CHANGES IN THE SEROTONIN CONCENTRATION IN THE HYPOTHALAMUS OF RATS AT LATE PERIODS AFTER IRRADIATION

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UDC 617-001.28-036.8-07:616.831.
41-008.937.56-074

A significant decrease in the serotonin level in the hypothalamus of rats was observed 6-12 months after x-ray irradiation in a dose of 460 R. The change in the serotonin concentration was not the direct result of irradiation, for in the early periods (1 and 3 months) its concentration was the same as in the control. Changes in the serotonin level in the hypothalamus showed a definite correlation with the state of the hypophyseo-adrenal system in the late periods after irradiation.

Much interest has recently been shown in the role of the serotoninergic structures of the brain (particularly the hypothalamus) in reactions of the organism to extremal stimuli. For this reason particular attention is paid to the role of these structures in regulation of the function of the hypophyseo-adrenal system as one of the protective and adaptive systems of the body.

Information in the literature on the effect of ionizing radiation on the serotonin concentration in the brain is very limited in amount and contradictory in nature [1, 3, 6, 7, 9, 10, 12, 13]. The most interesting observations are changes in the serotonin concentration in the hypothalamus. Renson and Fischer [11] demonstrated a decrease in the serotonin level in the hypothalamus 2 h after irradiation of rats in a dose of 1000 R. Serokina [4] investigated the serotonin concentration in different parts of the brain after irradiating guinea pigs in doses of 100, 300, and 600 R. She showed that 5 min after irradiation the serotonin concentration in all parts of the brain was increased, but a steady decrease in its level in the hypothalamus, thalamus, and pons was then observed after 1 h and until the end of the period of observation (25 days). However, in none of these investigations was the serotonin concentration in the brain compared with the functional state of the hypophyseo-adrenal system. There is no information in the literature on changes in the serotonin concentration in the hypothalamus in the later periods after irradiation.

The object of this investigation was to determine the serotonin concentration in the hypothalamus of animals after acute radiation sickness. The importance of the study of this problem lies in the fact that in previous investigations [2] significant changes in the functional state of the hypophyseo-adrenal system were demonstrated in the late periods after irradiation.

EXPERIMENTAL METHOD

Experiments were carried out on 186 male rats weighing initially 180-240 g. The animals were irradiated with x-rays on the RUM-3 apparatus (175 kV, 15 mA, 0.5 mm Cu + 1 mm Al filters, distance 40 cm, dose rate 44.1 R/min). The rats were irradiated in transparent plastic boxes surrounded beneath and at the sides with paraffin wax diffuser. The dose of irradiation was 460 R. The animals were used in the

Laboratory of Radiation Genetics and Late Effects of Irradiation, Central Research Roentgeno-Radiological Institute, Ministry of Health of the USSR, Leningrad. (Presented by Academician of the Academy of Medical Sciences of the USSR S. V. Anichkov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 74, No. 8, pp. 34-36, August, 1972. Original article submitted March 26, 1971.

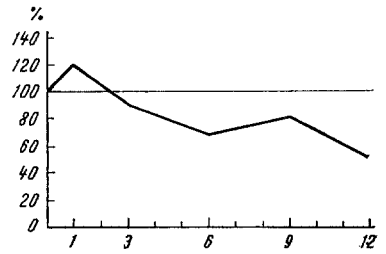

Fig. 1. Serotonin concentration in the hypothalamus of irradiated rats. Abscissa, time after irradiation (in months); ordinate, serotonin concentration in irradiated rats (in percent of control).

experiment 1, 3, 6, 9, and 12 months after irradiation. Control animals of the corresponding age group were sacrificed at the same times. The rats were decapitated under Nembutal anesthesia. The hypothalamus was removed as quickly as possible and immersed in liquid nitrogen. Serotonin was determined fluorometrically by the method of Kuntzman et al., [8], and its concentration was expressed in $\mu g/g$ fresh weight of tissue studied. The serotonin concentration in the hypothalamus of the irradiated animals was expressed as a percentage of the corresponding control value. For each determination material was taken from three animals. For the statistical analysis of the results the method of correlated series was used.

EXPERIMENTAL RESULTS AND DISCUSSION

The serotonin concentration in the hypothalamus of the control animals was 0.81 ± 0.15 $\mu g/g$, in agreement with data in the literature.

Changes in the serotonin level in the hypothalamus of the irradiated animals are shown in Fig. 1. An increase in the serotonin concentration (by 20%) compared with the control animals was observed 1 month after irradiation. However, this change was not statistically significant ($P > 0.05$). Three months after irradiation the change in the serotonin level in the irradiated rats was equivocal. During this period the serotonin concentration on the average was slightly lowered, although the difference from the control was not statistically significant ($P > 0.05$). Six months after irradiation a statistically significant decrease in the serotonin concentration in the hypothalamus to 68% of the control level ($P < 0.05$) was observed. The serotonin concentration remained at about this same level until 9 months after irradiation, when it was 80% of the control value ($P < 0.05$). However, by the 12th month after irradiation a further decrease in the serotonin concentration in the hypothalamus was observed, down to 50% of the control level ($P < 0.05$).

It can be concluded that in the later periods after irradiation there is a gradual but sufficiently marked decrease in the concentration of one of the mediators. This may reflect significant changes in the functional state of the hypothalamus, which must undoubtedly manifest themselves as a disturbance of its regulatory capacity. A previous investigation did in fact show that it is at these periods after irradiation (6–12 months) that the reactivity of the hypophyseo-adrenal system to exposure to functional loads is reduced [2]. This synchronization in the appearance of the pathological changes suggests that a disturbance of hypothalamic function leads to changes in the hypophyseo-adrenal system.

It is an interesting fact that the changes observed in the hypothalamus in the late periods after irradiation are not the direct result of exposure but a secondary phenomenon. This is confirmed by results showing that after a considerable decrease in the serotonin concentration in the hypothalamus during acute radiation sickness [4] not only is its normal level restored by the time of clinical recovery, but there is even a tendency for its concentration to be higher than normal 1 month after irradiation, evidently through some form of compensatory process. However, the serotonin level was unchanged 3 months after irradiation in only some of the animals studied, and in most animals pathological changes indicating a breakdown of the compensation mechanism had begun to appear. They were more marked still 6–12 months after irradiation, when they were very stable in character.

The results of this investigation indicate the presence of substantial disturbances in the centers of regulation of the endocrine system in the later periods after irradiation.

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