# TOPOGRAPHY OF SUBNUCLEI OF THE HYPOTHALAMIC PARAVENTRICULAR NUCLEUS IN RATS AND SENSITIVITY OF THEIR NEURONS TO INSULIN DEFICIENCY

E. I. Goufman

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The hypothalamus is an important center regulating carbohydrates metabolism, as many clinical and experimental observations have confirmed. Meanwhile there is no unanimity on the role of particular hypothalamic structures in the regulation of glucose metabolism. Direct nervous connections of the paraventricular nuclei (PVN) of the hypothalamus with autonomic centers in the medulla, involved in nervous regulation of the pancreatic islets [1], discovered in recent years, suggest that PVN participate in the central control of carbohydrate metabolism. However, as the results of recent neuronanatomical studies have shown [2], PVN is heterogeneous in composition and consists of about 10 subnuclei, which differ in their morphology, nervous connections, peptides and mediators synthesized in their neurons and, possibly, their physiological features.

In connection with the facts described above the investigation described below was undertaken to study the reaction of PVN subnuclei to insulin deficiency and to elevation of the blood glucose level under conditions of experimental alloxan diabetes.

TABLE 1. Parameters of Distribution of Areas of Cell Nuclei in Subnuclei Distinguished in Rat PVN ($\mu^2$, $\bar{X} \pm \bar{m}$)

| Subnucleus | Control | Experiment | $t$ | $P$ |
|---|---|---|---|---|
| AMS | 72,7±0,5 | 95,3±0,4 | 33,93 | <0,001 |
| APS | 55,2±0,6 | 54,2±0,6 | 1,22 | >0,05* |
| MMS | 67,8±0,5 | 86,1±0,5 | 26,14 | <0,001 |
| PVMS | 53,1±0,5 | 83,4±0,6 | 41,13 | <0,001 |
| LMS | 78,9±0,5 | 102,6±0,5 | 33,17 | <0,001 |
| VMS | 73,1±0,5 | 93,7±0,5 | 28,56 | <0,001 |
| DC | 72,3±0,6 | 87,3±0,6 | 17,97 | <0,001 |
| PS | 79,9±0,5 | 104,8±0,5 | 33,54 | <0,001 |
| PVPS | 50,7±0,6 | 52,2±0,6 | 1,72 | >0,05* |
| MPS | 45,0±0,6 | 51,1±0,6 | 7,18 | <0,001 |

Legend. In each case 1000 nuclei were measured. Distributions of areas of nuclei of neurons of all cell groups corresponded to theoretical frequencies of normal distribution. *) Assessment of changes in diabetes in these subnuclei by the chi-square test likewise did not reveal significant differences ($P > 0.1$).

