CONDITIONED REFLEXES IN RATS AFTER A SINGLE PRENATAL EXPOSURE TO X RAYS (1 R)

(UDC 612.825.1 : 612.684.014.482-019)

V. N. Semagin

Institute of Higher Nervous Activity and Neurophysiology
(Director—Corresponding Member of the Academy of Sciences of the USSR,
Professor É. A. Asratyan), Academy of Sciences of the USSR, Moscow
(Presented by Active Member of the Academy of Medical Sciences of the USSR, V. V. Parin)
Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 60, No. 9,
pp. 43-46, September, 1965
Original article submitted April 2, 1964

It was shown in earlier investigations [8, 9, 10, 11] that prenatal exposure of rats to x rays in dosage of 1 R daily for 20 days damaged the developing nervous system. Other investigators [1, 3, 7, 15] found that single irradiations of 25 R or 10 R also damaged the developing brain of the embryo, as evidenced by disruption of higher nervous activity. From a consideration of the results of research carried out in the Institute of Higher Nervous Activity and Neurophysiology, together with the results of certain other investigations [13, 14], Piontkovskii [6] has expressed the opinion that the brain of the embryo may be damaged by ionizing radiations in doses of the order of 1-2 R.

This view has been examined in the present investigation, which may therefore represent a step towards determination of the threshold dose of radiation damaging to the brain of the embryo.

EXPERIMENTAL

The uterus of female rats (Wistar) was brought out through an incision in the abdominal wall on the 18th day of pregnancy. The rest of the body was screened with lead. The uterus and the contained embryos were exposed to x-rays in dosage of 1 R. Conditions were: voltage 190 kV, current strength 15 mA, filters 0·5 mm Cu and 1·0 mm Al, focal distance 3 m, dose rate in air 1 R/min. After irradiation the uterus was returned to the abdominal cavity and the abdominal wall was sutured. Similar operations were performed on other rats, the controls, but without irradiation. Parturition occurred naturally. Eight mothers produced 53 young rats which had been irradiated prenatally, and another 8 mothers produced 62 control rats. The fathers were different in all cases. A study of motor-food conditioned reflexes by (with certain modifications) a method described earlier [2, 4, 5, 9, 10, 12] began at the age of 45 days in 26 male rats which had been irradiated and 25 controls.

RESULTS

A conditioned reflex to a tone of 400 cps took longer to establish in irradiated (26·0 ± 2·43 combinations) than in control rats (20·8 ± 0·73 combinations) (P 0.05). The difference between the two groups was particularly evident in the coefficients of variation, that for the controls being 24·7 ± 3·5, compared to 93·5 ± 12·8 for the group of experimental rats (P 0.001). A conditioned reflex to light also took longer to establish in the irradiated than in the control rats (27·2 ± 3·19 paired stimulations compared to 18·5 ± 0·25 in the controls) (P 0.01). This value also varied more in the irradiated rats, the respective values of the coefficient of variation for irradiated and control groups being 110·0 ± 5·7 and 52·7 ± 7·44 (P 0.01).

The table gives details of positive conditioned, unconditioned and intersignal reflexes when the conditioned reflexes were established and when differentiation was being elaborated. The latent period of the conditioned reflex was longer, its duration was shorter, its magnitude less and the number of conditioned reflex thrust reactions at the door was less in the irradiated than in the control animals. An interesting and characteristic feature of irradiation

Characteristics of Positive Conditioned Reflexes during Period of Stabilization and during Elaboration of Differentiation

Stage	Conditioned signal	Animals	Conditioned: Latent period	Conditioned: duration	Conditioned: value	Conditioned: number	Unconditioned: value	Intersignal: number	Intersignal: value
Stabilized conditioned reflex	Tone 400 cps	Control	0,77±0,04	2,33±0,08	52,8±2,44	4,0±0,14	40,0±1,31	13,5±0,65	212±12,8
		Irradiated	1,07±0,06[1]	1,88±0,08[1]	43,0±2,21[2]	2,5±0,08[1]	39,0±1,09	9,6±0,51[1]	90±6,3[1]
	Red light	Control	0,92±0,04	2,54±0,07	67,6±2,48	4,1±0,15	43,0±1,35	7,0±0,39	127±8,2
		Irradiated	1,40±0,08[1]	1,99±0,07[1]	49,8±2,31[1]	3,4±0,13[1]	46,2±1,46	7,5±0,44	102±6,4[3]
Elaboration of differentiation	Tone 400 cps	Control	0,74±0,01	2,70±0,02	66,3±0,82	4,0±0,05	40,6±0,46	3,3±0,09	54±1,2
		Irradiated	0,81±0,01[1]	2,41±0,03[1]	63,8±0,89[4]	3,2±0,04[1]	43,6±0,50[1]	1,8±0,06[1]	156±3,6[1]
	Red light	Control	0,78±0,01	2,75±0,02	76,3±0,91	4,2±0,05	45,7±0,47	4,8±0,13	89±2,0
		Irradiated	1,00±0,02[1]	2,12±0,03[1]	58,5±0,87[1]	3,6±0,05[1]	49,2±0,57[1]	2,2±0,07[1]	141±3,2[1]

[1] P 0,001.
[2] P 0,01.
[3] P 0,02.
[4] P 0,05.

