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BRIEF COMMUNICATION

Lack of Behavioural Effects Following Intraventricular Infusion of Somatostatin in the Conscious Goat

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GORDIN, A., L. ERIKSSON, A. K. BLOM, M. R. TASKINEN AND F. FYHRQUIST. *Lack of behavioural effects following intraventricular infusion of somatostatin in the conscious goat.* PHARMAC. BIOCHEM. BEHAV. 9(2) 255–257, 1978.—The effect of IV or intracerebroventricular (ICV) administration of somatostatin was studied on the behaviour of conscious goats. The doses of somatostatin infused IV were 100 and 300 μg for 30 min and 600 μg for 6 min. The doses infused ICV were 10 and 100 μg for 30 min and 600 μg for 6 min. In contrast to earlier reports on experiments with rats, no behavioural effects whatsoever were seen in goat. IV infusion of 100 to 600 μg and ICV infusion of 600 μg of somatostatin caused a definite reduction in the secretion of insulin and growth hormone, but had no effect on the concentration of blood glucose. The reason why neither IV nor ICV administration of somatostatin had any behavioural effects in the conscious goat, in contrast to the effects in rat, cannot be explained with certainty. This may be due to species specificity, to the amount of somatostatin reaching the central nervous system, or to some metabolic changes in rat but not in goat.

Behaviour Intraventricular administration Somatostatin Blood glucose Insulin Growth hormone

IT HAS been shown in several recent reports that both systemic and direct intracerebroventricular (ICV) administration of somatostatin induces a variety of motor, behavioural, electrophysiological and biochemical phenomena in rat [3, 4, 6, 9]. These effects seem to be unrelated to the well-known endocrine effects of this hormone.

We have studied behavioural, motor and some hormonal effects following IV and ICV infusion of somatostatin in the conscious goat. In contrast to earlier reports on rat, no behavioural or motor abnormalities due to somatostatin were seen in goat.

MATERIAL AND METHODS

Animals and Animal Care

Nine adult female and two castrated male goats (weighing 28–47 kg) were used for repeated experiments. The animals were kept in metabolism cages, where the experiments were conducted. The goats had free access to hay and water.

Procedure

The goats were prepared with a permanent cannula in the anterior part of the lateral cerebral ventricle at least 2 weeks prior to the experiments. The implantation and ICV infusion techniques have been described earlier [2]. IV infusions were given via the jugular vein.

Cyclic somatostatin (Ferring International, Malmö, Sweden) was infused ICV in doses of 10 and 100 μg/0.3 ml of physiological saline (at a rate of 10 μl/min) or IV in doses of 100 and 300 μg/15 ml of saline for 30 min. Blood samples were obtained via a Braunule cannula inserted into the jugular vein 30 min and 2 min before the start of the infusion and at 15 min intervals for 60 min followed by 30 min intervals for another 60 min. In another series 600 μg somatostatin was infused over 6 min either ICV (at a rate of 50 μl/min) or IV in 0.3 or 6 ml of saline, respectively. Blood samples were taken 30 min and 2 min before and 10, 30, 45 and 60 min after the start of the infusion. Each dose of somatostatin was tested in 2–5 animals.

Blood samples for the determination of plasma glucose, insulin and growth hormone (GH) were collected in prechilled tubes containing 0.25 ml of EDTA (0.3 M) and 500 IU of aprotinin (Apronin®, Medica, Finland) per 8 ml of blood. The samples were immediately cooled and centrifuged at 4°C.

Behavioural Observations

The goats are well accustomed to the laboratory conditions and are alertly following their environment without any signs of stress and fear. They can move within the metabolism cages and the infusions can be performed without the animal noticing it. Therefore it is easy to observe

TABLE 1

EFFECT OF INTRACEREBROVENTRICULAR (ICV) AND INTRAVENOUS (IV) INFUSION OF 600 μG OF SOMATOSTATIN FOR 6 MIN (0–6 MIN) ON PLASMA GLUCOSE, INSULIN AND GROWTH HORMONE (GH) LEVELS IN CONSCIOUS GOATS

Animal No.	Route of administration	−30	−2	+10	+30	+45	+60 min
Plasma-glucose (mmol/l)							
7	icv	3.3	3.1	3.0	2.8	3.0	3.1
8	icv	2.9	2.7	3.2	3.5	3.4	3.0
9	icv	2.6	2.5	2.5	2.9	2.8	2.8
10	iv	2.7	2.7	2.7	3.0	3.1	2.9
11	iv	3.4	3.4	3.6	3.8	3.9	3.9
Insulin (μU/ml)							
7	icv	7	7	3	4	4	7
8	icv	6	6	5	5	6	6
9	icv	14	14	9	7	10	10
10	iv	11	11	7	7	11	10
11	iv	9	9	4	5	9	10
GH (ng/ml)							
7	icv	2.7	3.0	—	2.7	2.5	2.7
8	icv	5.3	7.2	4.5	4.2	4.0	4.6
9	icv	30.0	30.0	19.0	24.5	27.5	31.7
10	iv	4.7	4.5	3.2	4.0	3.8	3.9
11	iv	3.5	3.2	1.0	1.0	1.3	4.5

