CHANGES IN CELLS OF THE ANTERIOR HYPOTHALAMUS AFTER DIVISION OF THE OPTIC NERVE

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Efferent connections of the hypothalamus with the peripheral part of the visual system have been found in several experimental investigations [1, 3-5, 9]. However, the structure of these connections has not been established. More recently, centrifugal fibers have been found in the optic nerve of the rabbit, cat, and man.

The aim of this investigation was to study connections of neurons in nuclei of the anterior hypothalamus with the peripheral part of the visual system.

EXPERIMENTAL METHOD

Experiments were carried out on eight cats aged 3-4 weeks. Under pentobarbital anesthesia the optic nerve was divided. The animals survived between 14 days and 2 years after the operation. Serial frontal sections through the brain in the region of the anterior hypothalamus were stained by Nissl's method.

EXPERIMENTAL RESULTS

After division of the optic nerve, changes were observed in the size of the neuron bodies, their shape, and internal structure, in the supraoptic and paraventricular nuclei of the anterior hypothalamus. Neurons showing such changes were most numerous on the side opposite to the divided optic nerve. In animals surviving 14 days after division of the optic nerve, the cytoplasm of neurons of the supraoptic and paraventricular nuclei had a honeycomb-like structure and contained large vacuoles (Fig. 1). The changed cell nuclei were oval, elongated, or rod-shaped, with irregular staining and with a large nucleolus. Individual neuron bodies were irregular in shape, with a large hyperchromic nucleus. The cytoplasm of the cell was finely honeycombed and the Nissl's substance present in the form of small conglomerates, lying at one pole of the cells. Processes of the cells were thickened and fused with the surrounding material. Isolated cells with similar changes also were found in the supraoptic and paraventricular nuclei on the same side as the divided optic nerve.

Comparison of the number of altered nerve cells in the supraoptic and paraventricular nuclei showed that they were rather more numerous in the supraoptic nucleus, both on the side of the operation and on the opposite side.

More marked and varied changes in nerve cells of the supraoptic nucleus were observed in experiments lasting up to 29 days. In nearly all sections through the supraoptic nucleus nerve cells of different types were seen. In experiments of longer duration (up to 2 months), degeneration of the neurons also was sufficiently well marked, and in the altered neurons the Nissl's substance, with the appearance of narrow, pressed conglomerate, was displaced to the periphery of the cell — the typical picture of perinuclear chromatolysis (Fig. 2). This picture, as we know [7], reflects a unique combination of retrograde changes in the nerve cells and it is the most constant morphological detail which is observed during changes arising in neurons after division of axons.

In these same experiments, greatly enlarged nerve cells with numerous outgrowths of cytoplasm with indistinct outlines were observed in the contralateral supraoptic nucleus. These cells had a honeycombed cytoplasm, and Nissl's substance in the form of a conglomerate was

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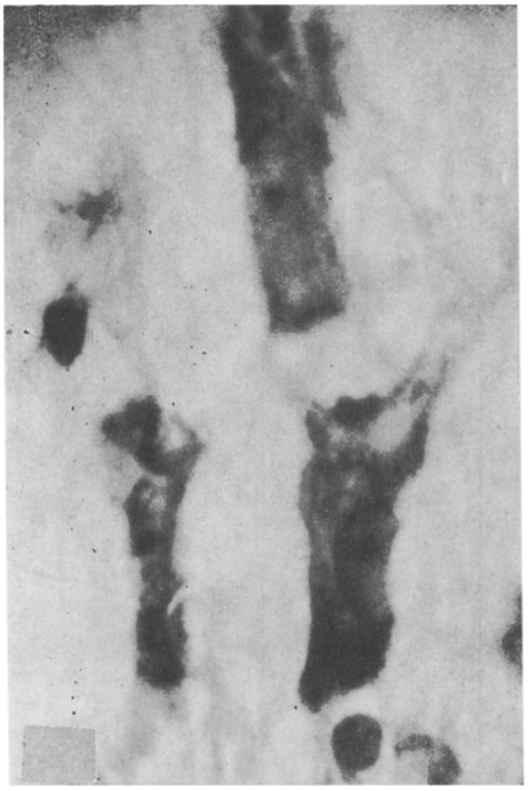

