mals with thermal injury led not only to a significant accumulation of BAA, which implies an inhibition of their incorporation into proteins, but also to a considerable increase of the content of FMFA (2-3-fold). Probably, excessive administration of nerobolil, inducing the accumulation of BAA, accelerates degradation of valine, leucine, and isoleucine with the simultaneous activation of the synthesis of fatty acids with odd numbers of carbon atoms from products of their incomplete degradation. Course administration of nerobolil exerting an anabolic effect in intact animals and in rats with thermal injury helped normalize the levels of the amino acids and albumins in question.

Thus, sex steroid hormones and their synthetic analog nerobolil regulate the relationship between the metabolism of essential BAA and FMFA with odd numbers of carbon atoms both under physiological conditions and in disturbed protein metabolism. It is well known (Fig. 3) that the biosynthetic and catabolic pathways of FMFA and BAA are characterized by some common intermediates: propionyl CoA, valeryl CoA, and isobutyryl CoA, which are probably the key intermediates in the realization of steroid activity. Moreover, anabolic steroids affect energy metabolism via regulation of the levels of free fatty acids and BAA, which in turn affect the energetics of muscle tissue [4] and some components of the citric acid cycle [3].

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Response of Hypothalamic Accessory Nonapeptidergic Centers to Hypophysectomy in Rats

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Accessory centers were calculated to contain more than 600 nonapeptidergic cells, most of which proved to be oxytocinergic. One week after hypophysectomy, morphometric measurements and morphofunctional changes in the nonapeptidergic cells of accessory centers indicated decreased synthesis of oxytocin and vasopressin by these cells as well as diminished transport of these neurohormones along their fibers. In contrast to the supraoptic, postoptic, and paraventricular nuclei, no degenerative cells were present in the accessory centers following hypophysectomy.

Key Words: *hypothalamus; accessory centers; oxytocinergic cells; vasopressinergic cells; hypophysectomy*

In addition to the supraoptic, postoptic, and paraventricular nuclei, the rat hypothalamus contains small accumulations of nonapeptidergic (NPE) neuroendocrine cells referred to as accessory centers (AC) [3,6,8,11]. The microanatomy of these centers has not been studied in sufficient detail, and the existing evaluations of their functional role are contradictory [1,2,7,12]. The question of how oxytocinergic (OTE) and vasopressinergic (VPE)

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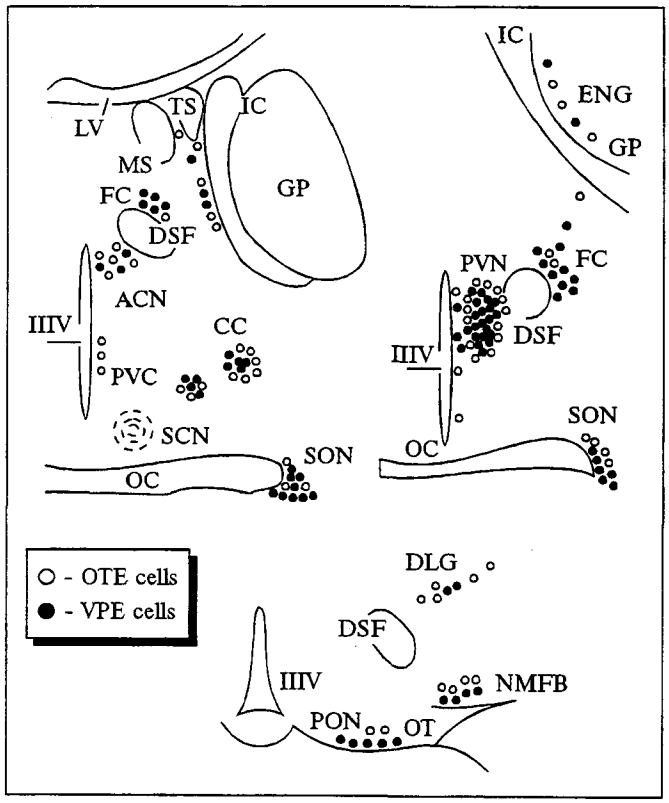

Fig. 1. Topography of the main and accessory hypothalamic nonapeptidergic neuroendocrine centers and the adjacent regions in rat brain. *IIIV*: third ventricle; *LV*: lateral ventricle; *GP*: globus pallidus; *IC*: internal capsule; *DLG*: dorsolateral group; *TS*: terminal stria; *DCF*: descending columns of the fornix; *MS*: medullary stria of the thalamus; *OT*: optic tract; *OC*: optic chiasm; *PVC*: periventricular cells; *PVN*: paraventricular nucleus; *ACN*: anterior commissural nucleus; *PON*: postoptic nucleus; *SON*: supraoptic nucleus; *SCN*: suprachiasmatic nucleus; *FC*: fornicate complex; *CC*: circular complex; *EHG*: extrahypothalamic groups; *NMFB*: nucleus of the medial forebrain bundle.

cells of the AC are related to the neurohemal regions remains open.

