ROLE OF DISTURBANCES OF ENDOCRINE EQUILIBRIUM IN INDUCTION OF BRAIN TUMORS WITH METHYLNITROSOUREA

UDC 616.831-006:092.9:616.43

V. A. Enish, R. Vartsok,
and D. Schreiber

Analysis of data in the literature and of experimental findings showed that disturbances of the endocrine balance in rats (after x-ray irradiation of the gonads, injection of methylthiouracil, or castration) does not affect the incidence of tumors of the nervous system induced by methylnitrosourea.

* * *

Recent experiments in neurooncology have shown that tumors of the nervous system can be induced by a number of chemical compounds, viruses, and biologically active radiations. By no means all animals respond in the same way to the carcinogen. Animals are always found which do not develop tumors under particular experimental conditions. It thus follows that additional and, as yet unknown, factors are present which exert some influence on neoplasm development.

Dimant and co-workers [1] have discussed an important problem in neurooncology, the conditions of appearance of brain tumors. They concluded from their experiments that: "Besides the direct action of the carcinogen on tissue of the central nervous system, an extremely important role in the genesis of brain tumors induced by methylnitrosourea is played by certain other factors, primarily the neuro-endocrine system regulating homeostasis."

In this paper the results obtained by Dimant and co-workers as well as personal observations on the role of endocrine disturbances in the induction of tumors of the nervous system in rats by methylnitrosourea are analyzed.

EXPERIMENTAL METHOD AND RESULTS

Dimant and co-workers carried out their experiments on 42 noninbred rats receiving weekly injections of methylnitrosourea solution. In addition, they induced a disturbance of "hormonal homeostasis" in 30 animals by x-ray irradiation of the gonads (group 1) or repeated injections of methylthiouracil (group 2). The remaining 12 animals acted as controls (group 3). They report that 34 rats remained alive at the

TABLE 1. Incidence of Brain Tumors from Data Given by Dimant and Co-workers [1]

Group	Number of rats	Number of brain tumors	Confidence interval (in %)	
			lower limit	upper limit
1	7	3	7.1	85.8
2	10	6	21.8	90.7
3	6	1	0.0	53.6

Here and in Table 2 the confidence intervals were determined by Weber's method [3]; level of significance P = 0.01.

TABLE 2. Results of Personal Experiments on Induction of Tumors of the Nervous System with Methylnitrosourea in Castrated and Intact Rats

Animals	Number of animals	Incidence of tumors		Confidence interval (in %)	
		of the brain	of nerves	lower limit	upper limit
Castrated	17	1	3	5.2	57.3
Control	18	2	5	14.5	68.7

Department of Pathological Anatomy, Medical Academy, Erfurth, East Germany (Presented by Active Member of the Academy of Medical Sciences of the USSR V. V. Zakusov). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 67, No. 1, pp. 64-66, January, 1969. Original article submitted June 20, 1968.

time when tumors appeared. However, in the subsequent discussion of their results, Dimant and co-workers cite figures given in Table 1. Their conclusions are thus apparently based on results obtained in 23 experimental animals.

The number of observations is of considerable importance in ensuring a correct interpretation of experimental results. Sound conclusions concerning the significance of observed changes can be deduced even from a small number of cases if their statistical analysis is correct. However, Dimant and co-workers did not use statistical methods when determining the significance of the differences which they found in the incidence of brain tumors in their experimental and control groups. However, even if they had used such an approximate statistical criterion as the confidence interval, it would have shown them the need for care when deducing their conclusions. Confidence intervals have been determined for Dimant's material (Table 1). It is clear from Table 1 that there is no significant difference between the results of the various experimental groups, and consequently, that disturbance of the endocrine balance had no effect whatever on the incidence of brain tumors. This was confirmed by our own experiments on adult male Wistar rats. Some animals were castrated a few days before the beginning of the experiments. A freshly prepared solution of methylnitrosourea [2] was then injected into the caudal vein once every two weeks (each dose 10 mg/kg body weight).

The results of these experiments are given in Table 2. Only those animals which survived 100 days after the beginning of the experiments were considered. As Table 2 shows, in these experiments the confidence intervals overlap almost completely. Consequently, the observed difference in the number of tumors in these experiments also is not statistically significant.

The paper of Dimant and co-workers contains other mistakes or inaccuracies. For instance, they describe that the experiments were carried out on male rats and a disturbance of endocrine equilibrium was produced by irradiation of the ovaries.* Later, the animals were injected with 1% methylnitrosourea in a dose of 5 mg/body weight. This means that a rat weighing 100 g received 0.05 ml of solution. It must have been very difficult to give the correct dosage with this concentration.

Hence, neither from the results of experiments undertaken by Dimant and co-workers nor our own findings can permit the conclusions to be drawn that a disturbance of the hormonal balance in rats influences the frequency of tumors of the nervous system induced by methylnitrosourea. This does not rule out the possibility that further investigations on a much larger series of cases would demonstrate such an influence.

LITERATURE CITED

1. I. N. Dimant et al., Byul. Éksperim. Biol. i Med., No. 3, 98 (1968).
2. W. Tänisch, D. Schreiber, V. Steffen, et al., Exp. Path., No. 1 (1967).
3. E. Weber, Grundriss der Biologischem Satistik, Jena (1967).

* This mistake was corrected in the English translation: Byul. Éksperim. Biol. i Med., 65, No. 3, 328 (1968).