

PATHOLOGICAL PHYSIOLOGY AND GENERAL PATHOLOGY

CHANGES IN THE HIGHER NERVOUS ACTIVITY OF DOGS AFTER EXPOSURE TO IONIZING RADIATION AT DIFFERENT PERIODS OF ANTENATAL DEVELOPMENT

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In previous investigations [1-3] we examined the early postnatal ontogenesis of higher nervous activity in puppies irradiated antenatally on the 13th, 20th, and 45th days of embryogenesis. In the present investigation the object was to determine whether restoration of disturbed brain functions, noticed in early postnatal ontogenesis, takes place in adult dogs irradiated before birth.

METHOD

Total irradiation of the animals with x-rays was given in utero as a single dose of 200 R at a dose rate of 6 R/min at different periods of antenatal development: on the 13th day (the beginning of organogenesis), the 20th day (the period of completion of organogenesis), and the 45th and 50th days (fetal period). The conditions of irradiation were: voltage 190 kV, current 15 mA, filters 0.5 mm Cu and 0.5 mm Al. Observations were made on 20 adult dogs; 4 animals were irradiated antenatally at each of the times mentioned above, and 4 were controls. The conditioned-reflex activity was investigated by the classical method of salivary reflexes conditioned to food.

RESULTS

We began to try to form a system of positive conditioned reflexes and differentiation in the animals at the age of about 1-2 years. The results given in the table show that the food conditioned reflexes and differentiation appeared and became firmly established sooner in the animals irradiated on the 55th day than in all the rest (at almost the same times as in the control animals).

The most marked disturbances of the reflex-forming function of the cerebral cortex and of the processes of internal inhibition were observed in the dogs irradiated on the 13th day of embryogenesis. In these animals the conditioned reflexes to both sound and light were formed with great difficulty, and stable differentiation was not found even after 200 applications. The conditioned-reflex activity was chaotic in character and omission of reflexes, refusal to eat in the experimental room, and phasic states (balancing and paradoxical phases) were frequently observed.

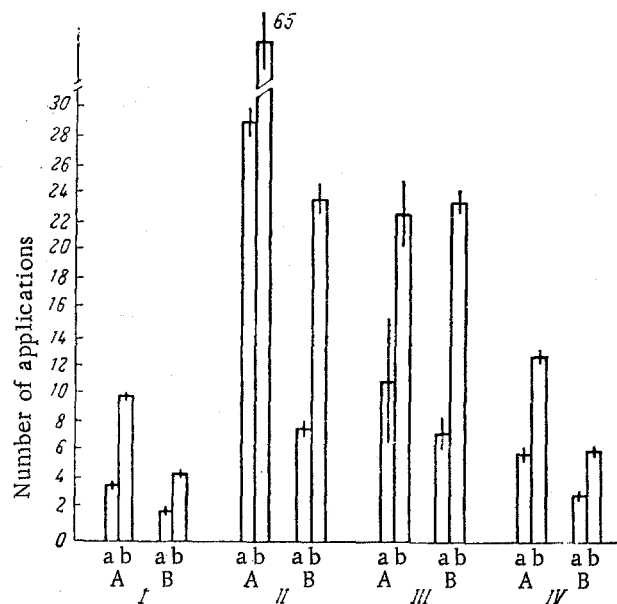
In the animals irradiated on the 20th day of embryogenesis the greatest difficulty was observed during the formation of the conditioned reflex to light. Conditioned reflexes to acoustic stimuli appeared comparatively early in these animals, whereas the conditioned reflex to light was formed later than in the controls (see table). Comparison of these animals with the animals irradiated on the 45th day shows that there was hardly any difference in the times of appearance and stabilization of the conditioned reflexes to acoustic stimuli, whereas the differences between the times of appearance and stabilization of the reflex to light were considerable ($P_{45} < 0.001$). This demonstrates that the disturbances taking place in the animals irradiated on the 20th day of embryogenesis affected mainly the functions of the optic analyzer.

