# ROLE OF THE PITUITARY IN GENERATION OF THE SLOW ELECTRICAL ACTIVITY OF THE HYPOTHALAMUS IN THE FROG

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In 1953, Euler [6] observed slow wavelike changes in the constant potential arising in the supraoptic region in response to osmotic stimulation. These single waves of emf, lasting about 1 min, were produced by injecting either a hypertonic or a hypotonic solution into the common carotid artery. N. A. Aladzhalova [1] recorded spontaneous slow waves of e.m.f. in the hypothalamus, almost sinusoidal in character, with a rhythm of 6-10 waves per min. Stimulation of this region led to a decrease in the period and an increase in the frequency: 18-24 waves per minute were observed.

The author has previously described spontaneous slow waves of potential in the hypothalamo-neurohypophyseal region of a grass frog after removal of the anterior lobe of the pituitary [2].

In the present investigation, the slow electrical activity of the hypothalamic and hypothalamo-neurohypophyseal regions of frogs was studied after the preliminary removal (2.5 weeks beforehand) of the pituitary or the adenohypophysis.

## EXPERIMENTAL METHOD

Experiments were carried out on male frogs (Rana temporaria) in the spring-summer period (May-August). The animals were immobilized with ditilin (succinylcholine) in a dose of 0.1-0.2 ml of a 1% solution, intramuscularly. Access to the pituitary was obtained by resecting the sphenoid bone in such a way that a bone segment was formed, supported by periosteum, which could be replaced after adenohypophysectomy or total hypophysectomy, and the skin then sutured.

In experiments on hypophysectomized frogs, which were kept (like the control animals) after the operation in a refrigerator at 4-8°, animals which remained light colored (melanophore index corresponding to Hogben's 1st degree) after the operation were chosen for the investigation. The temperature in the chamber during the experiment was 25°. The experiment began 40-60 min after the region to be investigated had been exposed. The bipotentials were recorded by nonpolarizing zinc electrodes on a Disa 51-B-00 oscilloscope fitted with a type 51-B-01 dc amplifier with asymmetrical input and a photorecording device. A downward deflection of the beam corresponded to electronegativity. The electrodes were placed in contact with the tissue by means of a wick, through a salt bridge. One electrode was applied to the hypothalamus (the region of the substantia grisea and the infundibulum) or the neurohypophysis, the other to the skin of the right thigh, inactivated by coagulation. To compare the reaction to a change in the external environmental conditions, in a series of experiments on preliminarily hypophysectomized and intact (only the adenohypophysis was removed) frogs, the animals were dehydrated by moving them before the experiment from the refrigerator to a dry terrarium at 25° for 4 h.

## EXPERIMENTAL RESULTS

The results of the chronic experiments on hypophysectomized summer frogs showed that 2 weeks after removal of the pituitary spontaneous activity was recorded in the hypothalamic region, but the amplitude of the slow waves was much less than in the animals in the acute experiment or in animals with an intact neurohypophysis. Their amplitude reached 0.1-0.4 mV and their period 6-20 sec, and these values were rarely exceeded. The constant potential of the investigated region was +16 mV. The variations in emf were rare and irregular, amounting to 1-3 waves in 5 min, and mainly positive (Fig. 1). In one animal, at the beginning of the experiment, a more regular rhythm was observed for a few minutes: 5 waves in 5 min, with an amplitude of 0.1-0.2 mV and a period of about 15 sec.

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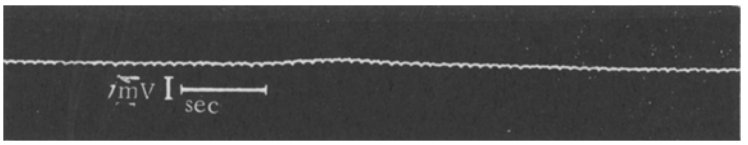


Fig. 1. Electrical activity of the hypothalamic region 2 weeks after hypophysectomy.

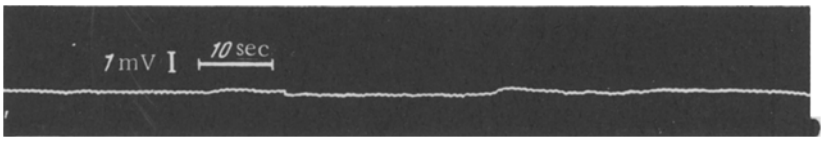


Fig. 2. Electrical activity of the hypothalamo-neurohypophyseal region 2 weeks after removal of the adenohypophysis.

