Differential sensitivity of neuronal stimulant responses to 5-hydroxytryptamine to inhibition by agonists at presynaptic receptor sites

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5-Hydroxytryptamine (5-HT) stimulates noradrenaline release from rabbit cardiac sympathetic nerves (Fozard & Mwaluko, 1976), by activating tryptamine receptor sites (Fozard & Mobarok Ali, 1976). Transmitter release from terminal sympathetic nerves evoked by depolarizing stimuli can be modified by a variety of compounds which activate presynaptic receptors (Starke, 1977). The present report compares the effects of three such drugs, apomorphine, clonidine and prostaglandin E_1(PGE_1) on responses to 5-HT with their effects on dimethylphenylpiperazinium (DMPP) and electrical stimulation of the nerves leaving the stellate ganglion.

Rabbit hearts, some with the sympathetic nerves attached (Huković & Muscholl, 1962), were perfused by the Langendorf technique at constant pressure with Tyrode solution containing atropine (0.5 μg/ml), at 37°C. Right atrial and ventricular tensions and cardiac rate were recorded as previously described (Fozard & Muscholl, 1971).

Cardiac rate responses to bolus injections of 5-HT (0.2 to 32 μg) were antagonized concentration-dependently by perfusion of hearts with apomorphine (0.31 and 1.25 μg/ml). At 1.25 μg/ml, responses to 5-HT did not exceed 20% of the control maximum. In contrast, responses to DMPP (5 to 80 μg) were only slightly reduced by the higher concentration of apomorphine. Responses to electrical nerve stimulation (0.5 ms; supramaximal voltage) were reduced at low (0.33 to 3.3 Hz), but unaffected at high (10 Hz) frequencies by apomorphine 1.25 μg/ml.

Clonidine (1 μg/ml) had no significant effect on responses to 5-HT, although it markedly reduced responses to low (0.33 to 3.3 Hz) rates of electrical nerve stimulation and, less effectively, responses to DMPP throughout the dose range.

PGE_1 (1 μg/ml) inhibited responses elicited to electrical nerve stimulation evenly over the frequency range 0.33 to 10 Hz. Both 5-HT and DMPP were inhibited to a lesser extent.

Responses to bolus injections of noradrenaline (0.04 to 10 μg) remained unaffected by clonidine (1 μg/ml), apomorphine (1.25 μg/ml) or PGE_1 (1 μg/ml), implicating a presynaptic locus for the modulatory effects observed.

At this stage, no conclusive data are available to explain the differential effects of activation of presynaptic receptor sites on the three depolarizing stimuli. One explanation for the differences seen may lie in the fact that the mode of action of 5-HT and DMPP in evoking transmitter release, unlike electrical nerve stimulation, does not involve the generation of action potentials in this tissue (Fozard & Mwaluko, 1976).

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