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Effects of autonomic drugs on the electrical activity of intestinal circular muscle

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Although a considerable amount of information is available on the intrinsic nervous control (Crema et al 1970; Hirst & McKirdy 1974) of the circular layer of intestinal smooth muscle, relatively little is known about the mechanisms subserving its excitation (Holzer et al 1980). Circular muscle is usually quiescent; fast electrical activity is absent or very rarely detectable in the resting state but can be easily recorded during peristalsis segmentation (Frigo et al 1972) or by the intestinal stimulant cerulein (Lecchini & Gonella 1973). Spike activity is also produced in circular muscle by tetrodotoxin, which may unmask tonically-inhibited myogenic activity (Tonini et al 1974; Bortoff & Muller 1975). Our aim has been to investigate the effect of hexamethonium, noradrenaline (NA) and isoprenaline on evoked and spontaneous electrical activity of circular muscle.

Rabbits of either sex (900–1800 g) were used. Segments (5–6 cm long) of terminal ileum were removed and mounted horizontally in a organ bath 100 ml containing Tyrode's solution aerated with 5% CO_2 in O_2, at 36 °C. The oral end of the segment was tied over a glass tube connected to a Mariotte bottle containing Tyrode's solution and the lumen was perfused continuously at a flow rate of 2 ml min^{-1}. The aboral end was connected to an isotonic force transducer under a tension of 1–2 g to measure smooth muscle contractions. The intraluminal pressure was measured by means of a pressure transducer as described by Gonella (1971).

Extracellular electrical activity was measured with glass electrodes, tip diameter 0·10–0·20 mm, filled with Tyrode's solution and placed on the serosal surface of the preparations. The electrode arrangement was of the floating type to permit flexibility of movement with that of the bowel. Signals were led via chlorided silver wires to an AC-preamplifier (time constant 0·2 s). The electromyograms were recorded on an inkwriting polygraph. Drugs used were: hexamethonium chloride, (−)-noradrenaline bitartrate, (−)-isoprenaline bitartrate, cerulein (Farmitalia) and tetrodotoxin.

The electrical activity of the small intestine of the rabbit consists of rhythmic fluctuations of resting membrane (slow waves) and of rapid action potentials (spikes) which appear during slow wave depolarization. Spikes are accompanied by contraction of muscular layers and it has been found that the spikes synchronous with the contraction of circular fibres always occur after spike activity of the longitudinal fibres (Gonella 1971).

In all preparations (25 experiments) the slow waves were accompanied by small spikes (2–4 mV) similar to those obtained from isolated longitudinal muscle by Small & Weston (1971) and associated with longitudinal contractions. The frequency of the waves was 10–14 cycles min^{-1}. As shown in Fig. 1a, faster action potentials (more than 8 mV), related to the circular activity, occurred in bursts during segmentation or peristalsis. The mean (±s.e.) frequency of burst was 6·8 ± 0·4 min^{-1} and lasted 2 ± 0·1 s. When propagated during peristalsis, each burst travelled aborally at a velocity of 2 ± 0·08 cm s^{-1}. Hexamethonium (at a final concentration of $5{\cdot}6 \times 10^{-5}$ M, 10 experiments) abolished both mechanical and fast electrical activity of circular layer. It has been found that NA is capable of inhibiting both the release of acetylcholine from Auerbach's plexus in ileal muscle (Paton & Vizi 1969; Kazic 1971) and the peristaltic reflex in isolated colon (Frigo et al 1974), these actions being mediated via α-adrenoceptors on presynaptic nerve terminals (Vizi 1979). As shown in Fig. 1b, NA (3×10^{-8} M, 10 experiments) abolished both mechanical and fast electrical activity of the circular muscle, the latter after a latency of 1 min. The inhibitory effect of isoprenaline has been considered in terms of a direct action on the smooth muscle of intestinal tract (Vizi 1979). In our preparations isoprenaline (3×10^{-6} M, 10 experiments) abolished both mechanical and electrical activity of the circular coat.

The cholecystokinin-related polypeptide caerulein increases peristaltic activity probably by acting on presynaptic enteric nervous structures (Frigo et al 1971). In 12

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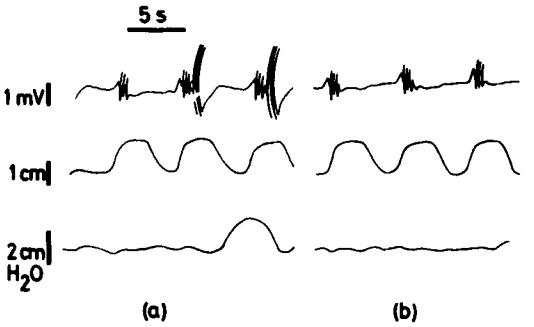

FIG. 1. Effect of NA on the electrical and mechanical activity of the isolated rabbit small intestine. From top to bottom records of extracellular electrical activity, longitudinal movements, and intraluminal pressure. a: control; b: in the presence of NA 3×10^{-8} M. Time bar, 5 s.

experiments, caerulein (8×10^{-10} M) antagonized the inhibiting effect of hexamethonium and NA, but not that of isoprenaline. Tetrodotoxin completely blocks intestinal peristalsis (Crema et al 1970). However, after the toxin myogenic activation appears in the circular muscle (Wood 1975; Bortoff & Muller 1975). This consists of a regular spike discharge at the beginning of each slow wave, associated with rhythmic oscillations of intraluminal pressure. In our preparations neither hexamethonium nor NA ($5{\cdot}6 \times 10^{-5}$ M and 3×10^{-8} M respectively) modified spikes evoked by tetrodotoxin (3×10^{-7} M). Isoprenaline (3×10^{-6} M) and NA (3×10^{-6} M) both inhibited the excitatory effect of the toxin.

Our results confirm that activity in circular smooth muscle can be both myogenic and neuronal in origin (Wood 1980). Since tetrodotoxin induces spontaneous firing, an underlying inhibitory mechanism may be active normally in the intestinal musculature (Tonini et al 1974; Wood 1975; Bortoff & Muller 1975). The activities of the circular muscle associated with peristalsis and spontaneous segmentation seem to be neurally-mediated and are suppressed by tetrodotoxin (Crema et al 1970). Nicotinic receptors at ganglionic sites are probably involved in such activities as indicated by the actions of both hexamethonium and caerulein. The inhibitory effect of adrenergic agonists (NA and isoprenaline) has usually been considered in terms of a direct action on the smooth muscle (Bülbring & Tomita 1969). However, recent findings show that NA is capable of inhibiting the acetylcholine release by axonal stimulation from Auerbach's plexus (Vizi 1979). NA control of circular electrical activity can be viewed as a kind of presynaptic inhibition. Moreover, recent anatomic and physiological findings have caused a re-evaluation of the classical concepts of sympathetic innervation of intestine (Silva et al 1971).

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