THE SIGNIFICANCE OF OVEREXCITATION OF THE CENTRAL NERVOUS SYSTEM IN THE GENESIS OF EXPERIMENTAL HYPERTENSIVE STROKE

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In previous investigations, it was established that in a portion (up to 15%) of intact rats that are highly sensitive to the sound of a bell (a line developed in the laboratory under the direction of Prof. L. V. Krushinskii), a fatal brain damage occurs in the setting of marked central nervous system excitation, caused by an intense, bell-ringing stimulus [6, 7]. It was also noted that in animals with hyperthyroidism, having a higher blood pressure level, the cerebral hemorrhages, with their lethal outcome, develop significantly more frequently than in the normal animals [1, 8]. Nonfatal brain hemorrhages were observed in rats with experimental renal hypertension [2, 3].

EXPERIMENTAL METHOD

In the experiment we used white rats, highly sensitive to the bell stimulus, with experimental renal hypertension, caused by the method of measured narrowing of one or both renal arteries, using metal spirals [5]. Functional trauma of the central nervous system was caused by prolonged (up to 20 minutes) action of a discontinuous electric bell [7].

The control consisted of animals in which the same surgical procedure was carried out, except without narrowing the renal arteries.

The arterial systolic pressure was determined in the caudal artery, using the platysmometric method [4].

A total of 74 rats were used in the experiment (37 with hypertension and 37 controls), ranging from 3 to 12 months in age.

EXPERIMENTAL RESULTS

The mean level of the arterial pressure in the rats with hypertension, prior to the action of the bell stimulus on the nervous system, was 160.2 mm, while in the controls—98.9 mm.

As a result of overexcitation of the central nervous system by the action of the bell stimulus, lethal brain hemorrhages, at different sites, arose in 27% of the experimental animals and 5.4% of the controls (Table 1). Most frequently, we observed extensive hemorrhages into the subarachnoid space, into the tissue, and into the ventricles of the brain (Fig. 1 and 2). The animals died immediately, or 2—5 minutes after termination of the exposure to the bell stimulus.

In the animals that died the starting arterial pressure, as a rule, was somewhat higher than in those that survived.

With the same starting level of arterial pressure, we observed fatal outcomes as a result of overexcitation of the central nervous system in animals with two ischemic kidneys more than twice as often as in animals with a single ischemic kidney (see Table 1). These data testify to the role of extensive ischemia of the kidneys as a factor predisposing to hemorrhages.

TABLE 1. Frequency of Lethal Brain Hemorrhages Arising as a Result of Marked Excitation of the Central Nervous System by Intense Bell Stimuli, in Rats with Hypertension and in Controls

Animals	Index	Rats with hypertension			Control rats		
		total	with a narrowed artery		total	prepared artery	
			on one side	on both sides		on one side	on both sides
Died	Number of Animals	10(27)*	4(18)†	6(40)†	2(5.4)*	2(9.5)†	–
	Arterial pressure ‡	164.3	160.7	169.7	100.5	100.5	–
Survived	Number of Animals	27			35		
	Arterial pressure‡	158.8			98.7		
Total	Number of Animals	37	22	15	37	21	16
	Arterial pressure‡	160.2	161.2	158.7	98.9	101.4	95.6

*The percent of the total number of animals used in the experiment is shown in parentheses

†The percent of the number of animals in this group used in the experiment is shown in parenthesis

‡Mean data for the arterial pressure is presented in millimeters of mercury

The level of arterial pressure in 26 of the 27 surviving rats with hypertension, and in 32 of the 35 surviving control rats, decreased by the end of the experiment with application of the bell trauma; in one of the surviving rats with hypertension, and in 3 of the surviving control rats, the arterial pressure rose.

The decrease in arterial pressure in the rats with hypertension was more intense than in the controls (in the former, by 47.7 mm; in the latter, by 34 mm). Due to their rapid death, it was not possible to determine the changes in arterial pressure.

It should be noted that in all the animals that died of brain hemorrhages (in the experimental and control groups), the excitability of the nervous system, as judged from the latent period of the motor reaction to the bell stimulus on its initiation, was always higher than in the animals that survived. The duration of the latent period in the rats that died was approximately half that in the surviving animals. This permits postulating that the level of excitability of the brain structures responsible for the motor reaction, under conditions of overexcitation of the central nervous system, is specifically related to the occurrence of brain hemorrhages. However, this factor by itself does not play a decisive role in the development of experimental hypertensive stroke since with almost the same, or even a somewhat lower, excitability of the central nervous system in rats with hypertension, as compared with the controls (Table 2),

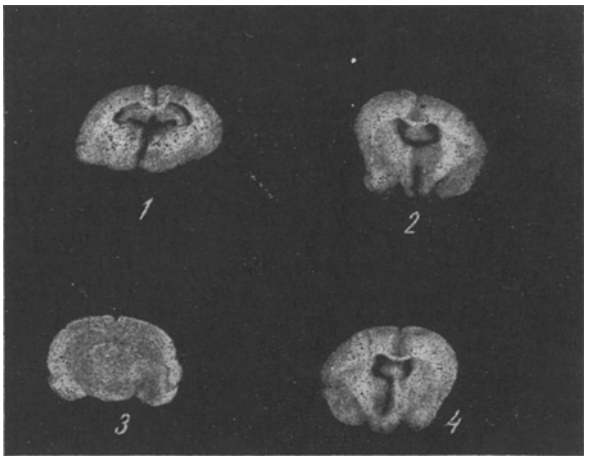

Fig. 1. Brain of a rat with hemorrhage in the ventricles, arising from marked excitation of the central nervous system (1, 2, 4), and the brain of a control rat (3).

