adenohypophysial tissue *in vitro* (Buckingham & Hodges, 1977b). Acetylcholine (10^{-12}–10^{-9} M) and 5-hydroxytryptamine (5-HT) (10^{-9}–10^{-6} M) caused dose-related increases in CRF synthesis and release and their effects were antagonized by atropine, (1.4×10^{-11} M) hexamethonium (10^{-9} M) and cyproheptadine (10^{-7} M) and by methysergide (5×10^{-7} M) and cyproheptadine (10^{-7} M) respectively. Noradrenaline (10^{-8} M) also reduced the responses to acetylcholine and 5-HT. The actions of noradrenaline were mimicked by adrenaline (10^{-7} M), phenylephrine (10^{-8} M) and methoxamine (10^{-8} M) but not by isoprenaline (10^{-6} M) and antagonized by phentolamine (10^{-8} M) but not by atenolol (10^{-7} M). The results indicate the existence of cholinoceptors, 5-HT receptors and α-adrenoceptors in the hypothalamus, all of which may be involved in the control of the synthesis and release of the corticotrophin releasing factor.

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Evidence for a presynaptic inhibitory receptor for 5-hydroxytryptamine in dog isolated saphenous vein

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5-Hydroxytryptamine (5-HT) inhibits sympathetic neuronal activity in anaesthetized animals (Page & McCubbin, 1953). More recently it has been suggested that 5-HT has a presynaptic inhibitory action on neurones in the dorsal raphe nucleus (Farnebo & Hamberger, 1974; Haigler & Aghajanian, 1977). Since the dog isolated saphenous vein is a useful vascular preparation for studying presynaptic inhibitory agents (Vanhoutte & Shepherd, 1973; Verhaeghe, Vanhoutte & Shepherd, 1977) we have used it to examine the effects of 5-HT on contractile responses produced by electrical stimulation.

Dog saphenous vein strips were prepared as described previously (Apperley, Humphrey & Levy, 1977). The strips were mounted between platinum electrodes in Krebs solution at 37°C which contained indomethacin (2.8×10^{-6} mol/l) and cocaine (3.0×10^{-5} mol/l) to inhibit endogenous prostaglandin biosynthesis and uptake$_1$ respectively. The isometric contractions produced by electrical stimulation (0.1 ms, supramaximal voltage for 10 s) were frequency dependent (0.5–10 Hz). Stimulation at 2 Hz produced submaximal contractions of 0.75 ± 0.10 g (mean ± s.e. mean, $n = 20$). These contractions were almost completely blocked by tetrodotoxin (3.1×10^{-8} mol/l) or phentolamine (1.0×10^{-6} mol/l) but unaffected by mecamylamine (1.0×10^{-5} mol/l), suggesting that they were mediated predominantly via noradrenaline release from post-ganglionic neurones. Contractions of the saphenous vein induced by electrical stimulation were inhibited by 5-HT (1.0×10^{-9}–1.0×10^{-7} mol/l) in a concentration-dependent manner. The concentration of 5-HT which produced 50% inhibition was $3.2 \pm 0.6 \times 10^{-8}$ mol/l ($n = 20$); the maximal inhibition obtained was $67 \pm 4\%$. 5-HT slightly potentiated contractile responses to exogenous noradrenaline (1.0×10^{-8}–1.0×10^{-4} mol/l) which suggests that the site of the inhibitory action is presynaptic. The inhibitory effect of 5-HT was potentiated by cyproheptadine (1.0×10^{-6} mol/l) but was not antagonized by phentolamine (5.0×10^{-8} mol/l), propranolol (1.0×10^{-6} mol/l), morphine (1.0×10^{-5} mol/l), atropine (1.0×10^{-6} mol/l), mepyramine (1.0×10^{-6} mol/l) or cimetidine (1.0×10^{-5} mol/l). 5-HT also contracted the saphenous vein, although the threshold concentration was about 10 times higher than that required for inhibition of electrically induced contractions. These contractions to 5-HT were almost completely blocked by cyproheptadine (1.0×10^{-6} mol/l).

Our findings are in accord with a preliminary report that 5-HT inhibits electrically-induced release of tritiated noradrenaline from the dog saphenous vein (McGrath & Shepherd, 1976) and suggest that activation of an inhibitory presynaptic 5-HT receptor is involved. The receptor has yet to be fully characterized but, like the central inhibitory receptor (Haigler & Aghajanian, 1977), it is not blocked by the classical D-receptor antagonist cyproheptadine.

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Characterization of the β-adrenoceptors in the mesovarium of the rat

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The mesovarium is the peritoneal fold which holds the ovary in place. In the rat the mesovarium consists of connective tissue, adipose tissue and smooth muscle. Nelson & Kelly (1971) have reported that prolonged oral administration of the selective β_2-stimulant soterenol, 4.6–21.5 mg/kg daily for 18 months, resulted in the formation of benign tumours of the smooth muscle (leiomyomas) in the mesovarium of Sprague–Dawley rats. In this or in a Sprague–Dawley-derived strain of rat, prolonged oral administration of high doses of all other β_2-stimulants examined, including mesuprine (Nelson, Kelly & Weikel, 1972) and salbutamol (Poynter, Harris & Jack, 1978), caused mesovarian leiomyomas. Since mesovarian leiomyomas are normally uncommon, it is possible that the effect is mediated through activation of β-adrenoceptors. Therefore, we have investigated whether the rat mesovarian smooth muscle contains β-adrenoceptors and, if so, which subtype is present.

Isolated mesovarian strips from Charles River CD (Sprague–Dawley derived) rats, 300–400 g, were set up in Krebs solution at 37°C bubbled with 5% CO_2 in O_2. Since the preparation has no spontaneous tone the relaxant effects of β-stimulants were determined in preparations contracted with KCl ($3–6 \times 10^{-2}$ mol/l); phenoxybenzamine (7×10^{-7} mol/l) was present to eliminate actions at α-adrenoceptors. (−)Isoprenaline (0.01–100 ng/ml), (−)adrenaline

Table 1 Relative β-stimulant potencies of (−)isoprenaline, (−)adrenaline, (±)salbutamol and (−)noradrenaline on isolated rat mesovarium and guinea-pig trachea and atria

Preparation and response measured	*Receptor type*	*Mean equipotent concentration (95% confidence limits)* (−)*Isoprenaline*	(−)*Adrenaline*	(±)*Salbutamol*	(−)*Noradrenaline*
Rat mesovarium Relaxation of KCl-induced contraction	β_2	1	5 (3–8)	30 (20–47)	344 (129–914)
Guinea-pig tracheal strip Relaxation of tone	$\beta_2 > \beta_1$	1	9 (8–10)	28 (21–38)	24 (18–30)
Guinea-pig right atria Increase in rate of contraction	β_1	1	31 (16–58)	1222* (552–2707)	13 (8–20)
Guinea-pig left atria Increase in force of contraction	β_1	1	45 (26–79)	>10000*	16 (8–30)

* Partial agonist. All experiments were carried out in presence of phenoxybenzamine (7×10^{-7} mol/l). Each mean equipotent concentration was obtained from not less than 5 individual experiments.