Short Communication

SOME EFFECTS OF A HEMICHOLINIUM COMPOUND (HC-3) ON NEUROMUSCULAR TRANSMISSION IN THE CAT

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THE hemicholinium compound 4,4′-biphenylylenebis[carbonylmethyl-(2-hydroxyethyl)dimethylammonium bromide] (HC-3) (Long and Schueler, 1954) has been shown to produce a neuromuscular block in rabbits which is of gradual onset, long duration (Reitzel and Long, 1959) and dependent on the frequency of nerve stimulation (Wilson and Long, 1959).

An attempt has been made in the present study to determine the effect of HC-3 on neuromuscular transmission in the cat by using the tibialis anterior muscle-sciatic nerve preparation. Some effects on this preparation have already been described by Bowman and Rand (1961).

EXPERIMENTAL

Method

Cats (2 to 5 kg.) were anaesthetised with intraperitoneal pentobarbitone (35 mg./kg.) and the hind limbs supported in a Brown-Schuster myograph. The tendon of each tibialis anterior muscle was attached to a flat steel spring and the movements recorded on smoked kymograph paper. Twice maximal rectangular pulses of 0·05 msec. duration were applied to the cut sciatic nerve by silver electrodes. In experiments in which innervated muscles were stimulated directly, the stimulus duration was 0·10 msec. The blood pressure was recorded from the carotid artery by a mercury manometer and the vagus nerves were cut in the neck. HC-3 was administered intravenously.

RESULTS

Preliminary studies showed that the maximum dose of HC-3 which could be used without lowering the blood pressure was 500 μg./kg. but it was necessary to stimulate the nerve at a frequency of 1 or 2/sec. to produce an effect on the muscle response. Before investigating these effects, however, it was established that the response of the muscle to nerve stimulation at these frequencies was constant.

The effects produced by 100, 250 and 500 μg./kg. of HC-3 on the response of the muscle to nerve stimulation at a frequency of 1/sec. are compared with control results in Fig. 1*a*. This shows that 100 μg./kg. failed to produce a significant effect after 3 hr. A depression of the muscle response was produced, however, by doses of 250 and 500 μg./kg. The onset of the depression was similar for both doses and the maximum

effect occurred in approximately 90 min. Recovery from the effects of these doses occurred in 180 and 230 min. respectively.

Fig. 1*b* shows how the muscle response was modified by increasing the frequency of nerve stimulation to 2/sec. In contrast to Fig. 1*a* 100 μg./kg. caused a depression of the muscle response. Increasing the dose to 250 and 500 μg./kg. produced a successively greater depression. The rate of onset was similar for each dose but the times required to produce the maximum effects were 50, 70 and 80 min. respectively. Recovery from the effects of these doses of HC-3 occurred in 180 min. after 100 and 250 μg./kg. and in 280 min. following 500 μg./kg.

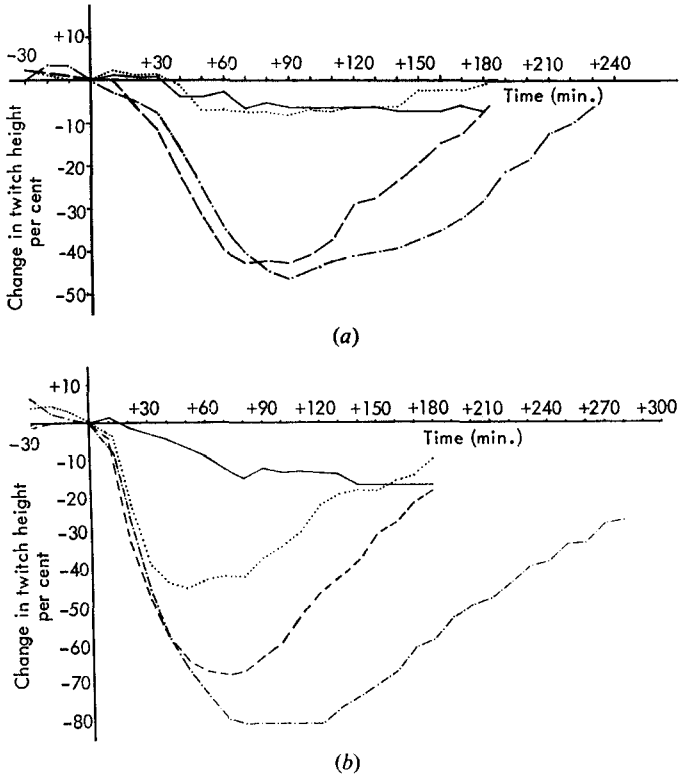

FIG. 1. The mean percentage change in twitch height produced on the cat tibialis anterior muscle stimulated by its nerve at a frequency of (*a*) 1/sec., (*b*) 2/sec. after intravenous injections of saline (——) and HC-3 in doses of 100 μg./kg. (. . . .), 250 μg./kg. (– – –) and 500 μg./kg. (–·–·–).

Point of intersection of the co-ordinates represents the point of drug administration.

Further experiments showed that when the response of the muscle to nerve stimulation was reduced by HC-3, the muscle was fully responsive to direct stimulation. This finding together with the observation that HC-3 failed to influence nerve conduction (Longo, 1959) indicates that

the effects described above are due to an action at the neuromuscular junction.

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