Short communications

Central adrenoceptors concerned in the release of adrenocorticotrophic hormone

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The effect of injecting the α-adrenoceptor stimulating drugs adrenaline, noradrenaline and phenylephrine and the β-adrenoceptor stimulating drug, isoprenaline into the lateral ventricles (i.c.v.) of the brains of dogs on the plasma cortisol concentration was investigated. Adrenaline, noradrenaline and phenylephrine produced a significant rise in the plasma cortisol concentration. Isoprenaline had no effect on the plasma cortisol concentration. The effect of noradrenaline and phenylephrine on the plasma cortisol concentration was completely blocked by yohimbine (i.c.v.). This indicates that the stimulation of central α-adrenoceptors can cause the release of adrenocorticotrophic hormone.

The peripheral administration of adrenaline to albino rats has been shown to cause a depletion of the adrenal ascorbic acid and cholesterol contents (Long & Fry, 1945; Gershberg, Fry, Brobeck & Long, 1950; Hodges, 1953; Guillemin, 1955; Arimura & Long, 1962). These effects could be abolished by hypophysectomy (Long & Fry, 1945), administration of α-adrenoceptor blocking agents (Guillemin, 1955) or a lesion in the median eminence (Royce & Sayers, 1958). Injection of adrenaline into the third ventricle of the rat brain induced changes in the integrated multiple-unit electrical activity of the median eminence which was possibly related to the secretion of ACTH (Weiner, Rubinstein & Sawyer, 1971). An increase in the plasma steroid concentration has been observed in man after the injection of adrenaline (Corcoran & Page, 1948).

In the present study, the effect of an injection into a lateral cerebral ventricle of adrenaline, noradrenaline, phenylephrine or isoprenaline on the plasma cortisol concentration was studied in dogs.

Methods.—Mongrel dogs of either sex were anaesthetized with pentobarbitone sodium (30 mg/kg i.v.) and a permanent cannula was implanted into a lateral cerebral ventricle under aseptic conditions. Peripheral blood (6 ml) was collected in tubes containing heparin to obtain plasma for the estimation of cortisol. Blood samples were collected 24 h after the operation (control samples) and 30 min after the intracerebroventricular administration of each drug. The plasma cortisol concentrations were estimated by the fluorescence method of Mattingly (1962).

Results.—The effects of the intracerebroventricular (i.c.v.) injection of adrenaline, noradrenaline, isoprenaline, phenylephrine and yohimbine on plasma cortisol concentration are shown in Table 1. Adrenaline and noradrenaline which act on α-adrenoceptors caused a significant rise in the plasma cortisol concentration, whereas isoprenaline, which acts on β-adrenoceptors, failed to change the plasma cortisol concentration. Phenylephrine, a more specific α-receptor stimulating drug also caused an increase in the plasma cortisol concentration, which was dose-dependent. In another series of experiments on twelve dogs, the effect of an i.c.v. injection of yohimbine, a drug which blocks α-adrenoceptors, on the plasma cortisol concentration was studied. Table 1 shows that yohimbine had no significant effect on the concentration of cortisol in the plasma and that the subsequent administration of noradrenaline or phenylephrine no longer resulted in an increase in the concentration of plasma cortisol.

Discussion.—Noradrenaline and adrenaline are found in high concentrations in the hypothalamus (Vogt, 1954). Furthermore, recent histochemical studies employing fluorescence histochemical techniques have demonstrated the presence of catecholamine-containing neurones in certain areas of the hypothalamus with their terminal axons in the region of the median eminence (Fuxe, 1964; Fuxe & Hokfelt, 1968). Endocrinological effects of drugs that interfere with monoamine metabolism suggest the participation of monoaminergic mechanisms in the regulation of hormone secretion from the anterior pituitary (Gold & Ganong, 1967). It is well known that the corticotrophin releasing factor (CRF) is transported to the anterior pituit-

TABLE 1. *Effect of intracerebroventricular injection of α- and β-adrenoceptor agonists and an α-adrenoceptor blocking agent on plasma cortisol concentration in dogs*

Adrenoceptor agonists	Dose μg (i.c.v.)	Pre-treatment dose μg (i.c.v.)	Plasma cortisol concentration (μg %±S.E.)	*P* value (comparison with control)
Control (0·9% w/v NaCl solution)	0·2 ml (11)	—	16±2·1	—
(−)-Adrenaline	5 (5)	—	37±7·6	<0·01
(−)-Noradrenaline	5 (5)	—	49±12·6	<0·01
(−)-Phenylephrine	2 (3)	—	22±2·3	>0·05
	5 (5)	—	45±4·1	<0·001
	10 (5)	—	52±2·2	<0·001
(±)-Isoprenaline	5 (4)	—	10±3·5	>0·05
	25 (3)	—	18±5·3	>0·05
	50 (3)	—	16±1·8	>0·05
—	—	Yohimbine 1,500 (4)	9±3·5	>0·05
(−)-Noradrenaline	5 (4)	Yohimbine 1,500 (4)	11±3·5	>0·05
(−)-Phenylephrine	5 (4)	Yohimbine 1,500 (4)	13±0	>0·05

Figures in parentheses indicate number of animals.

ary via the pituitary portal circulation to bring about the release of adrenocorticotrophic hormone which is responsible for the release of cortisol from the adrenal cortex.

Since the central administration of α-adrenoceptor agonists induced a significant rise in the plasma cortisol concentration and this effect was fully blocked by the α-adrenoceptor blocking agent, yohimbine, it may be concluded that the central adrenoceptor involved in the release of CRF in our experiments is of the α-type. β-Adrenoceptor participation is ruled out because isoprenaline did not cause an increase in the plasma cortisol concentration when injected into the cerebral ventricles.

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