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Vasopressin Inhibits Food Intake in Pygmy Goats by Activation of α_1-Adrenergic Receptors

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ROSSI, R. AND E. SCHARRER. *Vasopressin inhibits food intake in pygmy goats by activation of α_1-adrenergic receptors.* PHARMACOL BIOCHEM BEHAV **49**(4) 897–900, 1994.—Vasopressin (VP) is known to reduce food intake in pygmy goats. The hypophagic effect of intraperitoneally injected VP (1.5 μg/kg) was blocked by concomitant injection of the α_1-adrenergic antagonist prazosin (27 and 40 μg/kg). Both the α_2-adrenergic antagonists idazoxan (300 μg/kg) and yohimbine (500 μg/kg) and the β-adrenergic antagonist propranolol (500 μg/kg) failed to block the hypophagia induced by VP (1.5 μg/kg). The results suggest that the hypophagic effect of VP is mediated by α_1-adrenergic receptors.

Vasopressin Food intake α_1-Adrenergic receptors Pygmy goats

THE neurohypophyseal hormone vasopressin (VP) is one of the hormones that coordinates the response to stress (10). Stressful stimuli eliciting anorexia (3,15) often trigger an increase in plasma VP level (6,7,19). Because VP has been shown to reduce food intake in rats (9) and pygmy goats (13), it has been associated with stress-induced anorexia (13). The hypophagic effect of VP seems to be mediated by an activation of adrenergic mechanism because phentolamine, an antagonist blocking α_1 and α_2-adrenergic receptors eliminated this effect (9,13). In the present study, we wanted to find out which subtype of adrenergic receptor mediates VPs anorectic effect. VP induced hypophagia as affected by α_1- and α_2-adrenergic antagonists was, therefore, investigated. For comparison, a β-adrenergic antagonist was also tested in this regard.

METHOD

Twelve adult nonlactating female African pygmy goats (age: 4–8 years), with a body weight of 25 to 40 kg, were used for the experiments. The goats were housed in pens (1.25 × 1.35 m) in a room that was kept on an artificial light : dark cycle (light: 0900–2100). They were fed a pelleted diet (Hypona Optimal 888, Volg, Winterthur, Switzerland). Water was always available. Food was offered in spill-resistant food containers that were fixed on scales (8). The actual weight of the food containers was checked each minute by a Hewlett-Packard personal computer (HP85). Every 2 h cumulative food intake was recorded by the computer for each animal. On test days, the goats were food deprived for 2 h (0900–1100). Injections were given intraperitoneally (IP) at 1100, and the cumulative food intake was recorded for the following 10 h. Control animals received an equivalent volume (injection volume: 1 ml/10 kg body weight) of the vehicle. All drugs except prazosin and yohimbine were dissolved in saline (0.9% NaCl). Prazosin and yohimbine were dissolved in a 30% (vol/vol) solution of ethanol. Injected solutions were freshly prepared on test day. For each experiment six control goats were compared to six goats receiving the test substance. Two days later, the trial was repeated in counterbalanced order. The data of both trials were combined. The interval between the experiments was about 1 week.

Seven experiments were conducted (in chronological order):

1. injection of VP (1.5 μg/kg) or saline (control);
2. injection of yohimbin (500 μg/kg) or yohimbine (500 μg/kg) + VP (1.5 μg/kg);

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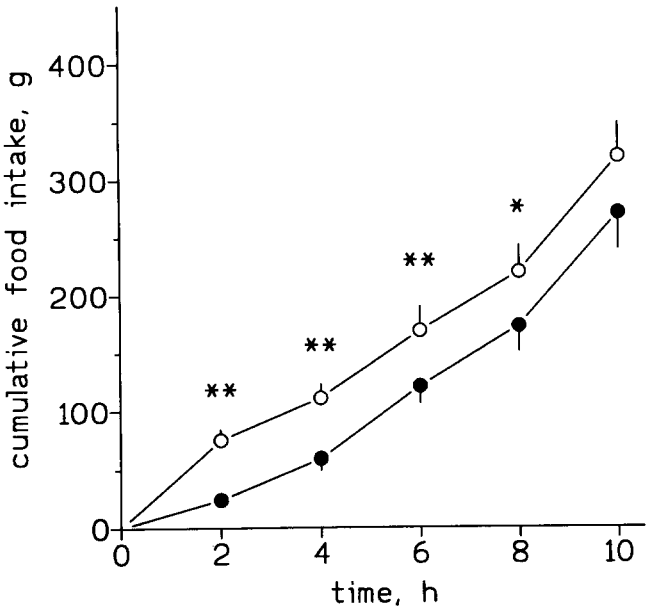

FIG. 1. Depressed food intake after VP injection (1.5 μg/kg IP, filled circles) in comparison to controls (open circles). *,**Significantly different from control values, $*p < 0.05$, $**p < 0.01$.

