

PATHOLOGICAL PHYSIOLOGY AND GENERAL PATHOLOGY

ON CERTAIN CHARACTERISTICS OF HIGHER NERVOUS ACTIVITY IN ANIMALS SUBJECTED TO ANTENATAL IONIZING RADIATION

REPORT VI. CHARACTERISTICS OF HIGHER NERVOUS ACTIVITY DURING THE POSTNATAL ONTOGENESIS OF RABBITS IRRADIATED WITH ROENTGEN RAYS IN THE PERIOD OF ORGANOGENESIS

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Embryologists distinguish three independent periods within the intrauterine period of development: 1) embryonal (preimplantation); 2) prefetal (organogenesis); 3) fetal [6]. In rabbits, out of the total duration of the 30-32 day intrauterine period, the embryonal period lasts up to 8 days, and the prefetal - from 8 to 18 days.

In a series of previous investigations, we studied postnatal functional initiation in higher divisions of the central nervous system of rats, subsequent to their irradiation in the fetal period, on the 23rd day of antenatal development [2, 3, 4]. We considered it of interest to investigate the characteristics of disturbances in higher nervous activity associated with irradiation at different intervals in antenatal development.

In this report, we consider certain characteristics of higher nervous activity in rabbits irradiated with roentgen rays during the prefetal period (organogenesis).

EXPERIMENTAL METHOD

On the 15th day after mating, pregnant rabbits were subjected to a single, whole-body irradiation with roentgen rays. The conditions of the irradiation were the following: force of 190 kv, current intensity of 15 ma, filters of 1 mm Al and 0.5 mm Cu, dose of 400 r, dose output of 16.5 r/min. The progeny of the irradiated and respective control animals were studied, starting with the 3rd day after birth. Observations were carried out on the development of the animals (weight dynamics, development of vision, etc.), motor activity, behavior, orientating reflex to sound, development and stabilization of the "shaking-off" conditioned reflex (according to the method of Volokhov and Obratsova [1]), and stabilization of differentiation. Bells of different timbres served as the conditioning stimuli, and an alternating current of threshold intensity represented the direct stimulus. The positive and inhibitory stimuli were presented in an alternating stereotype. We also carried out hematological investigations on both the mothers and the irradiated progeny. A total of 41 animals were used in the experiment, of which 17 were irradiated in the antenatal period and 24 represented controls.

EXPERIMENTAL RESULTS

At birth, the weight of the irradiated rabbits did not differ from the weight of the controls (45.8 ± 1.1 and 47.5 ± 1.7 grams). Subsequently, the experimental animals somewhat lagged in weight behind the controls, but this difference was not shown to be statistically significant. Thus, at the age of 1 month, the weight of the irradiated rabbits was equal to 348.0 ± 30.0 grams, and of the controls, 373.7 ± 9.3 grams, and at the age of 3 months, 1241.0 ± 67.2 and 1314.0 ± 35.5 grams respectively. In the newborn irradiated animals the peripheral blood leukocyte count was 3070 ± 362 , and in the controls - 2565 ± 183 (the difference is not statistically significant). By the 20th-30th day, the blood leukocyte count in the control and irradiated animals was more equal. Resistance and viability fell sharply in the irradiated animals. Out of 7 litters (45 rabbits) that were in the experiment designed to study the higher

Development of Certain Functions of Higher Divisions of the Central Nervous System in Rabbits Irradiated on the 15th and 23rd Days of Embryogenesis

Experimental conditions	Time intervals (in days)				
	appearance of the orientating reflex	vision	development of the conditioned reflexes	stabilization of the conditioned reflexes	stabilization of differentiation
Irradiation on the 15th day	6.22±0.22	9.75±0.66	11.12±0.41	16.69±0.70	Successful in only 3 rabbits
Irradiation on the 23rd day	5.40±0.17	9.07±0.23	8.8±0.29	16.52±0.73	65.23±4.28
Control	6.43±0.16	9.81±0.10	10.05±0.25	13.19±0.33	28.50±1.91

nervous activity, it was possible to use the animals of only 3, since the remaining litters died in the age range of 2-5 days.

