QUANTITATIVE MEASUREMENTS OF THE SENSITIVITY OF THE CENTRAL NERVOUS SYSTEM TO IONIZING RADIATION

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One of the most fundamental and pressing problems concerning the biological effects of radiation is to determine the sensitivity to radiation and the conditions which determine it. Nevertheless we are still a long way from having found the answers. Although it is admitted, for instance, that the nervous system responds to comparatively small doses of ionizing radiation, until now little work has been done on the quantitative aspect of this response.

Detailed quantitative work has been carried out on nervous and muscular tissue using electrical stimulation. It has been shown that the strength of the current and its duration are the two parameters which determine excitability. From the facts and direct observations of Gorveg, Weiss, and Lapique the relationship between the value of the threshold voltage and its time of action has been determined. The mathematical relationship between the two has been shown by the so-called strength – duration curve. This curve shows that for each value of the current a corresponding minimal duration of its action on the tissue is required in order that an excitation may be produced.

Following the suggestion of M. N. Livanov, we decided to find to what extent the laws governing electrical stimulation applied also to the action of ionizing radiation on the nervous system.

Until the present time, studies of radiation sensitivity have as a rule been conducted on the basis of determining some end effect such as for instance the period elapsing before a batch of animals died. This approach obviously does not allow the sensitivity to radiation of any part of the body to be determined, i.e., by this means it is not possible to find the threshold value of the radiation which will evoke a response from one particular system.

As an index of the sensitivity of the central nervous system, we used the earliest responses which could be shown on the electroencephalogram. The advantage of this method is that the earlier responses are recorded during the period of irradiation, i.e., during the period in which radiation is being absorbed; this arrangement made it possible to determine the threshold dose.

METHOD

The experiments were carried out on 200 sexually mature chinchilla rabbits weighing 2.5-3 kg. Gamma irradiation was used in order to avoid the possibility of any additional effects arising from electromagnetic fields such as occur when working with x-ray apparatus.* As a source of gamma irradiation we used the original ÉGO-2 and OKFO-1 instruments; this made it possible to expose the animals to a general irradiation of different doses. Among others, we carried out the following experiments: (1) 15 rabbits, dose 7.5 r/sec; (2) 15 rabbits, 5 r/sec; (3) 34 rabbits, 2.5 r/sec; (4) 34 rabbits, 1 r/sec; (5) 34 rabbits, 0.35 r/sec; (6) 34 rabbits, 0.13 r/sec; (7) 34 rabbits 0.013 r/sec. All the animals were irradiated for 5 minutes during which time the electroencephalogram was recorded.

In experiments (1) to (4) the irradiation was absolutely evenly applied, as the cobalt sources were arranged in a ring around the animal. In experiments (5) to (7) the sources were arranged above the animal so that there was a dosage gradient between the upper and lower parts of the body.

The sources were taken from store and transferred to the operating position by mechanical means. Any possible noise effect associated with the operation of the apparatus was excluded by control experiments. In 95% of the animals used, hearing was destroyed by an operation. Also, we carried out experiments in which the Co^{60} was replaced by pieces of metal of the same size and weight. Under these conditions, when all conditions were the same except that there was no radiation actually delivered, no reaction occurred.

As we have pointed out, the index of sensitivity of the nervous system to radiation was taken as the change in the electrical activity of the brain. Poten-

* We gave a report of the biological effect of electromagentic fields developed during the use of x-ray apparatus at the All-Union Conference on Electrophysiology. Report of the All-Union Conference of Electrophysiology (Moscow, 1958).

Time of Development and Extent of Response in Relation to Dose

Number of experiment	Dose rate r/sec	Number of animals in experiment	Onset of response: during first second	Onset of response: during remaining period	Extent of response: Actual numbers	Extent of response: in %	No response during period of observation
1	7,5	15	15	—	15	100	—
2	5	15	15	—	15	100	—
3	2,5	34	32	1	33	97	1
4	1	34	21	11	32	94	2
5	0,35	34	17	14	31	91	3
6	0,13	34	1	23	24	74	10
7	0,013	34	—	16	16	47	18

