STATE OF SYNAPTIC STRUCTURES AT NERVE CELLS OF THE SPINAL CORD OF IRRADIATED RATS

I. D. Lev

From the Chair of Normal Anatomy, S. M. Kirov Military Medical Academy, Order of Lenin, Leningrad

(Received April 15, 1957. Presented by V. N. Chemogovsky, Member AMS USSR)

The first convincing evidence of the effect of irradiation of frogs with x-rays was provided by L. R. Tarkhanov [19, 20]. It was later shown that radioactive substances cause degenerative changes in the nerve cells and fibers of the central nervous system [3]. Other authors [24, 26], however, reported that x-rays have no effect on nervous tissues, which remain intact after irradiation of the organism.

I. R. Tarkhanov's views were supported and further developed by M. I. Nemenov [16], F. P. Maiorov, M. I. Nemenov and L. F. Vasileva [13], E. I. Bakin [1], N. N. Lifshits [12], R. Liman, P. Kupalov and W. Scholz [25], D. G. Shefer [21], P. F. Minaev [14, 15], and others, who found that the nervous system is quite sensitive to penetrating radiation. M. I. Nemenov [16] definitely established that x-rays adversely affect cortical activity. D. G. Shefer [21] showed that irradiation caused degenerative changes in the cells of the cerebral cortex and of the subcortical ganglions.

These divergent views on the sensitivity of the nervous system to the action of radiant energy are also reflected in the textbooks. V. V. Efimov [6] classes nervous tissue as being the least sensitive to radiation of all the tissuer and cells of the body. While B. N. Tarusov [18] concedes on the one hand that the central nervous system is very sensitive to direct irradiation, on the other hand he considers that "the tissues of the nervous system are best of all protected against secondary toxic products formed during irradiation."

Of recent times, morphological data have been added to clinical and physiological observations indicative of the sensitivity of the nervous system to x-rays.

- V. V. Portugalov et al. [17] have shown that irradiation of animals causes damage to the nerve cells of different levels of the brain, and of the sympathetic and spinal ganglions, and leads to changes in nerve fibers and receptors.
- A. G. Beglaryan, K. A. Kyandaryan and S. A. Papoyan [2] came to the conclusion that irradiation affects receptor nerve fibers and cells of spinal ganglions (crenellation, hyperchromatosis, central chromatolysis). They also found changes in the lateral horns of the spinal cord (karyocytolysis, ghost cells), and, to a lesser degree, in the cells of the higher levels of the central nervous system.

The least affected were the cells of the cerebral cortex, which is, in the opinion of these authors, due to differences in the functional state of different parts of the central nervous system.

V. V. Kupriyanov [10, 11] subjected dogs and cats to irradiation, and found significant changes in the cardiac receptors and in the intramural nerve cells of the heart; he observed degenerative changes in the pericellular formations.

Irradiation restricted to the temporal or frontal lobes of the brain of apes was followed by acute inflammatory or necrotic processes in the irradiated parts of the brain, according to the amount of radiation administered [22]. Changes in the glia cells of irradiated apes were also observed [23]. A. D. Zurabashvill and B. R. Naneishvill [8] examined the condition of certain parts of the brain and the spinal cord of 4 irradiated dogs and 4 irradiated apes. They came to the conclusion that the central nervous system, consisting as it does of highly differentic and cells, is sensitive to irradiation.

The impression given by this short survey of the literature is that nervous elements are very sensitive to irradiation with x-rays. One may agree with N. A. Kraevsky's view [9] that the alleged insensitivity of the nervous system to radiant energy was based on superficial morphological observations.

The question of the effect of x-rays on the nervous system is, of course, still far from being finally elucidated; in particular, virtually no attention has been paid to the state of the synaptic structures, which are abundantly distributed around the neurons of the central nervous system.

For the explanation of the processes of stimulation and inhibition taking place in the central nervous system, present-day physiology attaches great importance to the function of the complex synaptic apparatus distributed around nerve cells and their protoplasmic processes (dendrites). B. A. Dolgo-Saburov [4, 5] has, on morphological grounds, advanced the suggestion that the concept of the neuron as a structural and physiological element of the reflex arc should be extended to include its surrounding neuroglia and blood capillaries. It was found [4, 5] that these elements are also supplied with synaptic structures, which appear to be terminations of nerve cell dendrites and axons (i.e., of conducting systems).

EXPERIMENTAL METHODS

We examined the condition of synaptic structures around spinal cord cells of rats which had been subjected to x-ray irradiation, at a dosage of 450-600 r, causing acute radiation sickness. The spinal cord of 5 rats killed on the 5-12th day after irradiation was studied in complete serial sections. The sections were impregnated by D. I. Deinek's modification of the Golgi method. This procedure gives a very clear picture of normal and pathologically changes synaptic structures at nerve cells and their dendrites. The capillary network is also well shown: for greater contrast we stained the capillaries with iodoeosin.

