The particular vulnerability of MRF, where brain vessels are damaged first and most severely in emotional stress, may be due to a certain specific feature of the energy metabolism of this part of the brain — relatively high activity of anaerobic and relatively low activity of aerobic energy metabolism [3].

LITERATURE CITED

1. T. I. Belova and G. Jonsson, Usp. Fiziol. Nauk, 16, No. 2, 61 (1985).
2. T. I. Belova, N. V. Petrova, and G. Jonsson, Byull. Éksp. Biol. Med., 101, No. 4, 395 (1986).
3. T. M. Ivanova and T. I. Belova, Byull. Éksp. Biol. Med., 102, No. 10, 397 (1986).
4. D. S. Sarkisov, Essays on the Structural Principles of Homeostasis [in Russian], Moscow (1977).
5. T. I. Belova and G. Jonsson, Acta Physiol. Scand., 116, 21 (1982).
6. E. Ben-Menachem, B. B. Johansson, and T. H. Svensson, J. Neural Transmiss., 53, 159 (1982).
7. S. I. Harik, Proc. Natl. Acad. Sci. USA, 83, 4067 (1986).
8. R. Kvetnansky and L. Mikulaj, Endocrinology, 87, 738 (1970).

RESPONSE OF SINGLE CELL POPULATIONS OF THE PARAVENTRICULAR HYPOTHALAMIC NUCLEI TO CARBOHYDRATE LOADING AND STARVATION IN RATS

O. S. Gorbatyuk, E. I. Goufman, A. A. Gusev, L. K. Starosel'tseva, and I. G. Akmaev

UDC 612.826.4.06:[612.396+612.391].08

KEY WORDS: paraventricular nuclei of the hypothalamus; regulation of carbohydrate metabolism

With the discovery of direct nervous connections between the paraventricular nuclei (PVN) of the hypothalamus and the dorsal nuclei of the vagus (DNV) in the medulla [4, 8] a possible role for PVN in the regulation of the hormonal basis of carbohydrate homeostasis via the paraventriculovagal nerve pathway began to be postulated [1, 3]. Experimental confirmation of such a possibility could be given by observations on insulin-dependent food responses, which have been studied in animals with different procedures aimed at the PVN region [5, 6]. With an increase in interest in the study of the role of PVN in the regulation of homeostatis functions, it has become increasingly evident that in modern research changed ideas on the structure of these nuclei must be taken into account. At the present time about 10 cell populations are distinguished in them, differing in the character of their nervous connections and the composition of their neuropeptides and neurotransmitters [2, 7]. Hence it is clear that any attempt to study the role of PVN in the regulation of carbohydrate homeostasis requires clarification of the individual contribution of each separate subnucleus in the regulation of this homeostatic function.

In the investigation described below correlation was studied between structural changes in the cells in each subnucleus of PVN and experimental changes in the parameters of the blood sugar: lowering of their values by starvation and their elevation as a result of drinking 12% glucose solution instead of water.

EXPERIMENTAL METHOD

The test object consisted of 30 mature male Wistar albino rats weighing 180-200 g, of which 10 were deprived of food for 6 days but allowed free access to drinking water; 10 animals were kept on a standard diet but, instead of drinking water, they were given a 12% solution of glucose for 20 days; 10 animals served as the control and received a pellet diet and

---

Laboratory of Experimental Morphology and Laboratory of Biochemistry and Pathology of Metabolism, Institute of Experimental Endocrinology and Hormone Chemistry, Academy of Medical Sciences of the USSR, Moscow.

(Presented by Academician of the Academy of Medical Sciences of the USSR, D. S. Sarkisov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 108, No. 7, pp. 105-107, July, 1989. Original article submitted November 5, 1988.

