THE EFFECT OF TOTAL X-RAY IRRADIATION ON THE THALAMUS

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The object of the present work has been to study the functional condition of sympathetic centers in the hypothalamus during acute radiation sickness, and also to determine thresholds for hypothalamic effects produced by ionizing radiation.

Central autonomic regulatory function is of great importance in connection with the extensive evidence of destruction of the innervation of endocrine glands by radiation. The quantity measured was the change in the potentials developed by the sweat-secreting surface of the cat's paw in response to hypothalamic electrical stimulation. It is known that this reaction is mediated nervously, and that the hypothalamic excitation is conducted to the effector organ (the sweat gland) by sympathetic cholinergic fibers.

METHOD

The experiments were carried out on 20 cats, 12 of which received a dose of 600 r and 4 a dose of 50 r, while the remaining 4 served as controls. The electrodes were implanted in the hypothalamic region using Hess's method. Postmortem observations on the position of the tips of the electrodes showed that they lay in the anteromedial hypothalamic areas (mainly in the nucleus supraopticus, nucleus medialis, and nucleus lateralis).

Stimulation was applied to the hypothalamic region with a sinusoidal voltage from a ZG-10 oscillator at 50 cycles per seconds at intervals of 2-3 minutes. The strength of the stimulus varied according to the threshold, and varied from 0.2 to 3.6 volts.

The sweat secretion was recorded by the method of Weng and Brown, as used for measuring the cutaneous-galvanic reflex.

Change in skin potential, and respiration, were recorded from the ensuing reaction after the end of the stimulation on a two-channel electrocardiograph (mingograph 24 Elema). A feature of the apparatus was the inertia-free inkwriter. The paper speed was 0.25 cm/second. The magnitude of the reaction was expressed in millivolts.

The electrodes were clips of chemically pure sheet zinc firmly fixed to the front paw: one electrode was applied to a pad of the foot (sweat-secreting surface), and the other to the shaved dorsal surface. A layer of gauze soaked in a paste consisting of a mixture of kaolin and saturated zinc sulfate solution was placed between the skin and electrode. All the experiments were carried out under ether anesthesia.

RESULTS

A preliminary study was made of the sweat-secreting reaction in response to hypothalamic stimulation in normal cats. The baseline curve in anesthetized animals was usually straight. Sometimes potential variations not exceeding 0.3-0.4 mv were observed. Isolated spontaneous waves occurred frequently.

The threshold value of the stimulus required to elicit a change in potential from the sweat glands varied in different animals by as much as from 0.2 to 2.5-3 volts (see table).

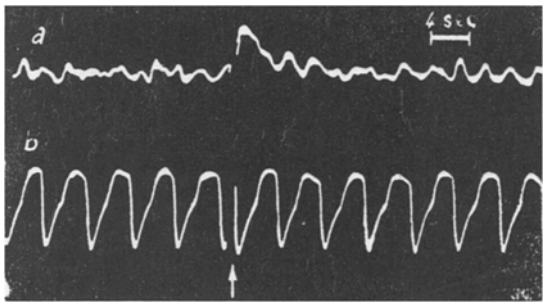

Fig. 1. Change in (a) potential difference of sweat glands, and (b) respiration, on stimulating hypothalamus (control). Arrow (↑) indicates moment of stimulation (0.2 volt, 30 seconds).

Variation in Successive Experiments of Hypothalamic Stimulus Threshold in Control Animals (results given in volts, interval between experiments 2-3 days)

No. of cat	Expt. No. 1	Expt. No. 2	Expt. No. 3
22	0,2	0,2	0,2
29	0,2	0,2	0,2
34	1,3	1,5	1,5
36	1,0	1,3	1,3

The sweat-secretion reaction in response to hypothalamic stimulation developed gradually, and it was always possible to record it after the end of the stimulation. It was very rare for the potentials to begin as early as 10-15 seconds after the onset of stimulation, but they usually occurred after the stimulus had ceased. The potential change was always in the same direction. The magnitude of the effect obtained was 0.6-1 mv, and was not always a function of the strength of the stimulus.

As a rule, the respiration after the stimulus had been given did not differ from the normal condition. In some experiments, when very strong stimuli were used, it was slowed, and respiratory movements might even cease.

Fig. 1 shows the baseline curve, as well as the reaction of the sweat glands to the hypothalamic stimulus.

After preliminary results had been obtained, 12 cats were exposed to a dose of 600 r, administered as follows: whole animal irradiated, three-tube apparatus potential 180 kv, current 20 ma, focusing distance 60 cm, dose rate 22.2-24.9 r/minute, filters 0.5 mm Cu + 1 mm Al.

