INTERACTION BETWEEN NEUROGENIC AND RENAL FACTORS IN THE PATHOGENESIS OF HYPERTENSION

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According to the theory of G. F. Lang and A. L. Myasnikov [3, 4], the neurogenic factor plays the leading role in the origin of hypertensive disease, although other factors predisposing to this disease are also very important in the development of hypertension.

Among these factors, transient diseases of the kidneys are especially important for the etiology of essential hypertension. The interconnection between renal pressor factors and the neurogenic mechanism has received little study and is unexplained.

Because of the important role of the kidneys in the development of essential hypertension, it was considered that this problem should be studied further.

The object of the present investigation was to study the development of neurogenic hypertension in animals with pre-existing kidney disturbances.

The most intensively studied method of obtaining experimental renal hypertension is the method of constricting the renal arteries or injuring the kidney tissue. At the same time, it has been found that after constriction of one renal artery or injury to one kidney, the arterial pressure in the animals does not always rise, or it rises only for a short time, and only occasionally does it remain permanently elevated in individual animals.

EXPERIMENTAL METHOD

Experiments were carried out on 78 rats, divided into seven groups. Of the 4 experimental groups (with 12 rats in each), in the rats of groups 1, 2, and 3 a unilateral injury to the kidneys was first produced, and group 4 consisted of rats with intact kidneys. The animals of all these groups were later exposed to neurogenic stress.

In the 3 control groups (with 10 rats in each) the results of various procedures carried out on one kidney were observed for 5-6 months.

Ischemia of the kidney tissue in experimental group 1 and the control groups of rats was produced by application of a coil of wire to constrict the right renal artery by A. Kh. Kogan's modification [1, 2] of Goldblatt's method [7]. With the same aim, in the animals of the 2nd experimental and control groups the right kidney was wrapped in cellophane by Page's method [9], and in the 3rd experimental and control groups a figure-of-8 ligature was applied to the right kidney by the method suggested by Grollman [8].

EXPERIMENTAL RESULTS

In most of the rats the arterial pressure was raised temporarily to a varied degree. As a rule this hypertension was moderate—not more than by 30-35 mm—and of short duration (Table 1).

The pressure rose slowly, starting approximately at the end of the 1st week after the operation, and it reached its maximum usually in the course of the next 10-15 days; in individual cases the hypertension continued for 4 weeks. No significant differences were observed in the value of this hypertension in the animals of the three experimental groups. The mean data for the 1st and 2nd months after the operation on the rats of the experimental groups and the mean data for the rats of the control groups 5-6 months after the operation are given in Table 1.

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TABLE 1. Arterial Pressure (in mm) after Unilateral Injury to the Kidneys in Rats of Various Groups

Group of rats	Normal value before operation	Method of injury to kidney	After operation					
			1st month	2nd month	3rd month	4th month	5th month	6th month
Experimental animals								
1	93,8±2,2	Goldblatt's	109,2±4,4	97,1±2,3				
2	94,6±1,7	Page's	112,6±2,06	93,6±2,06				
3	90,3±1,9	Grollman's	107,4±4,9	102,5±4,3				
Control animals								
1	97,3±1,3	Goldblatt's	113,2±9,0	110,3±2,6	101,2±1,9	96,4±1,3	98±1,7	99±1,6
2	100,3±1,4	Page's	125,7±9,7	107,5±10,5	97,1±2,7	94,7±2,1	91±2,9	91±2,4
3	90,7±1,3	Grollman's	99,9±3,1	91,9±2,0	94,07±0,8	94,2±2,5	94,2±2,7	—

After a short time had elapsed (2 months after the operation), when the arterial pressure in the experimental animals had returned to normal, all these rats and also the rats of experimental group 4, in which no manipulations were carried out on the kidneys, were exposed to a strictly measured neurogenic agent, identical in strength for all groups. For this purpose the rats were placed in specially constructed cages, the floors and walls of which were made of drawn metal (stainless steel) wire, so that strong acoustic stimuli (a loud bell or 85 dB, 1000 cps) could be combined with periodic, brief pulses of electric current (140 V). This led to the formation of a conditioned motor-defensive reflex.

By means of a special automatic device, the application of the stimuli could be repeated many times in the following order: action of the bell in isolation for 30 sec and together with 3 brief pulses of electric current for 3 sec, followed by a pause of 30 sec. The total duration of the session was 3-4 h, and it was repeated daily or every other day for 3 months.