0007-4888/89/0007-1030$12.50

TABLE 1. Areas of Nucleoli (1), Nuclei (2), and Cytoplasm (3) in Different Cellular Subdivisions of Rat PVN during Experimental Procedures

Subnucleus	Control	Starvation	p	Glucose loading	p
AM					
1	3,6±0,2	3,7±0,1	0,05	3,1±0,1	0,05
2	73,6±1,3	74,1±1,1	0,05	72,6±1,3	0,05
3	93,3±3,1	94,9±4,8	0,05	56,2±3,7	0,001
PVM					
1	3,5±0,1	3,4±0,1	0,5	3,4±0,2	0,05
2	68,3±1,1	62,5±1,2	0,001	59,7±0,9	0,001
3	87,5±2,7	50,5±4,1	0,001	63,8±4,2	0,001
MM					
1	4,0±0,2	3,5±0,1	0,05	4,5±0,2	0,05
2	68,3±0,7	66,9±0,9	0,05	70,3±1,1	0,05
3	113,5±2,6	82,9±3,4	0,001	77,5±3,4	0,001
AP					
1	2,5±0,1	2,9±0,1	0,05	2,4±0,1	0,05
2	62,5±1,8	61,2±0,8	0,05	56,8±1,2	0,01
3	62,3±2,5	54,4±2,6	0,05	51,0±3,3	0,05
PVP					
1	2,7±0,1	3,2±0,1	0,01	3,6±0,2	0,001
2	61,6±1,6	59,8±1,1	0,05	63,6±1,3	0,05
3	49,6±2,1	53,6±3,0	0,05	77,5±4,6	0,001
MP					
1	2,3±0,1	2,1±0,1	0,05	2,4±0,2	0,05
2	55,7±1,1	50,8±1,2	0,01	61,8±1,8	0,01
3	62,1±2,1	48,2±2,9	0,001	63,1±4,1	0,05
VS					
1	3,2±0,1	2,4±0,1	0,001	3,7±0,1	0,01
2	72,6±1,2	63,4±1,6	0,001	71,6±1,4	0,05
3	108,2±4,4	88,3±4,1	0,001	104,6±4,5	0,05
LM					
1	4,5±0,2	3,5±0,2	0,001	4,1±0,1	0,05
2	77,6±0,7	75,2±1,4	0,05	74,4±0,9	0,01
3	137,0±3,7	91,8±5,0	0,001	95,7±3,6	0,001
DS					
1	3,0±0,2	2,3±0,1	0,01	3,5±0,1	0,05
2	70,4±1,1	65,4±1,2	0,001	69,4±1,5	0,05
3	80,4±2,1	63,2±3,0	0,001	57,1±3,8	0,001
PS					
1	3,7±0,2	3,3±0,1	0,05	4,1±0,1	0,05
2	78,6±1,5	86,9±1,6	0,001	75,2±1,4	0,05
3	109,0±3,1	129,0±5,7	0,01	110,1±5,1	0,05

Legend. Subnuclei of PVN: AM) anterior magnocellular, PVM) periventricular magnocellular, MM) medial magnocellular, AP) anterior parvocellular, PVP) periventricular parvocellular, MP) medial parvocellular, VS) ventral subnucleus, LM) lateral magnocellular, DS) dorsal subnucleus, PS) posterior subnucleus.

water ad lib. The state of the carbohydrate metabolism of the control and experimental animals was judged by their blood levels of glucose (the glucose level was determined on a "Beckman" automatic analyzer) and insulin (the insulin level was measured with the aid of standard radioimmunoassay kits). The plasma glucose and insulin levels were respectively as follows: in the control animals (on average) 6.1 ± 0.3 mmoles/liter and 28.6 ± 8.1 mU/ml, in the starving animals 4.0 ± 0.2 mmoles/liter and 10.6 ± 6.3 mU/ml, in animals with carbohydrate loading 7.5 ± 0.5 mmoles/liter and 49.1 ± 11.4 mU/ml. The animals were killed by decapitation. The hypothalamic region of the brain was fixed in Bouin's and Susa's fluids. Serial celloidin and paraffin sections through the region of the hypothalamus to be studied were stained with hematoxylin and eosin and with Gabe's paraldehyde-fuchsine method, followed by counterstaining with azocarmine. The response of the subnuclei of PVN was judged from the results of measurement of the areas of the cell nuclei, nucleoli, and cytoplasm, and also by determining the quantity of stained neurosecretion in the cell bodies, processes, and their terminals in the posterior principal part of the neurohypophysis. All the measurements mentioned above were carried out by means of a "Vidiomat-1" television image analyzer. The results of the measurements were subjected to statistical analysis on the "Pidipi-12/20" computer. In each case 100 cells were measured; distributions of areas of the nuclei, nucleoli, and cytoplasm of the neurons corresponded to theoretical parts of the normal distribution.

