CELLULAR RESPONSES OF THE NUCLEUS OF THE TRACTUS SOLITARIUS AND ITS INDIVIDUAL SUBNUCLEI TO CHANGES IN CARBOHYDRATE METABOLISM IN RATS

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UDC 616.379-008.64-092.9-07:616.831.8-076

KEY WORDS: carbohydrate homeostasis; nucleus of the tractus solitariusi nervous regulation

The attempt to explain the absence of a pituitary trophic hormone for the pancreatic enzyme apparatus was the basis for the hypothesis that activity of pancreatic islets may be controlled by nerve fibers incorporating hypothalamic and bulbar levels of regulation [1]. The key stage in the organization of the bulbar level of regulation is considered to be the nuclei of the tractus solitarius (NTS), where taste and visceroceptive afferents, playing an important role in the trigger mechanisms of food responses, relay [3].

The hypothesis concerning involvement of NTS in the regulation of carbohydrate metabolism required experimental proof. However, this was not easy to obtain, because according to existing data, many cell populations differing in the histophysiology and biochemistry of their component neurons, and also in the range of functions controlled by them, can be identified in NTS [2, 4-6]. Consequently, in order to investigate the role of NTS in the regulation of carbohydrate homeostasis, information was needed on the state of each of the individual cell populations in the nucleus during experimentally induced changes in carbohydrate metabolism.

This paper describes a study of the response of individual subnuclei of NTS to experimental disturbance of carbohydrate homeostasis, in a model of alloxan diabetes.

EXPERIMENTAL METHOD

Experiments were carried out on 10 control and 10 experimental mature male Wistar rats kept on a standard diet. The experimental animals received a single intraperitoneal injection of alloxan-4-hydrate ("Chemapol") in a dose of 26 mg/100 g body weight. The animals were decapitated 30 days after the injection of alloxan and the medulla was removed and fixed in Bouin's and "Susa" fluids. Serial paraffin and celloidin sections were stained with hematoxylin and eosin and by Einarson's gallocyanin method. Since alloxan diabetes is accompanied by disturbance of the water and electrolyte balance, 10 rabbits loaded with water and salt were used as an additional control group. Instead of drinking water, the rats of this group received a 2.5% solution of sodium chloride for 20 days. Cellular responses of each subnucleus of NTS were judged by the results of karyometric tests. The areas of the neurons were measured by means of an "Ibas-2" television image analyzer.

EXPERIMENTAL RESULTS

The results of the karyometric study of neurons in different subnuclei of NTS in animals of the control and experimental groups are given in Table 1. Analysis of the results indicates that in alloxan diabetes the nuclei are enlarged in neurons of all subnuclei of NTS except the medial small-cell subnucleus (MSC). Changes also are found in the morphol-

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 0007-4888/91/0009-1338$12.50

TABLE 1. Parameters of Distributions of Areas of Cell Nuclei (in μ^2) in Individual Subnuclei of Rat NTS ($X \pm m$)

Subnucleus	Control	Diabetes	p	Water and salt loading	p
RM	50,0±1,2	58,1±1,3	<0,01	56,2±2	<0,05
RI	62,6±2,0	68,1±1,8	<0,05	71,0±1,4	<0,01
RVL	76,6±1,8	86,2±1,2	<0,01	84,0±2,0	<0,01
VL	88,6±1,8	95,8±2,8	<0,01	83,0±1,2	<0,05
DL	52,3±2,3	58,7±1,0	<0,05	47,3±1,0	>0,05
D	66,7±1,2	71,2±1,4	<0,05	70,0±1,2	<0,05
DL	85,4±1,4	92,1±2,3	<0,05	92,2±2,0	<0,05
DM	66,1±1,5	74,3±1,2	<0,01	78,3±1,2	<0,01
ML	60,3±1,1	69,5±1,2	<0,01	71,7±1,1	<0,01
MM	56,9±1,4	65,1±1,1	<0,01	54,4±1,3	>0,05
C	76,9±1,9	99,3±3,2	<0,001	81,4±2,8	>0,05
IS	69,6±2,2	74,1±2,2	<0,05	73,5±2,3	<0,05
MSC	44,1±1,2	47,6±2,4	>0,05	36,5±1,0	<0,01
I	85,4±2,4	104±2,8	<0,001	90,1±2,2	>0,05

Legend. p) evaluation of changes compared with control.

ogy of the nuclei: the area of the Nissl's substance and its basophilia are increased, the grains of heterochromatin in the nuclei are reduced in size, and the karyoplasm is translucent. These findings are evidence of intensified synthetic activity of the NTS subnuclei studied. However, the degree of activation of the responding neurons differed significantly. Cell responses of the intermediate (I) and commissural (C) subnuclei were most marked, and neurons of the medial (MM) and lateral (ML) parts of the medial subnucleus, dorsomedial (DM), ventrolateral (VL), rostroventrolateral (RVL), and rostromedial (RM) subnuclei exhibited high but weaker activation of synthesis, and the dorsolateral (DL), rostrointermediate (RI), dorsal (D), and interstitial (IS) subnuclei and the dorsal cellular band (DB) exhibited even fewer signs of increased cellular activity. During water and salt loading changes on the whole similar to those of alloxan diabetes were observed in neurons of DM, ML, RVL, DB, and RI. Neurons of RM, D, and IS gave a much weaker response than that in diabetic animals. Virtually no changes were found in the response of neurons to water and salt loading in C, DL, MM, and I. Additionally, in the cellular responses of MSC and VL to this loading, both the sign and the magnitude of the deviations changed: the nuclei were reduced in size, the area occupied by the Nissl's substance was reduced, basophilia of the karyoplasm was increased, and the heterochromatin was condensed into numerous medium-sized and large granules.

The absence of any cellular response or the presence of cellular responses significantly weaker than those of diabetic animals, in MM, C, I, DL, IS, and VL in the control experiment with water and salt loading suggest that the individual subnuclei respond selectively to changes in the parameters of carbohydrate homeostasis. These changes could be those affecting the blood glucose and insulin levels.

Comparison of the results relating to activity of ML, DM, DB, D, RM, RI, and RVL in the two experimental models makes their interpretation even more difficult, for this type of response of the neurons of these subnuclei, whether in the first or in the second experiment, does not allow the factor leading to a change in the histophysiology of the cells to be definitely identified.

The results of this investigation thus demonstrate a marked response of the seven cellular subdivisions of NTS to changes in carbohydrate homeostasis, confirming experimentally the hypothesis that NTS is involved in the regulation of carbohydrate metabolism.

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