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Is the latency of parasympathetic nerve effects due to a slow activation of muscarinic receptors? An iontophoretic study.

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The latency between parasympathetic nerve stimulation and the response of the smooth muscle membrane is in the range 0.07-0.4 s (Gillespie, 1962; M.R. Bennett, 1966; Ohashi & Ohga, 1967; T. Bennett, 1969; Furness, 1969; Ito & Kuriyama, 1971). A possible explanation of this latency is that it is caused by a combination of slow conduction and synaptic delays in the nerve pathways by which excitation reaches the muscle membrane. If this was the case then one would expect the response to iontophoretically applied acetylcholine or carbachol to have a latency much shorter than 0.1 second.

Experiments were therefore done in which carbachol was applied from iontophoretic pipettes (resistance about 200 MΩ) to the surface of smooth muscle from guinea-pig ileum and taenia in isotonic or in sucrose hypertonic physiological salt solution. Simultaneously intracellular records were made from the smooth muscle by microelectrode which was inserted as close as possible to the tip of the carbachol pipette. In most experiments the distance between electrode and pipette was proably not more than 20 μm.

In isotonic solution spikes were often discharged spontaneously. When carbachol was applied iontophoretically no latencies less than about 0.1-0.2 s were observed. The depolarization produced by carbachol invariably triggered a spike or spikes and the electrode was usually dislodged by the contraction of the muscle.

In sucrose hypertonic solution the muscle does not contract and the membrane potential is stable. The sensitivity to carbachol (either applied in the perfusate or iontophoretically) was reduced. Iontophoretic application of carbachol produced small depolarizations of up to 10 mV. Their latency was again never less than 0.1-0.2 seconds.

In these experiments carbachol was released onto the surface of the muscle strip. Presumably therefore it must first cross a layer of serosal cells before it can affect the muscle. By 0.1 s after beginning release of carbachol, it can be calculated that a patch of muscle surface some 100 μm in diameter must be exposed to a suprathreshold concentration of carbachol in these experiments. The observed latency could be explained by invoking some special property of the serosa or associated connective tissue. However, Purves (1974) observed similar latencies when acetylcholine was applied iontophoretically to cultured taenia smooth muscle cells where presumably serosa is absent. A simple explanation of the latencies observed in his experiments and in mine, or following parasympathetic nerve stimulation, is that it represents mainly the time required to produce the responses associated with activation of the muscarinic receptor.

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