THE DYNAMICS OF THE FUNCTIONAL STATE OF THE NEUROMUSCULAR APPARATUS IN EXPERIMENTAL TUMORS

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 55, No. 2,
pp. 96-99, February, 1963
Original article submitted June 8, 1961

The single work devoted to the subject under study [1] gives rise to a number of questions. Investigation of chronaxie under clinical conditions excludes the possibility of recording individual characteristics, of comparing the results obtained with starting data (before illness), and of performing investigations in the so-called pretumoral period. In addition, at the present time one must apparently approach data just on chronaximetry alone with a critical attitude, especially in view of the series of comments made by Academician D. N. Nasonov [2, 3, 4] et al. in a discussion of the theoretical nature of the chronaxie.

We investigated the functional state of the neuromuscular apparatus in experimental homotransplanted tumors of rats and mice, from the moment of transplantation up to the death of the animal.

EXPERIMENTAL METHOD

We described the method of the investigations in detail earlier [5].

The animals were fixed to the edge of a special table. The inactive anode electrode – a lead disk (30 cm^2) – was fastened to the thorax. The active cathode electrode – a silver needle – was inserted into the gastrocnemius muscle. Stimulation was carried out with impulses of rectilinear form. The motor effect was recorded on an electrokymograph (speed of 2 mm/sec). Transplantation of the tumor was performed by subcutaneous injection of 0.6 ml of a 10% emulsion, prepared in sterile physiological saline. The rats were inoculated with lymphosarcoma, and the mice, with Ehrlich's carcinoma, which strains were obtained from the Leningrad Institute of Oncology.

EXPERIMENTAL RESULTS

The experiments were carried out on 38 rats and 20 white mice. We obtained 610 myograms, 45 electroexcitability curves, and we completed 635 chronaxie determinations.

In the first series of experiments, we performed comparative investigations of lability in 13 healthy rats and 8 rats with already developed tumors. In the healthy rats, the optimum frequency for tetanic stimulation ranged from 50 to 100 pps; the development of complete pessimum was not observed, even at a frequency of 1500-2500 pps (Fig. 1, a). The relationship between stimulus strength and the responding reaction of the muscle was always proportional (Fig. 1, b). In the process of multiple recording of the myograms, we observed the phenomena of assimilation of the excitation rhythm, and elevation of lability in the course of the reaction.

In 6 rats with tumors, stable tetanus – the optimum frequency – was observed in the range of 30-40 pps, and in the other 2 rats, in that of 80-100 pps. In isolated cases, we observed a decrease in lability in the course of the reaction.

In the second series of experiments, we studied the dynamics of changes in the physiological lability, from the moment of transplantation up to the death of the animal. For the purpose of more fully studying the functional state of the neuromuscular apparatus, in 5 rats we also investigated the motor chronaxie and the electroexcitability curve (strength-duration). In the mice we only investigated the motor chronaxie.

The course of the tumor process can be divided arbitrarily into 3 periods.

The first – pretumoral – lasted for 2 to 5 days. Out of the 15 rats investigated in this period, we observed a drop in lability in 14. Thus, in rat No. 3, diminishing tetanus was already recorded at 50-100 pps, and complete pessimum at 800-1000 pps (Fig. 1, c).

