The depolarizing action of 5-hydroxytryptamine on sympathetic ganglion cells

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5-hydroxytryptamine (5-HT) is known to alter the excitability of sympathetic ganglion cells and can stimulate both excitatory and inhibitory neurones in the intestine (Gershon, 1967). In the work reported here, the action of 5-HT on the excised superior cervical ganglion of the rabbit has been examined by means of the sucrose-gap apparatus (Kosterlitz & Wallis, 1966). Ganglia were superfused with Krebs solution at 22° C and potential changes displayed on a potentiometric chart recorder.

The threshold concentration for depolarization was around 10^{-5} M 5-HT, which also depressed the height of the transmitted action potential. 10^{-4} M consistently produced depolarizations, but with this and higher concentrations repolarization began during the course of perfusion. This was followed by prolonged tachyphylaxis. Tachyphylaxis was largely avoided if injections of 5-HT were made into the perfusion stream. Estimates of dilution by the perfusion stream suggest an injection is dispersed in a volume of about 5 ml; thus, the standard injection of 80 μg gave a concentration around 40 μM. Responses to 5-HT were similar in magnitude and rate of onset to those elicited with acetylcholine and choline.

Depolarizations elicited by 40–80 μg 5-HT were followed by hyperpolarizations; the latter tended to decline after repeated exposures to 5-HT. Depolarization amplitude and area were related to the concentration, but response area tended to increase further even when amplitude had reached a maximum. The after-hyperpolarization was also concentration dependent; it was selectively depressed by ouabain.

Attempts to characterize the 5-HT receptors mediating depolarization are in progress with a variety of blocking agents. Picrotoxin and BOL 148, 10^{-5} to 10^{-4} M, is an effective blocking agent, as are morphine and phenyl biguanide in similar concentrations. Methysergide and LSD produced less complete block of the 5-HT responses at these concentrations. Atropine (3×10^{-6} to 3×10^{-5} M) reduced the amplitude and particularly the area of 5-HT responses, but hexamethonium (3×10^{-4} to 10^{-3} M) produced a considerable enhancement of both the amplitude and the area of the responses.

Leading from the proximal pole of the ganglion and a point on the cervical sympathetic nerve yields records of membrane potential change in the presynaptic terminals (Koketsu & Nishi, 1968). The presynaptic terminals were also depolarized by 5-HT, but these depolarizations were not usually enhanced by the presence of hexamethonium.

We conclude that ganglionic 5-HT receptors are located both pre- and postsynaptically and can mediate relatively large and rapid changes in membrane potential. The receptors of this preparation may provide a model for neuronal 5-HT receptors in general, including those of the CNS.

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Some characteristics of calcium accumulation at motor endplates of mouse diaphragm

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Carbachol causes the progressive accumulation of labelled calcium at the junctional region of mouse diaphragm muscle and this effect occurs in the absence of nerve terminals