One experiment on each cat was performed before irradiation. After it, the first test was made after 1-3 hours or after 24 hours, and subsequently after 3 and after 6-7 days. In all, 3-4 experiments per animal were performed.

Irradiation with 600 r caused acute radiation sickness in all the animals. After 3 days, there was generally a severe leukopenia, with a white cell count of 2500-600 cells per mm^3, and there was a noticeable loss of weight.

Death occurred from radiation sickness when practically no leukocytes remained in the blood stream (150-250 cells per mm^3), and after considerable loss in weight had occurred. Of the 12 cats, 3 died within the first 3 days, 3 after 4-5 days, and 5 after 7-10 days. One died under anesthesia 3 days after irradiation.

In the irradiated animals there was a definite phasic disturbance of the functional condition of the hypothalamic region; this took the form of variation in the threshold stimulus required to obtain the reaction of the sweat glands. There was no change in the spontaneous fluctuations recorded from the sweat glands, nor in the type or magnitude of the reaction itself.

Fig. 2 shows separately the results for animals with initially high and low hypothalamic stimulation thresholds (low and high excitability respectively).

Of the 12 cats irradiated with 600 r, in 7, before irradiation, the threshold varied between 1.5 and 3 volts, and in 5, from 0.2-0.5 volt; in all these animals, before irradiation, application of these stimuli to the hypothalamus caused a very definite electrical change in the sweat glands.

In Fig. 2, it can be seen that in the first few hours after the irradiation, there is a considerable increase in the excitability of the hypothalamic centers. At this period, experiments were carried out on 9 cats. In 6 of them there was a marked reduction in the threshold (from 2-2.5 to 0.2-0.5 volts). In one animal there was no reaction from the sweat glands, and in 2 which had low initial thresholds no change was recorded.

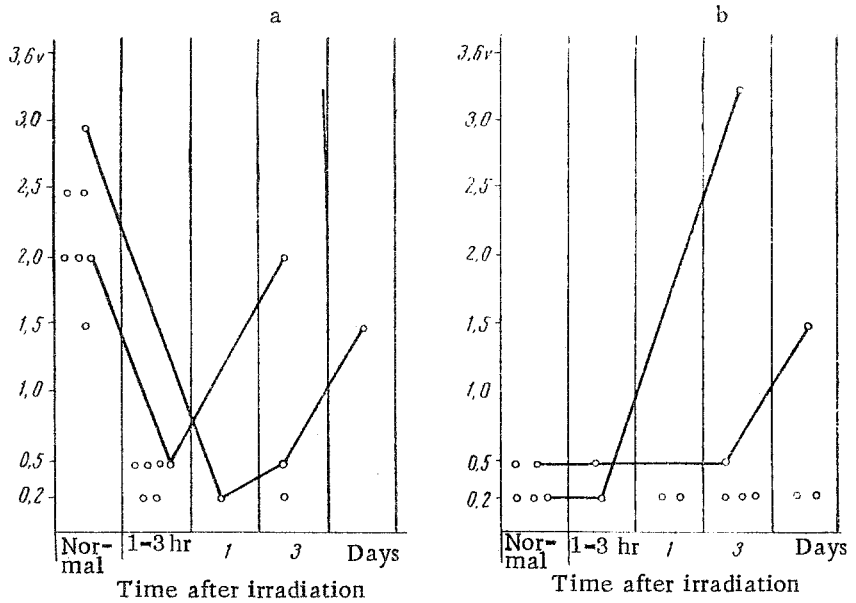

Fig. 2. Variation in hypothalamic stimulus threshold following irradiation of cats with (a) a high initial threshold and (b) a low initial threshold, with 600 r.

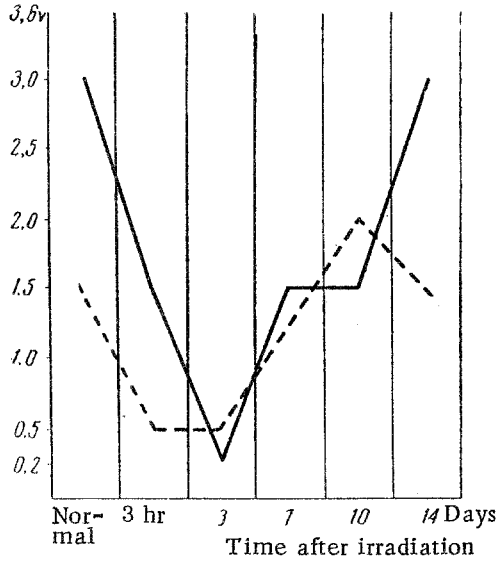

Fig. 3. Changes in threshold of excitability of the hypothalamus after irradiating with a dose of 50 r.

