THE MECHANISM OF THE CENTRAL ACTION OF HYPERTENSIN AND PITUITRIN

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We have shown that hypertensin and pituitrin cause similar changes in the electrical activity of the brain, coinciding with elevation of the blood pressure. On the grounds that similar changes in the EEG have been obtained by other researchers during stimulation of the pressure receptors of the carotid sinus, the aorta, and the superior vena cava [2,4], we have postulated that the changes in the EEG under the influence of hypertensin and pituitrin are associated to some degree with afferent impulses from the pressure receptors.

In order to elucidate this problem, we have studied the electrical activity of different levels of the brain during the action of hypertensin and pituitrin after prebulbar transection of the brain, thereby excluding afferent influences from the pressure receptors.

EXPERIMENTAL METHOD

Experiments were conducted on 16 cats. The animal was immobilized by an intravenous injection of tubocurarine (0.1 mg/kg) and maintained on artificial respiration. The brain was divided by means of a spatula, introduced through a trephine hole in the skull (from the side, in the bone over the cerebellum).

Hypertensin (0.08-2.0 μg/kg) and pituitrin (0.6-0.8 unit/kg) were injected intravenously 1 h after the transection of the brain. The electrical activity of the brain and the arterial pressure were recorded simultaneously. The arterial pressure was recorded in the femoral artery on a kymograph by means of a mercury manometer.

We recorded the electrical activity of the frontal, sensomotor, and occipital regions of the cerebral cortex, and of the region of the posterior hypothalamus and the reticular formation of the midbrain by means of a "Kaiser" electroencephalograph. Bipolar leads were used to tap the potentials. The electrical activity of the cortex was recorded by means of needle electrodes fixed epidurally, the distance between the electrodes being 4-5 mm. The potentials of the subcortical structures were recorded by means of tantalum electrodes with a diameter of 0.3 mm, insulated with varnish except at their tip; the distance between the electrodes was 2 mm. The electrodes were inserted into the subcortical structures in the planes 190 and 350 according to Jasper's stereotaxic coordinates [5].

The actual site of the electrodes was checked histologically by means of the method of coagulation of the brain tissue with an electric current [1] and subsequent treatment by Nissl's technique.

EXPERIMENTAL RESULTS

The EEG of the intact brain was characterized by potentials of relatively high frequency (15-30 cps) and an amplitude of 30-60 μV. The intravenous injection of hypertensin or pituitrin caused the appearance of fusiform volleys of impulses, with a frequency of 5-9 per sec and high amplitude (about 200 μV) after a delay of 1-2 min in all leads of the EEG. These electroencephalographic changes coincide with a high level of the arterial pressure, caused by injection of these substances.

Prebulbar transection of the brain has been shown [2] to be accompanied by a change in the normal background pattern of the EEG. The electrical activity was characterized by predominance of slow waves, against the background of which fusiform volleys of impulses with a frequency of 8-11 per sec and a high amplitude reaching 200 μV were observed from time to time (Fig. 1A; Fig. 2A).

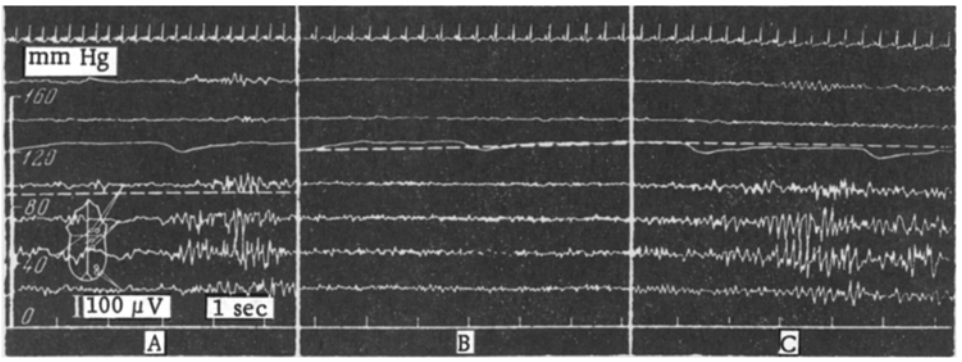

Fig. 1. Changes in the EEG and level of the arterial pressure after injection of 0.6 unit pituitrin per kg body weight into cats after immobilization with tubocurarine (0.1 mg/kg) and prebulbar transection of the brain. Significance of the curves (from above down): ECG; EEG of the posterior hypothalamus, of the reticular formation of the midbrain; respiration; EEG of the frontal, sensomotor, occipital, and sensomotor regions of the cerebral cortex; broken line, arterial pressure level, the value of which is shown on the scale on the left. A) Before injection of pituitrin; B) 17 sec after injection; C) 1 min 15 sec after injection.

