

HYPOTHALAMIC INFLUENCES ON MOTOR ACTIVITY OF THE SMALL INTESTINE OF DOGS WITH ACUTE RADIATION SICKNESS

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Considerable disturbances of hypothalamic influences on motor activity of the small intestine have been found, depending on the severity of radiation sickness. Changes in function of the hypothalamic region itself have also been discovered after x-ray irradiation

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Too little attention has been paid to the study of changes in functions of the gastrointestinal tract in radiation sickness and, in particular, of the pathogenesis of the intestinal syndrome which, according to some investigators [6, 7, 8], is of decisive importance in determining the outcome of the disease. The importance of disorders of the central links of neurohumoral mechanisms has been particularly neglected. The hypothalamus is particularly interesting in this respect, and its connections with digestive functions are well established [2-5]. However, no details can be found in the radiobiological literature of hypothalamic influences on the digestive system.

The object of this investigation was to study hypothalamic influences on motor activity of the small intestine during exposure to ionizing radiation.

EXPERIMENTAL METHOD

Chronic experiments were performed on 4 dogs in which a fistula was first formed into the proximal portion of the intestine, or part of the intestine was isolated by the Thiry-Vella method. Intestinal contractions were recorded graphically by means of a balloon.

Bipolar electrodes were inserted into the hypothalamus with a stereotaxic apparatus using the atlas of O. S. Andrianov and T. A. Mering [1]. Stimulation was with square pulses (0.6 mA, 1 msec, 50-100 cps, duration of stimulation 1 min), but 1 dog was stimulated with sinusoidal current from a ZG-10 audio-frequency generator. The electrogram of the hypothalamic region of the experimental animals also was recorded.

After determination of the initial data, the animals were subjected to whole-body x-ray irradiation (bilaterally, using two apparatuses simultaneously) in a dose of 500 R (187 kV, 15 mA, filter 0.5 Cu, distance 100 cm, dose rate 12.5 R/min, duration of irradiation 40.6 min). As a rule the experiments were carried out on fasting animals (18-20 h after feeding). The severity of the radiation sickness was judged from the hematologic indices.

EXPERIMENTAL RESULTS

Electrical stimulation evoked an inhibitory response in all animals. Histologic analysis showed that the electrodes were in the lateral and preoptic areas of the hypothalamus. The intestinal contractions ceased after a short latent period (a few seconds), and this effect stopped immediately after switching off the current. Before irradiation, the thresholds of the responses, and also the intensity of stimulation evoking complete cessation of intestinal contractions, remained unchanged in all experiments. No significant differences were observed in responses of dogs with intestinal fistulae and with loops of intestine isolated by the Thiry-Vella method to stimulation of the hypothalamus.

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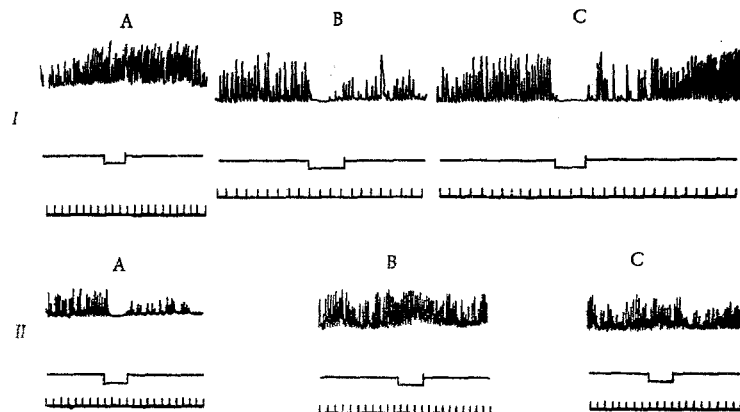


Fig. 1. Effects of electrical stimulation of lateral area of hypothalamus. I) Before irradiation; A) during stimulation with current of 0.6 mA (subthreshold stimulation); B) threshold response to 0.7 mA; C) stimulation with current of one mA (complete cessation of intestinal contractions); II) after irradiation: A) on the 14th day after irradiation (stimulation 0.6 mA); B) on the 24th day (stimulation 0.7 mA); C) on the 30th day (stimulation 1 mA).

