Adrenergic effector mechanisms in the stomach of the sheep

SIR,—Miert & Huisman (1968) reported evidence for the presence of α-stimulatory and β-inhibitory receptors in the wall of the rumen of the sheep.

We, too, find similar adrenergic effector mechanisms in another part of the stomach of the sheep, the reticulo-omasal orifice. Our experiments were made in decerebrate preparations of wholly milk fed lambs (up to 10 kg in weight and 6 weeks of age) and in lambs and normally fed sheep anaesthetized with chloralose (60–70 mg/kg). In all experiments anaesthesia was induced by the inhalation of halothane. Access to the reticulo-omasal orifice was obtained through an incision made in the reticulum after a mid-ventral laparotomy. The activity of the reticulo-omasal orifice was recorded from a water filled balloon retained in it and connected to a transducer (Setekleiv, 1964) to obtain either isotonic or isometric recordings with a Siemens Mingograph jet writing recorder. The results obtained from both records were similar and were confirmed by direct observation of the reactions of the reticulo-omasal orifice in the absence of the balloon. The drugs used were: (−)-adrenaline (Parke Davis), (−)-noradrenaline (Winthrop), isoprenaline (Winthrop), the α-adrenergic blocking agents tolazoline (CIBA) and phentolamine (CIBA) and the β-blocking agent propranolol (I.C.I.). They were injected into a saphenous vein or into the aorta cranial to the origin of the coeliac trunk. Both vagus nerves had been cut in the neck in all the experiments.

After intravenous or intra-aortic injections of adrenaline or noradrenaline (in doses, as the base, of 1–10 μg/kg) there was a closure of the reticulo-omasal orifice. This effect was obtained in all the preparations and proved to be repeatable in all. Recurrent openings and closures of the orifice, such as were detected before the amines were injected, ceased for a period after the contraction. The effect of these amines is thus interpreted as being excitatory in causing a closure of the orifice and inhibitory in producing a reduction in tonic activity. Adrenaline was more potent in causing a closure of the orifice than were equal doses of noradrenaline, but was less potent in producing an inhibition of tonic activity and an opening of the reticulo-omasal orifice than was noradrenaline.

When the α-blocking agents phentolamine and tolazoline (0·2–1·0 mg/kg) had been given intravenously there was no longer a closure of the reticulo-omasal orifice after the injection of adrenaline or noradrenaline; however, the inhibitory effects of these agents remained, and noradrenaline again proved more potent in causing an opening of the orifice.

Isoprenaline (1–10 μg/kg) was found to have a purely inhibitory effect on the reticulo-omasal orifice. Its effects and the inhibitory effects of adrenaline and noradrenaline were abolished by the administration of the β-blocking agent propranolol (0·1–0·3 mg/kg).

Evidence (cited by Miert & Huisman, 1968) for adrenergic excitatory effects on different parts of the ruminant stomach now includes the rumen, omasum and abomasum, and confirms the effect on the reticulum reported by Comline & Titchen (1951), who also obtained effects with sympathetic nerve stimulation.

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Aggressive behaviour provoked by pargyline in rats pretreated with diethyldithiocarbamate

SIR,—We have previously described various forms of aggressive behaviour induced by drugs affecting the brain amines (Randrup & Munkvad, 1966; 1968).

An excitation characterized by fighting, vocalization together with sudden bursts of fast running was reported in experiments with rats treated with monoamine oxidase inhibitors + L-dopa, the physiological precursor of the catecholamines, dopamine and noradrenaline. Biochemically this behaviour was connected with high levels and turnover of dopamine and noradrenaline (Scheel-Krüger & Randrup, 1967).

The present paper deals with an aggressive behaviour induced by the monoamine oxidase inhibitor pargyline in rats pretreated with repeated doses of disodium diethyldithiocarbamate $2H_2O$ (DDC).

DDC inhibits the synthesis of brain noradrenaline by blockade of the enzyme dopamine-β-oxidase (Goldstein & Nakajima, 1966; Carlsson, Lindqvist & others, 1966).

Male Wistar rats weighing 225–275 g were used. Rats (22) were observed after four doses of DDC given subcutaneously; 18 hr after the first dose of 500 mg/kg, the rats received 500, 50 and 500 mg/kg subcutaneously at intervals of 2 hr.

Another 35 rats were given pargyline hydrochloride (150 mg/kg s.c.) 2 hr before the last DDC injection, while 21 rats received pargyline alone.

The brain content of dopamine, noradrenaline and their respective 3-*O*-methylated metabolites, 3-methoxytyramine and normetanephrine, was analysed by a method involving chromatographic separation of the amines followed by a fluorimetric determination (Scheel-Krüger & Randrup, 1967; Jonas & Scheel-Krüger, unpublished).

The rats treated with the four injections of DDC were already sedated (no spontaneous activity in the home cage) before the last dose of DDC. The sedation persisted for at least 6 hr.

A striking contrasting behavioural excitation of aggressive character was provoked by the additional dose of pargyline.

The aggressive behaviour began 4–5½ hr after pargyline and increased in intensity during the following 2–3 hr.

Bursts of spontaneous vocalization were sometimes heard from rats kept in individual cages. Two rats placed in the same cage reared face to face in defence posture striking at each other with their forelegs. Much vocalization was heard in this situation (26/35 rats showed this behaviour). Rats receiving pargyline only as a control did not show these aggressive features. Vocalization and stereotyped sniffing have been observed after monoamine oxidase inhibitors