

BIOCHEMISTRY AND BIOPHYSICS

CERTAIN SPECIFIC FEATURES OF THE HIGHER NERVOUS ACTIVITY OF FULLY GROWN ANIMALS IRRADIATED ANTENATALLY WITH IONIZING RADIATION

COMMUNICATION I. THE INFLUENCE OF IONIZING RADIATION ON THE OFFSPRING

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Irradiation of pregnant female animals and women with ionizing radiation may cause the appearance of a variety of congenital deformities in the offspring and may interfere with their postnatal development [2-6].

L. Hicks [4] points out the particular sensitivity of the nervous system of the embryo to ionizing radiation. Thus irradiation of rats on the 9th, 11th, 12th and 13th days of prenatal development may cause, in addition to somatic deformities, anencephaly (on the 9th day), hydrocephaly (on the 11th day), microcephaly (on the 12th-13th day)— failure of development of the subcortical structures, the corpora callosa and so on.

The influence of ionizing radiation on the nervous system during antenatal irradiation has been studied mainly morphologically [1, 4]. There are no indications in the literature of the state of the higher nervous activity of fully grown animals exposed at various periods of their antenatal development to the action of ionizing radiation.

This impelled us to investigate the effect of ionizing radiation, applied in various doses and at different stages of embryonic development, on the state of the higher nervous activity of animals.

EXPERIMENTAL METHOD

The day of semination was determined in female white rats by the presence of sperm in a vaginal smear. On the 12th day of pregnancy the animals were subjected to a single total irradiation with γ -rays from radioactive cobalt (dose strength — 200 r, dosage rate — 8.3 r/min.). The present report is based on observations made on 52 rats: 30 irradiated (experimental) and 22 controls, born at the same period, but not exposed to the action of ionizing radiation in utero.

Among the group of irradiated rats, in one marked hydrocephalus was observed, in four — anophthalmia, in one — bilateral microphthalmia and in four — unilateral microphthalmia; in addition one blind animal had a deformity of the tail. The remaining 20 animals showed no external, visible congenital deformities. None of the control animals had any visible defects.

Investigations of the higher nervous activity of the experimental and control animals began at the age of 45-50 days (when they had reached a weight of 70-80 g). The experiments were carried out in 2 series, and the motor-alimentary method of L. I. Kotliarevskii was used (the work was undertaken by V. E. Miklashevskii and N. G. Mikhailova).

Initially a conditioned reflex was established to a sound (tone 1), then differentiation to a higher tone was produced (tone 2), after which a conditioned reflex was developed to a light stimulus; a stereotype was then created. In the group of animals with anophthalmia and microphthalmia no reflex to light was established;

both positive reflexes were established to sounds of different frequency. Tone 1 was a sound with a frequency of 400 cps (attenuation 20 db), tone 2 — a sound with a frequency of 800 cps (attenuation 40 db). The light stimulus was the red light from an incandescent lamp (voltage 6v). The duration of the conditioned stimulus was 10 sec: 5 sec in isolation and the next 5 sec in association with unconditioned alimentary reinforcement.

EXPERIMENTAL RESULTS

Observations on the behavior of the animals. During investigation of the conditioned reflexes the normal animal at first usually gives an orientational reflex, which is extinguished after the animal has been placed 4 or 5 times in the chamber. In the experimental animals the orientational reflex is extinguished more slowly. As a rule the experimental animals give a greater number of intersignal reactions. They relatively often show aggressiveness towards each other and towards the experimenter for no cause.

Rate of Appearance and Consolidation of the Conditioned Reflex to Sound

Series of experiments	Experimental animals			Control animals		
	no. of animals	no. of combinations (mean) for the appearance	for the consolidation of the conditioned reflex	no. of animals	no. of combinations (mean) for the appearance	for the consolidation of the conditioned reflex
1st (expts. by V.E. Mikla-shevskii)	18	4.5	42	13	5.5	13.5
2nd (expts. by N.G. Mik-hailova)	12	10.1	52.6	9	9.3	16.3

Rate of formation and consolidation of the conditioned connections. In the experimental animals the first appearance of the conditioned reflex to sound sometimes takes place rather sooner than in the controls*. Consolidation of the conditioned reflex in the experimental animals always takes place more slowly and requires a larger number of combinations (see Table).

Consolidation of the artificial reflex to light and to the second sound signal also required a greater number of combinations in the experimental group of animals than in the control group.

A difference between the experimental and control groups is also observed when comparing data on the establishment of differentiation, its appearance and consolidation. In the 1st series of experiments the time of appearance of the first negative conditioned reflexes in the experimental and control groups was only very slightly different, but complete differentiation was not achieved in practice in all cases. Of 18 animals in the experimental group consolidation arose in only 12, the number of combinations required being about 20; in the control group, of 13 animals consolidation appeared in 12, the number of combinations being about 12. In the second series of experiments, in the control group of 9 animals complete differentiation was obtained in 8, and on the average 24.8 combinations were required, whereas in the experimental group of 12 animals it was not possible to obtain complete differentiation in all, in spite of a large number of combinations.

Observations on the stereotype. Comparison of the latent periods of the reaction to the positive signals, the magnitudes of the conditioned reflexes and the percentage of loss shows that antenatal irradiation of rats causes a characteristic deterioration in their conditioned reflex activity. On the average the latent period to sound in the experimental animals is equal to 2.65 seconds, and that of the control animals 2 seconds; the magnitude of the reflex is 21.5 and 32 cm respectively; the corresponding percentage loss — 21.5 and 2.5.

*The phenomenon noted may depend on the longer preservation of the orientational reaction in the experimental animals, masking the true time of appearance of the conditioned reflex.

Depression of the conditioned reactions in the second half of the stereotype was observed in a much higher percentage of cases in the experimental rats than in the controls. In 20 experiments the successive inhibition in a group of experimental animals amounted to 40%, and in the control rats — 18%.

Functional tests. In order to ascertain the strength, the mobility and the equilibrium of the nervous processes tests were carried out with an external inhibitor, with prolongation of the differential stimulus to 120-180 seconds, a test of extinction and restoration, and positive induction. In the majority of rats irradiated before birth, on the introduction into the stereotype of an excessively strong stimulus (external inhibitor) a deterioration of conditioned reflex activity was observed, the percentage loss of the conditioned reflexes to sound and light was increased and their magnitude was reduced, and the latent period increased. Tests in which the differentiation was prolonged showed that in the experimental rats in 100% of cases differentiation was disinhibited, whereas the control animals maintained differentiation in 30% of cases.

The study of extinction and restoration of the conditioned reflex showed that the animals irradiated before birth could be distinguished into two groups by the character of extinction of the reflex. In some experimental animals extinction was observed to be more rapid than in the controls. Thus in the control animals complete extinction of the reflex (00000) was reached after 20 stimulations without combination, and in the experimental animals — after 11 (V. E. Miklashevskii). On the other hand in some of the experimental animals extinction took place very slowly. Whereas in the experimental and control groups the beginning of extinction appeared with approximately the same number of combinations, complete extinction was not observed after 70-80 stimulations without reinforcement. The extinguished conditioned reflex was restored slightly more slowly in the experimental than in the normal animals, in the control group — after 2-3 combinations, but in the experimental group — after 2-3-4 combinations.

In the control rats, when the time of action of the positive stimulus was directly after the differentiation, as a rule positive induction was observed, but in the experimental animals this did not happen in the great majority of cases.

The main distinctive feature of the higher nervous activity of rats irradiated before birth, compared with normal animals, is a congenital reduction in the working capacity of their cortical cells. In the rats irradiated before birth the two main nervous processes are less powerful, less mobile and not so well balanced with respect to each other.

In rats irradiated before birth by γ -rays from radioactive cobalt changes were found in the process of internal inhibition, especially extinctive and differential. It can be seen from a number of pointers that sometimes weakening of the process of stimulation did not allow the detection of any disturbance of the process of internal inhibition which might have been present.

The experimental animals also showed a disturbance of the equilibrium of the nervous processes: processes of stimulation were considerably in excess of inhibition. This was shown by the great motor excitation, by the slow attenuation of the orientational reaction and by the large number of intersignal reactions. The mobility of the nervous processes was also disturbed; they showed inertia, reflected in phenomena of successive inhibition.

It may be considered that rats, irradiated before birth by ionizing γ -rays from radioactive cobalt, belong, from the point of view of their type of higher nervous activity, to a weak type in the majority of cases, verging on the pathological — neurosis. It should also be mentioned that as the animals develop and in the course of the work with them, the difference in the indices of conditioned reflex activity between those irradiated before birth and controls becomes smoothed out and less conspicuous.

Morphological examinations of the brain of normal animals and rats irradiated before birth, carried out on the 2nd, 7th, 14th, 30th, 180th and 450th days after birth (by N. L. Artiukhina) revealed a number of characteristic features. In the first seven days of life no difference could be observed in the thickness of the cortex of the experimental and control animals, but in the 14-day-old animals of the control series the cortex was twice as thick as in the experimental animals, in both the frontal and occipital regions. On the 30th and 180th days the thickness of the cortex of the experimental and control animals was the same, but on the 450th day the thickness of the cortex in the frontal region of the experimental animals was again less than in the control animals.

A histological study showed that the nerve cells of the cerebral cortex of the animals irradiated before birth were delayed in formation and maturation. In the control animals the cerebral cortex developed intensively in the period from the 7th to the 14th day of postnatal development, and in those irradiated before birth -- in the period from the 14th to the 30th days; in the animals irradiated before birth marked atrophy of the cerebral hemispheres was observed at later periods in consequence of death and atrophy of the nerve cells.

We also observed developmental anomalies as already [4] described in the literature. In 28% of cases the animals irradiated before birth showed developmental defects of the hippocampus, the corpus callosum, the basal ganglia, the optic tubercle, displacement of the rudiments of the subcortical ganglia and hydrocephalus.

SUMMARY

This work was conducted on white rats. On the 12th day of pregnancy the animals were subjected to a total single irradiation (200 r) by γ -rays of radioactive cobalt. The study of the highest nervous activity of rats irradiated during the antenatal period reveals a congenital decrease of the working capacity of their cortical cells as compared to the normal animals. Both fundamental nervous functions are not as strong in the animals irradiated antenatally. These processes are less mobile and less interbalanced. The processes of internal inhibition, especially of extinction and differentiation, are particularly affected.

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* In Russian.