LOW-MOLECULAR WEIGHT NITROGEN COMPOUNDS IN EXPERIMENTAL BRAIN TUMORS OF ALBINO MICE

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The content of ammonia and urea in brain tumors of albino mice is increased, that of γ-aminobutyric acid is reduced, and the content of aspartic and glutamic acids is the same as in the control. Aspartate aminotransferase activity in tumor tissue is reduced to half its level in normal brain tissue.

The object of this investigation was to study the metabolism of certain low-molecular weight nitrogen compounds in primary brain tumors (of the oligodendroglioma* type) in albino mice and to compare it with that in brain tissue adjacent to the tumor and in normal brain tissue.

EXPERIMENTAL METHOD

The content of free ammonia, urea, and aspartic, glutamic, and γ-aminobutyric (GABA) acids was investigated. Tumor tissue for analysis was taken at the height of development of the tumor (12th-14th day after transplantation). In one experiment a pooled sample from 5 animals was studied. Brain tissue adjacent to the tumor was obtained from three animals, and in the same way a weighed sample of brain was taken from intact albino mice. Tests were carried out on 105 albino mice with brain tumors and 36 control animals. A weighed sample of tissue was fixed in 12% TCA, homogenized, and the proteins were separated by centrifugation at 3000 rpm for 10 min. The supernatant was investigated.

Ammonia was determined by Silakova's modification [2] of Seligson's microdiffusion method using Nessler's reagent. Aspartic and glutamic acids and GABA were determined by electrophoresis by Dose's method [4]. Aspartate aminotransferase activity was determined by Greenwood and Greenbaum's modification of Awapara's method [1].

EXPERIMENTAL RESULTS

The content of free ammonia in the tumor tissue was increased (Table 1). The possible cause of its accumulation was an increase in the rate of protein renewal and breakdown of proteins in necrotic areas of the tumor, with subsequent deamination of the amino acids thus liberated.

This increase in the urea content in brain tumors of albino mice is most probably due to increased arginase activity. According to Greenstein [5], arginase activity is increased in tumors arising from tissues in which its normal activity is low.

The content of GABA, specific for nerve tissue, in the tumor tissue was reduced. This observation is not in agreement with the writer's previous findings or with observations made by other workers [3, 7], to the effect that GABA is absent in human brain tumors and that glutamate-decarboxylase activity in them is low.

* This strain of tumor was obtained in the laboratory of neurooncology of the N. N. Burdenko Research Institute of Neurosurgery by Dr. Med. Sci. L. Ya. Yablonovskaya.

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TABLE 1. Content (in mg/100 g fresh tissue) of Ammonia, Urea, Aspartic and Glutamic Acids, and GABA in Brain Tumors, in Brain Tissue Adjacent to Tumor, and in Normal Brain in Mice (M±m)

Material tested	Ammonia	Urea	Aspartate	Glutamate	GABA
Control	1.5±0.1 (12)	21.6±0.79 (12)	35.3±0.83 (12)	112.5±7.61 (12)	40.0±1.54 (12)
Surrounding tissue	3.3±0.36 (21)	24.8±2.01 (16)	25.1±1.71 (19)	88.7±5.20 (19)	35.9±2.65 (17)
Tumor	7.4±0.97 (19)	33.0±2.94 (16)	35.1±3.54 (20)	94.2±9.47 (21)	29.5±3.73 (18)

Note. Number of experiments given in parentheses.

TABLE 2. Activity of Aspartate-aminotransferase in the Brain

Tissue tested	No. of animals	Quantity of aspartic acid formed per gram fresh tissue in 30 min (in μmoles)	P
Normal brain tissue	12	1700±50	
Oligodendroglioma	20	760±40	< 0.001
Brain tissue adjacent to tumor	20	1540±80	> 0.05

No significant differences were found in the content of aspartic and glutamic acids in the brain tumors of albino mice compared with control brain tissue.

Changes in the level of these metabolites in the brain tissue surrounding the tumor compared with the control were due primarily to the fact that these tissues contain elements of the diffusely growing tumor. At the same time, an influence of the tumor on the course of metabolism in adjacent and remote organs and tissues cannot be ruled out. In this connection it was interesting to study the activity of aspartate-aminotransferase (2.6.1.1), catalyzing the principal pathway of aspartate synthesis in the brain [6].

The results (Table 2) indicate that while aspartate-aminotransferase activity in the tumor tissue was low, the content of aspartic acid in the tumor tissue was indistinguishable from its content in the control. Conversely, high activity of the enzyme in brain tissue adjacent to the tumor was accompanied by a significant decrease in the content of aspartic acid in it (Table 1).

These observations suggest that a decrease in the activity of transamination enzyme systems leads to depression of amino-acid synthesis in tumor tissue. The demands of the tumor for amino acids as precursors of protein are evidently satisfied by the amino-acid reserves of the brain tissue and by the incoming blood.

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