THE ACTION OF HYPERTENSIN AND PITUITRIN ON THE ELECTRICAL ACTIVITY OF THE BRAIN IN ANIMALS

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 54, No. 10,
pp. 85-89, October, 1962
Original article submitted October 24, 1961

Hypertensin and vasopressin are known to play an active part in the regulation of vascular tone [2, 5, 12, 13]. The action of humoral pressor factors (including hypertensin and vasopressin) is particularly increased during depression of the metabolic antihypertensive function of the kidneys [6].

Vasopressin is a hormone of central origin, whereas hypertensin is of peripheral origin. The comparative study of the action of these hormones on the functional state of the central nervous system is of much interest.

One method of determining the functional state of the central nervous system is by studying the electrical activity of the various parts of the brain. This method has been used with success to study other pressor hormones such as adrenalin, noradrenalin, etc. [8, 14, 16].

The object of the present investigation was to study the changes in the electrical activity of the different levels of the brain during the action of hypertensin and pituitrin (one component of which is vasopressin) and to compare them with the changes in the level of the arterial pressure.

EXPERIMENTAL METHOD

Experiments were carried out on 63 cats, either unanesthetized or anesthetized with urethane (1 g/kg body weight, intraperitoneally), using a stereotaxic technique. The unanesthetized animals were immobilized by intravenous injection of tubocurarine (0.1 mg/kg) or myorelaxin (0.2 mg/kg), and maintained on artificial respiration. Hypertensin (0.08-2.0 μg/kg) and pituitrin (0.6-0.8 unit/kg) were injected into the femoral vein.

The electrical activity of the brain and the blood pressure were recorded simultaneously during the experiments. The latter was recorded in the femoral artery on a kymograph by means of a mercury manometer. The electrical activity of the brain was recorded from the frontal, sensomotor, and occipital regions of the cerebral cortex, and from the posterior hypothalamus and reticular formation of the midbrain by means of a Kaiser electroencephalograph. Bipolar electrodes were used to pick up the potentials. Needle electrodes were used for recording the cortical activity; they were fixed epidurally and the distance between them was 4-5 mm. The potentials of the subcortical structures were recorded by means of tantalum electrodes, 0.3 mm in diameter, insulated with varnish except at their tips. The distance between the electrodes was 2 mm. The electrodes were introduced into the subcortical structures in sections 190 and 350 of Jasper's coordinates [11].

The position of the electrodes was confirmed histologically by coagulating the brain tissue with an electric current [4] and staining by Nissl's method. In some experiments the reticular formation in the midbrain was stimulated for 5 sec with pulses of current of voltage 3 V, duration 1 msec, and frequency 100 cps.

EXPERIMENTAL RESULTS

Two series of experiments were conducted: 1) on curarized animals, and 2) on animals under urethane anesthesia.

The EEG of the curarized cats, immobilized with tubocurarine or myorelaxan, had the characteristic appearance of the waking brain (Fig. 1, A; Fig. 2, A). In most experiments the frequency of the waves of potential in the

posterior hypothalamus and reticular formation of the midbrain ranged between 20 and 30 cps, and their amplitude was about 30 μV. In the sensomotor occipital regions of the cortex, the most common frequency of the potentials was 15-20 cps, and their amplitude about 60 μV. These findings were in agreement with those reported by other workers [9, 3], showing that this pattern of electrical activity corresponds to the waking state of the animal.

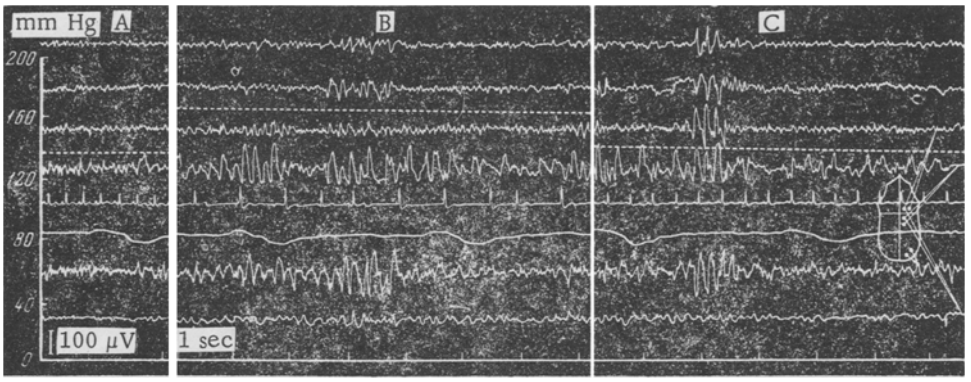

Fig. 1. Changes in the EEG and the level of the arterial pressure after injection of 1.9 μg/kg hypertensin into cats curarized with myorelaxin (0.2 mg/kg). From above down: electrograms of the posterior hypothalamus, the reticular formation of the midbrain, and the frontal and sensomotor areas of the cortex, ECG, respiration, EEG of the occipital and sensomotor areas; broken line—level of the arterial pressure (scale on the left). A) Before injection of hypertensin; B) 1 min 10 sec after injection; C) 4 min after injection.