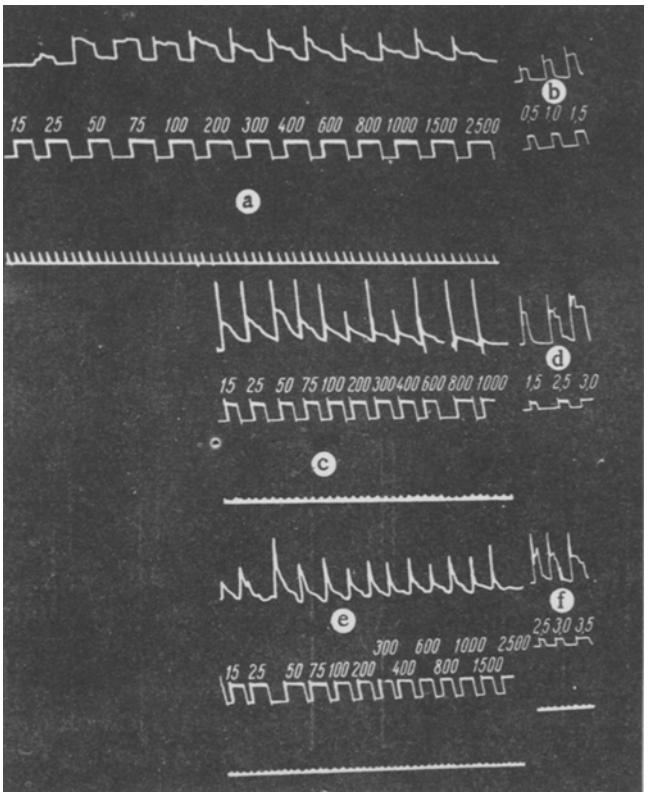

Fig. 1. Change in the physiological lability of the gastrocnemius associated with homotransplanted lymphosarcoma in rats: a) before transplantation (current intensity of 1.5 mA); b) before transplantation (frequency of 50 pps); c) on the 5th day after transplantation (current intensity of 3 mA); d) on the 4th day (frequency of 50 pps); e) on the 23rd day (current intensity of 3.5 mA); f) on the 25th day (frequency of 50 pps). Meaning of the curves (from above downward): myogram; stimulation markings with indication of the frequency of impulses (in pps) on myograms a, c, e, and the intensity of the stimulus (in mA) on myograms b, d, f; time markings (1 sec). Duration of the rectilinear impulses was 0.05 msec in all the myograms. Speed of the electrokymograph was 2 mm/sec.

We observed signs of disturbance of the rhythm assimilation and reduction of lability in the course of the reaction. In a number of rats we observed a discrepancy between the reaction of the muscle and the strength of the stimulus – a leveling phase (Fig. 1, d). In those animals in which we investigated the strength-duration curve in this period, comparison with the curve seen prior to transplantation (Fig. 2, a) showed movement of the curve away from the axes, in both the horizontal and vertical areas (Fig. 2, b). This testified to a reduction in electroexcitability, in the zone of both long (1.0-0.5 msec) and short (0.2, 0.1, 0.05, 0.02 msec) stimulation impulses. The magnitudes chronaxie in the rats were in the range 0.015-0.3 msec (before transplantation, 0.02-0.2 msec), while in the mice, the range was 0.01-0.08 msec (before transplantation, 0.012-0.07 msec).

Thus, the chronaxie was rather varied: we observed both shortening and lengthening of it, despite a general drop in excitability and lability.

The second period was the appearance and development of the tumors (8-12 days). The animals' condition (appetite, activity, mobility) remained good. In this period, as compared with the previous one, 5 rats showed a further drop in lability and 10 rats, a certain elevation of it; in 4 of the 10, it did not reach the normal level, in 4 it returned to normal, and in the remaining 2, it somewhat exceeded the normal level (see table). The strength-duration curves indicated a further decrease in excitability (Fig. 2, c). Fluctuations in the chronaxie were replaced by its prolongation in some rats to 0.56 sec, and in mice to 0.1 msec.

The Dynamics of the Physiological Lability Associated with Homotransplanted Lymphosarcoma in Rats

Rat No.	Before transplantation	Periods in the course of the tumor process		
		first (2-5 days)	second (8-12 days)	third
1	75—100	50—75	50—75	25—50
2	75	25—50	50—75	25—50
3	75—100	50	50	25—50
4	80—100	Not investigated	30—40	30—40
5	50—75	50	75—100	25—50
6	75—100	75—100	50—75	25—50
7	50—75	25	Not investigated	Not investigated
8	75	15—25	25—50	Not investigated
9	50—75	50	50—75	25—50
10	40—60	Not investigated	30—40	30—40
11	40—60	30—40	40—60	Not investigated
12	40—60	30—40	40—60	Not investigated
13	50—75	50	50—75	50
14	50	25—50	25—50	50
15	40—60	40	60—80	Not investigated
16	75	50—75	25—50	75—100
17	50—75	25—50	75	100—200

Note. The figures designate the number of impulses per second in the stimulation which caused stable tetanus – the optimum frequency.