Fig. 1

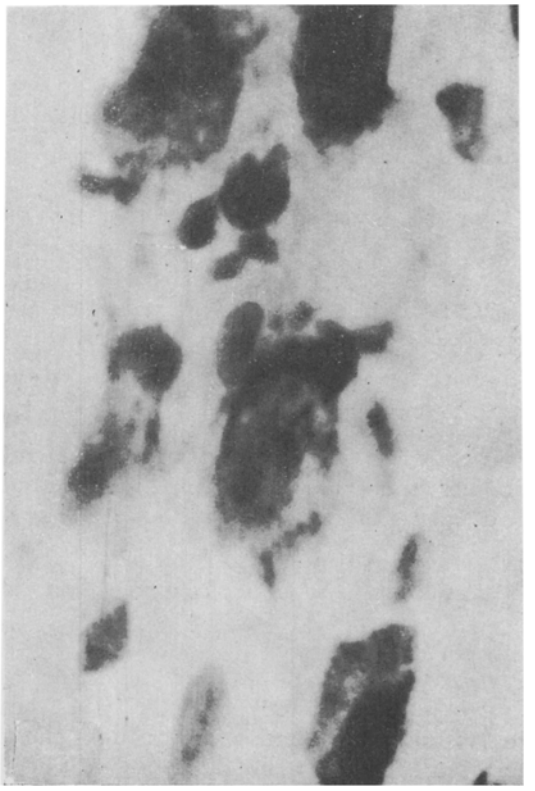

Fig. 2

Fig. 1. Nerve cells of right supraoptic nucleus of a cat 14 days after division of left optic nerve. Here and in Figs. 2 and 3, staining by Nissl's method, × 800.

Fig. 2. Nerve cell of right supraoptic nucleus of a cat 29 days after division of left optic nerve.

located at one pole of the cell. The basophilic nucleus, irregular in shape, had an enlarged nucleolus, around which the nuclear substance was palely stained (Fig. 2).

In an experiment which lasted about 2 years, the histological sections showed changes in 10 neurons of the contralateral supraoptic nucleus, whose bodies were palely stained, grossly enlarged, and had indistinct, hazy outlines. Some neurons showed signs of degeneration. Even in animals which survived so long after the operation, the cells evidently possessed special resistance and reacted weakly to division of the axon or not at all (Fig. 3).

In experiments lasting 14 days, over 2 months, and also in an experiment which lasted about 2 years, investigation of the paraventricular nucleus revealed (by contrast with the supraoptic) only single changed nerve cells, mainly on the side opposite to the divided optic nerve. The nerve cells had a finely vacuolated cytoplasm and the Nissl's substance was displaced toward one pole of the cell. In other altered cells of the paraventricular nucleus, besides concentration and displacement of the Nissl's substance (chromatolysis) vacuolation of the cytoplasm giving a finely or coarsely honeycombed appearance, and destruction or total disappearance of the cell processes could also be observed.

In the remaining nuclei of the anterior hypothalamus (suprachiasmatic medial and lateral nuclei of the preoptic region) under the same experimental conditions only single neuron bodies were observed, in which various manifestations of destruction could be seen. In the medial and lateral nuclei, they were seen mainly on the contralateral side, but in the suprachiasmatic nucleus on the ipsilateral side also.

The results of these experiments thus indicate that neurons of all nuclei of the anterior hypothalamus send axons into the optic nerves of the ipsilateral and contralateral eye, but the contralateral representation is stronger. During analysis of the results of the study of retrograde changes in neuron bodies in the anterior hypothalamic nuclei, the morphology of neurosecretory neurons in the hypothalamic region under normal conditions was taken into consideration.

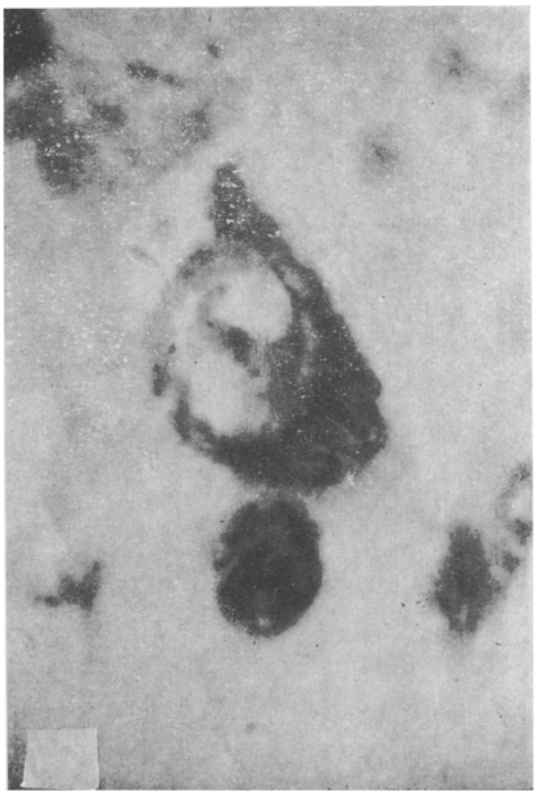

Fig. 3. Nerve cell of right paraventricular nucleus of a cat 14 days after division of left optic nerve.

