animals cannot be consistently shown to correlate with blood pressure changes as a result of increased sympathetic activity. However, raised circulating levels of DBH have been observed in certain types of hypertension in man and animals (De Champlain, Farley, Cousineau & van Ameringen, 1976; Schanberg & Kirshner, 1976).

Circulating DBH is believed to be derived from monoaminergic nerve-endings of all sympathetically innervated tissues, therefore estimation of DBH in the circulation is not a satisfactory measurement of the stimulated release of neuronal DBH. An alternative is described below.

Experiments were performed on female rats (C.F.E. derived strain) weighing 200–240 grams. The animals were prepared for stimulation of the sympathetic outflow using a modification of the Gillespie and Muir preparation (1967) and artificially respired. The splenic vein of eight rats was cannulated and connected to a cannula in the left femoral vein to maintain haemodynamic continuity. The hepatic-portal vein of a further eight rats was cannulated and similarly connected to a femoral vein cannula. The blood pressure was monitored in all animals by means of a cannula placed in the left carotid artery. Blood samples were collected from the spleen or hepatic-portal vein following selective stimulation of the sympathetic outflow supplying the coeliac and superior mesenteric ganglia (T10-L1), at frequencies between 1 and 25 Hz (20 V, pulse-width 0.3 ms for 5 s). At the same time blood samples were taken from the carotid artery to serve as controls. DBH released from heart tissue was measured by sampling from the aortic arch of eight rats following selective stimulation at frequencies between 0.5 and 5 Hz (30 V, pulse-width 0.5 ms for 15 s) of the spinal outflow to the stellate ganglion (C7-T1). Serum was removed simultaneously from the femoral vein to serve as a control. These experiments were repeated using various types of hypertensive rats. The animal models used were spontaneously hypertensive, renal hypertensive and deoxycorticosterone acetate/NaCl rats.

The serum was assayed for DBH activity by the spectrophotometric method of Kato, Kuzuya & Nagatsu (1974).

In each of the three tissues, DBH was shown to be released in a frequency dependent manner. The maximum enzyme levels released in response to stimulation expressed as $nmol.ml^{-1}.h^{-1} \pm$ s.e. mean, were spleen, 25.25 ± 2.25, (25 Hz); mesentery, 14.3 ± 0.95, (25 Hz); and heart 9.1 ± 1.7 (5 Hz). The stimulated release of the enzyme in hypertensive animals did not differ significantly from those of the normotensive rats.

These results provide further evidence for the combined release of DBH and noradrenaline at nerve endings. They also suggest that biochemical mechanisms associated with the release of transmitter at the sympathetic postganglionic nerve-ending do not differ significantly in hypertensive rats.

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Evidence for tryptamine receptors on cardiac sympathetic nerves

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5-Hydroxytryptamine (5-HT) stimulates noradrenaline release from rabbit cardiac sympathetic nerves (Fozard & Mwaluko, 1976). Despite the fact that classical tryptamine receptor antagonist drugs displayed no selective blocking activity, the possibility was considered that tryptamine receptors (Gaddum & Picarelli, 1957) exist on the terminal fibres which evoke transmitter release when activated (Fozard & Mwaluko, 1975). In an attempt to clarify the situation, the effects of several analogues of 5-HT have been investigated on the rabbit heart and comparisons have

Table 1 Equivalent molar ratios for stimulation of the cardiac sympathetic nerves and the ileal cholinergic nerves

Compound	Molar dose ratio $\frac{ED_{50}\ drug}{ED_{50}\ 5\text{-}HT}$	
	Heart	*Ileum*
5-HT	1	1
N-methyl-5-HT	2.2 (1.7–2.8) (4)	1.2 (0.3–4.5) (4)
N,N-dimethyl-5-HT	2.3 (1.8–3.0) (5)	2.9 (1.2–6.6) (7)
5,6-dihydroxytryptamine	4.7 (3.2–6.9) (3)	3.5 (3.0–4.0) (4)
Tryptamine	302* (135–676) (4)	328* (133–807) (5)

Figures presented are mean values with 95% confidence limits. * Molar dose ratio $\frac{ED_{25}\ drug}{ED_{25}\ 5\text{-}HT}$

been made with their potency as stimulants of the cholinergic elements of the guinea pig ileum.

Hearts were perfused with modified Tyrode solution containing atropine (1.4 μM) and right atrial and ventricular tensions and cardiac rate were recorded as previously described (Fozard & Muscholl, 1971). Segments of guinea pig ileum were set up in modified Tyrode solution containing methysergide (2.8 μM).

Bolus injections of 5-HT, tryptamine, 5,6-dihydroxytryptamine, *N*-methyl-5-HT and *N,N*-dimethyl-5-HT increased the force and rate of cardiac contraction. With the exception of *N,N*-dimethyl-5-HT, the ED_{50} responses of all the compounds were abolished by perfusion with 5-HT (7.1 μM), colchicine (1 mM) or propranolol (0.34 μM) indicating a basically similar mechanism of indirect sympathomimetic action. Responses to *N,N*-dimethyl-5-HT were abolished by colchicine or propranolol, but a small residual response occasionally remained during perfusion with 5-HT. All the compounds also stimulated the guinea pig ileum treated with methysergide. Responses to the ED_{50} of all the compounds were abolished by morphine (1.3 μM) or atropine (1.4 μM) confirming activation of the cholinergic neuronal elements of the ileum. The equiactive molar ratios for stimulation of the cardiac sympathetic nerves and the ileal cholinergic nerves are presented in Table 1.

Thus, four closely related analogues of 5-HT stimulate transmitter release from rabbit cardiac sympathetic nerves by a mechanism basically similar to 5-HT itself. The close similarity between the potencies of these compounds relative to 5-HT in this respect and on the cholinergic nerves of the guinea pig ileum would implicate a common receptor site.

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