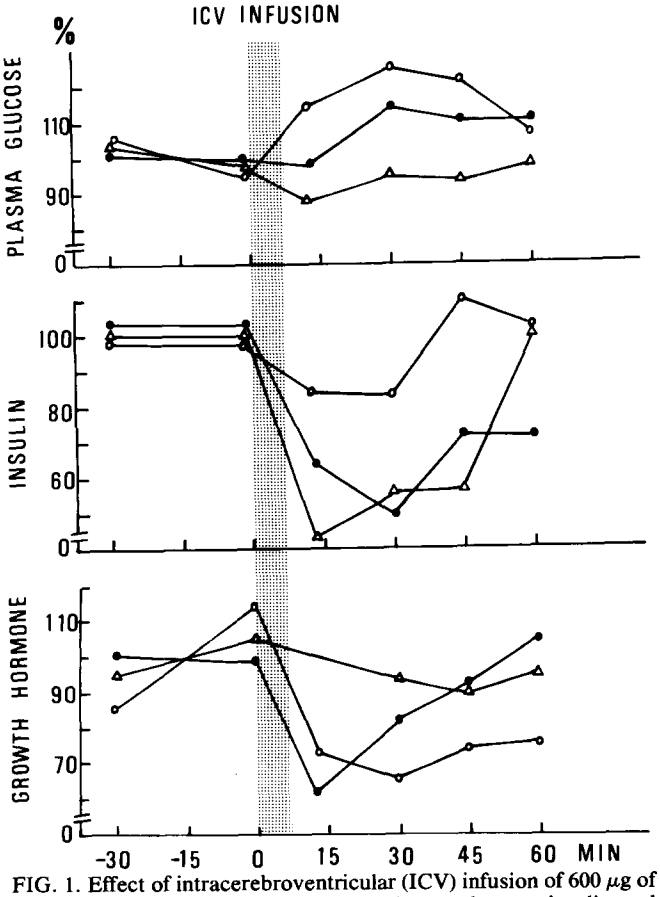

FIG. 1. Effect of intracerebroventricular (ICV) infusion of 600 μg of somatostatin for 6 min (0–6 min) on plasma glucose, insulin and growth hormone levels in three conscious goats. The results are expressed as % of the baseline values, which were calculated as the mean of the two preinfusion samples.

changes in behaviour (any exceptions from normal behaviour). The behavioural parameters followed were: alertness, drinking of water, eating, ruminating, spontaneous motility, vocalisation and pattern of respiration.

Assays

Plasma glucose was determinated using a Beckman glucose-analyser by a polarographic method and insulin and GH by radioimmunoassay [8].

RESULTS

No pathological behavioural or motor effects were seen after either ICV or IV infusion of somatostatin even if given in huge pharmacological doses.

IV infusion of somatostatin in doses of 100–300 μg for 30 min or 600 μg for 6 min caused a definite decrease in insulin and GH without affecting the glucose concentration. ICV infusion of 10 and 100 μg for 30 min did not change the glucose, insulin or GH levels. On the other hand, infusion of 600 μg of somatostatin ICV caused a definite reduction in the secretion of insulin and GH, but had no effect on plasma glucose (Fig. 1, Table 1).

DISCUSSION

The conscious goat with a permanent ICV cannula provides an excellent animal model for testing the central effects of various psychoactive substances. These animals are very cooperative and behavioural patterns can easily be recorded [1].

This is why we chose to study the central effects of somatostatin in this species. However, no pathological behavioural or motor effects whatsoever were seen during or after the administration of even 600 μg of somatostatin over a period of a few minutes. This is in contrast with earlier reports on experiments in rat [4,6], where central infusion of

somatostatin introduced a variety of behavioural and motor effects. These included excitation, barrel rotation, facial and generalised tremors, motor coordination difficulties and even tonic-clonic seizures. The behavioural pattern varied depending on the site of infusion and the dose used, the effects of small doses differing from those of larger ones [10, 11, 12, 13].

IV infusion of somatostatin decreased the insulin and GH concentration as expected, while it did not affect the blood glucose level. One possible explanation for the fact that the glucose concentration did not decrease is that volatile fatty acids are the main energy source in ruminants, while glucose plays a minor role in this respect [5]. Rapid infusion of 600 μg of somatostatin ICV caused a reduction in the serum insulin and growth hormone levels, comparable to that seen after similar IV infusion. These effects may be due to a direct central effect of somatostatin or most probably of the diffusion of this peptide into the peripheral circulation.

It cannot be explained with certainty why somatostatin did not cause any behavioural effects in goat in contrast to those seen in rat, though it is possible to theorize on this matter. First, this may simply be due to species specificity. Secondly, the amount of somatostatin reaching the central nervous system might be greater in the rat, in spite of quite comparable doses used, since the cerebral ventricles are naturally much smaller in the rat than in goat. Again, experiments with psychoactive drugs would lead one to expect even smaller doses applied ICV to be effective. Thirdly, the effects seen in the rat may be due to metabolic changes (i.e. hypoglycaemia) not occurring in the goat.

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