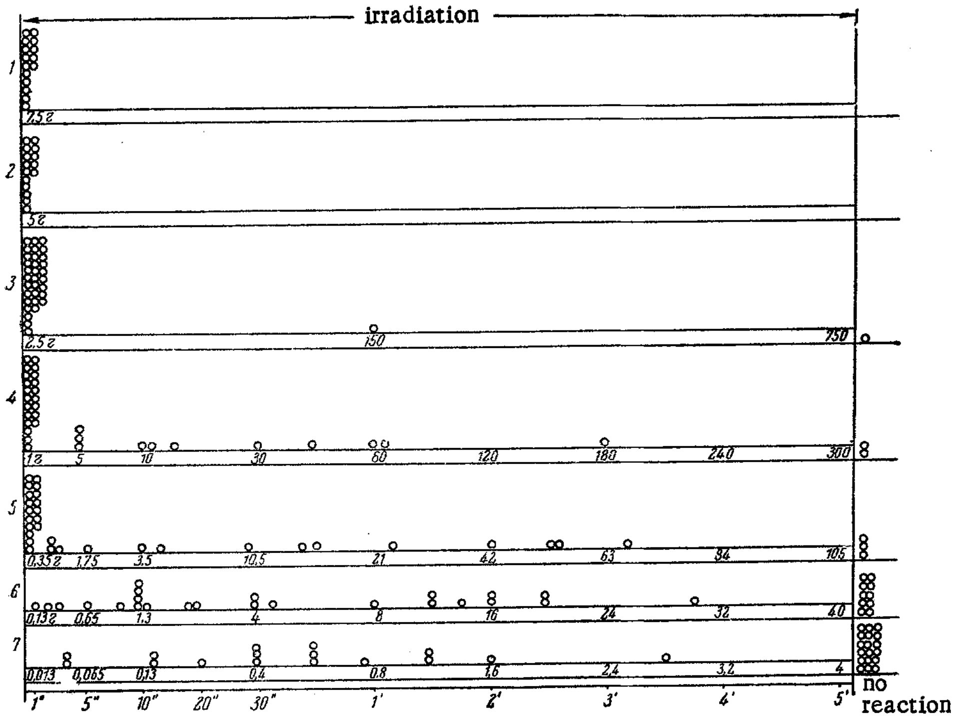

Fig. 1. Time of response occurring during a 5-minute irradiation at different intensities (reaction of each rabbit during irradiation shown by a circle.) Time along abscissa measured from onset of radiation, the number of the experiment is shown on the ordinate as well as the corresponding dose applied.

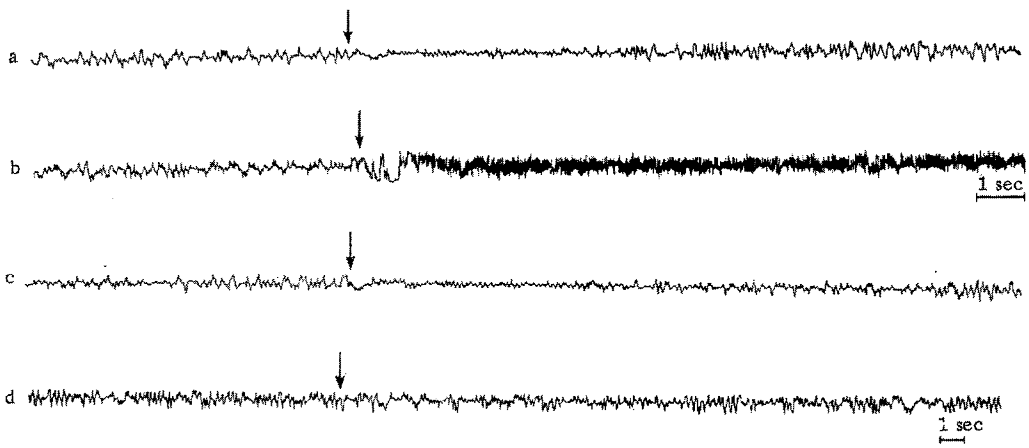

Fig. 2. Type of early change in electrical activity of cerebral cortex of rabbit brain during irradiation (↓).

tials were recorded from the parietal region of the cerebral cortex by a monopolar electrode, an indifferent electrode being applied to the skull bone in the midline at the junction of the frontal and nasal bones. The potentials were amplified by a four-stage AC-coupled amplifier. A 100-μv signal applied to the amplifier input gave a deviation of the penwriter of 0.7-0.8 cm. The recording apparatus had a frequency response extending up to 70 cps.

