Further evidence for two types of excitatory receptor for 5-hydroxytryptamine in dog vasculature

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It has been suggested that the excitatory receptor for 5-hydroxytryptamine (5-HT) in the dog femoral artery differs from that in the dog saphenous vein (Apperley, Humphrey & Levy, 1977). In order to characterize these receptors further, we have examined the effect of the 5-HT-antagonist cyproheptadine (Stone, Wenger, Ludden, Stavorski & Ross, 1960) on contractile responses to 5-HT and methysergide in the two vessels. In addition, there other vessels, from the dog carotid vasculature, have been included in the study.

Beagle dogs of either sex were anaesthetized with barbitone sodium (300 mg/kg i.p.) and portions of the femoral artery, saphenous vein, external carotid artery, lingual artery and intermediate auricular artery removed. The intermediate auricular artery was perfused with Krebs solution at a rate of 2–6 ml/min to give a resting perfusion pressure of 15–25 mmHg. Changes in perfusion pressure were recorded under constant flow conditions. The remaining vascular preparations were cut spirally into strips and isometric contractions recorded from a resting tension of 0.2–0.5 gram. The experimental conditions and design were the same as those described previously (Apperley, Humphrey & Levy, 1976).

In the femoral artery 5-HT, but not methysergide, produced concentration-dependent contractions, the maximum response occurring at about 5.0×10^{-6} mol/l. Cyproheptadine (2.5×10^{-9}–2.5×10^{-7} mol/l) was a potent antagonist of 5-HT, producing parallel displacements to the right of the concentration-effect curve. The pA_2(30 min) for cyproheptadine against 5-HT in the femoral artery was 8.73 ± 0.13 (mean ± s.e. mean, $n = 4$), with a slope of 1.18 ± 0.10, indicating competitive antagonism (Arunlakshana & Schild, 1959).

In the saphenous vein both 5-HT (1.0×10^{-8}–5.0×10^{-6} mol/l) and methysergide (5.0×10^{-8}–1.0×10^{-5} mol/l) produced concentration-dependent contractions. Cyproheptadine (1.0×10^{-8} mol/l) had little or no effect on these contractions. Higher concentrations of cyproheptadine (1.0×10^{-7}–1.0×10^{-5} mol/l) produced only slight displacement of the 5-HT and methysergide concentration-effect curves but a concentration-dependent reduction of the maxima, indicating non-competitive antagonism.

The results obtained in the other vessels were compared with those obtained in the femoral artery and saphenous vein. The profile of activity of methysergide and cyproheptadine in the external carotid and lingual arteries was the same as that in the femoral artery, while the profile of activity in the intermediate auricular artery was the same as that in the saphenous vein.

These findings add support to the suggestion that there are two types of excitatory receptor for 5-HT in dog vasculature. At one type methysergide and cyproheptadine are potent competitive antagonists. At the other type methysergide is an agonist and cyproheptadine is a weak non-competitive antagonist. Stimulation of the latter type by methysergide could account for its selective vasoconstrictor action in the dog carotid artery bed (Saxena, 1974).

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