Hence, the rats were exposed to the action of a strong acoustic stimulus, as shown above, while at the same time the nervous processes were overstrained, with development of a "conflict" in the sphere of the conditioned defensive reflexes. This conflict was brought about by the periodic extinction and restoration of the conditioned defensive reflex by I. P. Pavlov's method.

The maximal arterial pressure was measured by the method of Williams and co-workers [10], modified by A. Kh. Kogan [2], twice or three times a week for 2 months before the beginning of the experiments (control period), during them, and also after the cessation of the exposure to the neurogenic stimuli. Simultaneous observations were made on the animals' weight and general behavior.

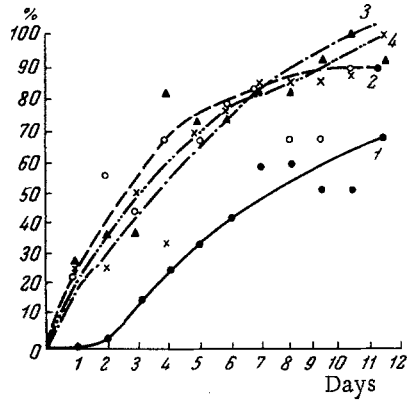
The maximal arterial pressure was measured in 147 healthy rats of different weights (the weight of the animals varied from 120-130 to 400-430 g) for a period of 1.5 years. The observations on the healthy rats lasted 1-5 months. The maximal arterial pressure in normal conditions was on the average 95±1.6 mm. In some healthy animals it was constantly higher than 140 mm or lower than 65 mm. Such rats were not used in the experiments.

At the beginning of neurogenic stimulation, the rats were very restless, running about the cage and trying to force their way out.

After 10-15 days the severe motor excitation was temporarily replaced by the development of a state of inhibition, during which the animals sat motionless in the cage and reacted weakly to the application of the conditioned and unconditioned stimuli (the motor components of the conditioned and unconditioned reactions are implied). The posture characteristic of the state of inhibition was observed in these circumstances—downward flexion of the head and curling the body into a ball. The animals sometimes remained in this state throughout the experiment. In such cases, however, after the experimental session had ended the rats' behavior showed a transition from a depressed state to one of marked excitation—they jumped on one another, squeaked and bit. These changes in the animals' behavior indicated the development of a neurotic state.

TABLE 2. Mean Increase of Arterial Pressure (in mm) in Experimental Rats during Neurogenic Stress, for Each Week

Group of animals	Method of injury to kidneys	Increase of arterial pressure
1	Goldblatt's	24,92±2,0
2	Page's	21,52±1,21
3	Grollman's	24,37±1,07
4	Rats with intact kidneys	15,14±0,94



Rate of development of neurogenic hypertension. Methods of injury to kidneys: 2) Goldblatt's; 3) Page's; 4) Grollman's. 1) Control.

Systematic measurement of the arterial pressure revealed the gradual development of a hypertensive state in the rats of group 4, starting from the 3rd week after the beginning of neurogenic stress, whereas in the rats with renal injuries, i.e., in groups 1, 2, and 3, there was a tendency for the arterial pressure to rise at the end of the 1st week.

Meanwhile, significant differences were observed in the rate and degree of development of hypertension between the group of rats with intact kidneys and the three groups of animals in which the procedures described above had been carried out on one of the kidneys.

It is clear from these results that in the rats previously subjected to unilateral injury to the kidneys, accompanied by a transient elevation of the arterial pressure, and then subsequently exposed to neurogenic stress, a tendency appeared for the arterial pressure to rise actually in the 1st week; in the rats with intact kidneys, on the other hand, this tendency was not seen until the 3rd week (see figure).

In addition, the level of the arterial pressure in the rats with the intact kidneys was always lower during stress and after cessation of action of the neurogenic factor than in the animals with unilateral injury to the kidneys.

Table 2 shows that the mean rise in the arterial pressure during each week in the rats with the intact kidneys was appreciably less than in the remainder ($P < 0.05$); no significant differences were found in this respect between the three groups with injured kidneys.

The author's previous investigation showed that patients with transient diseases of the kidney suffer from essential hypertension more often than the other inhabitants of Moscow. The results of the present experiments are in agreement with the clinical observations.

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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 the first issue of this year.