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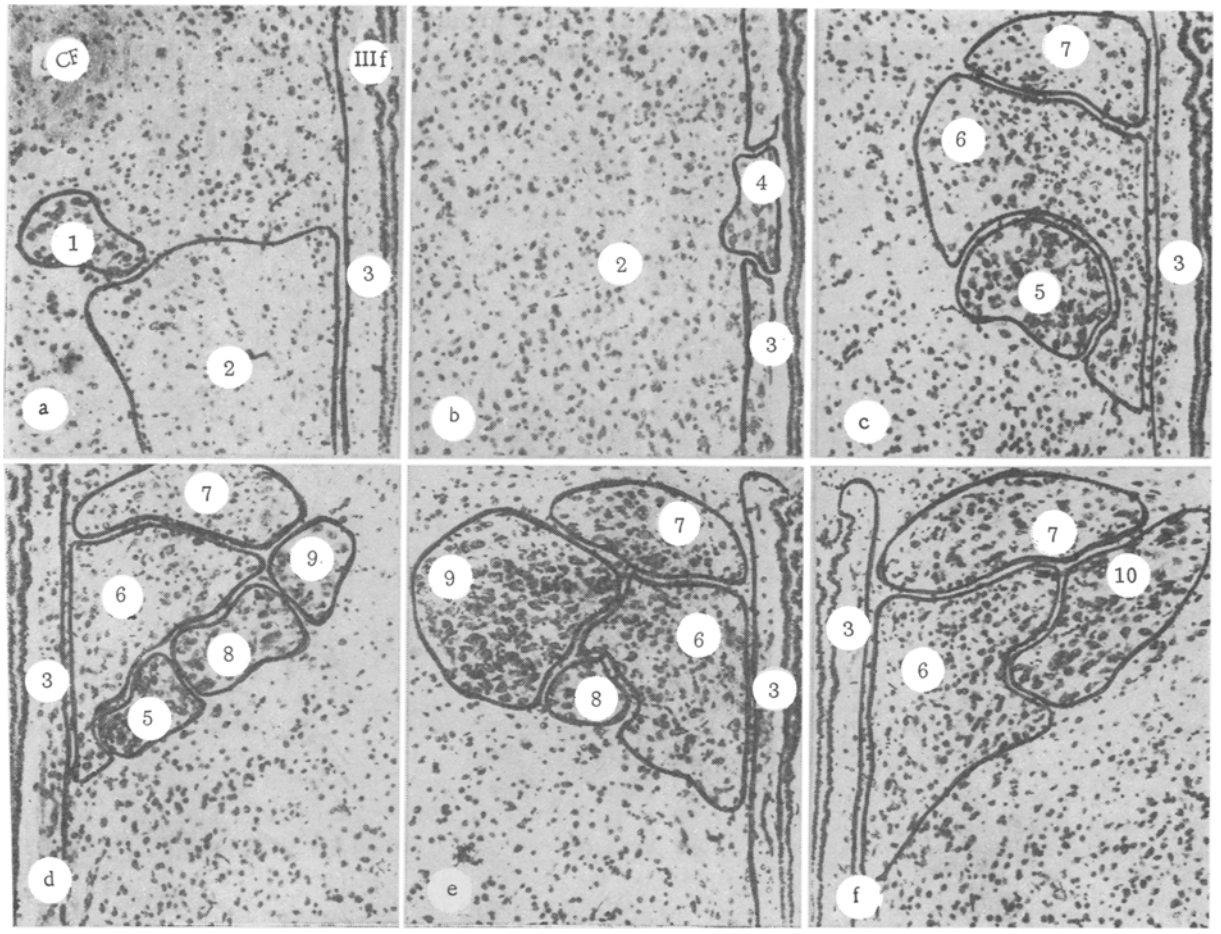


Fig. 1. Topography of subnuclei distinguished in rat PVN. Frontal sections through hypothalamus, cut at level of 550 μ (a), 850 μ (b), 1000 μ (c), 1030 μ (d), 1090 μ (e), and 1210 μ (f) from zero vertical plane passing through the bregma (calculations based on Szentagothai's cytoarchitectonic atlas). 1) AMPS, 2) APS, 3) PVPS, 4) PVMS, 5) MMS, 6) MPS, 7) DC, 8) VMS, 9) LMS, 10) PS. f) Fornix, IIIv) third ventricle. Stained with hematoxylin and eosin, 40 ×.

## EXPERIMENTAL METHOD

Experiments were carried out on 15 control and 15 experimental mature male Wistar rats, kept under identical conditions on a standard diet. Alloxan was injected intraperitoneally into the experimental animals in a single dose of 26 mg/100 g. The animals were decapitated 30 days after injection of alloxan. The state of the carbohydrate metabolism of the diabetic and control animals was judged by the blood glucose and radioimmune insulin levels.* The hypothalamic region was fixed in 10% buffered neutral formalin, Carnoy's fluid, and Susa fixative. Serial paraffin-celloidin sections were stained with hematoxylin and eosin, with methylene blue by Nissl's method, and with gallocyanin by Einarson's method. The reaction of the various cell populations of PVN was judged from the results of their karyometric and morphologic investigations. Areas of neurons were measured by means of a "Videomat-1" television image analyzer and the results of the measurements were subjected to statistical analysis on the "Pidipi-12/20" computer.

