Corticotrophin production by rat adenohypophysial segments *in vitro*

JULIA C. BUCKINGHAM* & J.R. HODGES

Department of Pharmacology, Royal Free Hospital School of Medicine, London WC1N 1BP

A method for the direct assessment of the adrenocorticotrophic activity of pituitary segments has been developed using the cytochemical bioassay for corticotrophin (ACTH) (Chayen, Loveridge & Daly, 1972; Alaghband-Zadeh, Daly, Bitensky & Chayen, 1974). The responsiveness of the rat adenohypophysis *in vitro* to some substances known to affect adrenocorticotrophic activity has been studied. Anterior pituitary glands were rapidly removed from freshly killed male albino Sprague-Dawley rats, carefully bisected and incubated for 2.5 h at 37°C in an artificial medium (Bradbury, Burden, Hillhouse & Jones, 1974) gassed with 95% O_2/5% CO_2. The medium was then replaced with similar medium containing the test substance. Fifteen minutes later the ACTH contents of the medium and the adenohypophysial tissue were determined separately. Lysine vasopressin, arginine vasopressin and acid hypothalamic extracts (Hiroshige, Kunita, Yoshimura & Itoh, 1968) resulted in marked, dose-related increases in both pituitary ACTH release and content. Cortisol (10-500 ng/ml) added to the final incubation medium inhibited the release but not the synthesis of ACTH induced by these substances. The method is potentially useful both for the identification and the assay of corticotrophin releasing hormone (CRH).

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The effects of glucagon on the hepatic arterial vasculature of the dog: an inhibition of the effects of vasoconstrictor agents

P.D.I. RICHARDSON* & P.G. WITHRINGTON

Department of Physiology, The Medical College of St. Bartholomew's Hospital, Charterhouse Square, London EC1M 6BQ

Glucagon is released from the pancreas and small intestine, and its effects on the hepatic vasculature may well be of functional significance. In these experiments, the action of glucagon, and its effects on responses of the hepatic arterial vasculature to noradrenaline, angiotensin and vasopressin have been examined.

Seven female dogs (10-16 kg) were anaesthetized with chloralose (Kuhlman, Paris; 50 mg kg^{-1}) and urethane (BDH; 500 mg kg^{-1}) i.v., after induction with methohexitone sodium ('Brietal', Lilly; 7.5-10.0 mg kg^{-1}, i.v.). The hepatic artery, dissected free from its periarterial sympathetic nerves which were then divided, was cannulated close to its origin from the aorta, and perfused with blood from a cannulated femoral artery. The hepatic arterial perfusion pressure was measured close to the cannula in the hepatic artery, and blood flow in this system measured with a cannulated flow probe and electromagnetic flowmeter.

The initial control values (means ± s.e. means) were hepatic arterial mean perfusion pressure (HAPP), 119.2±5.9 mmHg and hepatic arterial blood flow (HABF) 38.8 ± 5.3 ml min^{-1} 100 g^{-1}. The calculated hepatic arterial vascular resistance (HAVR) was 3.31 ± 0.38 mmHg ml^{-1} min 100 g. *Post-mortem*, the livers weighed 324.8 ± 69.6 (mean ± s.d.) grams.

In 5 experiments, noradrenaline acid tartrate ('Levophed', Winthrop; 10 μg base, i.a.) caused a significant ($P < 0.001$; paired t-test) increase in hepatic arterial vascular resistance (HAVR) of 129.8 ± 19.7% ($n = 11$ injections). Angiotensin amide ('Hypertensin', Ciba; 0.5 μg salt, i.a.) caused a significant ($P < 0.001$) rise in HAVR of 161.1 ± 25.5% ($n = 12$), and vasopressin ('Pitressin', Parke-Davis; 0.1 unit, i.a.) caused a significant rise ($P < 0.01$) in HAVR of 98.7 ± 22.4% ($n = 9$).

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

G. METCALF* & R.D. MYERS

Laboratory of Neuropsychology, Department of Psychological Sciences, Purdue University, West Lafayette, Indiana 47907, USA

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