Glucagon hydrochloride (Lilly; 100 μg base, i.a.) was injected on 14 occasions to 5 preparations, causing a transient but significant ($P < 0.001$) reduction in HAVR of 19.9 ± 3.3%, an effect similar to that found by Bashour, Geumei, Nafrawi & Downey (1973). One minute after these glucagon injections, the increase in HAVR in response to noradrenaline (10 μg, i.a.) was 14.9 ± 4.2% of the control effect to angiotensin (0.5 μg, i.a.) 5.1 ± 2.4%, and to vasopressin (0.1 u, i.a.) 11.0 ± 4.5% showing highly significant ($P < 0.001$) attenuation of the vasoconstrictor effects of these compounds. The vasoconstrictor responses progressively returned to control values within 8-10 min after the glucagon injections.

When glucagon was infused into the hepatic artery in dose from 10-50 $\mu g\ min^{-1}$ for 11-13 min, the vasoconstrictor effects of noradrenaline, angiotensin and vasopressin were suppressed throughout the course of the infusions.

Glucagon has been shown to reduce the effects of α-adrenoceptor stimulation on the superior mesenteric arterial vascular bed (Kock, Tibblin & Schenk, 1971); the present study has shown that a similar attenuation of the effects of vasoconstrictor agents on the hepatic arterial bed is not limited to α-adrenoceptor agonists. This action of glucagon represents a protection of the hepatic arterial vasculature from the effects of circulating vasoconstrictor agents in states by hypoglycaemia when mobilization of hepatic glycogen would be necessary.

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Investigations concerning TRH-induced hypothermia in cats

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Thyrotrophin releasing hormone (TRH) has been known to exert an essential function in normal thyroid metabolism for some years but recently it has been investigated in a wider context. In 1974 Metcalf reported that TRH produced hypothermia when injected into the cerebral ventricles of the unanaesthetized cat but hyperthermia when injected similarly into the rabbit. The present experiments were undertaken to compare the hypothermic effect of TRH with that of noradrenaline (NA) and calcium ions (Ca^{++}) both of which cause hypothermia in the cat (Feldberg & Myers, 1963; Myers & Veale, 1971). In addition experiments were undertaken with the amino acids which compose TRH and the thyroid hormones which it releases to ascertain whether the hypothermic action of TRH was related to its endocrine functions.

TRH (50-200 ng), NA (25-200 μg), and Ca^{++} (20-80 mM in excess of the amount found in CSF) all produced dose-related falls in body temperature when injected intraventricularly (i.c.v.) into the unanaesthetized cat. Of the three TRH was the most potent and it was estimated that the equi-potent molar ratio TRH; NA; Ca^{++}; was 1; 900; 27,000. Unlike NA or Ca^{++} the doses of TRH necessary to produce hypothermia compared well with the estimated endogenous concentration of TRH (Winokur & Utiger, 1974). In addition to hypothermia TRH induced profuse salivation, tachypnoea, cutaneous vasodilatation and frequent defecation and vomiting. Animals given NA or Ca^{++} rarely exhibited these symptoms and usually appeared quiet or sedated. Statistical analysis demonstrated a positive correlation ($r = +0.82$; $P < 0.001$) between the increased respiratory rate and the fall in temperature observed after TRH injections. Thus, the heat loss caused by panting is considered an important factor in TRH induced hypothermia in the cat but does not explain other central actions reported for TRH.

Prior treatment of cats with α-methyltyrosine (100 mg i.c.v.) depletes cerebral stores of noradrenaline (Cranston, Hellon, Luff & Rawlins, 1972) and prevents the hypothermia induced by tyramine which acts indirectly via noradrenaline release (Metcalf & Myers, 1975). Pretreatment with α-methyltyrosine did not prevent hypothermia induced by either TRH or Ca^{++}. Similarly

the α-receptor antagonist, phentolamine (125 μg i.c.v.), did not affect TRH or Ca^{++}-induced hypothermia but antagonized hypothermia provoked by NA. Although TRH is a tripeptide composed of pyroglutamic acid, histidine and prolineamide, none of these amino acids (0.1 μg, i.c.v.) produced effects similar to TRH. Thyroxine (0.25-1.0 μg, i.c.v.) caused a dose-related rise in temperature of slow onset (2 h) consistent with its known effect as a metabolic stimulant whereas thyrotropin (TSH) (0.2-0.8 i.u., i.c.v.) produced a gradual, sustained hypothermia which was unrelated to dose and which was not accompanied by an increase in respiratory rate.

It is concluded that the hypothermia produced in the cat by the i.c.v. injection of TRH is unrelated to its endocrine function and is not mediated by cerebral noradrenaline.

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Central hypertensive action of histamine in rats

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Intraventricular (i.c.v.) injection of histamine in cats has been shown to produce a short lasting rise in blood pressure, with an associated tachycardia (Trendelenburg, 1957; White, 1965; Sinha, Gupta & Bhargava, 1969). Similarly Brezenoff & Jenden (1969) were able to show a pressor response to intrahypothalamic injection of histamine in rats. However, Corrêa & Graeff (1969) and Jagiello-Wojtowicz (1973) failed to demonstrate the hypertensive response to i.c.v. histamine in rats.

In this study we have shown that i.c.v. administration of histamine elicits increases in blood pressure and heart rate in anaesthetized rats and we have examined possible mechanisms of action involved in these histamine-mediated cardiovascular changes.

Histamine (0.1-10 μg i.c.v.) caused a dose-related increase in blood pressure and heart rate in urethane-anaesthetized rats. Pretreatment with mepyramine (50 μg and 100 μg i.c.v.) produced a dose-related antagonism of the cardiovascular effects induced by a sub-maximal dose of histamine (1.0 μg i.c.v.). However pretreatment with metiamide, a histamine-H_2 receptor antagonist, in doses of 100 and 200 μg i.c.v., or procaine (300 μg i.c.v.) did not significantly modify the cardiovascular effects of histamine (1.0 μg i.c.v.) ($P > 0.05$).

Intraventricular administration of phentolamine (100 and 200 μg i.c.v.) caused a dose-dependent antagonism of the histamine-induced pressor effect, whilst peripheral administration of phentolamine (5 mg/kg i.v.) totally abolished this hypertensive response. Neither treatment significantly modified the positive chronotropic effect produced by histamine ($P > 0.05$).

6-Hydroxydopamine (3 x 250 μg i.c.v.) or mecamylamine (5 mg/kg i.v.) abolished both the pressor response and tachycardia to i.c.v. administered histamine, while atropine (100 μg i.c.v.) or propranolol (1 mg/kg i.v.) abolished the tachycardia without modifying the blood pressure rise. Acute bilateral vagotomy or adrenal demedullation failed to modify either cardiovascular change.

The results demonstrate that i.c.v. administration of histamine elicits blood pressure and heart rate increases in anaesthetized rats and are consistent with the view that centrally increased sympathetic nerve activity mediates these responses. Furthermore the central action of histamine appears to be mediated via histamine-H_1-receptors, although central adrenergic and cholinergic mechanisms also appear to be involved.

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