A combination of changes associated with retrograde degeneration is known to develop at longer intervals after division of the axon than anterograde changes. However, optimal times of retrograde degeneration have not yet been precisely established for neurons in different species of animals. That is why, like other workers [2, 3], we had to keep the animals for different periods after the operation. Retrograde changes were represented more especially in neurons of the supraoptic nucleus, followed by the paraventricular nucleus. In many nerve cells of the supraoptic and paraventricular nuclei, vacuoles of different sizes could be seen as a manifestation of different stages of the neurosecretory cycle. This naturally complicated the assessment of retrograde changes in the present experiments, for vacuolation is also evidence of initial changes in neurons undergoing destruction [10].

Accordingly, during analysis of retrograde changes, only those cells which had a marked axonal reaction were taken into account. This reaction is characterized by perinuclear chromatolysis, which reflects the response of the neuron to injury to the axon [1]. The presence of nerve cells with such changes in the nuclei of the anterior hypothalamus after division of the optic nerve is evidence that axons of these neurons of the above-mentioned nuclei are represented in the optic nerve. Meanwhile, a problem which remains for discussion is that of the extremely little studied relations between centrifugal and centripetal fibers present in the composition of the optic nerve. Our data confirm that at least some of these centrifugal fibers belong to neurons of the anterior hypothalamic nuclei. They also are evidence of the unequal representation of neurons in different nuclei of the anterior hypothalamus in the composition of the optic nerve. As regards the fact that there are more of these fibers in the optic nerve on the contralateral side, this is in agreement with observations of other workers [8]. The fact that centrifugal fibers are present in the optic nerve can itself be interpreted as evidence that, besides specific visual functions, for which centripetal fibers of the optic nerve act as carriers, there are also other, "nonvisual functions," as has already been stated, in whose regulation the hypothalamus plays a part [6].

The fact that centrifugal fibers are present in the optic nerves, as we have shown, can be regarded as the morphological basis for conduction of impulses from the hypothalamus to the eye. Two hypotheses can be deduced from this fact: First, these centrifugal fibers may be important

for their role in transmitting the influence of the hypothalamus; second, these fibers are perhaps feedback channels in the neuronal net of the eyes and hypothalamus, in agreement with modern views on two-way connections between an organ and the CNS.

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EFFECT OF HYPOTHYROIDISM ON METABOLIC MATURATION OF HIPPOCAMPAL PYRAMIDAL NEURONS IN RATS

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The effect of hypothyroidism on developing nerve tissue has been investigated in the greatest detail, chiefly by biochemical methods, with respect to the cerebral cortex and cerebellum [3]. The main effect of hypothyroidism has been shown to be marked depression of synthetic processes in developing nerve tissue. From this aspect, the limbic region of the brain, with which learning, memory, and emotions are connected, has received comparatively little study [6].

The aim of this investigation was to study, by interference microscopy, the time course of growth of neurons and accumulation of protein products in the pyramidal cells of hippocampal areas CA1 and CA3, as the major part of the limbic region of the rat brain.

EXPERIMENTAL METHOD

Hypothyroidism was induced by intraperitoneal injection of methylthiouracil (MTU) into a lactating Wistar rat in a dose of 100 mg in 0.5 ml physiological saline daily during the first week of life of the progeny, and thereafter on alternate days throughout the period of lactation (1 month). The brain of animals aged 14 and 21 days and 2 months was studied under normal conditions and in hypothyroidism. Animals with hypothyroidism for 2 months thus did not receive MTU in the 2nd month of life. After decapitation, pieces of brain containing the anterior hippocampus were fixed in formalin–alcohol–acetic acid (9:3:1) mixture. The thickness of frontal paraffin sections for interference microscopy was measured by the method in [1]. Parallel sections were stained with cresyl violet. The concentration of dry substances ($\Delta\phi$), and the area of the nucleus and perikaryon of the neurons (S) in areas CA1 and CA3 of the hippocampus were measured for 100 cells from each animal (2-3 animals in each age group). The area of the nucleus and perikaryon was determined by the formula $S = \pi Rr$; the radii were measured on projections drawn with the RA-6 drawing apparatus or by means of an ocular micrometer. The dry weight of the neurons was calculated for an area of section 5 μ thick. The numerical results were subjected to statistical analysis, the significance of differences between means being assessed by the t test.

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