current on A fibers to the minimum, identification of the type of fibers always began by passing a weak (1 μA) current, and the stimulation was repeated, by increasing the current until complete disappearance of the C wave (as a rule a current of 2 μA was sufficient for this purpose).

The use of the method described above is illustrated by Fig. 2. CAP of the strand (Fig. 2a) indicate that it contains active C fibers (the wave in the center of the trace). As a result of the action of the current (2.2 μA for 10 sec) the C wave in the CAP disappeared (Fig. 2c). Meanwhile, the spike (4) on the trace recorded during chemical stimulation of the receptor zone with K^+ ions also disappeared (Fig. 2b, d). Consequently, the two spikes which remained (3 and 5) were A spikes, and the one which disappeared (4) was a C spike.

Differences in the resistance of A and C fibers to the action of a direct current can thus be used to identify afferents of each type. Since C spikes were not restored after being inhibited, the identification must be carried out at the end of any investigations on the particular strand of nerve fibers.

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ANGIOTENSIN II IN THE ORGANIZATION OF FEEDING BEHAVIOR OF RATS

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The renin-angiotensin system plays an important role in the formation of food motivation [2-5]. In most animals, including rats, a close interlinking between drinking and feeding behavior has been discovered [2, 7]. With an increase in thirst, food intake of animals is reduced [8]. However, the neurochemical mechanisms of the interlinking of these forms of natural biological motivations have received little study.

In the investigation described below the role of the dipsogenic neuropeptide angiotensin II in the realization of feeding behavior of animals was studied, with particular reference to the time course of food and water consumption by hungry rats receiving central and peripheral injections of angiotensin II.

EXPERIMENTAL METHOD

Experiments were carried out on 75 noninbred male rats weighing initially 200-300 g. As a first step, all the animals were deprived of food for 48 h. The hungry rats received injections of angiotensin II or saralasin 10 min, and in some experiments 60 min also, before receiving food and water, and in other experiments, angiotensin II was injected after preliminary administration of saralasin. Asp^1-Val^5-angiotensin II diacetate ("Berlin Chemie," East Germany), dissolved in physiological saline, was injected into the lateral ventricles (in a volume of 5 μl) or intraperitoneally (in a volume of 0.5 ml) of the rats in concentrations of 100 and 10 ng/kg body weight respectively. Saralasin (Sar^1-Val^5-Ala^8-angiotension II;

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TABLE 1. Mean Statistical Amounts of Food and Water Consumed by Rats per Hour after Food Deprivation for 48 h, and Receiving Angiotensin II and/or Saralasin by Intraventricular or Intraperitoneal Injection

Injection	Substance injected	Latent period of onset of feeding behavior, sec	Quantity of food consumed, g/kg	Quantity of water drunk, ml/kg	Number of rats
Intraperitoneal	Physiological saline	201±23,8	101,2±13,6	7,9±2,88	10
Intraventricular	Angiotensin II	60±13,5	40,7±15,4**	1,8±0,9	8
Intraventricular	Saralasin	160±24,7	29,3±9,9***	6,3±3,9	7
Intraventricular	Saralasin + angiotensin II	180±60	73,5±15,8	1,9±1,5	7
Intraperitoneal	Saralasin	211±18,5	49,3±12,1*	1,7±0,9	13
Intraperitoneal	Angiotensin II (1st phase of action)	224±39,6	94,9±17,4	9,6±2,48	8
Intraperitoneal	Angiotensin II (2nd phase of action	158,8±29,8	150,9±9,49*	8,6±2,53	8
Intraperitoneal	Saralasin + angiotensin II (2nd phase)	214±25,8	55,8±10,1*	2,6±1,38	8

Legend. *p < 0.05, **p < 0.01, ***p < 0.001.

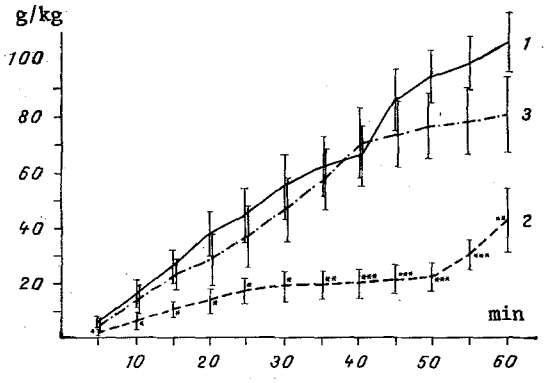

Fig. 1. Dynamics of food consumption (in g/kg body weight) by hungry rats during 1 h after injection of physiological saline (1), intraventricular microinjections of angiotensin II (2), and a combination of saralasin with angiotensin II (3). Here and in Fig. 2: *p < 0.05, **p < 0.01, ***p < 0.001.

