EFFECT OF PANCREATECTOMY AND OF CHOLINACETYLASE INHIBITORS ON POSTTETANIC POTENTIATION OF NEUROMUSCULAR TRANSMISSION

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Experiments on frog nerve-muscle preparations showed that disturbance of acetylcholine synthesis by preliminary pancreatectomy or perfusion of the muscles with cholinacetylase inhibitor (2-methylnaphthoquinone) diminishes, and in some cases abolishes posttetanic potentiation in the myoneural junction.

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The object of this investigation was to study posttetanic potentiation (PTP) at the myoneural junction when synthesis of the mediator is disturbed.

EXPERIMENTAL METHOD

Experiments were carried out on isolated perfused nerve-muscle preparations from pond frogs. Muscle activity was recorded myographically and electrographically. The PTP were investigated against a background of fatigue of the nerve-muscle preparation produced by single indirect stimuli at a frequency of 0.5/sec, when the amplitude of contractions was reduced to 1/3 of its initial value (frequency of tetanization 30/sec, duration 4 sec). Acetylcholine synthesis was disturbed in 68 experiments by preliminary (6-9 days before the experiment) pancreatectomy [2], and in 50 experiments by perfusion of the muscle with a solution of the cholinacetylase inhibitor 2-methylnaphthoquinone [1, 5] in concentration of 1:10,000–1:50,000.

Significance of the differences between the control and experimental preparations was determined by the signed rank test and in some cases by the paired-sample test [4].

EXPERIMENTAL RESULTS

In normal animals the amplitude of the contractions increased by 96.5% after tetanization, on the average from 14.35 to 28.2 mm (Fig. 1, A). The amplitude of the action potentials (AP) was increased by a rather smaller amount (by 63.9%) after a short period of tetanization, on the average from 14.43 to 23.64 mm (Fig. 1, a, b). The duration of the AP remained unchanged or was slightly reduced. The time for transmission of excitation from nerve to muscle [3] was shortened after tetanization on the average from 3.8 to 3.56 msec.

In preparations of pancreatectomized frogs the PTP was much less marked. Greatest depression of PTP of the contractions was found on the 8th day after the operation, when single contractions were increased by 51.8% after tetanization (on the average from 13.5 to 20.5 mm). Every day after the operation the contractions increased on the average from 13.2 to 23.4 mm (177.3%). The duration of PTP was shortened: in preparations of pancreatectomized frogs it averaged 25 sec (32 sec in the control).

Similar changes took place in the muscle AP. After tetanization their amplitude increased from 8.5 to 12.7 mm, i.e., by 49.3%. The duration of the AP under these circumstances rose only slightly (on the average from 6.4 to 6.8 msec). Changes in the time of transmission of excitation from nerve to muscle differed particularly sharply. After tetanization the time was not shortened, as usually occurs, but was lengthened on the average from 3.9 to 4 msec, i.e., to 103%.

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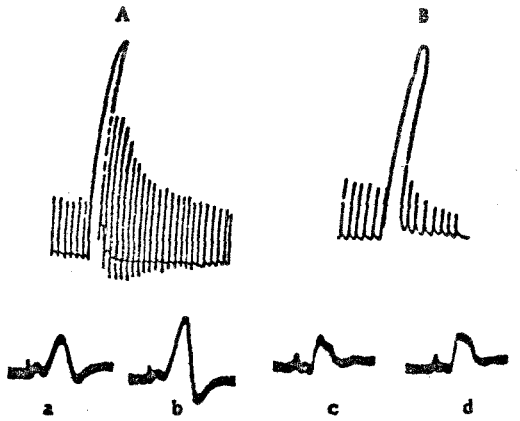

Fig. 1. Posttetanic potentiation of muscle contractions in fatigued preparations perfused with Ringer's solution (A) and with a solution of 2-methylnaphthoquinone (B). Single action potentials before (a, c) and after (b, d) short tetanization.

Changes in posttetanic potentiation in the experimental changes described above are statistically significant ($\Delta\bar{x} \pm S\Delta\bar{x}$ for contractions, amplitudes of action potentials, and transmission times are -3.65 ± 1.21, -4.51 ± 1.4, and $+0.34 \pm 0.09$ respectively; $P \ll 0.05$).

After administration of acetylcholine, no increase was found in the posttetanic effects compared with those observed in the pancreatectomized animals (except for shortening of the time of transmission of excitation from nerve to muscle, on the average to 98.4%).

Results similar to those described above were obtained with perfusion of the muscle with a solution of the cholinacetylase inhibitor 2-methylnaphthoquinone. Development of fatigue of the nerve-muscle preparation and diminution of the contractile effects and AP of the muscle were shortened somewhat in duration, while posttetanic potentiation was considerably weakened and, in some cases, disappeared completely (Fig. 1, B). The amplitude of single contractions increased after tetanization on the average to 125% of their initial value (from 19.6 to 24.5 mm), compared with an increase to 196.5% in the control. The duration of posttetanic potentiation (if it was present) was considerably shortened, and averaged 12 sec (32 sec in the control). The amplitude of the muscle AP increased slightly, on the average from 15.7-17.3 mm, i.e., 110% of their initial value compared with 163.9% in the control (Fig. 1, c, d). The duration of the potentials was either unchanged or increased, whereas in the control it fell to 96%. The time of transmission of excitation from nerve to muscle was distinctly increased. The mean transmission time in the control experiments fell to 93.7%, while during the action of 2-methylnaphthoquinone it increased from 3.2 to 3.4 msec (106.3%).

The results demonstrate that disturbance of acetylcholine synthesis by preliminary pancreatectomy or by perfusion with 2-methylnaphthoquinone causes a decrease, and in some cases complete disappearance, of posttetanic potentiation.

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