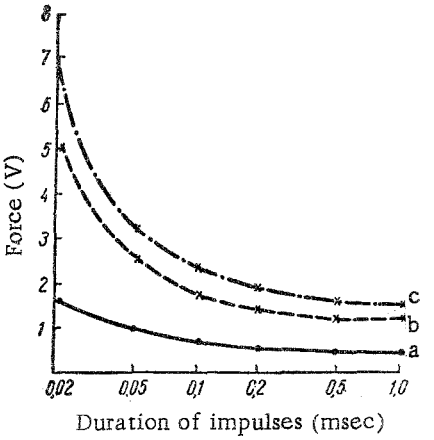

Fig. 2. Changes in the electroexcitability curve (strength-duration) for the gastrocnemius muscle, associated with homotransplanted lymphosarcoma in rat No. 7, before transplantation (a), in the pretumoral period (b), and with the appearance and growth of the tumor (c).

The third period was characterized by the development of large tumors, sometimes with disintegration in the center and small necrosis of the skin over the tumor. The condition of the animals gradually worsened. Signs of cachexie rapidly developed. The ratio of the weight of the tumor to the weight of the animal, after its death, was equal to 1:4, 1:3, and in isolated cases, even 1:1.

The duration of life of the animals following the transplantation was equal to an average of 25-35 days. In this period, the lability progressively fell in the majority of the rats (see table). Thus in rat No. 3, at a frequency of 25-50 pps, we already recorded manifest diminishing tetanus, and at frequencies of 1000-1500 and 2500 pps, only an initial shudder of the muscle, and then rapid development of complete pessimum (Fig. 1, e).

We noted leveling, or even distortion, of the relationship between stimulus strength and the magnitude of the responding muscle reaction – a leveling and paradoxical phase of parabiosis (Fig. 1, d, f).

Data from investigation of the strength-duration curve and the motor chronaxie indicated a further reduction in electroexcitability. We observed prolongation of the chronaxie in mice to 0.15 msec, and in the rats, even to 0.7 msec. Only in 2 rats (Nos. 16 and 17), in 6 experiments in the terminal period, did we register comparatively high indices of lability. It is interesting to note that the certain increase in lability in these animals, in contrast to the others, coincided in time with progressive disintegration of the tumor, wide ulcerations, and the onset of secondary infection.

Thus, the course of the tumor process was accompanied by profound changes in the functional condition of the neuromuscular apparatus, which, according to the mechanism of their development, apparently may be regarded as the pattern of a parabiotic process. The development of the latter may be the result of a disturbance in the subordination effects of the central nervous system, and may be the sequela of cachexie.

SUMMARY

To assess the functional state of the neuromuscular apparatus in experimental homotransplanted tumors in mice and rats a study was made of the motor chronaxie electroexcitability curve and physiological lability. After transplantation of Ehrlich's carcinoma to mice and of lymphosarcoma to rats marked changes occur in the functional state of the motor apparatus. Reduction of physiological lability is observed already during the pretumoral period. With growth of the tumors and development of cachexie there is a progressive reduction of excitability and lability, disturbance of correlations between the strength of the stimulus and the muscular response, development of equalizing and paradoxical phases – parabiosis.

LITERATURE CITED

1. L. V. Latmaniozova and G. G. Ivanov, Byull. éksper. biol., 1951, No. 2, p. 80.
2. D. N. Nasonov and D. L. Rozental', Fiziol. zh. SSSR, 1953, No. 4, p. 405.
3. D. N. Nasonov and D. L. Rozental', Fiziologicheskii zhurnal SSSR, 1953, No. 4, p. 39.
4. D. N. Nasonov and D. L. Rozental', Fiziol. zh. SSSR, 1955, No. 1, p. 121.
5. A. I. Plaksin, Byull. éksper. biol., 1959, No. 12, p. 42.

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.
