SYMPATHETIC NEURONS IN THE SUPERIOR CERVICAL GANGLION ARE MORE NUMEROUS IN SHR AND WISTAR-KYOTO RATS THAN IN WISTAR RATS

I. M. Rodionov, V. N. Yarygin,
Kh. M. Markov, V. G. Pinelis,
F. K. Lakgueva, O. S. Tarasova,
I. A. