alanine. Glutamic acid also inhibits caffeine sensitization to potassium ions, which is similar to that caused by veratrine [8]. It also reduces the potassium reaction of a nonsensitized muscle somewhat and diminishes the contracture induced by caffeine and quinine.

Therefore, glutamic acid inhibits not only effects associated with the synaptic region (contractions and sensitization to potassium induced in skeletal muscles by guanidine, tetraethylammonium and aminopyridine), but effects resulting from action on the muscle itself (veratrine and caffeine sensitization to potassium, contractures induced by potassium, caffeine and quinine) as well.

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