MORPHOLOGICAL BASIS OF THE PHASIC COURSE OF POSTTRAUMATIC DIABETES INSIPIDUS

E. M. Parshkov

UDC 616.631.11-02:614.8]-091

In sexually mature male Wistar rats in which electrolytic injury to the median eminence of the hypothalamus was followed by the development of a triphasic disturbance of water metabolism, an ultrastructural study was made of the neurohypophysis at the periods of greatest abnormality. Correlation was obtained between the physiological parameters (the volume of fluid consumed and of urine excreted) with the morphological data in the posterior lobe of the pituitary (the relative numbers of neurosecretory granules with dense and optically empty centers, the number of synaptic vesicles, and the state of the pituicytes).

Lesions localized in the region of the median eminence and stalk of the pituitary gland lead to the development of the symptom-complex of diabetes insipidus [2, 4, 5, 6, 9, 14]. Some workers have observed a triphasic disturbance of water metabolism under these circumstances; i.e., after a brief increase in diuresis there is a short period of oliguria, followed by polyuria and polydipsia [8, 10, 11]. Morphological analysis carried out at the height of these phases showed that the content of Gomori-positive material in the neurohypophysis is virtually unchanged [3, 8]. Conversely, in the later postoperative periods, when the neurohypophysis undergoes atrophy and contains no neurosecretion [8, 12], the normal water intake and urinary excretion are restored in the animals [4, 5]. The evident discrepancy between the physiological indices and the morphological data can probably be explained by the low resolving power of the light microscope, which does not permit the fine changes taking place in the neurohypophysis to be studied.

The investigation described below was accordingly carried out to study the posterior lobe of the pituitary at the ultrastructural level in various phases of disturbance of water metabolism.

EXPERIMENTAL METHOD

Pituitary glands of sexually mature male Wistar rats which developed the symptom-complex of diabetes insipidus after electrical coagulation of the median eminence of the hypothalamus by a direct current (1-2 mA, 10-20 sec) were subjected to histological and electron-microscopic investigation. Animals with no signs of polyuria or polydipsia were used as the control. The animals were killed by decapitation 1, 2, 5, 9, 30, and 40 days after the operation. The pituitary gland was divided into two parts in the sagittal plane. One part was fixed in Bouin's fluid and then used for light microscopy; the other part was again divided into two or three narrow strips which were fixed by Palade's method and embedded in Araldite or Epon after standard treatment. Ultrathin sections were studied in the JEM-5Y electron microscope. The region of injury was localized in serial frontal and sagittal sections through the hypothalamus stained with paraldehyde-fuchsin by the Gomori–Gabe technique.

EXPERIMENTAL RESULTS

In rats with features of diabetes insipidus foci of destruction were found in the rostral and central regions of the median eminence; in the latter case the stalk of the pituitary gland also was damaged. In

Laboratory of Experimental Pathomorphology, Department of Pathomorphology, Institute of Medical Radiology, Academy of Medical Sciences of the USSR, Obninsk. (Presented by Academician of the Academy of Medical Sciences of the USSR G. A. Zedgenidze.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 76, No. 12, pp. 102-106, December, 1973. Original article submitted December 14, 1972.

