THE EFFECT OF GAMMA-AMINOBUTYRIC ACID ON THE POTASSIUM AND ACETYLCHOLINE CONTRACTIONS OF SKELETAL MUSCLE

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Translated from Byulleten Eksperimental'noi Biologii i Meditsiny, Vol. 55, No. 8, pp. 75-76, August, 1963
Original article submitted January 8, 1963

According to the widely accepted opinion, γ-aminobutyric acid is a metabolite of medullary tissue, participating in the regulation of synaptic excitation. However, the numerous investigations carried out with γ-aminobutyric acid contain contradictory data on its role in this regulation. On the basis of these data, some authors regard γ-aminobutyric acid as an inhibitory agent or an antagonist of acetylcholine [4]. In the opinion of other investigators, γ-aminobutyric acid does not influence the effects of acetylcholine [2, 7]. A number of authors contend that it takes part in the formation of a mediator of excitation [5] or is a synergist of acetylcholine [8].

We studied the effect of γ-aminobutyric acid on excitation in the central and peripheral synapses. In the first series of experiments, carried out on white mice [1], it was established that γ-aminobutyric acid exerts an anticonvulsive effect in association with cardiazol poisoning, and has no action in the presence of poisoning with strychnine or like substances, suppressing the enzymatic hydrolysis of acetylcholine by proserine.

In this work, we investigated the effect of γ-aminobutyric acid on acetylcholine and potassium contractions of skeletal muscle.

EXPERIMENTAL METHOD

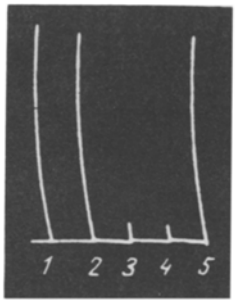
The experiments were carried out on the isolated rectus muscle of the frog's abdomen. The muscle was maintained undisturbed for a period of 1-2 h in a small beaker filled with Ringer's solution, through which oxygen was bubbled. After establishing the effective concentration of acetylcholine or potassium chloride and replacement of the Ringer's solution, a freshly prepared solution of γ-aminobutyric acid, made by the Sigma Chemical Co., was added to the beaker (acid concentration in the vessel was $1 \cdot 10^{-6} - 1 \cdot 10^{-3}$). After 30 min, we again added the previous concentration of acetylcholine or potassium chloride. Muscle contractions were recorded over a period of 30 sec – 1 min on a stationary kymograph.

EXPERIMENTAL RESULTS

γ-Aminobutyric acid in a concentration of $1 \cdot 10^{-3}$ suppresses potassium contractions of skeletal muscle. This effect was observed in 22 tests out of 25 (Fig. 1). It also suppresses the sensitization of the muscle to potassium ions, which is caused by guanidine, aminopyridine, and veratrine (15 experiments). These results are in agreement with the data in the literature on the capacity of γ-aminobutyric acid to prevent the effect of potassium and veratrine on the miniature potenitals of the mammalian end plate [6].

In the experiments with acetylcholine, the application of γ-aminobutyric acid did not yield a clear effect. No effect was present in 11 out of 25 tests (Fig. 2), a minimal decrease in the acetylcholine contractions was observed in 7, and a slight intensification in the contractions was seen in the remaining 7.

Thus, γ-aminobutyric acid manifested a marked inhibitory effect on potassium contractions of skeletal muscle, but not on acetylcholine contractions.



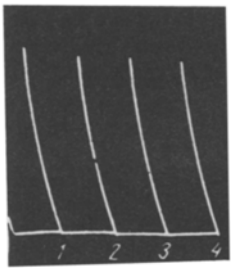


Fig. 1. Contractions of the rectus abdominus muscle under the influence of potassium chloride (1:1250), before (1 and 2) and after a 30 min treatment with γ-aminobutyric acid in a concentration of $1 \cdot 10^{-3}$ (3 and 4), and also after washing away of the acid (5).

Fig. 2. Contractions of the rectus abdominus muscle under the influence of acetylcholine (1:5,000,000) before (1 and 2) and after a 30 min treatment with γ-aminobutyric acid in a concentration of $1 \cdot 10^{-3}$ (3 and 4).

It is known that γ-aminobutyric acid possesses the capacity to increase potassium excretion from the cerebral cortex [3]. The possibility has not been excluded that the same thing occurs in muscle, and this may express itself on the muscle's reactivity to potassium.

SUMMARY

Gamma-aminobutyric acid depressed the potassium contraction of the skeletal muscles and its sensitization to potassium ions caused by guanidine, aminopyridine, veratrine, and had no material effect on the aceytlcholine muscle contractions.

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