Rate of Appearance and Stabilization of Conditioned Reflexes and Differentiation in Irradiated and Control Dogs (M ± m)

Group of animals	No. of animals	Conditioned reflex								Differentiation	
		Rattle (No. of comb.)		Tone 600 (No. of comb.)		Light (No. of comb.)		Tone 300 (No. of application)		Appeared	Stabilized
		Appeared	Stabilized	Appeared	Stabilized	Appeared	Stabilized	Appeared	Stabilized		
Control dogs	4	3, 25±0, 25	10, 5±0, 29	2, 75±0, 25	9, 0±0, 41	4, 5±0, 29	11, 25±0, 25	7, 25±0, 25	12, 5±0, 5		
Dogs irradiated on 13th day of embryogenesis *	4	4, 25±0, 25	22, 5±0, 96	4, 75±0, 48	21, 0±0, 91	7, 0±0, 41	21, 75±0, 96	21, 5±0, 5			
P _c †		0, 05	0, 001	0, 02	0, 001	0, 01	0, 001	0, 001			
P ₂₀		0, 40	0, 001	0, 30	0, 01	0, 05	0, 20	0, 01			
P ₄₅		0, 20	0, 001	0, 05	0, 001	0, 02	0, 01	0, 01			
P ₅₅		0, 60	0, 001	0, 05	0, 001	0, 01	0, 001	0, 001			
Dogs irradiated on 20th day of embryogenesis	4	3, 75±0, 48	15, 75±0, 85	3, 25±0, 25	15, 25±0, 85	8, 5±0, 29	24, 0±1, 08	13, 75±1, 31	30, 0±1, 08		
P _c		0, 40	0, 01	0, 30	0, 001	0, 001	0, 001	0, 01			
P ₄₅		0, 9	0, 20	0, 30	0, 05	0, 001	0, 001	0, 40			
P ₅₅		0, 70	0, 01	0, 70	0, 01	0, 001	0, 001	0, 005			
Dogs irradiated on 45th day of embryogenesis	4	3, 8±0, 25	13, 8±0, 63	3, 2±0, 25	12, 2±0, 75	5, 0±0, 41	15, 8±0, 48	11, 5±1, 85	17, 8±1, 8		
P _c		0, 9	0, 01	0, 9	0, 01	0, 3	0, 001	0, 1			
P ₅₅		0, 50	0, 05	0, 70	0, 40	0, 70	0, 001	0, 60			
Dogs irradiated on 55th day of embryogenesis	4	3, 50±0, 29	11, 25±0, 63	3, 0±0, 41	11, 25±0, 63	4, 75±0, 25	12, 0±0, 41	10, 25±0, 48	14, 25±0, 48		
P _c		0, 60	0, 40	0, 70	0, 05	0, 60	0, 60	0, 01	0, 05		

* Complete stabilization of reflexes was not observed in the dogs irradiated on the 13th day of embryogenesis.

† The index attached to the criterion of significance of differences denotes the group of animals in respect of which the significance has been calculated.



Modification of the signal value of an associated pair of conditioned stimuli. I) Control; II) animals irradiated on the 20th day of embryogenesis; III) on the 45th day; IV) on the 55th day. A) Modification of the positive value of the stimulus to negative; B) modification of the negative value of the stimulus to positive; a) modification registered; b) modification completed.

Another characteristic feature of all the irradiated dogs was the relatively early appearance of the conditioned reflex (see table), which was not accompanied by a correspondingly early stabilization, indicating the absence of concentration of the nervous processes in the irradiated animals. Whereas, for example, the conditioned reflex to the rattle appeared in the dogs irradiated on the 13th day of embryogenesis after 4.25 combinations, compared to 3.25 combinations in the controls ($P < 0.05$), it was stabilized in the irradiated animals only after 22.5 combinations, compared with 10.5 combinations in the controls ($P < 0.001$). The same relationship was also observed in respect of the formation of the other reflexes.

