Presynaptic action of 5-hydroxytryptamine in the myenteric plexus of the guinea-pig ileum

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5-Hydroxytryptamine (5-HT) is known to inhibit the peristaltic reflex when applied to the serosal aspect of the isolated guinea-pig ileum (Kosterlitz & Robinson, 1957) by an action which has been noted to be similar to that of the ganglion-blocking drugs (Kosterlitz & Lees, 1964).

Individual ganglia of the myenteric plexus of the guinea-pig ileum were immobilized by careful pinning and bathed in an organ bath in the manner previously described (Nishi & North, 1973a). Neurones were clearly observed by means of differential interference contrast microscopy (magnification x500) and were impaled with glass micro-electrodes filled with a solution of 3M KCl. Intracellular recordings were obtained from single cells for periods as long as 8 hours. Excitory post-synaptic potentials (e.p.s.p.) were elicited by focal stimulation of the ganglion within a distance of 100 μm from the impaled cell, using a low resistance micro-electrode filled with Krebs solution. A micro-electrode filled with 2M acetylcholine (ACh) chloride solution was manipulated under visual control on to the surface of the impaled neurone. After appropriate adjustment of the position of the micro-electrode tip, iontophoretic currents (retaining current 5-20 nA; ejecting current 10-100 nA, 10-25 ms duration) produced a depolarization of the impaled cell (ACh potential) with a rise time, amplitude and total duration closely similar to the e.p.s.p. in the same cell.

Changes in membrane potential imposed by passing hyperpolarizing or depolarizing currents through the recording micro-electrode affected the e.p.s.p. and the ACh potential in a proportionate manner; the equilibrium potential for the action of the synaptic transmitter was close to that for the iontophoretically applied ACh. Hexamethonium bromide (10-100 μM) reversibly abolished the e.p.s.p. and the ACh potential with a similar time course of action in the two cases.

In confirmation of an earlier report (Nishi & North, 1973b), noradrenaline (1-10 μM) reversibly abolished the e.p.s.p. in all cells to which it was applied. Noradrenaline caused no consistent change in postsynaptic membrane potential or resistance, or in the amplitude of the ACh potential. 5-HT (25 nM – 1 μM) reversibly abolished the e.p.s.p. in most cells, without affecting the amplitude of the ACh potential or changing the postsynaptic membrane potential or resistance. The depression of the e.p.s.p. amplitude produced by 5-HT (200 nM) was rapidly reversed by washing out and could be repeated every 4 min; larger doses of 5-HT caused tachyphylaxis. Methysergide (1.7μ M), which itself slightly depressed the e.p.s.p. amplitude, prevented the action of 5-HT. In a few cells, 5-HT (up to 10 μM) did not change the e.p.s.p. amplitude although noradrenaline had its usual effect.

These findings indicate that 5-HT reduces the release of ACh from most presynaptic terminals within the myenteric plexus. As the only excitatory pathway within the plexus appears to be cholinergic, such as action would inhibit the peristaltic reflex.

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