## EXPERIMENTAL RESULTS

Ten cell groups can be distinguished in PVN (Fig. 1), which differ in topography and morphological features of their component neurons. About 100-120 μ rostrally to the beginning of the supraoptic nuclei, below and medially to the descending columns of the fornix, a small collection of compactly arranged magnocellular neurons was observed. The bodies of these neurons were oval shaped and oriented mainly mediolaterally. Large round nuclei were sur-

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rounded by a dense border of Nissl's substance. This group of cells, described by Peterson [4], we called the anterior magnocellular subnucleus (AMS). An extensive group of parvocellular neurons is located from the beginning of AMS to the level of the posterior third of the supraoptic nuclei, occupying the space between the ventricle and fornix, along the extent of the upper two thirds of the third ventricle. It consisted of small and medium-sized neurons with small round nuclei and very little cytoplasm. This subnucleus was classed with PVN [5] and called the anterior parvocellular subnucleus (APS). Throughout the extent of PVN, directly against the wall of the third ventricle, there is a group of small fusiform cells, oriented vertically, and characterized by oval nuclei and weakly basophilic cytoplasm. This subdivision has been called the periventricular parvocellular subnucleus (PVPS) and has been described by a number of workers [3, 5]. In the periventricular region, a little caudally to AMS, we observed large neurons, stretching along the third ventricle. They had oval nuclei and cytoplasm with well-marked Nissl's substance. These neurons form a subnucleus, also described previously [5], which we called the periventricular magnocellular nucleus (PVMS). At the level of the posterior third of the supraoptic nuclei, adjacent to the periventricular zone there is a compact selection of oval and round neurons with large nuclei and abundant cytoplasm. In accordance with existing descriptions [2, 5] it has been named the medial magnocellular subnucleus (MMS). Dorsolaterally to the latter, magnocellular neurons are oriented at an angle of about 45° to the wall of the third ventricle. Their bodies are longer than the nerve cells of the medial subnucleus. This region has been called the ventral magnocellular subnucleus (VMS). Above and laterally to the ventral subnucleus lies the lateral magnocellular subnucleus (LMS), consisting of round neurons with abundant cytoplasm and large oval nuclei. Dorsally, the lateral subnucleus is bounded by medium-sized oval or fusiform neurons. They form a group of cells resembling in shape an inverted saucer, and named, in accordance with data in the literature [2], the dorsomedial "cap" (DC). The space bounded by this subnucleus and also by the lateral, ventral, and medial magnocellular and the periventricular parvocellular subnuclei is filled with small neurons, composing the medial parvocellular subnucleus (MPS). The posterior part of LMS is bordered by neurons with a very large nucleus and scanty cytoplasm. Caudally they replace cells of the lateral subnucleus and form a triangular cell group, which continues above the fornix into the dorsolateral hypothalamic region. It is called the posterior subnucleus (PS).

The results of the karyometric investigation of neurons of the structures described in intact and experimental animals showed (Table 1) that only neurons of the anterior and periventricular parvocellular subnuclei did not exhibit a significant reaction of the cell nuclei to alloxan diabetes. A bright reaction was demonstrated by neurons of PVMS, AMS, LMS, and PS (an increase in area of their nuclei by 57.06 ± 1.47%, 31.08 ± 0.88%, 30.03 ± 0.89%, and 31.16 ± 0.88% respectively compared with the control).

Observations on morphologic changes in neurons of subnuclei of PVN in alloxan diabetes agreed with the karyometric data. The cytoplasm of neurons of the magnocellular subnuclei was enlarged, its basophilia was intensified, and the Nissl's substance was more clearly demonstrated. These changes were most marked in MMS and LMS. In the magnocellular subnuclei, and also in PS and DC, vacuolated cells were found. In some parvocellular neurons basophilia of the cytoplasm was intensified and pale, swollen nuclei were observed.

The results of these investigations are evidence that both magnocellular and parvocellular neurons of PVN react to alloxan diabetes, and this is an argument in support of the hypothesis that PVN of the hypothalamus participates in the control of carbohydrate metabolism.

## LITERATURE CITED


1. I. G. Akmayev, Acta Morphol. Hung., 31, 137 (1983).
2. W. E. Armstrong, S. Warach, G. I. Hatton, et al., Neuroscience, 5, 1931 (1980).
3. S. McKellar and A. D. Loewy, Brain Res., 217, 351 (1981).
4. R. Peterson, J. Comp. Neurol., 128, 181 (1966).
5. L. W. Swanson and H. G. J. M. Kuypers, J. Comp. Neurol., 194, 555 (1980).