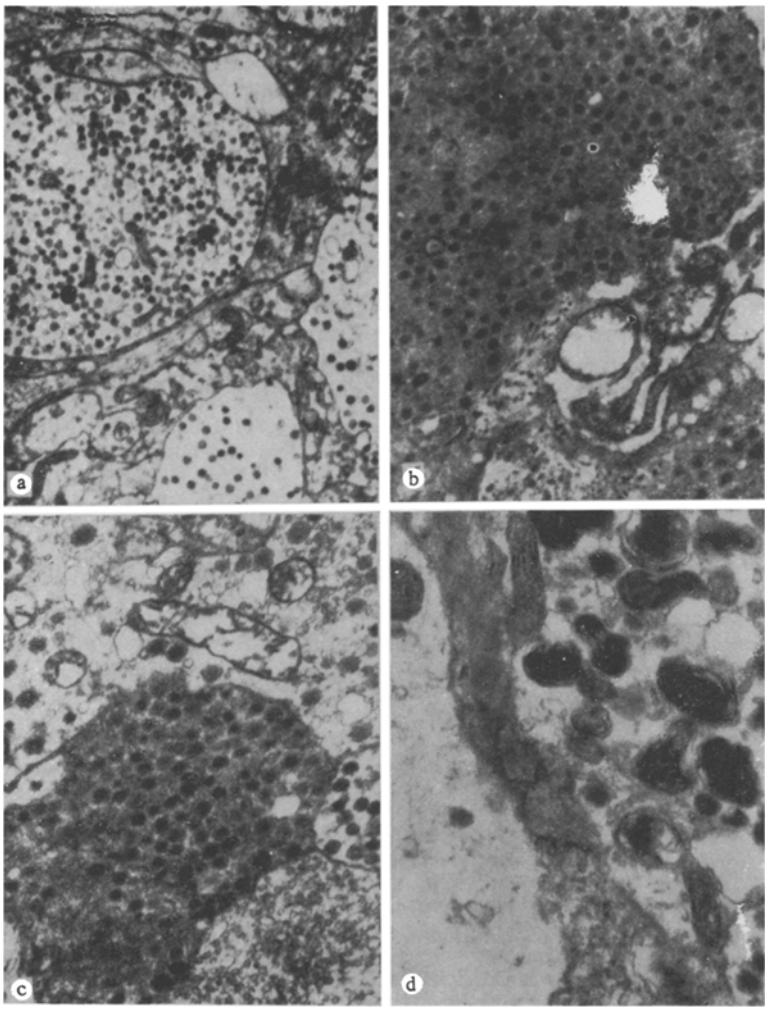

Fig. 1. Ultrastructure of posterior lobe of pituitary: a) posterior lobe of control rat; b-d) areas of posterior lobe of pituitary of rats with electrical coagulation of rostral region of median eminence, on 2nd (b), 5th (c), and 30th (d) days after operation. Magnification 5000 × (a); 12,000 × (b-d).

such animals a considerable accumulation of Gomori-positive material was found 1, 2, 5, and 9 days after the operation, anteriorly to the focus of injury, indicating destruction of most of the axons of the magnocellular nuclei. In the late stages after the operation (30-40 days) a glial scar was formed at the site of the focus of electrical coagulation. Neurosecretion in the median eminence was represented at this time by single granules.

In rats with no signs of disturbance of water metabolism the focus of electrical coagulation was outside the median eminence or in its caudal part. Under these circumstances no accumulation of neurosecretion took place in the median eminence. No changes could be detected in the neurohypophysis of these animals.

In the first week after destruction of the rostral and central regions of the median eminence, when a disturbance of the water balance was observed in the animals, the content of neurosecretion in the neurohypophysis was unchanged although it lost its customary granularity and became homogeneous. A study of the fine organization of the neurohypophysis showed that most nerve fibers and, in particular, their terminals were distended with neurosecretory granules, most of which had no limiting membrane. The density of the hyaloplasm reached the density of most of the secretory granules, and for that reason the granules appeared to merge with it. The whole nerve ending, under these circumstances, appeared osmiophilic (Fig. 1b). No synaptic vesicles were present in these structures. The pituicytes had little cytoplasm and were

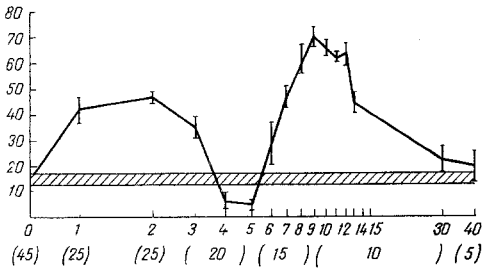

Fig. 2. Volume of urine excreted after electrical coagulation of medium eminence of hypothalamus. Abscissa, days after operation (logarithmic progression); ordinate, volume of urine excreted (in ml). Shaded band represents rat undergoing mock operation: continuous line with confidence limits represents experimental rats. Number of animals undergoing operation given in parentheses.

compressed by the hypertrophied axon terminals. In the control the nerve endings were typically few in number and they contained many neurosecretory granules and solitary microvesicles.

At this time the animals developed polyuria, which was soon followed by a short period of oliguria (Fig. 2).

In the phase of oliguria the number of optically dense terminals and their ultrastructural organization were virtually unchanged, but individual nerve endings which were evidently undamaged by electrical coagulation were filled with granules with an optically light center. The total number of neurosecretory granules fell sharply under these circumstances while the number of synaptic vesicles increased (Fig. 1c).