MATERIALS AND METHODS

Male Wistar rats weighing 120-150 g were used for the study. Five of them were hypophysectomized by the transsphenoidal route and decapitated on day 7 after the operation. Five intact rats served as controls. The brains of all rats were fixed in a picric acid:40% formalin mixture (3:5) at 37°C for a week. OTE and VPE structures were identified in serial paraffin-embedded sections immunohistochemically by the PAP method. Part of the material was stained with paraldehyde-fuchsin by Gomori-Gabe's method and counterstained with azan according to Heidenhain.

In the serial immunohistochemical preparations, OTE and VPE cells were counted on both sides in each AC (only those cell sections containing a nucleolus were taken into account). Diameters of cell bodies, nuclei, and nucleoli were measured with an eyepiece micrometer at a 15×90 magnification, and the cross-sectional areas of the nucleoli, nuclei, and cell bodies were calculated. The significance of differences between the test and control groups was evaluated by Student's *t* test.

RESULTS

The following AC were examined in the hypothalamus: circular and fornicate complexes, nucleus of the medial forebrain bundle, periventricularly situated NPE cells; extrahypothalamic groups were also considered (Fig. 1).

The circular complex was located above and somewhat lateral to the suprachiasmatic nucleus. NPE cells of this structure formed "cuffs" around sinusoidal capillaries (Fig. 2). In the control rats, the circular complex contained 230±3.46 cells, with OTE cells making up slightly more than a half of all cells (54%). In the hypophysectomized rats, the nucleoli of OTE and VPE cells were found to have decreased in area significantly ($p<0.01$) to similar extents (from 5.61±0.15 to 3.92±0.08 m^2 in OTE cells and from 5.21±0.18 to 3.43±0.1 m^2 in VPE cells), but the sizes of nuclei and cell bodies remained unchanged.

The perifornicate complex was located at the level of the paraventricular nucleus over the column of the fornix. Arterioles were surrounded by large NPE cells. In the control rats, this complex contained 101.67±3.28 cells, 68% of which were VPE cells. In the hypophysectomized rats, nucleolar areas in VPE cells had not undergone significant change, whereas their nuclear areas had increased significantly from 65.25±3.54 to 75.71±1.65 μ^2; $p<0.01$); cell body areas had increased only slightly. In OTE cells, nucleolar areas had decreased significantly from 6.51±0.22 to 5.12±0.16 μ^2; $p<0.01$; nuclear areas remained unchanged, while cell body areas had decreased slightly.

The nucleus of the medial forebrain bundle was located above the optic tract. In the control rats, NPE cells formed cuffs around arterioles. This nucleus contained 100.0±5.03 cells, with OTE and VPE cells being present in equal numbers. Following hypophysectomy, OTE cells had insignificantly increased nucleolar and cell body areas and significantly increased ($p<0.01$) nuclear areas (71.97±1.93 μ^2 vs. 59.66±1.3 m^2 in the control group). In VPE cells, hypophysectomy led to a significant decrease ($p<0.01$) in the nucleolar area (from 6.89±0.23 to 5.07±0.28 μ^2), to some in-

crease in the nuclear area, and to some decrease in the cell body area.

The dorsolateral group was located above and lateral to the column of the fornix at the level of the optic tract. This group contained 74.33±6.69 cells, most of which (72%) were OTE cells. OTE and VPE cells showed similar responses to hypophysectomy, with a significant decrease ($p<0.01$) in the nucleolar area (from 6.39±0.16 to 5.37±0.19 μ^2 in OTE cells and from 6.3±0.29 to 4.84±0.38 μ^2 in VPE cells), a significant increase ($p<0.01$) in the nuclear area (from 63.19±1.62 to 86.01±3.64 μ^2 in OTE cells and from 61.29±1.57 to 81.55±7.03 μ^2 in VPE cells), and virtually no change in the cell body area.

In the anterior hypothalamus, along the wall of the third ventricle in depressions of its ependymal lining, there lay small NPE cells, mostly of the OTE type (49.33±1.76 cells). The OTE cells of hypophysectomized rats had significantly decreased ($p<0.01$) nucleolar and cell body areas (3.37±0.14 μ^2 vs. 5.01±0.03 μ^2 and 140.29±4.33 μ^2 vs. 183.37±10.18 μ^2, respectively).

The region of the internal capsule was the site of extrahypothalamic groups of NPE cells. These groups contained 45.67±1.45 cells, most of which (82%) were OTE cells. In the hypophysectomized rats, both OTE and VPE cells had significantly decreased ($p<0.01$) nucleolar areas (4.77±0.18 μ^2 vs. 5.8±0.19 μ^2 in OTE cells and 4.03±0.34 μ^2 vs. 5.41±0.12 μ^2 in VPE cells) and slightly increased nuclear and cell body areas.

On day 7 after hypophysectomy, increased functional heterogeneity of NPE cells was observed in all AC (i.e., the cells were in different phases of the secretory cycle), as were appreciably increased numbers of fibers filled with neurosecretion. There were also increased numbers of cells containing nucleolus-like bodies in their nuclei, which is an indication of reduced functional activity of NPE cells [4]. It should be stressed that neither signs of NPE cell destruction nor the presence of pycnomorphic cells were observed in any of the AC (Fig. 3).