EXPERIMENTAL RESULTS

We compared our observations with those of A. D. Zurabashvili [7] and of B. A. Dolgo-Saburov [4], which describe the structure and distribution of synaptic structures of nerve cells of the spinal cord of normal rats. The terminal interneuronic apparatuses connecting spinal cord nerve cells of rats—the synapses—are normally in the form of slender ringlets or loops situated on the body of the cell and on the dendrites [4, 7]. Their number is fairly large, and their dimensions vary, but in general they give the impression of being extraordinarily thin. The synaptic ringlets are sometimes supplied by short preterminal segments of afferent nerve fibers, being axons of another nerve cell. Some of the synaptic structures are located between cells. These synapses, which had earlier been termed "free synapses" by Lorente de No, are in fact, according to B. A. Dolgo-Saburov [4, 5], terminations of nerve fibers at nerve cells and their dendrites which had not fallen within the plane of the section, at neuroglia cells, and, finally, at the walls of the multiplicity of capillaries which ramify in this region.

Many cells are literally covered with hypertrophied synaptic structures (Figs. 1 and 2). Some of these terminations lie close to the cell, within the perineural space. Synaptic terminations, including those located at interdendritic bridges between cells, undergo enlargement. Many synaptic structures not apparently connected with cells or their processes ("tree" synaptic structures, according to the old terminology) are visible in the field of vision; many of these are also hypertrophied, and are located on the walls of capillaries (see Fig. 3). It may be concluded that all types of synaptic structures are affected; axosomatic, axodendritic, and axovasal, i. e., located at the walls of capillaries,

The morphological picture of the reactively modified synaptic terminations is distinguished by its lack of uniformity. The structures vary from barely perceptible enlargements and swellings of the synaptic loops to filled-in loops, many times greater than the original ones, and with indistinct contours. There are also a large number of intact synaptic structures.

Apart from the forms described, there are also more considerably modified synaptic structures; these have undergone transformations into swollen, mace-like forms (Fig. 4), or into plates of irregular shapes. These

synaptic terminations do not have a uniform structure. They contain vacuoles and granulations, their contours are irregular, and the perisynaptic fibers are split in places (see Figs. 1 and 2).

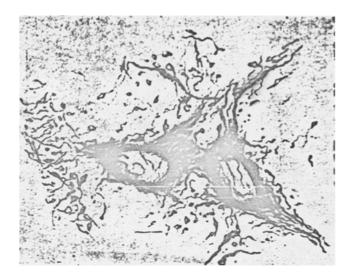


Fig. 1. Cervical segment of the spinal cord. Hypertrophied synaptic structures on the bodies of nerve cells and on their dendrices.

The synaptic structures seen to the left of the drawing are located on the walls of a capillary. Impregnated according to Golgi-Deinek. Oil immersion.

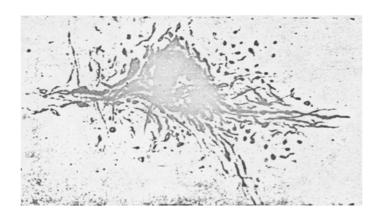


Fig. 2. Lumbar segment of the spinal cord. Hypertrophied synaptic structures on the body and the processes of a nerve cell. Impregnated according to Golgi-Deinek. Oil immersion.

It cannot be maintained that the above changes in synaptic structures are specific effects of radiation damage to the nervous system. It is known that the nervous system reacts fairly uniformly to different pathologically inadequate stimuli. Similar, although less pronounced, changes in synaptic structures at nerve cells of the spinal cord of cats, following ligation of the portal vein, have been described by B. A. Dolgo-Saburov [5].

The reactively modified synaptic structures represent an adaptive reaction. The neuron, of course, reacts as a unit to any agents acting on it, but the visible structural changes are evidently most readily observed

at its terminations (receptors, pericellular apparatuses, synaptic formations at cells of the central nervous system).

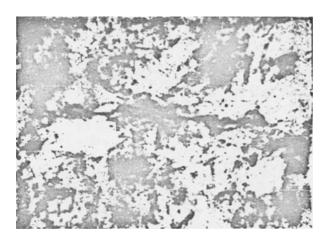


Fig. 3. Cervical segment of the spinal cord. Hypertrophied axovasel terminations on the wall of a blood capillary. Photomicrograph. Impregnated according to Golgi-Deinek. Oil immersion.

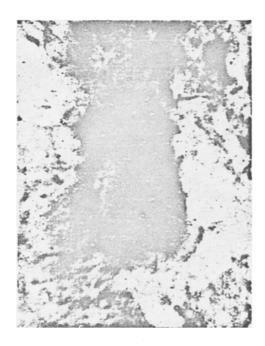


Fig. 4. Cervical someont of the spinal cord. Two very enlarged synaptic terminations, in the form of plates (one of them with a pre-synaptic fiber), may be seen at the upper end of the cell, at its axon root. Photomicrograph. Impregnated according to Golgi-Deinek. Oil immersion.

Apparently different parts of a neuron vary in their morphophysiological properties. This conclusion may be drawn from published data [8, 10, 11] and from the results of our experiments. The presence of intact synaptic structures side by side with reactively changed ones is striking evidence of the plasticity of the nervous system, which is responsible for maintaining the level of vital processes at the optimum for the given conditions.