So far as differentiation is concerned, in all the irradiated animals this appeared and became stabilized later than in the controls, and in the animals irradiated on the 13th day, moreover, in general differentiation was not stabilized. The stabilization of differentiation was also difficult to produce in the dogs irradiated on the 20th day.

In order to ascertain the state of mobility of the nervous processes in the animals after the establishment of a constant background, a two-way modification of the signal value of the associated pair of conditioned stimuli was carried out. This test could not be performed on the dogs irradiated on the 13th day.

It follows from the results given in the figure that modification was most difficult to introduce in the case of the dogs irradiated on the 20th day of embryogenesis. Modification of the positive stimulus into negative was most difficult for both the irradiated and the control animals. On the whole the irradiated animals accomplished the modification much later than the controls, revealing marked inertia of their nervous processes. The decrease in the mobility of the nervous processes was also clearly demonstrated in a special test in which a stereotype (applied over 100 times) was replaced by one stimulus. The reproduction of the complex stimulus was more complete than in the control animals, especially in dogs irradiated on the 13th and 20th days of antenatal development.

Another test was carried out in which the animals were deprived of food for 24 h in order to study the strength of the process of stimulation. In the control dogs the magnitude of the positive conditioned reflexes as a rule increased, whereas in the irradiated animals it either remained unchanged (55th day), fell very slightly (45th day and, partially, 20th day), or fell considerably as far as the total disappearance of the reflexes (13th day and, partially, 20th day). The results of the fasting test demonstrate the obvious weakness of the process of stimulation in the irradiated animals, especially in those irradiated on the 13th and 20th day of embryogenesis.

In a further test, differentiation was prolonged to 3 min. In the control animals the secretion of saliva after application of the differential stimulus for a period of 3 min amounted to 5-9 drops, distributed relatively evenly in time. In the animals irradiated on the 20th and 45th days, and to a lesser extent on the 55th day of embryogenesis, de-inhibition was more marked and was observed mainly at the beginning of action of the stimulus—during the first minute; hardly any secretion was produced during the next 2 min. This indicates that in the course of the first minute cortical inhibition became overstrained, with the development of limiting inhibition.

In the animals irradiated on the 13th day of embryogenesis the total secretion was less than in the controls. Immediately after prolonged differentiation, disappearance of reflexes and refusal to eat were observed in all the dogs. Consequently, limiting inhibition developed very early in the animals irradiated on the 13th day of antenatal development, and was maintained for a long time. The results of the test of prolongation of differentiation indicate weakness of the processes of internal inhibition in the irradiated animals.

In a test in which excessively strong stimuli (tone 600 with a strength of 110 dB) were used, the total disappearance of all the reflexes was observed on the day of the test and on the next day in the irradiated animals (except those irradiated on the 55th day), and on the following days the conditioned-reflex activity of most of them was within the limits of the original background, whereas in the control animals the disturbances of the conditioned-reflex activity after this test persisted for 4-8 days. The reason for the short duration of the disturbances of conditioned-reflex activity in the irradiated animals may have been that limiting, protective inhibition developed instantaneously in them, protecting their nervous system against the further injurious action of the stimulus. The disturbance of the reflex-forming function of the cerebral cortex in animals irradiated antenatally is not, therefore, compensated with age, but continues to be manifested in adult life.

LITERATURE CITED

1. M. G. Airapetyants, Abstracts of Proceedings of the 19th Conference on Problems in Higher Nervous Activity [in Russian], Pt. 2, Leningrad (1960), p. 173.
2. M. G. Airapetyants, Transactions of the Institute of Higher Nervous Activity, AN SSSR, Pathophysiological Series [in Russian], 10, Moscow (1962), p. 11.
3. I. A. Piontkovskii and M. G. Airapetyants, Byull. éksper. biol., 1 (1953), p. 26.

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.