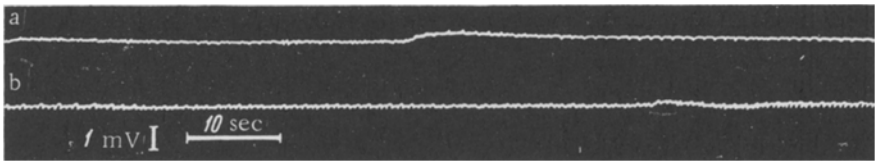


Fig. 3. Reaction to dehydration of an animal with an intact neurohypophysis (a) and a hypophysectomized frog (b).

In the animals with an intact neurohypophysis a more constant rhythm was observed: the fluctuations of the emf were positive, at the rate of 3-8 waves in 5 min, with a period of 6-30 sec or sometimes longer, and with an amplitude of up to 0.5 mV (Fig. 2).

In the dehydration experiments, the reaction to a change in the external environmental conditions differed in the intact and the hypophysectomized animals. The frogs in which the posterior lobe of the pituitary remained intact responded to dehydration by an increase in the electrical activity of the hypothalamo-neurohypophyseal region, manifested primarily by an increase in the frequency of the waves of emf — up to 10 or more in 5 min, and also by an increase in their amplitude and period. In the character of the observed effects, this reaction to dehydration was similar to those observed in the acute experiments [2].

In the hypophysectomized frogs after several hours of dehydration, the electrical activity of the hypothalamic region remained weak, or it actually diminished in intensity by comparison with that in the animals not undergoing dehydration. Long intervals were observed between individual waves (5-10 min), and the period of the waves was 6-30 sec. Their amplitude was 0.1-0.3 mV (Fig. 3).

In some experiments, against the background of the prolonged absence of fluctuations in emf, periods of between 1 and 3 min were observed during which not separate, but almost continuous waves appeared, distinguished by their low amplitude (0.1 mV or less) and short duration (5-10 sec). The constant potential of the investigated region in the dehydrated frogs was +22 mV.

Hence, even in the absence of the neurohypophysis, the hypothalamic region generates slow biopotentials. However, the electrical activity of the hypothalamus in the hypophysectomized frogs was much less intensive than in the animals with an intact neurohypophysis.

The functional disturbance of the hypothalamic mechanism after hypophysectomy was clearly seen in cases when the animal was exposed to considerable changes in the external or internal environment (dehydration in the present experiments or transfer from the refrigerator to an ordinary room, with a change of temperature of 20° in the author's previous experiments).

From a comparison of these facts, and also bearing in mind that the slow electrical activity of the hypothalamo-neurohypophyseal region is associated with its secretory activity [1,8], it may be concluded that the decrease in electrical activity after total hypophysectomy in animals during chronic experiments is associated with the decrease

in the secretory activity of the region under investigation as a result of disturbance of the normal relationships between the pituitary and the hypothalamus, and it may be a consequence of the removal of the hormone depot (the neurohypophysis) and of the degenerative changes which develop in the neurosecretory nuclei of the hypothalamus after extirpation of the pituitary or division of its stalk [3,4,7,10, etc.].

The problem of the secretory activity of the hypothalamus after hypophysectomy has not been finally solved. Removal of the pituitary or division of its stalk is known to cause retrograde degeneration of the secretory hypothalamic neurons. Several authors [4,7,10] have reported that removal of the neurohypophysis or division of the pituitary stalk is accompanied by the almost total degeneration of the secretory neurons forming the supraoptic nucleus, and only a very few neurons do not degenerate. V. F. Maiorova [3] reports that 1 month after hypophysectomy, the supraoptic nucleus shrinks to one-third of its normal size and the cells of the paraventricular nucleus also degenerate although, according to Sager [4], the neurons of the paraventricular nucleus do not degenerate. Meanwhile, several authors have found that after hypophysectomy regeneration of the fibers of the suptraoptico- and paraventriculo-hypophyseal tracts is observed. Moll [9] observed that in young rats these fibers started to regenerate in the 2nd week after hypophysectomy.

Simultaneously with the regenerative processes, reorganization of the stump of the pituitary stalk takes place and neurosecretory material begins to accumulate in it. With time the remnant of the pituitary stalk becomes transformed and it resembles in structure the posterior lobe of the pituitary. The histological data indicating partial replacement of the neurohypophysis in the functional respect by this transformed stump of the pituitary stalk have been confirmed by physiological and biochemical investigations [3,5,9].

On the basis of the results described above, indicating the character of the slow electrical activity of the hypothalamo-neurohypophyseal and hypothalamic regions, and considering the influence of neurohypophysectomy on this activity, it is concluded that this activity reflects primarily the activity of the secretory system of the anterior hypothalamus and neurohypophysis.

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