ROLE OF THE HYPOTHALAMUS IN DISTURBANCES OF PROTEIN METABOLISM AFTER BURNS

T. L. Zaets, V. B. Golovchinskii, and L. I. Muzykant

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In animals in which the hypothalamic nuclei have been destroyed, burn injuries do not lead to the accumulation of amino nitrogen in the muscle tissue or to increased autolysis of muscle proteins, as are usually observed in intact animals after burns.

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The problem of the role of the neuro-endocrine system in the development of the burn syndrome is one of the most interesting and promising in the pathogenesis of this condition. Luccioni and co-workers [9] regard the burn syndrome as a neuro-hormonal reaction to severe specific trauma. One of the main links in the mechanism of neuro-endocrine changes, in their opinion, is the hypothalamus. The work of several investigators [1, 4-8, 12] has demonstrated the importance of various zones and nuclear groups of the hypothalamus in the regulation of water-salt, lipid, carbohydrate, and protein metabolism.

In previous investigations we showed that if a rabbit in which the supraoptic nuclei of the hypothalamus have been destroyed is burned, the intensity of protein synthesis in the muscles and wall of the small intestine of the animal is unchanged, whereas usually burns inhibit uptake of methionine-S^{35} into proteins by several organs. On this basis we assumed that the hypothalamus, with its role in regulation of protein metabolism, also participates in the development of disturbances of protein metabolism after burns. Changes in protein metabolism in the burn syndrome are characterized not only by a disturbance of protein synthesis in various tissues [2], but also by intensification of protein breakdown both in the burned area and in intact tissues. Under these circumstances the activity of cathepsins is increased in the liver, kidneys, and skeletal muscles, and the intensity of autolysis rises [3]. Having determined on the basis of our own and published data that the state of function of the supraoptic zone of the hypothalamus is connected with the processes of protein synthesis, our next task was to examine the importance of this region of the hypothalamus in activation of protein breakdown processes in burned animals.

Accordingly, we investigated the effect of burns on the intensity of protein catabolism in the liver, muscles, kidneys, and intestine of animals in which the supraoptic nuclei of the hypothalamus has been destroyed. The indices used as criteria of catabolic processes were the content of free amino acids in the tissues and the intensity of autolysis.

EXPERIMENTAL METHOD

Experiments were carried out on male rabbits weighing 2-3 kg. The animals were divided into four groups: group 1—control intact rabbits; group 2—rabbits with destroyed supraoptic hypothalamic nuclei, group 3—burned rabbits, and group 4—rabbits burned 10 days after destruction of the supraoptic nuclei.

To destroy the supraoptic nuclei, monopolar electrodes were inserted stereotaxically in accordance with the following coordinates: plane A-2, 2 mm laterally, depth of insertion 16 mm (using the stereotaxic atlas of Sawyer and co-workers [11]). Destruction was carried out with a direct current (anode) of 1 mA acting for 30 sec. Completeness of destruction of the nuclei was verified morphologically.

In this paper we describe results obtained in animals with completely destroyed supraoptic nuclei of the hypothalamus on both sides. The animals were burned 10-12 days after coagulation of the nuclei by

Laboratories of Biochemistry, Physiology, and Morphology, A. V. Vishnevskii Institute of Surgery, Academy of Medical Sciences of the USSR, Moscow (Presented by Active Member of the Academy of Medical Sciences of the USSR A. A. Vishnevskii). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol 66, No. 8, pp. 48-50, August, 1968. Original article submitted July 8, 1967.