Permanent polyuria and polydipsia were established in the animals 9 days after destruction of the rostral and central regions of the median eminence (Fig. 2). Terminals with an extremely dense center predominated in the neurohypophysis. The limiting membrane of the granules was clearly distinguishable, and the hyaloplasm was translucent. Such endings either had no synaptic vesicles or they were concentrated in the central parts of the endings. The pituicytes were moderately hypertrophied, and their cytoplasm began to develop appendages. It contained a few mitochondria and a poorly developed endoplasmic reticulum. The Golgi complex consisted of short dictyosomes and small vesicles.

Later during the investigation (30-40 days) of the rats with diabetes insipidus their neurohypophysis had lost nearly all its Gomori-positive material. The normal water intake and urinary excretion were restored by this time (Fig. 2). Besides nerve endings, which have already been described, terminals completely devoid of secretory granules and of synaptic vesicles appeared in the neurohypophysis (Fig. 1d), and they were accompanied by large formations filled with atypical structures of curious shape with a strongly osmiophilic center and with numerous single membranes at the periphery (Fig. 1d). These formations are evidently a reflection of advanced degenerative changes in the terminals, and later they probably atrophy. Among the terminals listed above there were nerve fibers indistinguishable in structure from those in the control animals and animals undergoing the mock operation. Most of these terminals contained many synaptic vesicles and electron-empty granules. Individual endings were filled entirely with synaptic vesicles.

In the first phase of disturbance of water metabolism (1-2 days after destruction of the rostral and central regions of the medium eminence) deposition of neurosecretory material was observed in the posterior lobe of the pituitary. It spread both to endings whose nerve fibers had been damaged by the electric current and also to endings which were evidently unharmed by electrical coagulation but which, in all probability, were compressed by the reactive inflammation developing around the zone of destruction. In the phase of oliguria (4th-5th day after the operation), when the inflammation in the median eminence had subsided and information was beginning to reach the neurohypophysis along undestroyed axons from the hypothalamic centers, the nerve endings began to respond with a massive liberation of neurosecretion into the blood stream. An increase in the number of synaptic vesicles and secretory granules with an optically empty center was then observed in the terminals. This state of the terminals is interpreted as increased function [1, 13]. The content of antidiuretic hormone in the neurohypophysis in this phase was considerably reduced, while its excretion in the urine was greater than normal [10, 11]. Since the number of undestroyed axons and, consequently, of functioning neurocytes was small, they could not satisfy the animal's requirement for ADH and for that reason the stage of compensation quickly changed into a stage of decompensation. The animals therefore developed prolonged polyuria and polydipsia. Destructive changes in the endings which were seen during the first days after the operation were probably reversible, for later well-marked polymorphism of the nerve endings was found in the neurohypophysis and some of them regained their ultrastructure completely. Transport of neurosecretion was increased at this stage of the investigation, as shown by the absence of Herring's bodies and the appearance of many terminals with optically empty granules and synaptic vesicles. The result of this process was the virtually complete disappearance of the polyuria and polydipsia in these animals.

LITERATURE CITED

1. M. A. Belen'kii, Dokl. Akad. Nauk SSSR, 202, 449 (1972).
2. I. A. Ben'kovich, Probl. Éndokrinol., No. 4, 70 (1964).
3. E. M. Parshkov, The Hypothalamus and Pituitary after Electrolytic Injury to the Neurosecretory System and Irradiation, Candidate's Dissertation, Moscow (1970).
4. J. H. Adams, P. M. Daniel, and M. M. L. Prichard, J. Comp. Neurol., 142, 109 (1971).
5. S. M. Friedman, M. Nakashima, and C. L. Friedman, Endocrinology, 81, 1231 (1967).
6. M. Fusco, R. L. Malvin, and P. Churchill, Endocrinology, 79, 301 (1966).
7. C. C. Gale, S. Taleisnik, and S. M. McCann, Am. J. Physiol., 201, 811 (1961).
8. R. L. Holmes, J. Endocrinol., 22, 7 (1961).
9. S. Kawashima and N. Takusugi, J. Fac. Sci. Univ. Tokyo, 11, Sec. 4, 207 (1967).
10. F. A. Laszlo and D. de Wied, J. Endocrinol., 36, 125 (1966).
11. F. A. Laszlo and D. de Wied, Endocrinology, 79, 547 (1966).
12. J. Moll, Z. Anat. Entwickl.-Gesch., 124, 184 (1964).
13. J. Nagasawa, W. W. Douglas, and L. A. Schulz, Nature, 227, 407 (1970).
14. Y. Yamane and K. Kunishige, Jap. Circulat. J., 30, 1381 (1966).