PROTECTING THE CENTRAL NERVOUS SYSTEM OF ANTENATALLY IRRADIATED RATS AGAINST RADIATION

I. A. Piontkovskii and M. B. Gol'dberg

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The conditioned reflex method was used to study the antiradiation action of aminoethylthiouronium BrHBr (AET) on the higher levels of the central nervous system of antenatally irradiated rats. AET weakened the radiation response and created conditions for an improvement in conditioned-reflex activity of the antenatally irradiated rats during postnatal ontogenesis.

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The need for studying the structure and function of the central nervous system during radiation protection is determined by the fact that the survival rate of animals, the main criterion used to judge the effectiveness of protectors [2-8], in all probability depends primarily on the influence of the protected nervous structures in regulating and normalizing physiological processes.

The object of the present investigation was to study the antiradiation action of the chemical compound aminoethylisothiouronium (AET) on the conditioned-reflex activity of antenatally irradiated rats.

EXPERIMENTAL METHOD

Experiments were carried out on male Wistar rats. The control animals (50) received neither irradiation nor AET, while one group of rats (21) were irradiated antenatally in a dose of 150 R on the 16th day of embryogenesis, and the other group (12) were irradiated antenatally in the same dose and at the same time, but were protected by AET, which was injected into the mother rats of these animals during pregnancy in a dose of 200 mg/kg.* The higher nervous activity of the rats was studied by the conditioned-reflex method in a Kotlyarevskii chamber modified by workers at the Neuroradiology Laboratory [1]. The rats were 50 days old when they took part in the experiments. Nervous processes were investigated in stages: during formation and stabilization of conditioned reflexes, in a stereotype of stimuli, and in association with function tests. The positive stimuli were a tone of 400 cps from a type ZG-10 audiofrequency generator, with attenuation of 10 dB, and red light from an incandescent lamp (12 V), while the differential stimulus was a tone of 800 cps with attenuation of 20 dB. Single whole-body irradiation was given by a type RUM-11 apparatus (190 kV, 15 mA, filters 0.5 mm Cu and 1 mm Al, focal length 50 cm, dose rate 20 R/min).

EXPERIMENTAL RESULTS

Stabilization of the conditioned response in the 150-R rats to acoustic stimuli took place on the average after 33.8 ± 8.88 combinations and to photic stimulation after 31.2 ± 6.66 combinations, while the corresponding figures for the protected rats were 18.7 ± 2.95 and 11.6 ± 0.38 combinations and for the controls 17.7 ± 1.06 and 14.3 ± 1.72 combinations. The results show that stabilization of conditioned reflexes to positive stimuli takes place later ($P < 0.01$) in the 150-R rats than in the protected and control animals. Analysis of the conditioned reflexes to invidividual stimuli showed that with respect to criteria of conditioned-reflex activity characterizing excitation, the protected rats surpassed the 150-R rats in every case by a statistically significant degree, but showed very little difference from the controls. The mean latent period of the conditioned response to acoustic stimulation was 1.06 ± 0.015 sec for the control rats, 1.08 ± 0.09 sec for the protected rats, and 1.48 ± 0.03 sec for the 150-R rats; the response was present in 96.6 ± 0.26, 96.2 ±

*Subsequently these rats will be described as control rats, 150-R rats, and protected rats.

Laboratory of Neuroradiology, Institute of Higher Nervous Activity and Neurophysiology, Academy of Sciences of the USSR, Moscow (Presented by Academician V. V. Parin). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 65, No. 5, pp. 41-44, May, 1968. Original article submitted March 18, 1966.

0.52, and 90.4 ± 0.65% of the animals, respectively ($P < 0.001$). The latent period of the responses to photic stimulation was 1.51 ± 0.2 sec for the control rats, 1.61 ± 0.038 sec for the protected rats, and 2.39 ± 0.05 sec for the 150-R rats ($P < 0.001$); the magnitude of the responses was 49.6 ± 0.62, 44.2 ± 0.99, and 27 ± 1.03 conventional units, respectively ($P < 0.001$); responses were found in 93 ± 0.51, 96.9 ± 0.59, and 85.6 ± 1.23% of animals, respectively ($P < 0.001$).