TABLE 1. Effect of Burns and Destruction of Supraoptic Nuclei of Hypothalamus on Intensity of Autolysis and Amino Nitrogen Content in Tissues

Groups of animals	Autolysis (in μg tyrosine/ml protein)				Amino nitrogen (in μg/g fresh wt. of tissue)			
	liver	muscles	kidneys	intestine	liver	muscles	kidneys	intestine
I healthy rabbits (control)	7,2±0,25	0,35±0,06	11,2±0,6	4,7±0,3	289±16	149±10	289±20	325±31
II rabbits with destroyed supraoptic nuclei	8,8±0,4 <0,05[1]	0,38±0,01 >0,05[1]	12,2±0,9 0,05[1]	5,1±1,2 >0,05[1]	265±12 >0,05[1]	109±4 <0,05[1]	226±6 <0,05[1]	259±17 >0,05[1]
III burned rabbits	11,1±1,5 <0,05[2]	0,98±0,08 <0,02[2]	13,5±1,1 >0,05[2]	4,2±0,2 >0,05[2]	517±16 <0,01[2]	350±21 <0,01[2]	388±9 <0,05[2]	320±14 >0,05[2]
IV burned rabbits with destroyed hypothalamic nuclei	11,8±0,8 >0,05[3]	0,31±0,05 <0,02[3]	12,1±0,5 >0,05[3]	3,7±0,2 >0,05[3]	363±10 <0,02[3]	163±12 <0,02[3]	307±15 <0,02[3]	309±14 >0,02[3]

Significance of differences (P) between groups I and II, Ditto between groups I and III, Ditto between groups III and IV.

immersing the hind limbs for 15-20 sec in water at a temperature of about 100°. The investigation was carried out 5 days after burning. The amino-acid nitrogen content in a protein-free filtrate of the tissues was determined by the method of Moore and Stein [10] after precipitation of proteins of the tissue homogenate with alcohol. The intensity of autolysis was investigated in tissue homogenates after incubation for 2 h at 37°, on the basis of the increase in tyrosine in protein-free filtrates of the homogenates determined by the color reaction with Folin's reagent.

EXPERIMENTAL RESULTS AND DISCUSSION

Burn trauma caused intensification of autolysis in the liver and skeletal muscle and accumulation of amino nitrogen in the liver, muscles,and kidneys [Table 1), indicating predominance of catabolic processes in the rabbit at this period.

In the animals burned after destruction of the supraoptic nuclei the intensity of autolysis in the muscles was the same as in the control animals, whereas in the liver autolysis was at a higher level characteristic of burns. It may therefore be postulated that the effect of the supraoptic zone of the hypothalamus on autolysis of tissue proteins, associated with protein breakdown, is exerted only on the proteins of skeletal muscle. In animals with destroyed supraoptic nuclei the intensity of autolysis in the muscles was the same as in healthy animals.

Just as in the liver, in the muscles and kidneys of the rabbits burned after destruction of the supraoptic nuclei the accumulation of amino nitrogen typical of burned animals was not observed. The content of amino nitrogen in the muscles of the animals of this series fell to the normal level, while in the liver and kidneys it remained above normal, but nevertheless slightly lower than is usually observed after burns. It may be concluded from the data for the intensity of autolysis that the decrease in amino nitrogen in the muscles of rabbits burned after coagulation of the supraoptic nuclei was due to the retardation of protein breakdown under these conditions.

The study of the link between the hypothalamus and protein synthesis in burned animals showed that coagulation of the supraoptic nuclei increased the uptake of methionine-S^{35} into muscle proteins and shifted the peak of maximal uptake to earlier periods, thus influencing the rate of synthesis of muscle proteins.

We concluded from the results described in this paper and those obtained in previous investigations that the response of the organism to burns exhibits organ specificity. We could find no common response of all organs to burns, to blocking of the reticular formation with chlorpromazine, and to blocking afferent impulses from the burned area [3].

The results thus suggest that the supraoptic nuclei of the hypothalamus are concerned in activation of catabolism of muscle proteins after burns. The regulatory role of the hypothalamus in processes of protein breakdown in intact animals could not be demonstrated, for in healthy rabbits coagulation of the supraoptic nuclei led neither to changes in the intensity of autolysis nor to appreciable changes in amino acid

content. After severe burn injury, changes in functional activity of the supraoptic nuclei possibly occur, and in this case they take part in the activation of catabolic processes.

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