Congenital developmental malformations were not observed in either the experimental or control groups. Vision was observed in the irradiated animals on the 7th to 13th day of life, while in the controls, on the 9th to 12th day. Despite the earlier vision in individual irradiated animals, the difference between the means for the time vision occurred was not statistically significant, due to the high variability in the indices for the experimental rabbits.

In both the irradiated and control animals the orientating reflex to sound arose, on the average, on the 6th day (6.22 ± 0.22 and 6.43 ± 0.16 respectively); the differences were not significant. It must be noted, however, that in the control animals the orientating reflex to sound appeared no earlier than the 6th day, while in certain irradiated animals it could be observed as early as by the 5th day of postnatal development.

The conditioned defense reflex (in the form of a general motor reaction) arose, in the antenatally irradiated rabbits, on the 7th to 13th day of postnatal development (with a mean of 11.12 ± 0.41), and in the controls — on the 8th to 12th day (with a mean of 10.05 ± 0.26). Stabilization of the conditioned reflex in the experimental animals occurred on the 11th-21st day (with a mean of 16.69 ± 0.70), and in the controls — on the 11th-16th day (with a mean of 13.19 ± 0.33); the differences were statistically significant. The development of differentiation that was conducted after stabilization of the positive conditioned reflex demonstrated a marked deterioration of inhibitory function in the irradiated rabbits: it was practically impossible to develop stable differentiation in them. In the process of working out the differentiation in these rabbits, we observed numerous disappearances of the positive conditioned reflexes.

It is interesting to compare the indices studied with those obtained from investigating rabbits that were subjected to antenatal irradiation in a dose of 400 r on the 23rd day of antenatal development (see table).

As can be seen from the table, the animals that were irradiated on the 15th day differed substantially in several indices from both the controls and the animals that were irradiated on the 23rd day. Above all, with irradiation on the 15th day we did not observe the premature establishment of certain functions (vision, development of orientating and conditioned reflexes) which was noted with irradiation on the 23rd day of the antenatal period. In addition, it was practically impossible to develop differentiation in the animals irradiated on the 15th day.

In the animals irradiated on the 15th day, specialized subcortical reactions, such as washing and licking, appeared considerably more rarely than in those irradiated on the 23rd day.

In the first days of life of the irradiated rabbits, as well as at a later age in individual animals, we observed rotary movements, and also manifest side-to-side rocking.

Spastic paralysis of the posterior legs gradually developed in a number of the experimental animals (Fig. 1).

Morphological study of the brain of 7 animals, at the age of one year [5], showed atrophy of the cerebral cortices (the eminences of the corpora quadrigemina were not covered by cortex, the cerebellum was underdeveloped). At the same time we noted the absence or underdevelopment of the corpus callosum, and widening of the ventricular cavities. Microscopic investigation disclosed disruption of the cortical stratification, as well as of the cytoarchitectonics, and

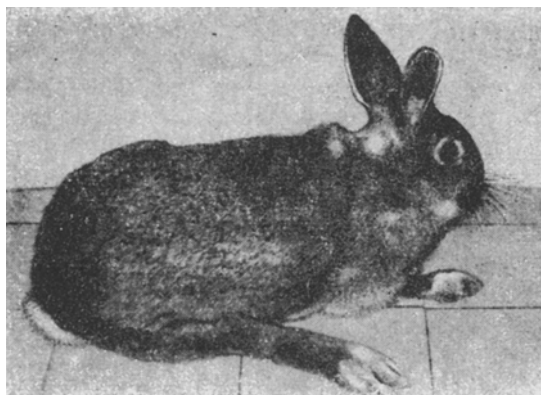


Fig. 1. Rabbit with spastic paralysis of the posterior extremity (irradiated on the 15th day of antenatal development).