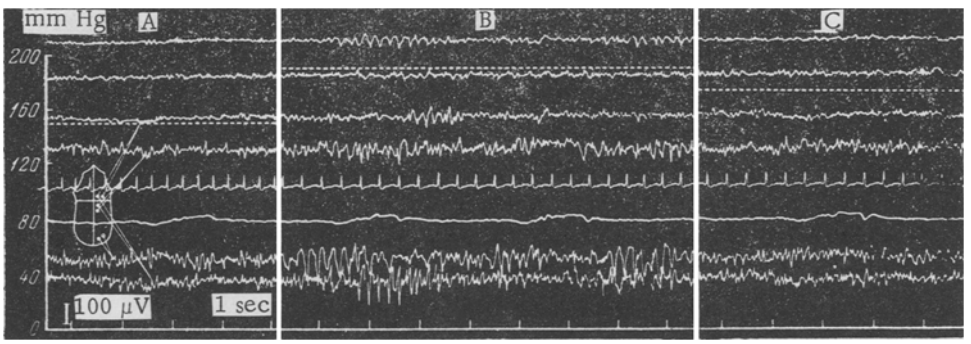

Fig. 2. Changes in the EEG and level of the arterial pressure after injection of 0.8 units/kg pituitrin into a cat curarized with tubocurarine (0.1 mg/kg). From above down: electrograms of the posterior hypothalamus, the reticular formation of the midbrain, and the frontal and sensomotor areas of the cortex, ECG, respiration, EEG of the occipital and sensomotor areas of the cortex; broken line—level of the arterial pressure. A) Before injection of pituitrin; B) 1 min after injection; C) 5 min after injection.

The experiments in which hypertensin and pituitrin were administered were carried out in the conditions described above.

After injection of hypertensin, a sharp rise in the level of the blood pressure and a slowing of the heart rate were observed, whereas the EEG remained unchanged at this stage. Between 1 and $1^1/_2$ min after injection of the substance, the blood pressure remained at a high level, but then began to fall. At this period the EEG, in all leads from the cortex and subcortical formations of the brain, showed characteristic changes in the form of spindle-shaped volleys of impulses with a frequency of 5-6 cps and a high amplitude—80-200 μV (Fig. 1, B). The volleys of impulses usually disappeared with the return of the blood pressure to its initial level, and the EEG resumed its former appearance (Fig. 1, C); except that in some experiments the volleys of impulses ceased after the restoration of the blood pressure to its original level.

Similar effects on the EEG and the blood pressure were shown by pituitrin (Fig. 2). However, after the injection of pituitrin, the volleys of spindle-shaped impulses were of a higher frequency—5-9 cps—and appeared later on the EEG, after 1-2 min. The arterial pressure was maintained longer at the high level, and the volleys of impulses on the EEG continued for a correspondingly longer period.

In a series of control experiments, physiological saline was injected intravenously in the same volume as the hypertensin and pituitrin. No change was found in the EEG and blood pressure in these experiments.

In order to study the mechanism of appearance of volleys of impulses in the EEG, in a series of experiments the reticular formation of the midbrain was stimulated by an electric current after the administration of hypertensin or pituitrin, at a period when spindle-shaped volleys of impulses were present in the EEG. Stimulation of the reticular formation led to the disappearance of the rhythmic potentials and to the appearance of waves of higher frequency and low amplitude in the EEG.

In the series of experiments on animals anesthetized with urethane, the EEG was characterized by a decrease of the electrical activity with groups of impulses at a frequency of 27 cps. The level of the blood pressure was also lowered (Fig. 3, A). In these experiments the injection of hypertensin and pituitrin gave quite different results. Despite the fact that in the anesthetized animal the increase in the level of the blood pressure after injection of these substances was of the same character as in the waking animal, no changes were seen in the EEG (Fig. 3, B).