The significance of our results is that they provide further support for the views of those authors who hold that the nervous system is highly sensitive to penetrating radiation. Apart from changes in the nerve cell bodies and their processes (which were observed by us), the greatest interest attaches to our findings on the reactivity of synaptic structures, to which there are very few references in the literature. It is known, for example, that irradiation of different parts of the central nervous system causes inhibition or stimulation of their activity, according to the dosage given [14].

These processes cannot proceed without the participation of the synapses, which connect one neuron with another. The changed synaptic structures may possibly interfere with proper functioning of reflex arcs, thus causing localized and generalized disturbances.

SUMMARY

Various changes were observed in synaptic structures following irradiation in the dose of 450 to 600 r. These structures were changed from delicate rings into button-like, mace-like structures and nodules of large size. All types of synaptic structures are subjected to hypertrophy—axosomatic, axodendritic and axovasal. However, there is a considerable number of synaptic structures which remain intact. This points to the high plasticity of the nervous system. Changed synaptic structures, probably, cause alteration of reflexes with ensuing local and general disturbances.

LITERATURE CITED

- [1] E. I. Bakin, Vesmik Rentgenol, i Radiol., No. 3, 3-8 (1951).
- [2] A. G. Beglaryan, K. A. Kyandaryan and S. A. Papoyan, Proc. Transcaucasian Radiol. Congress, pp. 27-32 (Tbilisi, 1955).
 - [3] A. M. Gorovits, Biological Significance of Radium Rays, St. Petersburg, 1906.
 - [4] B. A. Dolgo-Saburov, Zhur. Vysshei Nerv. Deyatel., 4, No. 6, 903-908 (1954).
 - [5] B. A. Dolgo-Saburov, Doklady Akad. Nauk SSSR, 103, No. 3, 521-524 (1955).
 - [6] V. V. Esimov, Biophysics for Medical Practitioners, Moscow, 1952.
 - [7] A. D. Zurabashvili, Synapses and Reversible Changes in Nerve Cells, Moscow, 1951).
- [8] A. D. Zurabashvili and B. R. Naneishvili. Contributions to the Patho-architectonics of Radiation Sickness, Tbilist. 1956.
- [9] N. A. Kraevsky, Transactions All-Union Congress of Pathological Anatomists, July 4-9, 1954, pp. 318-328. Moscow, 1956.
 - [10] V. V. Kupriyanov, Doklady Akad. Nauk SSSR, 106, No. 5, 921-922 (1956). **
 - [11] V. V. Kupriyanov, Transactions Naval Med. Acad., 4, 45-61 (Leningrad, 1956).
 - [12] N. N. Lifshits, Transactions, Congress of Biochem, of the Nervous System, pp. 36-37. Klev, 1953.
- [13] F. P. Maiorov, M. I. Nemenov and L. S. Vasileva, Transactions, Jubilee Sci. Session Celebrating the Centenary of the Birth of I. P. Pavlov, pp. 85-86 (Moscow, 1949).
 - [14] P. F. Minaev, Doklady Akad, Nauk SSSR, 95, No. 3, 693-696 (1954).
- [15] P. F. Minaev, Session of the AN SSSR on the Peaceful Uses of Atomic Energy, July 1-5, 1955. Meetings of the Division of Biol. Sci., pp. 51-67 (Moscow, 1955).
 - [16] M. I. Nemenov, Rentgenotherapy Mediated through the Nervous System.* Leningrad, 1950.

[•] In Russian

^{••} Original Russian pagination. See C.B. Translation.

- [17] V. V. Portugalov, Transactions, All-Union Congress of Pathological Anatomists, July 4-9, 1954, pp. 328-332 Moscow, 1956.
 - [18] B. N. Tarusov, Principles of Biological Action of Radioactive Radiations, Moscow, 1954.
 - [19] L. R. Tarkhanov, Izvest, St. Petersburg. Biol. Lab., 3, 47-52 (1896).
 - [20] I. R. Tarkhanov, Botkin Hospital Gazette, No. 33, 753-757 (1896); No. 34, 785-791 (1896);
 - [21] D. G. Shefer, X-Rays and the Central Nervous System, Rostov-on-Don, 1936.
 - [22] A. Arnold, P. Bailey, R. A. Harvey, L. L. Haas, J. S. Langhlin, Radiology, 1954, v. 62, N. 1, p. 37-46.
 - [23] A. Arnold, P. Bailey, Arch. pathol., 1954, v. 57, N. 5, p. 383-391.
 - [24] P. Krause, K. Ziegler, Fortschritte a. d. Geb. d. Rontgenstrahlen, 1906, Bd. 10, S. 126-182.
 - [25] R. Liman, P. Kupalov, and W. Scholz, Arch. Neurol. a. Psych., 1933, v. 29, p. 57-87.
 - [26] D. S. Russel, C. W. Wilson, and K. V. Tansler, Neurol., Neurosurg., Psych., 1949, v. 12, p. 187-195.
 - [27] M. Sicard and W. Bauer, Rev. Neuroi., 1907, v. 15, p. 903-903.

^{*} In Russian.