The AC of the diencephalon were calculated to contain about 600 cells, with a slight preponderance of OTE cells (58%). The only exceptions were the fornicate complex, where VPE cells predominated (68%), and the nucleus of the medial forebrain bundle, where OTE and VPE cells were present in equal numbers.

After hypophysectomy, nucleoli had significantly decreased sizes in the NPE cells of most AC. When the functional activity of NPE cells is evaluated, the nucleolus is accorded particular significance as the major structure associated with the production of ribonucleoproteins [4]. This suggests that the reduced sizes of NPE cell nucleoli observed after hypophysectomy in most AC were a reflection of reduced rates of protein production and, consequently, of oxytocin and vasopressin production. No significant changes in nucleolar areas occurred in the NPE cells surrounding arterioles (VPE cells of the fornicate complex and OTE cells of the medial forebrain bundle's nucleus), probably because the powerful oxygen flow in arterial blood can still maintain metabolic processes in NPE cells at a relatively high level under extremely adverse conditions such as those created by hypophysectomy.

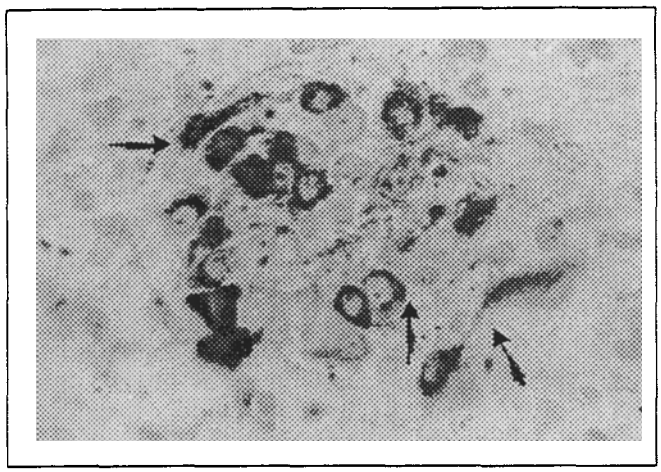

Fig. 2. The circular complex: control. Reaction with antiserum to oxytocin; counterstaining with Ehrlich's hematoxylin. ×280.

Nuclear and cell body sizes in AC cells underwent changes to lesser degrees than nucleolar sizes. In the dorsolateral group, however, whose cells are not in contact either with blood vessels or with the third ventricle, OTE and VPE cells had enlarged nuclei and diminished nucleoli,

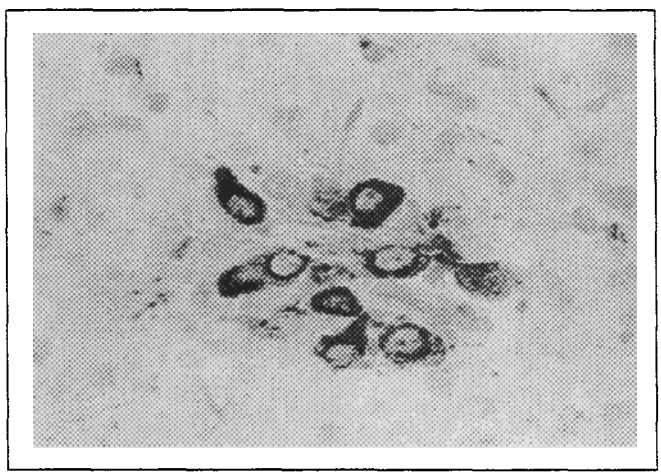

Fig. 3. The circular complex: day 7 after hypophysectomy. Reaction with antiserum to oxytocin; counterstaining with Ehrlich's hematoxylin. Arrows indicate oxytocin-immunoreactive fibers. ×280.

which appears to be an indication of degenerative processes in these cells and may be associated with the reaction to the trauma and with impairment of hormonal balance. Cell bodies were of decreased size only in the periventricularly located OTE cells, and the latter cells also had nucleoli of decreased size. This may be taken as evidence of considerably inhibited functional activity of the cells, probably as a consequence of their deteriorated nutrition following the postoperative disturbance of the cerebrospinal fluid dynamics.

Since 7 days after hypophysectomy no signs of NPE cell destruction were in evidence in the AC and none of these centers contained pycnomorphic cells, whereas many such cells were found in the supraoptic, postoptic, and paraventricular nuclei [9,10], we infer that NPE cells send their axons from the AC to the posterior pituitary. However, the changes observed in the AC, which were indicative of inhibited neurohormone transport along the fibers and of reduced synthesis in NPE cells, suggest that in most cases the posterior pituitary receives collaterals of axons that are damaged by hypophysectomy; this view is in accord with the data obtained by the method of retrograde labeling [5,13]. On the other hand, the results presented above do not rule out the possibility that NPE cell axons of accessory centers reach the medial eminence and make contact with capillaries of the pituitary portal system.

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