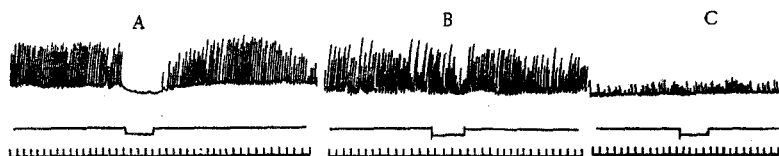


Fig. 2. Effects of electrical stimulation of preoptic area of hypothalamus. A) Before irradiation (stimulation with current of 6 V); B) on 3rd day after irradiation (stimulation of same intensity); C) on 19th day after irradiation (on day of death), absence of effect during stronger stimulation (8 V). From top to bottom: trace of contractions of small intestine, marker of stimulation, time marker (15 sec). Frequency of stimulating current 100 cps.

The results obtained demonstrate that x-ray irradiation appreciably modifies the periodic activity of the small intestine. In the initial period after x-ray irradiation, both periods of rest and periods of work were shortened. Subsequently, the changes became wavelike in character. After 10-20 days, the periods of complete rest disappeared and the amplitude of the contractions fell slightly. If the disease followed a favorable course (in dogs which recovered), the periodicity of the intestinal contractions was gradually restored. In the animals with severe radiation sickness, the motor activity of the small intestine was sharply depressed in the preterminal period.

From the first day after irradiation, the hypothalamic influences on motor activity of the small intestine were disturbed, and the changes taking place followed a pattern which was largely determined by the severity of the radiation sickness. In moderately severe radiation sickness, ending in recovery, stimulation of the hypothalamus on the first day after irradiation increased the inhibitory effect, as shown by a decrease in the thresholds of the responses and an increase in their intensity. Later, for about one month, a fluctuating picture was observed with predominantly an increase in the inhibitory effect of stimulation. However, 20-30 days after irradiation, at a time of relative clinical recovery of the animal, a sudden weakening of inhibition of the intestinal contraction took place in response to electrical stimulation. After a fairly long period (about 1.5 months), the indices returned almost to their initial level, although the thresholds remained slightly elevated (Fig. 1).

In dogs with a more severe type of radiation sickness, terminating in death on the 19th-22nd day, some decrease in the thresholds of the responses was observed on the first day after irradiation. Sometimes the responses were distorted, stimulation of the same intensity evoking an increase in motor activity as well as an inhibitory effect. Starting with the 3rd day, the thresholds of the responses increased. Electrical stimulation, normally leading to inhibition of intestinal contractions, became relatively ineffective or had no effect whatever on motor activity of the small intestine (Fig. 2).

These results show that whole-body irradiation of dogs with x-rays causes definite changes in the hypothalamic influences on small intestine motor activity. It was interesting to examine the changes in the functional state of the hypothalamus itself after irradiation, as reflected in its basic bioelectrical activity and its response to electrical stimulation. The electrohypothalamogram of the experimental dogs, recorded with bipolar leads is normally dominated by low-voltage waves (15-20 μ V, 10-15 cps). Stimulation of the hypothalamus against this background led to an appreciable increase in amplitude of the waves, lasting about 1-2 min after switching off the current. On the first day after irradiation, the electrical activity increased, and for the next few days the amplitude of the waves showed wavelike changes. Later, in dogs with severe radiation sickness, marked depression of the basic bioelectrical activity developed. Shortly before death discharges of large, pointed waves appeared, similar to those described by M. N. Livanov in experiments on rabbits. The response to electrical stimulation also showed wavelike changes in the course of radiation sickness. Where death supervened, the response gradually grew weaker or disappeared completely in the last days of life.

The results described above show that disorders of the central regulatory influences play a role in the mechanism of origin of disturbances of the motor activity of the small intestine developing in radiation sickness.

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