ROLE OF ANGIOTENSIN II IN FORMATION OF THE AVOIDANCE REACTION TO ELECTRICAL STIMULATION OF THE VENTROMEDIAL HYPOTHALAMUS IN RABBITS

T. N. Emel'yanova

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The presence of all components of the renin-angiotensin system (RAS) has been demonstrated in the brain [5, 6]. Participation of RAS in the formation of various forms of behavior has been shown [3], although its importance in the organization of emotional states has received little study.

The aim of this investigation was to study the specific role of angiotensin II (AII) as a component of RAS of the brain in the organization of emotional reactions in rabbits during electrical stimulation of the ventromedial hypothalamus (VMH). With this object in view the effect of AII, of specific antiserum to AII, of saralasin, a blocker of specific AII receptors, and of captopril, an inhibitor of AII-converting enzyme, on various behavioral manifestations of the avoidance reaction to electrical stimulation of the defense centers of VMH, were investigated.

EXPERIMENTAL METHOD

Experiments were carried out on 28 conscious adult male rabbits weighing 2.5-3 kg. Before the experiment, electrodes were implanted into the ventromedial nucleus of the animals' hypothalamus. Electrical stimulation of VMH of the unrestrained animals in a cage evoked a defensive avoidance reaction. The defensive reaction of the rabbits was manifested by the fact that after a certain period of time they curled into a ball, then began to run quickly around the experimental cage, attempting to escape from it. The animals' respiration rate increased sharply and in some cases micturition and defecation were observed. After the end of stimulation, the rabbits struck the floor of the cage several times in succession with considerable force with their hind limbs. The objective criterion for evaluation of the motor component of the avoidance reaction to electrical stimulation of VMH was the latent period (LP) — the time interval from application of stimulation to the beginning of the animal's motor activity. The background value of LP was determined three times, after which observations were made every 10 min during the first hour after injection of the test substances, and thereafter every 30 min for 2 h. AII (from Serva, West Germany), saralasin (Serva), and captopril (Squibb, England), were injected into the lateral ventricles of the rabbits' brain through metal cannulas, introduced previously, in a dose of 150 ng in a volume of 10 µl of distilled water. Antiserum to AII was injected in a volume of 30 µl.

EXPERIMENTAL RESULTS

The experiments showed that the effect of intraventricular injection of AII was manifested most clearly toward the end of the first hour: LP of the avoidance reaction under these circumstances was increased on average fourfold in all six experiments (Fig. 1a).

Injection of specific antiserum to AII shortened LP of the avoidance reaction by 50% of all six animals. The maximal effect was observed on average 40 min after injection of the antiserum. Toward the end of the third hour LP was increased, but it remained 25% shorter than the background value (Fig. 1b).

Intraventricular injection of saralasin, a blocker of specific AII receptors, into the rabbits caused facilitation of the avoidance reaction in all eight animals. LP 30 min after

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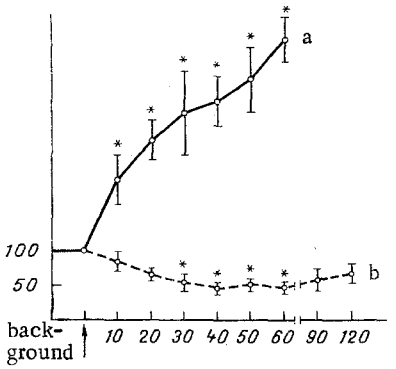

Fig. 1

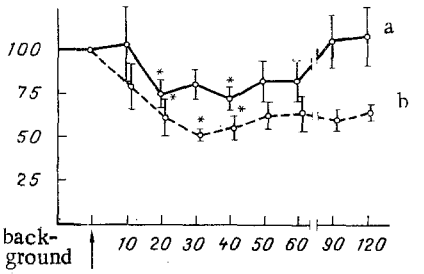

Fig. 2

Fig. 1. Time course of changes in KP of avoidance reaction following intraventricular injection of AII (a) and of antiserum to AII (b). Here and in Fig. 2: abscissa, time (in min); ordinate, LP (in %); number of animals given in parentheses.

Fig. 2. Time course of changes in LP of avoidance reaction following intraventricular injection of captopril (a) and saralasin (b).

injection of saralasin was reduced by half and remained low until the end of the experiment (Fig. 2b).

Injection of captopril, an inhibitor of the AII-converting enzyme, caused shortening of LP of the avoidance reaction by 25% after 20 min in all eight animals, and the effect lasted 30 min. Toward the end of the experiment the value of LP regained the background level (Fig. 2a).

The results show that AII is actively involved in the formation of negative emotional reactions evoked by electrical stimulation of the defensive centers of VHM. One probable pathway of the action of AII may be its binding with the specific receptors of different brain structures, including the para- and periventricular nuclei and the median eminence [7], followed by involvement of lysyl-vasopressin, which also effects negative emotional reactions of hypothalamic origin [2].

Meanwhile the possibility that other peptide or mediator systems of the brain may be involved by angiotensin cannot be ruled out, for the RAS has close anatomical and physiological connections with the catecholamine [4, 9] and opioid systems of the brain [8, 10]. In addition, the RAS is closely connected through AII-converting enzyme with the kallikrein-kinin system [10], one component of which, namely bradykinin, has a facilitatory action of the avoidance reaction of hypothalamic origin [1].

LITERATURE CITED

1. V. I. Badikov, Vasoactive Peptides [in Russian], Sofia, Bulgaria (1980), p. 12.
2. G. I. D'yachkov and V. I. Badikov, Vasoactive Peptides [in Russian], Sofia, Bulgaria, (1980), pp. 21-22.
3. V. V. Sherstnev et al., Usp. Fiziol. Nauk, 10, No. 3, 66 (1979).
4. K. Fuxe et al., Enzymatic Release of Vasoactive Peptides, New York (1980), p. 161.
5. M. Phillips et al., Fed. Proc., 38, 2260 (1979).
6. M. P. Printz et al., The Renin-Angiotensin System: A Model for the Synthesis of Peptides in the Brain, Berlin (1982), p. 3.
7. K. Shigematsu et al., Neurosci. Lett., 67, 37 (1986).
8. I. Summy-Long et al., J. Pharmacol. Exp. Ther., 217, 619 (1981).
9. C. Sumners and M. I. Phillips. Am. J. Physiol., 244, 257 (1983).