Activation of intramural inhibitory neurones of the rabbit caecum by nicotine

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Circular smooth muscle of the rabbit caecum had a non-adrenergic inhibitory innervation (Small, 1972) and is sparsely innervated by noradrenergic fibres. The inhibitory action of nicotine (1×10^{-6} to 1×10^{-4} M) upon this tissue has been analysed using tissue bath and sucrose gap recording techniques.

Muscle strips (which lack spontaneous activity or tone) were exposed to either atropine (1.7×10^{-7} M) or methacholine (2×10^{-6} M). In both cases the nicotine induced inhibition was assessed by the hyperpolarization produced. In the latter case a simultaneous reduction in mechanical activity could also be observed (Figure 1). The hyperpolarization induced by nicotine analysed similarly in both situations.

The action of nicotine was abolished by hexamethonium (5×10^{-4} M), strongly antagonized by tetrodotoxin (3.1×10^{-7} M) but unaffected by guanethidine (1×10^{-5} M). Pretreatment of animals with reserpine (2 mg/kg i.p. day 1, 2 mg/kg i.p. day 2, sacrifice day 3) or with 6-hydroxydopamine (30 mg/kg i.v. day 1, 2×20 mg/kg i.v. day 2, sacrifice day 3) each reduced the noradrenaline content of caecal tissue by more than 65% yet neither modified the response of the tissue to nicotine. Phentolamine (1×10^{-5} M) slightly reduced responses to nicotine. The hyperpolarizing action of nicotine was not shared by equimolar doses of tyramine but could be mimicked by large doses (10^{-5} moles) of ATP.

These results suggest that the action of nicotine in this tissue is mediated largely by excitation of non-adrenergic inhibitory neurones. A similar proposal was made for the action of nicotine on the
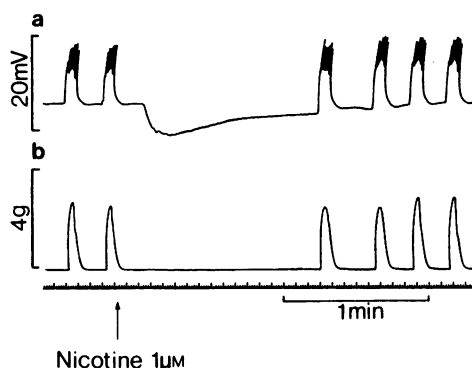

Fig. 1 Sucrose gap recording of the electrical (a) and mechanical (b) activity of circular smooth muscle from the rabbit caecum. The tissue was superfused with Kreb's solution containing methacholine (2×10^{-6} M) and at the arrow an E.D. 100 (10^{-6} moles) of nicotine was injected into the flow of solution. Note the hyperpolarization and abolition of mechanical activity induced by nicotine.

guinea-pig taenia caeci by Burnstock, Campbell & Rand (1966). Such findings are consistent with the suggestion of Burnstock (1972) that the preganglionic input to the intrinsic inhibitory neurone in some regions of the gut is cholinergic and plays onto nicotinic postsynaptic receptors.

The significance of the tetrodotoxin resistant component of the action of nicotine observed in the present study will be discussed.

References

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A quantitative assessment of the effects of clonidine on pre-ganglionic sympathetic nerve activity in the cat

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A method has been developed for the quantitative measurement of the effects of drugs on sympathetic nerve activity. It has been used to study the effects of clonidine, a drug known to inhibit spontaneous sympathetic activity (Schmitt, Schmitt, Boissier & Giudicelli, 1967).

Cats were anaesthetized with ether followed by chloraloseurethane and using gallamine and artificial respiration. Spontaneous preganglionic sympathetic nerve activity was recorded from a left splanchnic nerve, cut before its entry into the coeliac ganglion. The amplified neurogram was fed into a Nicolet 1072 laboratory computer which recorded the number of impulses above a pre-