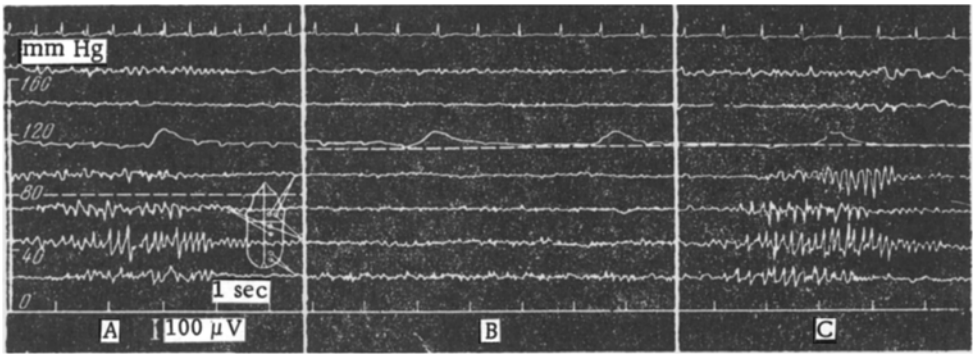

Fig. 2. Changes in the EEG and level of the arterial pressure after injection of 1.6 μg hypertensin per kg body weight into cats after immobilization with tubocurarine (0.1 mg/kg) and prebulbar transection of the brain. Significance of the curves as in Fig. 1. A) Before injection of hypertensin; B) 34 sec after injection; C) 1 min 10 sec after injection.

Hypertensin or pituitrin in these conditions caused, after a delay of 15-30 sec after injection, a change in the electrical activity of the cortical and subcortical structures of the brain: fast waves with a frequency of 15-25 per sec and a low amplitude (20-30 μV) appeared in all leads of the EEG (Fig. 1B; Fig. 2B). These changes were observed for 1-2 min, after which the EEG returned to its initial state (Fig. 1C; Fig. 2C). The electroencephalographic changes were accompanied by a marked increase in arterial pressure, which remained at a high level for a short time after the EEG had returned to its initial state.

Comparison between the electrical activity of the intact brain observed after injection of hypertensin and pituitrin and the initial EEG of the brain after prebulbar transection (Fig. 3) shows that, notwithstanding the presence of common features (fusiform volleys of impulses), the picture of the EEG differed in the two cases. The EEG of the intact brain after injection of these substances was characterized by volleys of impulses with a frequency of 5-9 per sec and a duration of 1.0-1.5 sec; electrical activity of low amplitude (20-30 μV) and high frequency (15-30 per sec) was observed between the volleys. The EEG of the brain after transection in the prebulbar region was characterized by volleys of impulses of a higher frequency (8-11 per sec) and a much longer duration (3-4 sec); low-frequency electrical activity was observed between the volleys.

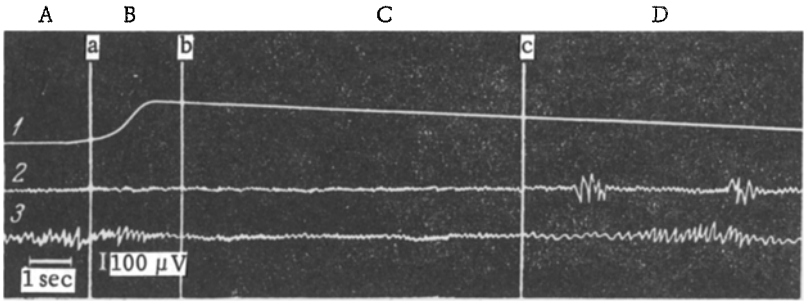

Fig. 3. Changes in the EEG of the intact brain of a curarized cat, in the EEG of a curarized cat after prebulbar transection of the brain, and in the arterial pressure level under the influence of hypertensin or pituitrin (scheme). Significance of the curves (from above down): arterial pressure; EEG of the intact brain; EEG of the brain after prebulbar transection. a) Beginning of injection of hypertensin or pituitrin; b) 15-30 sec after injection; c) 1-2 min after injection.

These experiments showed that prebulbar transection of the brain abolished the characteristic changes of the intact brain in the EEG, in the form of fusiform volleys of impulses, arising under the influence of hypertensin or pituitrin. Since prebulbar transection excludes the flow of afferent impulses from the pressure receptors, we may assume that these changes are associated with the pressure receptors.

However, changes do occur in the EEG after prebulbar transection of the brain in response to injection of hypertensin or pituitrin, although of a different character from those in the intact brain. Consequently, despite the fact that in these particular conditions the flow of afferent impulses is excluded to a considerable extent, hypertensin and pituitrin still manifest their action. It may be assumed that hypertensin and pituitrin act directly on the structures of the brain. Similar phenomena have been observed by other workers studying the action of adrenalin and noradrenalin [4].

The period of the EEG changes under the influence of hypertensin or pituitrin after prebulbar transection of the brain almost coincides with the period of absence of changes in the EEG of the intact brain after injection of these substances. It may therefore be suggested that the changes in the EEG of the intact brain arising under the influence of hypertensin or pituitrin also reflect the direct action of these substances on the structures of the brain. Hypertensin and pituitrin evidently act on the structures of the brain both indirectly, through afferent impulses from the pressure receptors, and directly.

SUMMARY

The electric activity of the cortical and subcortical formations of the brain in curarized cats was compared with the blood pressure level during the action of hypertensin and pituitrin prior to and after the prebulbar section of the brain. Prebulbar section of the brain eliminates the EEG changes occurring in the intact brain in the form of spindle shape impulse discharges, caused by the administration of these substances. It is supposed that this is due to the elimination of afferent impulsation from the pressoreception as a result of prebulbar section. Administration of hypertensin and pituitrin to animals with prebulbar division of the brain caused the appearance of high-frequency and low-amplitude biopotentials in the EEG. Evidently this was due to direct action of these substances on cerebral structures.

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