3. injection of prazosin (15 μg/kg) or prazosin (15 μg/kg) + VP (1.5 μg/kg);
4. injection of prazosin (27 μg/kg) or prazosin (27 μg/kg) + VP (1.5 μg/kg);
5. injection of prazosin (40 μg/kg) or prazosin (40 μg/kg) + VP (1.5 μg/kg);
6. injection of idazoxan (300 μg/kg) or idazoxan (300 μg/kg) + VP (1.5 μg/kg);
7. injection of propranolol (500 μg/kg) or propranolol (500 μg/kg) + VP (1.5 μg/kg).

The doses cited refer to the salt of drugs used.

Due to crossover design of the experiments, differences between treatments were statistically evaluated using two-way analysis of variance (ANOVA) and the Bonferroni post hoc test. p-Values less than 0.05 were considered significant.

Drugs

Chemicals used: Arg-vasopressin (No. 9879, Sigma, St. Louis, MO); DL-propranolol HCl (No. P-0884, Sigma); prazosin HCl (P-7791, Sigma); idazoxan HCl (No. 6138, Sigma); yohimbine HCl (No. 3125, Sigma).

RESULTS

As shown in Fig. 1, VP (1.5 μg/kg) caused a hypophagia that was not compensated within 10 h. Coinjection of the α_2-adrenergic antagonists idazoxan (300 μg/kg), yohimbine (500 μg/kg), and the β-adrenergic blocker propranolol (500 μg/kg) failed to reduce the hypophagic effect of VP (1.5 μg/kg) (Fig. 2). The injection of the α_1-adrenergic antagonist prazosin reduced the hypophagic effect of VP (1.5 μg/kg) dose dependently (15, 27, 40 μg/kg) (Fig. 3). Idazoxan (300 μg/kg), yohimbine (500 μg/kg), and propranolol (500 μg/kg) had no effect on cumulative food intake when injected alone. Prazosin (40 μg/kg) alone slightly depressed food intake after 6 h (23), whereas at a dose of 15 and 27 μg/kg, food intake was not affected (results not shown).

DISCUSSION

In the present study, the hypophagic effect of VP in pygmy goats was consistently reduced by the α_1-adrenergic antagonist prazosin, whereas the α_2-adrenergic antagonists idazoxan and yohimbine remained without effect. Also the β-adrenergic antagonist propranolol did not affect the hypophagic effect of VP. These findings suggest that the hypophagic effect of VP is mediated by activation of α_1-adrenergic receptors.

As reported by Meyer et al. (13), VP decreases rumination activity in pygmy goats. This effect could be due to an inhibitory effect of VP on reticuloruminal contractions (12,25, 28,30). The depression of rumen motility induced by VP may be related to the hypophagic effect of VP because there is evidence that food intake in ruminants is related to rumen motility (17,24). Although peripheral and central stimulation of α_2-adrenergic receptors inhibits rumen motility and food intake in ruminants (16,17,26,27), these receptors seem

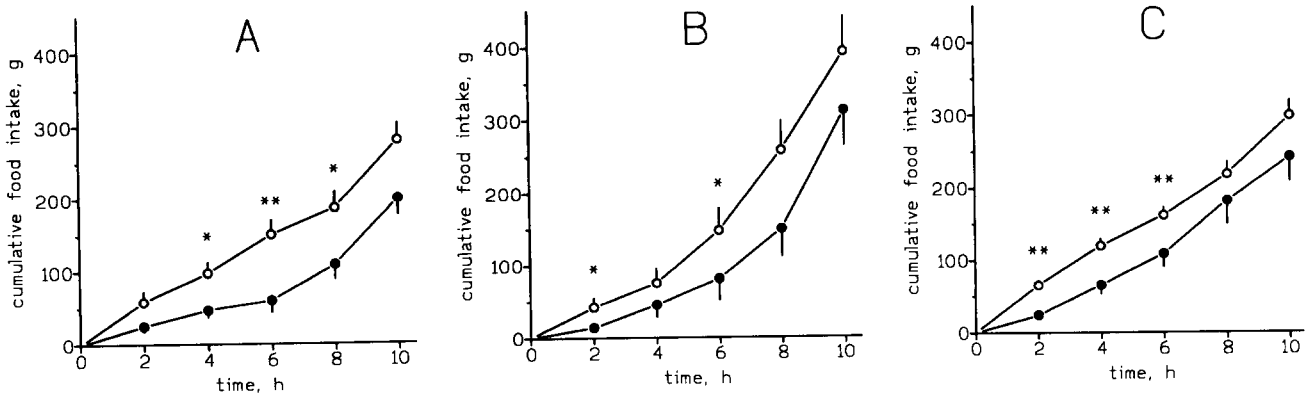

FIG. 2. Lack of effect of the α_2-adrenergic antagonists idazoxan (A, 300 μg/kg) and yohimbine (B, 500 μg/kg), and the β-adrenergic antagonist propranolol (C, 500 μg/kg) on the hypophagic effect of VP (1.5 μg/kg). Filled circles: VP + adrenergic antagonist, or open circles: adrenergic antagonist. *,**Significantly different from control value, $*p < 0.05$, $**p < 0.01$.

