On the neuromuscular blocking action of succinylmonocholine in the rat

In the cat the neuromuscular blocking action of succinylmonocholine, the first hydrolysis product of suxamethonium (Whittaker & Wijesundera, 1952), resembled that of a depolarizing rather than a competitive blocking agent (Ellis, Wnuck & others, 1953). However, Stovner (1958), using rat or kitten isolated nerve-diaphragm preparations reported the following findings, indicating competitive block. Eserine increased twitch height during partial block by succinylmonocholine, tetraethylammonium restored transmission and tubocurarine deepened the block. Furthermore, in the tibialis and soleus muscles of the cat, tetraethylammonium caused a slight antagonism of the block. Whittaker (1962), suggested that the competitive features of the blockade produced by suxamethonium in the rat isolated diaphragm preparation may be related to the enzymatic hydrolysis of suxamethonium to succinylmonocholine. More recently Ireson, Ford & Loveday (1969), have shown that, in anaesthetized rats, neuromuscular block by suxamethonium is competitive, again explainable by its metabolism to succinylmonocholine.

As studies on the neuromuscular blocking action of succinylmonocholine in the rat have been confined to isolated diaphragm preparations, it seemed relevant to investigate the neuromuscular blockade produced in the intact animal.

Male rats, 300 to 400 g were anaesthetized with pentobarbitone sodium (3 mg/100 g rat) plus urethane (60 mg/100 g rat), administered intraperitoneally in one solution.

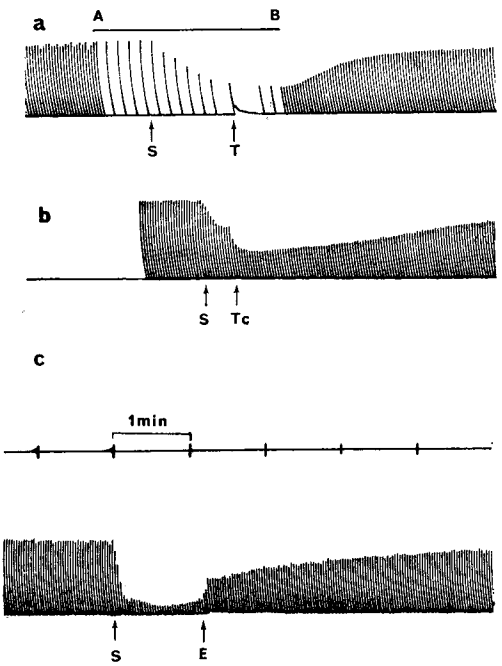

FIG. 1a. Maximal twitches of rat gastrocnemius muscle elicited by supramaximal stimuli to sciatic nerve, at a frequency of 0·2 Hz. At S, 80 μg succinylmonocholine injected intravenously. At T, tetanus was elicited by stimulation of nerve at 50 Hz for 10 s (oscillograph speed increased between A and B). b. At S, 60 μg succinylmonocholine and at Tc, 10 μg of tubocurarine injected intravenously. c. Maximal twitches of rat gastrocnemius muscle, elicited indirectly at 0·5 Hz. At S, 75 μg succinylmonocholine and at E, 50 μg of edrophonium injected intravenously.

The preparation of the sciatic nerve gastrocnemius muscle was similar to that of Van Maanen (1950), with the following modifications. The leg was held by an ankle clamp, the severed Achilles tendon was attached to a Statham linear transducer and the muscle contractions were recorded by a pen oscillograph. The sciatic nerve was stimulated once every 5 s in some experiments and once every 2 s in others by rectangular pulses of 1 ms duration and of approximately twice the strength required to evoke a maximal twitch. Drugs were injected intravenously through a cannula in the jugular vein. Succinylmonocholine, tubocurarine and edrophonium were used as the chlorides and doses quoted are in terms of these salts.

Succinylmonocholine produced a competitive neuromuscular block as indicated by the following features. Block was rapid in onset without prior twitch potentiation and when tetanic stimulation was applied through the sciatic nerve during partial block, muscle tetanus was not sustained, and after the tetanus, transmission was not further depressed (Fig. 1a). The injection of tubocurarine at the point of maximum blockade by succinylmonocholine intensified the block (Fig. 1b), and this additive effect was also seen when the order of injection was reversed. Edrophonium injected at the time of approximately maximum blockade caused an increase in twitch height (Fig. 1c).

These findings, from observations *in vivo* support the conclusions of Stovner (1958) from *in vitro* work. Furthermore, the present results could support the suggestion of Ireson & others (1969), that the metabolism of suxamethonium to succinylmonocholine might be responsible for the characteristics of suxamethonium block in the anaesthetized rat and the same suggestion made by Whittaker (1962) for the rat isolated diaphragm. However this is not the only possible explanation, since end plate depolarization by suxamethonium in the isolated rat diaphragm was hardly altered when cholinesterase activity was inhibited by neostigmine (Harris & Leach, 1968), and it is likely that unhydrolysed suxamethonium is also important in determining the nature of neuromuscular blockade in the rat.

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