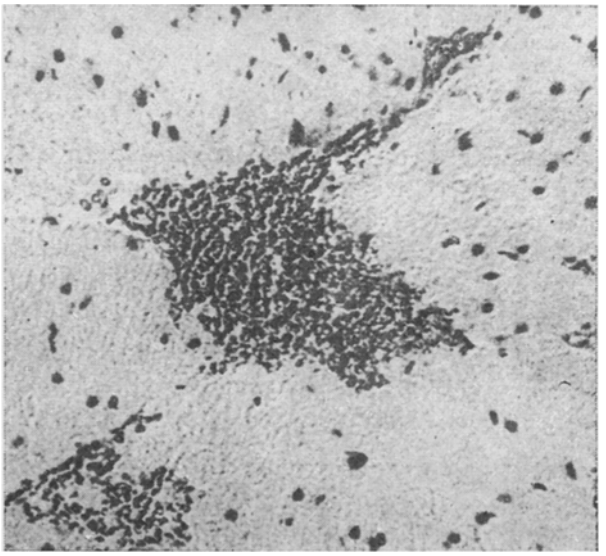

Fig. 2. Hemorrhage into the brain tissue. Microphotograph.

TABLE 2. Latent Period for the Motor Reaction of the Rats

	Animals	Number studied	Latent period (in sec)
Survived	with hypertension	25	6.6
	control	35	4.7
Died	with hypertension	10	2.7
	control	2	2.5
Total	with hypertension	35	5.4
	control	37	4.6

brain hemorrhages with lethal outcome were encountered in the former group approximately 5 times more often than in the latter. In all animals that died of brain hemorrhages, and in a portion of the surviving rats (both hypertensive and control), motor disturbances were noted during the period of action of the discontinuous bell stimulus—pareses, paralyses, disturbances in coordination of movements (Fig. 3), and also pronounced adynamia, which appeared in the hypertensive rats twice as frequently (40%) as in the controls (20%).

Thus, in the development of experimental hypertensive stroke, the following factors are of major significance: 1) the starting excitability of the central nervous system, particularly the structures determining the given motor reaction; 2) the total intensity of ischemia of both kidneys (the amount of ischemic kidney tissue); 3) the starting level of arterial pressure [8].

Fig. 3. Paralysis of the anterior paws in a rat, associated with the hypertensive condition.

Functional overexcitation of the central nervous system may play the role of the initial factor in the development of experimental hypertensive stroke; in this case, brain hemorrhages with fatal outcome arise in 27% of the animals. The latter fact, in essence, indicates the creation of a functional model for experimental hypertensive stroke.

SUMMARY

Experiments were conducted on 74 albino rats, highly sensitive to the bell (37 with renal hypertension and 37—control). In the development of experimental hypertensive stroke of great significance are: the initial excitation of the CNS (particularly of the structures determining the data of motor reaction); intensity of ischemization of both kidneys (the extent of the renal tissue ischemization), the initial blood pressure level (which coincides with Steshenko's observations—8). The role of the initial factor in the development of experimental hypertensive stroke may be played by the functional overexcitation of the CNS; fatal cerebral strokes occur in such cases in 27 percent of the animals. The latter circumstance indicates that a functional model of experimental hypertensive stroke has been created.

LITERATURE CITED

1. L. P. Dobrokhotova, The Role of the Thyroid Gland in the Development of Hemorrhagic Shock States, Avtoref. diss. kand., Moscow (1958).
2. A. Kh. Kogan, The Significance of Pregnancy in the Development of Experimental Renal Hypertension, Diss. kand., Moscow (1950).
3. A. Kh. Kogan, Arkh. pat., No. 2 (1952), p. 63.
4. A. Kh. Kogan, Byull. éksper. biol., No. 10 (1959), p. 109.
5. A. Kh. Kogan, Byull. éksper. biol., No. 1 (1961), p. 112.
6. L. V. Krushinskii, L. P. Pushkarskaya, and L. N. Molodkina, Vestn. Moskovsk. un-ta, No. 12 (1953), p. 25.
7. L. V. Krushinskii, The Formation of Animal Behavior Under Normal and Pathological Conditions [in Russian], Moscow (1960).
8. A. P. Steshenko, An Investigation of the Physiological Mechansims of Neurogenic Shock. Avtoref. diss. kand., Moscow (1960).