SENSITIVITY OF NEURONS OF THE PARAFASCICULAR COMPLEX OF THE RABBIT THALAMUS TO ANGIOTENSIN II DURING STIMULATION OF THE VENTROMEDIAL HYPOTHALAMUS

M. Colditz and A. N. Kravtsov

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The study of the role of peptides in the activity of the CNS and of single neurons is attracting ever-increasing attention [1, 2, 9]. A special place in this problem is occupied by research aimed at elucidating the mechanisms of the central action of various vasoactive peptides, notably angiotensin II (A-II). There is evidence in the literature that this peptide is present in various brain formations [10, 13, 15].

It is considered that A-II plays an important role in regulation of the blood pressure and the water and electrolyte balance and that it participates in the onset and development of emotional responses. However, despite research into various aspects of the action of vasoactive oligopeptides, the question of the mechanisms of their action at the molecular and cellular levels still remains open. There are data in the literature to indicate a direct action of A-II on neurons in different parts of the CNS [2, 6, 14]. However, the effect of this peptide on brain nerve cells in animals in different functional states remains virtually unstudied.

It is therefore interesting to study the sensitivity of neurons of the thalamus, a structure which plays an important role in the formation of pain integration, to A-II during stimulation of emotiogenic structures of the ventromedial hypothalamus.

EXPERIMENTAL METHOD

Acute experiments were carried out on unimmobilized, unanesthetized rabbits (males weighing 2.5-3 kg). The animals were fixed in a stereotaxic apparatus, a 0.5% solution of procaine was injected into the fixation points, and the animals also were scalped under local anesthesia. The bones of the vault of the skull were trephined at coordinates taken from the atlas [7].

Single unit activity was recorded in the parafascicular complex (PFC) of the thalamus by means of multiple-barreled glass microelectrodes with a total diameter of the tip of 3-6 μ. The barrel for recording extracellular activity was filled with 3M NaCl solution (resistance 5-15 mΩ). The other three barrels were filled with an aqueous solution (10^{-3} M, pH 5.5) of A-II (from VEB Berlin Chemic). A-II was injected into the zone of the cells chosen for study by currents of positive polarity (8-60 nA). The duration of microiontophoretic application of A-II varied from 10-20 sec to 1-1.5 min. The design of the apparatus for microiontophoresis provided for compensation of phoretic and holding currents.

To amplify and record single unit discharges a two-channel Amplior II-TP amplifier (from Alvar Electronic) and a Rostove-102 stereo tape recorder were used. The data were led from magnetic tape into a TA-1024 frequency analyzer. The results of processing of unit activity were recorded as a continuous frequency histogram on an N-327-5 automatic writer and NZ-891 digital printer.

The ventromedial hypothalamus was stimulated through bipolar nichrome electrodes (diameter 0.1 mm). Square pulses (0.1 msec, 4-5 V, 50 Hz) were applied for 1-3 sec from a Physiovar stimulator (from Alvar Electronic). The adequacy of stimulation of the negative emotiogenic zones of ventromedial hypothalamus (VMHT) was estimated by the use of criteria given in [5].

P. K. Anokhin Research Institute of Normal Physiology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR N. A. Fedorov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 97, No. 2, pp. 172-174, February, 1984. Original article submitted May 18, 1983.

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TABLE 1. Effect of Stimulation of VMHT on Responses of PFC Neurons to Microiontophoretic Application of A-II

Initial response to A-II	Response to A-II after stimulation of VMHT		
	activation	inhibition	no response
Activation 14 (100)	11 (78,6)	1 (7,1)	2 (14,3)
Inhibition 11 (100)	0	6 (54,5)	5 (45,5)
No response 27 (100)	10 (37,0)	0	17 (63,0)

Legend. Number of neurons and percentages (in parentheses) indicated.