Institute of Biologically Active Substances, Berlin, East Germany) was given in a dose of 100 ng by intraventricular microinjections and 50 ng/kg intraperitoneally. Animals of the control group received 0.5 ml of physiological saline intraperitoneally. After injection of either substance the rats were placed in individual cages equipped with graduated feeding and drinking bowls. The latent period of onset of feeding behavior was observed in all animals. Every 10 min for 1 h of observation the quantity of water and combined food consumed by the rats was recorded. The location of the tips of the cannulas in the lateral ventricles was verified against the atlas [6]. The results were subjected to statistical analysis by standard methods of determination of the arithmetic mean and by Student's test.

EXPERIMENTAL RESULTS

Comparative analysis of the time course of food and water consumption after intraventricular microinjections of angiotensin II and physiological saline 10 min before the hungry rats were given access to water and food gave the following results. Angiotensin II increased (on average by 70%) the latent period of onset of feeding behavior and reduced (on average by 63%) the total quantity of food taken per hour (Table 1; Fig. 1). Recording the time course of food consumption by the hungry rats revealed a decrease in food intake from the first minutes after intraventricular injection of angiotensin II (Fig. 1). The abovementioned inhibitory effect of angiotensin II on food intake was blocked by preliminary intraventricular injection of saralasin. Under these conditions no significant differences were observed in the latent period of onset of feeding behavior or in the quantity of food consumed per hour compared with the corresponding values in animals of the control group, receiving injections of physiological saline (Fig. 1).

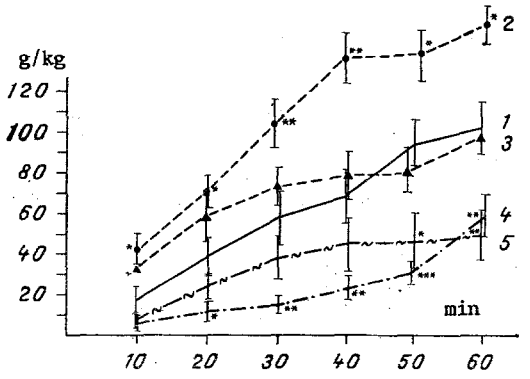

Fig. 2. Dynamics of food consumption by hungry animals after intraperitoneal injections of physiological saline (1), angiotensin II 10 min (3) and 60 min (2) before presentation of food, and a combination of angiotensin II with saralasin 60 min before presentation of food (4), and of saralasin alone, 10 min before presentation of food (5).

No significant differences were observed in the quantities of water consumed by the hungry rats in the course of 1 h after intraventricular injection of angiotensin II and control injections of physiological saline (Table 1).

The results suggest that inhibition of feeding behavior induced in hungry rats by angiotensin II is due to the direct effect of the peptide on CNS receptors specific for angiotensin II. It will be noted that cessation of food consumption by the hungry animals after intraventricular injection of angiotensin II was unconnected with the initiation of drinking behavior, as Rolls and Rolls [2] suggest.

Considering the different degree of involvement of central and peripheral components of the renin-angiotensin system in the regulation of thirst, in the next series of experiments the effect of peripheral intraperitoneal injections of angiotensin II on realization of feeding behavior of hungry rats was studied.

The experiments showed that intraperitoneal injection of angiotensin II 10 min before food was presented to hungry animals led to a tendency for food intake to be increased in the first 15-30 min of satiation of hunger (Fig. 2). In the case of intraperitoneal injection of angiotensin II 60 min before food consumption, however, significant shortening of the latent period of onset of feeding behavior and an increase (on average by 49%) in the quantity of food consumed during 1 h were observed, compared with the food intake of animals of the control group during a similar time interval (Table 1, Fig. 2). Intraperitoneal injection of saralasin 8-10 min before injection of angiotensin II prevented the increase in food intake induced by angiotensin II (Table 1, Fig. 2). Moreover, after intraperitoneal injection of saralasin alone, there was a significant decrease in food intake, which appeared 45-50 min after the hungry rats were allowed access to food.

No significant changes in water consumption by the hungry rats were observed after peripheral injections of angiotensin II (Table 1).

It can be concluded from these results that changes in the angiotensin II level in the CNS and plasma, caused by exogenous injection of the peptide, has a marked effect on realization of food-motivated excitation. Changes in food consumption under these circumstances, like changes in water consumption described by the writers previously [1], in response to central and peripheral injection of angiotensin II are opposite in nature, and in our view this is evidence of the existence of negative feedback between the peripheral and central components of the renin-angiotensin system.

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