CHOLINOMIMETIC EFFECT OF SOME SOVIET PREPARATIONS WITH CURARE-LIKE ACTION

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We noted earlier the ability of paramion—a preparation with pronounced curare-like action—to produce contraction of the tonic muscles. However, Hsaio K'un-tse [3] detected only a cholinolytic effect in paramion. The author did not succeed in producing contraction of an isolated rectus abdominis muscle, evidently as a result of insufficient duration of the observation.

This report presents the results of supplementary observations, in which we detected the possibility of producing cholinolytic and cholinomimetic effects through the use of the same substance.

EXPERIMENTAL PROCEDURE

The investigation was conducted on an isolated rectus abdominis muscle of a grass frog. Before the beginning of the test, the muscle was kept in Ringer solution, subjected to continuous aeration, for no less than 1 h. The cholinomimetic effect of paramion was investigated at concentrations of $1 \cdot 10^{-4}$-$1 \cdot 10^{-5}$ in 70 experiments. In addition to paramion, we tested other Soviet preparations with curare-like action: pyrolaxon, diplacin, and trimethyl-α-naphthylammonium iodide (the latter was synthesized in the laboratory headed by A. M. Khaletskii).

EXPERIMENTAL RESULTS

The results of the experiments, presented in the table, give evidence that paramion produces contraction of the tonic muscles (Fig. 1), while curare (Schuchardt Company) prevents it.

Action of Curare and Paramion on the Frog Rectus Abdominis Muscle

Conc. of curare (preliminary influence)	Conc. of paramion	Total no. of expts.	No. of expts. in which contraction was observed
	$1 \cdot 10^{-6}$	4	3
	$2 \cdot 10^{-6}$; $1 \cdot 10^{-4}$	66	66
$4 \cdot 10^{-6}$ (10-15 min)	$2 \cdot 10^{-6}$; $2 \cdot 10^{-5}$	12	0
$2.5 \cdot 10^{-6}$	$4 \cdot 10^{-5}$	12	5

Paramion in a $1 \cdot 10^{-6}$ concentration temporarily suppresses guanidine tremors (which possess a cholinergic origin) of the frog sartorius muscle; their permanent suppression arises at a paramion concentration of $0.25 \cdot 10^{-5}$ or $2 \cdot 10^{-6}$.

Thus, the paramion concentrations that are cholinolytic on the nontonic muscles produce a cholinomimetic effect on the tonic muscles. Paramion ($1 \cdot 10^{-4}$-$4 \cdot 10^{-6}$) suppresses guanidine tremors in an isolated frog rectus abdominis muscle, but in this case, after suppression of the tremors, muscle contracture develops (Fig. 2).

Pyrolaxon in a concentration of $1 \cdot 10^{-4}$ - $1 \cdot 10^{-5}$ produced contracture of isolated frog rectus abdominis muscle in 11 out of 24 experiments. This contracture also develops slowly and reached 1-3 mm in an hr.

Diplacin in a concentration of $1 \cdot 10^{-4}$ or $2 \cdot 10^{-5}$ produced no contracture of the tonic muscles in any of 6 experiments, in the case of observation for no less than an hour.

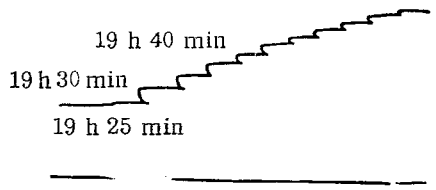

Fig. 1. Action of paramion on the frog rectus abdominis muscle. The arrow denotes the moment of introduction of paramion ($4 \cdot 10^{-6}$) into the beaker. At 19 h 40 min, muscle contracture arose. Subsequently, an increase in the contracture can be seen on the readings taken at 5 min intervals.

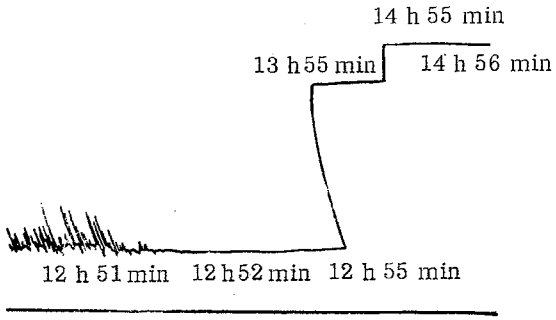

Fig. 2. Influence of paramion on the frog rectus abcominis muscle under conditions of guanidine hyperkinesis. To the left can be seen muscle contractions induced by guanidine ($1 \cdot 10^{-4}$), introduced into the beaker at 12 h 22 min: contractions began at 12 h 29 min. At 12 h 51 min, paramion ($4 \cdot 10^{-5}$) was added to the beaker: after a minute, the muscle contractions ceased, but then muscle contracture arose.

On isolated frog rectus abdominis muscle, triemthyl-α-naphthylammonium iodide, which exerted a curare-like action, produced contracture in concentrations of $1 \cdot 10^{-4}$, $2 \cdot 10^{-5}$, and $2 \cdot 10^{-6}$; in the case of strong concentrations of the preparation, the contracture reached 14-29 mm in 10 min.

During the first 10-20 min, contracture developed most rapidly. When the muscles were washed for 1.5 h, this contracture disappeared and could be repeatedly induced by the same concentrations of the preparation. Curare in a $4 \cdot 10^{-6}$ concentration prevented the development of contracture produced by trimethyl-α-naphthylammonium iodide ($2 \cdot 10^{-5}$) and reduced it upon subsequent influence on the muscle.

The ability to produce cholinomimetic contracture of the frog rectus abdominis muscle is characteristic not only of curare-like preparations classed among agents with depolarizing action (decamethonium, ditilin), but also of paramion and pyrolaxon.

The contrast of competing (competitive-blocking) and depolarizing types of agents, which disturb the transfer of an impulse in the neuromuscular synapses, in the opinion of V. M. Karasik, is terminologically improper, because the features according to which the classification is created differ: none of the numerous authors using this classification, beginning with Paton and Laimis, who proposed it [4], reported data or considerations according to which the depolarizing substances, for example, succinylcholine (ditilin) or decamethonium might be recognized as competitors for acetylcholine. It should be noted, in addition, that under conditions of suppression of the enzymatic cleavage of acetylcholine by eserine, stimulation of the motor nerve produces an "acetylcholine pessimum" [1], while when such cleavage is suppressed by proserine, acetylcholine leads to a suppression of guanidine tremors of a cholinergic nature [2]. All the main features of decamethonium blockage can be reproduced with acetylcholine or by tetanization of the motor nerve in the presence of anticholinesterase substances. Thus, decamethonium exerts a cholinolytic action and competes with acetylcholine, just like α-tubocurarine.

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