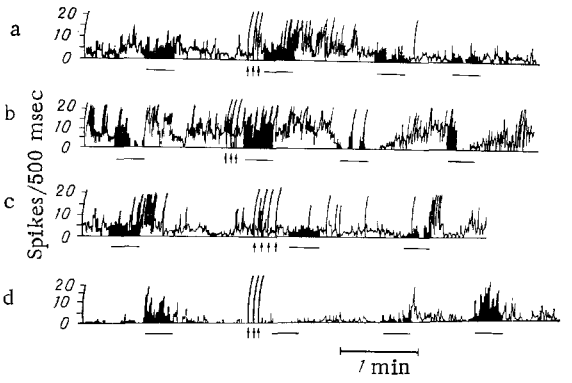

Fig. 1. Change in character of responses of thalamic neuron to A-II during hypothalamic stimulation. a-d) Continuous histograms of spike discharges of different PFC neurons; lines beneath histograms mark time of microiontophoretic application of A-II with a current of 45 nA; arrows show times of stimulation of VMHT (stimulation artefacts can be seen at that time on the histograms).

The locations of the electrode tips were determined in brain sections (frozen or embedded in celloidin), fixed in 10% formalin solution.

EXPERIMENTAL RESULTS

In 14 acute experiments activity of 99 PFC neurons was recorded. Analysis of the results showed that nearly half (48.5%) of the cells recorded responded to microiontophoretic application of A-II. On application of A-II the neurons either increased or reduced their discharge frequency virtually by an equal degree. Activation of the spike discharge was observed in 27 cells (27.3%), inhibition in 21 neurons (21.2%). The change in discharge frequency (activation or inhibition) occurred after a latent period of between 2 and 20 sec (mean 6.32 sec) and it lasted up to 10* sec after the end of microiontophoretic application of A-II. The intensity of responses of PFC neurons depended on the dose of A-II, and in some cases, if the strength of the electrophoretic current was increased, signs of desensitization were observed.

The results thus indicate that neurons sensitive to A-II are present in PFC. However, the possibility cannote be completely ruled out that the changes observed in unit activity under the influence of A-II are the result of its action on microvessels alongside the nerve cells. However, it has been shown that the A-II antagonist saralasin has a stronger action

*Russian original illegible. Possibly 10 sec is intended — Publisher.

on activation responses of the cells to A-II than on inhibitory responses [11, 12]. These facts suggest that A-II has both a specific and a nonspecific action on brain nerve cells.

To study the character of excitation effects evoked by stimulation of VMHT, 52 neurons were tested in five rabbits. The character of responses of the nerve cells of PFC to A-II was studied before and after stimulation of VMHT. Analysis of the results showed (Table 1) that nerve cells responding to application of A-II by activation virtually did not change the character of their responses after stimulation of VMHT. Of 11 cells which responded to microiontophoretic application of A-II by inhibition, five neurons ceased to respond after stimulation of VMHT, and of 27 nerve cells which did not respond to A-II, a response appeared in 10 cells. The change in the character of the responses to A-II took place at once (after 5-10 sec) after stimulation of VMHT, and restoration of the original response was observed after 90-180 sec.

As an example, histograms of discharges of various PFC neurons and their responses to microiontophoretic application of A-II before and after stimulation of VMHT are given in Fig. 1. A neuron not responding to A-II (Fig. 1a) began to respond to it by an increase in discharge frequency, whereas a cell with initially an inhibitory response (Fig. 1b) ceased to respond to microiontophoretic application of A-II. Of two neurons responding to application of the peptide by activation, one (Fig. 1c) ceased to respond to A-II, whereas the other (Fig. 1d) changed to the opposite type of response.

These results are evidence that during stimulation of VMHT the receptive properties of the PFC neuron membrane relative to A-II are modified and the character of responses of most cells to microiontophoretic application of this peptide is changed. There is evidence in the literature that stimulation of various hypothalamic zones causes changes in neuronal responses to various brain structures to microiontophoretically applied mediators and peptides [3, 4, 8]. It can accordingly by postulated that the character of synaptic organization of nerve cells and their sensitivity to different biologically active substances can be modified dynamically by excitation evoked by stimulation of hypothalamic emotiogenic structures.

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