RESULTS

It can be seen from Fig. 1 that in the first, second, and third experiments the reaction occurred in almost all the rabbits at the very onset of the radiation; it was not possible to record the start of the radiation more accurately than to half a second.

The response of the central nervous system was shown as the change in the electrical activity of the cerebral cortex. These changes appeared as frequency shifts and variation in amplitude. These are illustrated in Fig. 2.

Most often, there was a depressor response (see Fig. 2a), and this occurred independently of whether the radiation was given during a period of intense or of weak electrical activity. In some rabbits both the amplitude of the oscillations and the frequency were increased (see Fig. 2b); occasionally the effect of the radiation was to cause a slow regular rhythm to appear (see Fig. 2c). It must be noted that although most of the responses lasted as a rule for not more than 3-12 sec, the frequency change was sometimes maintained for longer, sometimes for the whole period of irradiation.

The reactions described were observed in all the animals in all the first three experiments, and they originated in the first second of the irradiation and were very marked. Two rabbits were exceptions: In one, the response occurred at the 60th second, and in the other no changes were observed for the whole of the 5 minute irradiation period.

In the fourth set of experiments where the power of the radiation was reduced to 1 r/sec, the response occurred in 94% of the animals. However, the time of occurrence and thenature of the response were somewhat different. In 11 of the rabbits, the change did not occur during the first second of irradiation, but later (see Fig. 1). In many cases the reactions were weaker and shorter lasting than previously (see Fig. 2d).

This same difference became accentuated as the dose was further reduced in successive experiments, as can be seen from Fig. 1.

The mean value of the time of onset of the reaction was calculated for each experiment, and the results plotted as a curve in Fig. 3.†

It can be seen from Fig. 3 that the sensitivity of the nervous system to irradiation has the same form as does the sensitivity to electrical stimulation. The curve approximates a hyperbola.‡

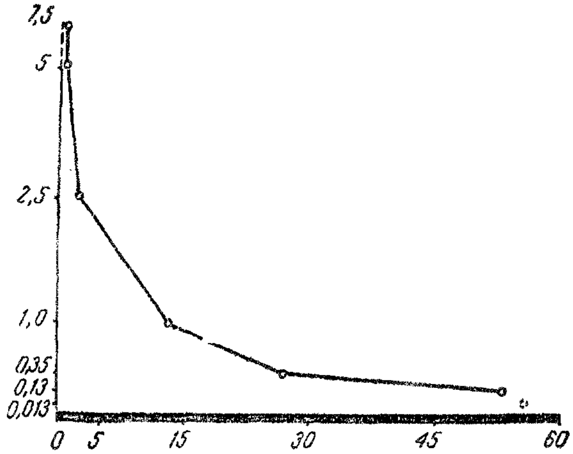

Fig. 3. Curve showing the sensitivity of the central nervous system to irradiation. Dosage is plotted as ordinate (in r sec), time of onset of the response is plotted as abscissa (in seconds).

It is not possible to determine how closely the left portion of the curve approaches the ordinate because it was not possible to determine the onset of the radiation more accurately than to 0.5 sec. As far as the right-hand part of the curve is concerned, there must be some minimal value of radiation which is capable of producing a response when operating for an indefinitely long period. By analogy with the electrical stimulus this value of the dose may be defined as the threshold.

By use of this curve it is possible to evaluate the sensitivity of the different excitable systems in different species, and to demonstrate more convincingly than otherwise would be possible the effect of individual variations. It can be seen from Fig. 1 that as the dose is increased, individual variations in sensitivity cause less alteration in the response to the irradiation.

The experiments we have performed have enabled us to obtain results giving a quantitative indication of the sensitivity of the central nervous system to ionizing radiation and to establish the relationship between excitable systems and radiant action, and also to reveal individual differences in sensitivity.

SUMMARY

This work deals with the quantitative characteristic of the sensitivity of the nervous system to ionizing radiation. The early reaction of the nervous system as revealed by the electroencephalogram was used as an index of sensitivity. The results show the relationship between the time of onset of the reaction and the dose rate. There was a general regularity in the response of the excitable systems to radiation.

† Experiments in which there was no reaction of the central nervous system during the whole of the 5-minute period were not included in calculating the mean values.

‡ The point on the curve referring to experiments with a dosage of 0.013 r/sec cannot be established with certainty by the mathematical treatment used because in 47% of the animals there was no response during the whole of the 5-minute period.