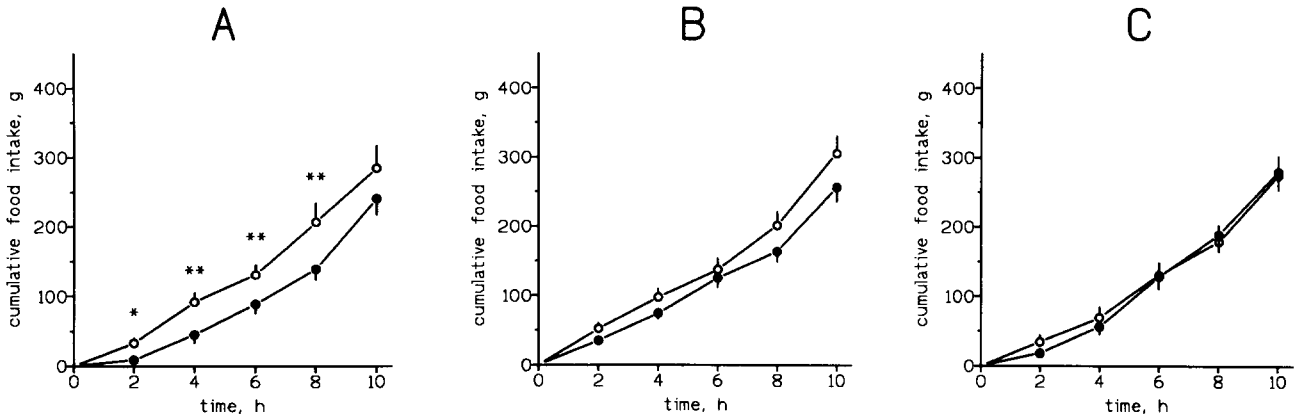

FIG. 3. Dose-dependent blockade of the hypophagic effect of VP (1.5 μg/kg) by the α_1-adrenergic antagonist prazosin (A: 15 μg/kg; B: 27 μg/kg; C: 40 μg/kg). Filled circles: VP + prazosin; open circles: prazosin. *,**Significantly different from control value, $*p < 0.05$, $**p < 0.01$.

not to be involved in VP induced anorexia, because the α_2-adrenergic blockers yohimbine and idazoxan, which cross the blood-brain barrier (4), failed to block the hypophagic effect of VP.

The hyperglycaemic action of VP (14,22) is probably not involved in its hypophagic effect, because hyperglycaemia does not influence food intake in ruminants (1) and the hyperglycaemic effect induced by VP was attenuated by the α_2-adrenergic antagonist yohimbine (22), which did not reduce VP-induced anorexia.

Because there is evidence that α_1-adrenergic agonists inhibit extrinsic reticuloruminal contractions as a consequence of increased tension receptor activity induced by an increase in smooth muscle tone (29), VP might reduce feeding in pygmy goats by inhibition of reticuloruminal motility through activation of α_1-adrenergic receptors in reticuloruminal smooth muscle. The antagonizing effect of prazosin, but not of propranolol, on the inhibitory action of adrenaline on reticuloruminal motility (28,29) and on the VP-induced anorexia (Figs. 2 and 3) is in keeping with this notion. It is well known that VP excites pre- and postganglionic sympathetic neurons (5,11,18,20,21) and, thus, may elicit release of catecholamines by sympathetic fibers and the adrenal medulla and, consequently, may reduce feeding in pygmy goats by inhibition of reticuloruminal motility through activation of α_1-adrenergic receptors. It is unlikely that VP induces anorexia through vasoconstriction, because angiotensin II (1.5 μg/kg), another potent vasoconstrictive agent, did not produce an inhibition of feeding in pygmy goats (13).

Because there is often a massive release of VP in stressful situations (6,7,10,19) and VP inhibits feeding, besides CRF (2,15), VP might be also causally related to stress-induced anorexia (13).

In summary, the present study suggests that the hypophagic effect of VP is mediated by activation of α_1-adrenergic receptors. The location of these adrenergic receptors remains to be assessed, but the findings discussed indicate that they may be located in the forestomachs.

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