One day after irradiating, in 2 out of 3 animals tested, the threshold remained at its initial value (0.2 volt), while in one the threshold was considerably below normal.

After 3 days, in 7 out of the 9 animals tested, the excitability was raised (in 2 of these, the thresholds were low even before irradiation). In the 2 others (Nos. 7 and 41) there was a marked fall in excitability. In cat No. 7 it had fallen to the initial threshold value of 2 volts, while in No. 41, the threshold before irradiation was low, having a value of 0.2 volt, and 3 days after it had risen to over 3 volts. Both animals died on the following day, i.e., 4 days after irradiation. After 6-7 days, 4 experiments only were carried out, since most of the animals had died by this time. In 2 of these, which had a high initial hypothalamic excitability, no change was observed. In one animal the threshold had fallen from 3 volts before irradiation to 0.2-0.5 volt on the 1-3rd day, and to 1.5 volts on the 6th day. In cat No. 10 there was a marked increase in threshold from 0.5 v before irradiation to 1.5 v on the 6th day; one day later the animal died.

Thus, immediately after irradiation, and also one day later, the excitability of the sympathetic hypothalamic area increased sharply, as was shown by the reduction in threshold stimulus strength; the same thing was true of most animals after 3 days. Just before death, there is a reduction in hypothalamic excitability, which, in animals having naturally high values, returns either to its initial value or falls considerably below it. Thus, two phases of the change of functional condition of the hypothalamic region can be distinguished in acute radiation sickness. At first it functions more vigorously, but toward the end the level of activity is reduced. These differences can be more clearly seen from the curves plotted for two different animals (Fig. 2, a and b). In some animals, with initially high hypothalamic excitability, no change occurred.

Experiments using a small dose (50 r) were made on 4 cats having initially high thresholds (1.3 to 3 volts), i.e., a low level of excitability. Total irradiation was carried out on a single tube apparatus, under conditions as follows: potential 180 kv, current 15 ma, focusing distance 120 cm, dose rate 4 r/minute, filters 0.5 mm Cu + 1 mm Al.

This irradiation dose caused no visible radiation sickness symptoms. During the whole two-week period of observation, the animals did not lose weight, and there was no change in the number of leukocytes in the blood stream. However, in two of the four animals there was a marked change in the functional condition of the higher automatic centers.

Threshold measurements were made after 2-3 hours, and after 3, 7, 10, and 14 days from the time of irradiation. Excitability changes in the hypothalamic area appeared at the same time and in the same direction as in experiments in which fatal doses were given. The results of this experiment on two cats are shown in Fig. 3.

Just as when irradiating with a dose of 600 r, there was a biphasic change in the fuctional condition of the hypothalamic area. In the first 3 days after the irradiation, excitability was increased. After 10 days, it was reduced. Subsequently, the thresholds returned to their initial values.

Thus, the hypothalamic sympathetic centers may be very sensitive to the action of ionizing radiation.

Some results obtained by A. L. Shabadash [6] are very interesting in this connection; using a histochemical method, he demonstrated disturbances of metabolism in cells of the diencephalon following total irradiation with 25-100 r of x-rays.

The results obtained demonstrate definitely the occurrence of a functional disturbance of the hypothalamic sympathetic areas following total irradiation. When these results are compared with the many other published observations, it can be seen that the part played by the hypothalamic area in the reaction of the organism to harmful radiations is complex. The effects appear soon after the radiation, and result in changes of excitability, in increased electrical activity [1, 2, 4], and also in the destruction of the neurosecretory regulatory mechanism [3, 5].

SUMMARY

A study was made of the functional condition of the hypothalamic area in cats following a total x-ray irradiation dose of 600 r. The functional condition of the sympathetic hypothalamic centers was measured in terms of the change in the skin potential of the sweat secreting surface of the cat's paw following electrical stimulation of the hypothalamus.

The excitability of the hypothalamic centers rose considerably after irradiation. The increased excitability was still present during the following 24 hours, and in most cases even after 3 days. Just before death, the excitability of the autonomic centers was reduced.

Analogous phasic changes of hypothalamic excitability were observed in a number of animals following their total irradiation with a dose of 50 r; these disappeared within 2 weeks after irradiation, and no radiation sickness developed.

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* In Russian