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Potentiation of the responses of the vas deferens of the guinea-pig to transmural stimulation and to noradrenaline, by triethylcholine and tetraethylammonium

The actions of triethylcholine (TEC) and tetraethylammonium (TEA) at cholinergic sites is well documented and an additional action at an adrenergic site was reported for TEA by Thoenen, Haefely & Staehelin (1967), who observed a potentiation by TEA of the contractile response of the cat spleen to stimulation of the splenic nerve. I now report a potentiation by TEC and TEA of the response of the vas deferens of the guinea-pig to adrenergic stimulation.

Adult male guinea-pigs, 500 g, were killed by stunning and bleeding and the vasa deferentia removed, stripped of their mesentery (Bentley & Sabine, 1963), and suspended in Krebs solution at 37°, bubbled with 5% carbon dioxide in oxygen. In some experiments the vasa were stimulated transmurally (Birmingham & Wilson, 1963) for 15 s every 4 min at a frequency of 20 impulses/s. Each impulse was of 500 μs duration and 100 V. In other experiments noradrenaline was added to the bath to stimulate the adrenergic receptors. Contractions were recorded by frontal writing levers on smoked paper. Concentrations of drugs are given in the weight of the base.

Each vas deferens was stimulated regularly until consecutive contractions were uniform. The tissue was then exposed to Krebs solution containing TEC (5×10^{-4} g/ml) or TEA (10^{-4} g/ml). In each experiment these concentrations of the drugs produced a potentiation of the response of the vas to transmural stimulation, although the extent of the potentiation varied from vas to vas it averaged $1\frac{1}{2}$ times. The potentiation was maintained while the drug remained in contact with the tissue, but was readily reversed. Control vasa, not exposed to the drug, showed no change in the size of the contractile response. The onset of the potentiation was rapid, maximum potentiation being reached within 30 s of administration of the drug.

Prior administration of cocaine (5×10^{-6} g/ml) or desipramine (10^{-6} g/ml) did not alter the potentiation.

A similar potentiating effect was described for choline by Bell (1967), but which differed from the present experiments in being blocked by hyoscine; the action of TEC and TEA did not appear to be at muscarinic or nicotinic ganglionic sites since neither atropine (5×10^{-6} g/ml) nor hexamethonium (5×10^{-6} g/ml) altered the potentiation.

In other experiments the effects of TEC and TEA on the response of vasa to a submaximal concentration of noradrenaline were tested. The response to $1{\cdot}6 \times 10^{-6}$ g/ml of noradrenaline (corresponding to about 30% of a maximal contraction) was, in the presence of TEC (5×10^{-4} g/ml) or TEA (10^{-4} g/ml), reproduced by a concen-

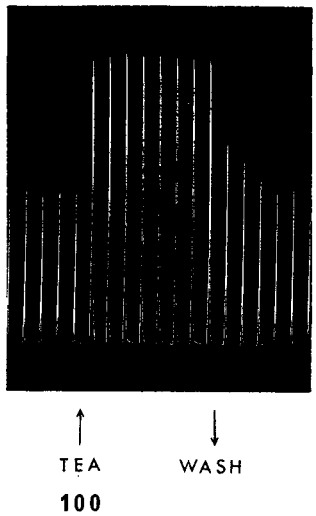

FIG. 1. The effect of tetraethylammonium (TEA) (μg/ml) on the responses of the guinea-pig vas deferens to transmural stimulation. Stimulation was for 15 s, every 4 min at a frequency of 20 impulses/s. Each impulse was of 500 μs duration and 100 V.

tration of noradrenaline of $2{\cdot}5 \times 10^{-8}$ g/ml. The action of the TEC or TEA in potentiating the response of the guinea-pig vas deferens to noradrenaline was not affected by prior administration of cocaine (5×10^{-6} g/ml) or desipramine (10^{-6} g/ml).

These experiments show TEC and TEA to have a potentiating effect at adrenergic neuroeffector junctions in the vas deferens. The action does not appear to be emdiated by blockade of the Uptake_1 mechanism since cocaine (Iversen, 1965) or desipramine, in concentrations which would be expected to inhibit the Uptake_1 process, have no effect on the potentiating action. Thoenen, Haefely & Staehelin (1967) found a measurable increase in the amount of noradrenaline released by nervous stimulation in the cat spleen after treatment with TEA; this effect may be contributing to the action of the drugs here. However, it does not explain the action of the drugs on the response to exogenous noradrenaline and for this reason it is suggested that the drugs may have a site of action at the post-synaptic membrane of the sympathetically innervated tissue.

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