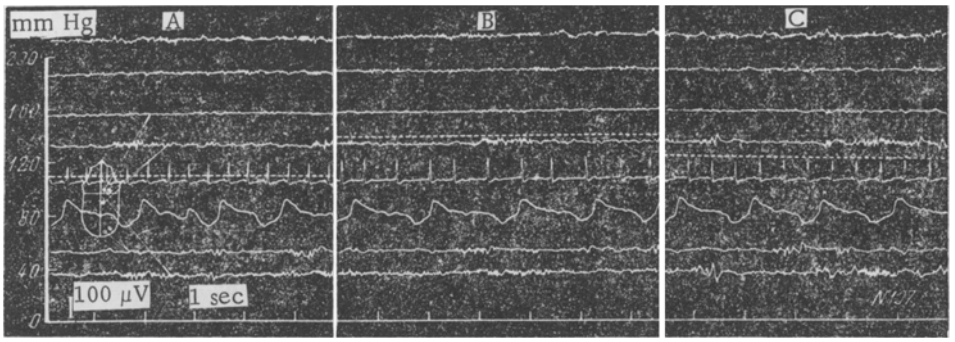

Fig. 3. Changes in the EEG and the level of the arterial pressure after injection of 1.8 μg/kg hypertensin into a cat anesthetized with urethane (1 g/kg). From top down: EEG of the posterior hypothalamus, the reticular formation of the midbrain, frontal and sensomotor areas of the cortex, ECG, respiration, EEG of the occipital and sensomotor areas of the cortex; broken line—level of the arterial pressure. A) Before injection of hypertensin; B, C) after injection of hypertensin.

Hence the injection of hypertensin and pituitrin caused similar changes in the level of the blood pressure and in the electrical activity of the brain. This indicates that the mechanism of action of these substances has something in common.

During the comparison of the changes in the EEG and the level of the blood pressure, we were struck by the fact that the volleys of impulses in the EEG appeared after injection of hypertensin and pituitrin at a time when the arterial pressure was high, and disappeared usually after the pressure had returned to its original level. It is interesting to compare these results with those obtained by other workers [7, 10, 17] who observed the appearance of similar volleys of impulses in the EEG after stimulation of the pressure receptors of the carotid sinus, the aorta, and the superior vena cava. These findings suggest that in our experiments too, the appearance of volleys of impulses in the EEG was associated with the increased blood pressure and, consequently, with increased stimulation of the pressure receptors. This hypothesis was also supported by the results of our experiments on animals anesthetized with urethane. If it is remembered that urethane blocks the transmission of afferent impulses [1], these results may be interpreted as due to exclusion of the pressor afferent impulses, causing changes in the EEG of the curarized animals after injection of hypertensin and pituitrin.

Another hypothesis may, however, be put forward to explain the mechanism of the appearance of volleys of impulses in the EEG under the influence of hypertensin and pituitrin. We know from clinical observations that a

lesion affecting the structures of the reticular formation is accompanied by the appearance of paroxysmal volleys of impulses in the EEG, similar to the rhythms of potentials which we have described. Some writers [15] regard the appearance of these high-amplitude, slow volleys of impulses as the result of the deactivation of the reticular formation of the brain, in consequence of which the rhythms of the diencephalic structures are "liberated."

We may suppose that in our experiments too, the appearance of these volleys of impulses was due to a change in the functional state of the reticular formation of the midbrain. Moreover, as we showed above, stimulation of the reticular formation was accompanied by the disappearance of the volleys of spindle-shaped rhythms from the EEG. It is evident that these two hypotheses are not mutually exclusive.

We may draw the following conclusions from these findings. The intravenous injection of hypertensin in doses from 0.08 to 2 μg/kg and of pituitrin in doses from 0.6 to 0.8 unit/kg into curarized animals is characterized by the appearance of volleys of spindle-shaped impulses of a frequency of 5-9 cps and a high amplitude in the EEG. The electroencephalographic changes are accompanied by a change in the level of the blood pressure. The injection of these substances in the same doses into animals anesthetized with urethane is not accompanied by any such changes in the EEG, notwithstanding the analogous change in the level of the blood pressure brought about by their action.

SUMMARY

A study was made of the electric activity of the cortical and subcortical formations of the brain as compared with the blood pressure level during the action of hypertensin and pituitrin on curarized cats and in conditions of urethane anesthesia. As shown, intravenous injection of these substances to curarized cats provoked EEG changes in the form of spindle-shaped impulse discharges and a rise of the blood pressure level. Administration of the same substances to the animals in conditions of urethane anesthesia was not associated with any EEG changes, notwithstanding the analogous blood pressure changes. As presumed, the appearance of spindle-shaped impulse discharges in the EEG was caused by the afferentation from the pressoreceptors, by the change of the functional state of reticular formation.

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