Similar results were obtained from the investigation in a stereotype. The mean latent period of the conditioned reflexes to acoustic stimulation was 0.77 ± 0.02 sec for the control rats, 1.02 ± 0.04 sec for the protected rats, and 1.21 ± 0.05 sec for the 150-R rats, respectively ($P < 0.001$ and $P < 0.01$). Responses were found in 98.5 ± 0.31, 99.16 ± 0.5, and 96.6 ± 1% of animals, respectively ($P < 0.05$). The latent period of the responses to photic stimulation was 1.46 ± 0.03 sec for the control rats, 1.55 ± 0.05 sec for the protected rats, and 2.10 ± 0.07 sec for the 150-R rats ($P < 0.001$); the magnitude of the responses was 57.7 ± 0.95, 51.1 ± 1.61, and 39.3 ± 1.72 conventional units, respectively ($P < 0.001$), and responses were found in 97.11 ± 0.45, 97.17 ± 0.88, and 93.4 ± 1.3% of animals, respectively ($P < 0.02$). The fact that excitation was stronger in the protected animals than in the 150-R rats was also confirmed by the results of the caffeine test. The latent period to acoustic stimulation before the injection of caffeine was 1.56 ± 0.22 sec for the protected rats, compared with 1.07 ± 0.18 sec after injection, and the latent period to photic stimulation was reduced by administration of caffeine from 2.84 ± 0.37 sec to 1.54 ± 0.27 sec ($P < 0.01$). Excitation in the control rats was also increased after injection of caffeine; the latent period to acoustic stimulation was 0.43 ± 0.02 sec before injection of caffeine and 0.34 ± 0.03 sec after injection ($P < 0.001$). The formation and stabilization of differentiation, and the study of negative conditioned reflexes in a stereotype also showed that inhibition was more marked in the 150-R rats than in the protected and control animals. The latent period of de-inhibition of differentiation was 1.96 ± 0.1 sec in the control rats, 2.13 ± 0.2 sec in the protected rats, and 4.31 ± 0.35 sec in the 150-R rats ($P < 0.001$), and the magnitudes of de-inhibition were 56.5 ± 1.75, 42.0 ± 3.27 ($P < 0.001$), and 28.3 ± 3.37 conventional units ($P < 0.001$), respectively; responses were found in 6.32 ± 1.12, 11.01 ± 2.88, and 23.1 ± 0.38% of animals, respectively ($P < 0.001$).

We interpret the fact that inhibition was stronger in the 150-R rats not as a sign that active inhibition was itself stronger, but that, on the one hand, excitation was weak and, on the other hand, protective inhibition developed because of radiation injury received by the animals during antenatal development. Protective inhibition was less marked in the protected rats than in the 150-R rats. This fact may be regarded as indirect evidence of strengthening of excitation in these animals. Evidence that internal inhibition was weaker in the 150-R rats and protected rats than in the control animals was given by the results of a reflex-extinction test. Extinction developed in the 150-R rats after 36.5 ± 3.58 applications of the stimulus, in the protected rats after 41 ± 4.2 applications, and in the controls after 32.7 ± 2.3. These findings suggest that AET has a protective action on the function of the higher structures of the central nervous system. It reduces the severity of radiation injury and improves conditioned-reflex activity of the animals. In rats receiving AET before irradiation, the level of excitation was higher than in the 150-R rats. The protected animals, occupying an intermediate position between the 150-R rats and the controls with respect to most criteria characterizing higher nervous activity, resembled the latter more closely. The mechanism of action of AET is in all probability twofold: it reduces the severity of radiation injury in the mother, thereby indirectly reducing the toxic effects on the fetus, and it penetrates from the mother to the fetus, on which it has a direct protective action.*

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