EXPERIMENTAL RESULTS

The results of the morphometric study of cellular responses in the various subnuclei of PVN on the experimental and control animals are given in Table 1. With both types of experimental

procedures, disturbing carbohydrate homeostasis, the neuronal response of the magnocellular subnuclei of PVN was on the whole fairly uniform (Table 1). In both cases structural evidence was obtained on inhibition of synthesis and release of neurosecretion. The dimensions of the nuclei and nucleoli and of the cytoplasm of the neurons were reduced. The quantity of condensed chromatin in the nuclei was increased. The content of stained neurosecretion in the cell bodies, processes, and their endings in the posterior, principal part of the neurohypophysis was considerably increased. The possibility cannot be ruled out that these changes do not reflect the specific response of neurons of the magnocellular subnuclei to disturbance of carbohydrate homeostasis, but are the result of increased water intake by the experimental animals.

Marked dependence of their histophysiology on the state of carbohydrate metabolism was exhibited by five subnuclei which, in accordance with the classification used [2] we included in the classes of parvocellular and intermediocellular: PVP, MP, VS, DS, and PS. In the starvation experiments, i.e., when the blood insulin level was lowered and when there was a corresponding decrease in the quantity of glucose entering the cells, neurons of PS responded with an increase of functional activity, which was more marked in the rostral zones of this subnucleus. Under the same conditions structural evidence was obtained of a reduction of functional activity of the neurons of VS, MP, and DS, which was most marked in VS. Nerve cells of PVP were activated by glucose loading, i.e., when blood insulin and glucose levels were raised. This effect was particularly marked in a group of neurons which could be clearly distinguished at the level of frontal sections where PVM ceases and the MM subnucleus begins. As will be clear from Table 1, each of the experimental models used induced changes in activity of these subnuclei in a particular combination. It is perhaps through a combined change of this kind in the activity of the latter that the mosaic pattern of incorporation of these subnuclei into the mechanisms involved in the regulation of carbohydrate homeostasis is achieved via different channels of communication: via the vagus system (through direct nervous connections of PS with DNV), via the sympathetic nerves innervating the pancreatic islets (through direct nervous connections of DS and VS with preganglionic sympathetic neurons in the spinal cord), and via the portal system of vessels of the pituitary gland, through which PVP and MP can control the secretion of pituitary counterinsulin hormones [8].

LITERATURE CITED

1. I. G. Akmaev, Usp. Sovrem. Biol., 103, No. 1, 109 (1987).
2. E. I. Goufman, Byull. Éksp. Biol. Med., No. 2, 194 (1985).
3. I. G. Akmaev (I. G. Akmayev), O. V. Vikhreva, and L. K. Konovalova, Brain Res., 230, 342 (1981).
4. I. G. Akmaev (I. G. Akmayev), Exp. Clin. Endocrinol., 88, 129 (1986).
5. S. F. Leibowitz, Physiol. Behav., 14, 731 (1975).
6. S. F. Leibowitz, Pharmacol. Biochem. Behav., 8, 163 (1978).
7. P. E. Sawchenko and L. W. Swanson, J. Comp. Neurol., 205, 260 (1982).
8. L. W. Swanson, P. E. Sawchenko, S. J. Wiegand, and J. L. Price, Brain Res., 198, 190 (1980).