Two types of excitatory receptor for 5-hydroxytryptamine in dog vasculature?

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It is known that there are two types of excitatory receptor for 5-hydroxytryptamine (5-HT) in the gastro-intestinal tract (Gaddum & Picarelli, 1957). The D-receptor occurs in the smooth muscle and is blocked by dibenzyline and methysergide; the M-receptor occurs in the ganglia and is blocked by morphine and phenylbiguanide (Drakontides & Gershon, 1968). We now present evidence to suggest that there are two different types of 5-HT-receptor in dog vascular smooth muscle, one of which does not have the characteristics of either the 'D' or the 'M' receptor.

Experiments were carried out in dog saphenous veins and femoral arteries. Male or female beagle dogs were anaesthetized with barbitone sodium (300 mg/kg i.p.) and the vessels removed and cut spirally into strips. Contractions were recorded isometrically and agonist–antagonist interactions were examined by the method of Arunlakshana & Schild (1959). The experimental conditions and design were the same as described previously (Apperley, Humphrey & Levy, 1976).

The effects of methysergide and phentolamine on the contractions produced by 5-HT and the α-adrenoceptor agonist methoxamine are summarized in Table 1. Phentolamine was a potent antagonist of methoxamine and a weaker antagonist of 5-HT in both preparations. Methysergide was a potent antagonist of 5-HT and a weaker antagonist of methoxamine in the femoral artery. In contrast, methysergide was not an antagonist of 5-HT in the saphenous vein, but was instead a potent agonist. This agonistic action was not mediated via α-adrenoceptors since it was only weakly antagonized by phentolamine (Table 1). Neither were M-receptors involved since responses to 5-HT and methysergide in the saphenous vein were not antagonized by morphine (1.0×10^{-6} mol/l) or phenylbiguanide (1.0×10^{-5} mol/l).

These results suggest that there are two distinct excitatory receptors for 5-HT in the vasculature of the dog. One type, at which methysergide is a potent antagonist, is like the 'classical' D-receptor, and the other type, at which methysergide is an agonist, has not previously been described.

Table 1 Interactions between agonists and antagonists in dog vascular smooth muscle

		pA_2 (30 min) against		
Vessel	*Antagonist*	*5-HT*	*Methysergide*	*Methoxamine*
Femoral artery	Methysergide	8.54 (8.19–8.89)	no contraction*	5.77 (5.45–6.09)
Femoral artery	Phentolamine	6.55 (6.15–6.95)	no contraction*	7.70 (7.25–8.15)
Saphenous vein	Methysergide	no antagonism at 1.0×10^{-7} mol/l	contraction†	5.63 (4.00–7.03)
Saphenous vein	Phentolamine	6.11 (5.92–6.30)	6.31 (5.80–6.82)	7.90 (7.66–8.14)

Each value quoted is the mean (95% confidence limits) of 4–8 determinations.
* Up to 10^{-6} mol/l.
† Concentration-dependent from 5.0×10^{-8}–1.0×10^{-5} mol/l with maximum equivalent to 40–100% of 5-HT maximum.

References

APPERLEY, EIRA, HUMPHREY, P.P.A. & LEVY, G.P. (1976). Receptors for 5-hydroxytryptamine and noradrenaline in rabbit isolated ear artery and aorta. *Br. J. Pharmac.*, **58**, 211–221.

ARUNLAKSHANA, O. & SCHILD, H.O. (1959). Some quantitative uses of drug antagonists. *Br. J. Pharmac. Chemother.*, **14**, 48–58.

DRAKONTIDES, ANNA, B. & GERSHON, M.D. (1968). 5-Hydroxytryptamine receptors in the mouse duodenum. *Br. J. Pharmac. Chemother.*, **33**, 480–492.

GADDUM, J.H. & PICARELLI, Z.P. (1957). Two kinds of tryptamine receptor. *Br. J. Pharmac.*, **12**, 323–328.