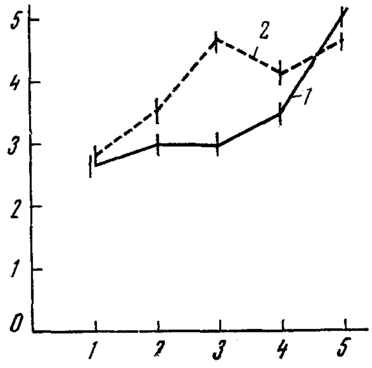

Fig. 1. Change in duration of latent period for conditioned reflex to unreinforced tone of 800/cps. Absicssa) stages in elaboration of differentiation; ordinate) seconds. 1) Rats of control group; 2) irradiated rats. Vertical lines) errors of mean.

at this particular time is, it is thought, the absence of any statistically significant differences between the two groups of rats in the value of the unconditioned reflex. Intersignal reflexes were on the whole weaker and less frequent. Correlation analysis [12] revealed that intersignal reactions depended on the strength of excitation when conditioned reflexes were being elaborated and on the strength of processes of internal inhibition when positive and negative conditioned reflexes were examined in stereotype. The intersignal reflexes were therefore indicative of weakening of the excitatory process in the irradiated rats. The positive conditioned reflexes to the acoustic and photic stimuli were also reduced when ability to distinguish between different acoustic and photic stimuli was being elaborated (the table).

Coefficients of variation with their errors were calculated for the results given in the table. Differences between irradiated and nonirradiated rats with respect to coefficients of variation were reliable in 14 instances. In 13 of these the coefficients for the prenatally irradiated rats were higher; in the other (latent period of established reflex to tone of 400/cps) the coefficient was higher for the control group.

Changes in latent periods (Fig. 1) indicate that both irradiated and control rats could be trained to distinguish acoustic stimuli. There was little difference between the two groups in the first and last stages of training. In the 2nd, 3rd and 4th stages, however, there were important differences. In the control group training to differentiate proceeded at an increasing pace, with maximum progress in the fifth stage (1·5 times or more than in the preceding three stages). In the experimental group there was rapid but constant increase of

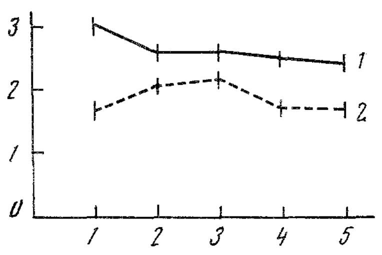

Fig. 2. Change in period of conditioned reflex responses to unreinforced yellow light. Notation as in Fig. 1.

latent period in the second and third stages, with no further increase thereafter. Differential inhibition had apparently reached its limit in the irradiated rats, and was weaker than in the controls. This conclusion would appear, however, to be incompatible with the rapid development of power to differentiate in the irradiated rats in the second and third stages, when latent periods for the control rats in these stages differed little from the latent periods in the first stage. Allowance must, however, be made for the fact that the excitation process was weaker in the irradiated than in the control rats, and that their latent period for the conditioned reflex to the tone of 400/cps was longer. It may therefore be assumed that the ability to differentiate developed more rapidly in the irradiated animals by virtue of the weakness of the excitation process. This is consistent with the fact that the limiting strength of differential inhibition was reached in the irradiated but not in the control rats.

The duration of the conditioned reflexes to the yellow light was less in the irradiated than in the control rats at all stages in the training of differentiation (Fig. 2). This was yet further proof of the weakness of inhibitory processes in the irradiated animals. Comparison of the first and fifth stages reveals significant reduction in the duration of the conditioned reflex to the yellow light in the control group (P 0.001), but no change in duration by the end of training of differentiation in the irradiated group (P 0.90). This constitutes proof of weakness of the inhibitory process in the irradiated rats.

The closing function of the brain was thus disturbed, and processes of excitation and inhibition were weakened in the fully grown rats which had been exposed to x-rays, in a dose of 1 R in 1 min, on the 18th day of embryonic development.

LITERATURE CITED

1. M. B. Gol'dberg, In the book: Problems of Neuroradiology [in Russian], Moscow (1962), p. 58.
2. M. B. Gol'dberg, I. A. Kolomeitseva, V. N. Semagin, et al., In the book: Problems of Neuroradiology [in Russian], Moscow (1962), p. 187.
3. I. A. Kolomeitseva, In the book: Problems of Neuroradiology [in Russian], Moscow (1962), p. 71.
4. L. I. Kotlyarevskii, Zh. Vyssh. Nervn. Deyat., No. 5 (1951), p. 753.
5. N. G. Mikhailova, Higher nervous activity in fully grown animals exposed to γ radiation in the middle period of embryonic development, Candidate's Dissertation [in Russian], Moscow (1961).
6. I. A. Piontkovskii, (Editor), Effects of Ionizing Radiation on Functions of Higher Divisions of Central Nervous System in the Offspring [in Russian], Moscow (1961).
7. I. A. Piontkovskii and I. A. Kolomeitseva, Radiobiologiya, No. 2 (1963), p. 220.
8. I. A. Piontkovskii and V.N. Semagin, Byull. Éksper. Biol., No. 11 (1961), p. 18.
9. V. N. Semagin, Higher nervous activity of albino rats regularly exposed to x rays in the embryonic period, Candidate's Disserataion [in Russian], Moscow (1959).
10. V. N. Semagin, In the book: Effects of Ionizing Radiation on Functions of Higher Division of Central Nervous System in the Offspring [in Russian], Moscow (1961), p. 79.
11. V. N. Semagin, In the book: Effects of Small Doses of Ionizing Radiation on Physiological Functions [in Russian], Moscow (1961), p. 117.
12. V. N. Semagin, In the book: Problems of Neuroradiology [in Russian], Moscow (1962), p. 158.
13. S. P. Hicks, J. Cell. Comp. Physiol., 43, Suppl. 1 (1954), p. 151.
14. L. B. Russell and W. L. Russell, J. Cell Comp. Physiol., 43 (1954). p. 103.
15. S. J. Kaplan, In the book: Response of the Nervous System to Ionizing Radiation, New York (1962), p. 645.