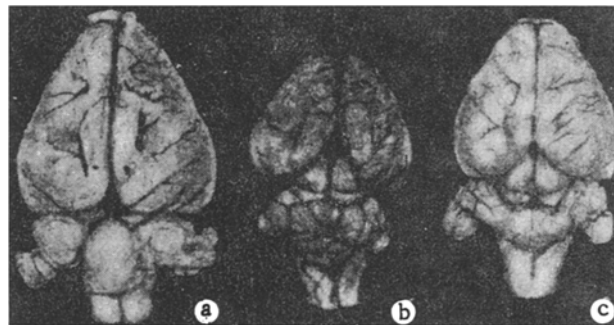


Fig. 2. Combined view of the brain of 1 year old rabbits, under normal conditions (a), irradiated on the 15th day (b), and irradiated on the 23rd day (c), of antenatal development.

irradiation on the 15th day of antenatal development, underdevelopment of the cerebral cortices was manifest more markedly than with irradiation at later periods. Figure 2 shows that the brain of a rabbit irradiated in the period of organogenesis was considerably reduced in volume as compared with the brain of a control animal and the brain of an animal irradiated at a later period of antenatal development.

rarefaction of the cells, particularly in the deep 5th and 6th layers of the cortex at various analyzer areas. With

Analysis of the data presented permits the statement of a number of aspects. Animals irradiated on the 15th day of antenatal development characteristically show profound injury in their inhibitory processes, which are disturbed much more intensely than in animals irradiated in the fetal period; conditioned reflex activity as a whole is also disrupted. A positive conditioned reflex arises later and is stabilized later; the inhibitory influences of the cortex on the subcortical structures apparently suffer less intensely. Heterochronism in the development of the brain structures causes varying radiosensitivity of the neural formations. With irradiation during the period of organogenesis, along with injury to the structures of the brain, which is also noted with irradiation at different intervals, the functional systems connected with the process of inhibition are selectively traumatized. With irradiation on the 15th day, it is possible to cause injury to different links in one functional system, responsible for inhibition and located in different levels of the brain. With irradiation at such times, the upper layers of the cortex apparently suffer less than the lower layers and the subcortical formations: this is also supported by the functional and morphological investigations.

SUMMARY

On the 15th day after coitus female rabbits were subjected to a single x-irradiation in a dose of 400 r. Stabilization of conditioned reflex activity was investigated in the progeny; observations covered the somatic state of the animals with determination of hematological indices and inquiry into the cerebral morphology. In animals irradiated during organogenesis there is a slower elaboration and a slower stabilization of conditioned positive reflexes; differential response to sound stimulus is not elaborated. By irradiated animals differed but little from the controls hematological and weight indices. Histological investigation disclosed a reduction of the brain mass, considerable atrophy of the cortex and its disturbed development; corpus callosum is either absent or underdeveloped and so is cerebellum. Clinically there appear rotational and pendulum-like movements and development of spastic paralyzes of hind extremities. According to the brain function indices subcortical formations are the ones to suffer most in these animals

LITERATURE CITED

1. A. A. Volokhov and G. A. Obratsova, *Byull. éksper. biol.*, No. 9, (1953) p. 58.
2. R. I. Kruglikov, in the book: *The Effect of Ionizing Radiation on the Nervous System of Progeny* [in Russian], Moscow, (1961) p. 102.
3. I. A. Piontkovskii and R. I. Kruglikov, *Dokl. AN SSSR*, Vol. 130, No. 4, (1960) p. 898.
4. I. A. Piontkovskii, *Works of the Tashkent Conference on the Peaceful Use of Atomic Energy* [in Russian], Vol. 3, (1961) p. 38.

5. I. A. Chernyshevskaya, in the book: The Effect of Ionizing Radiation on the Nervous System of Progeny [in Russian]. Moscow, (1961) p. 185
6. G. A. Shmidt, The Embryology of Animals [in Russian], Moscow (1951).

All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
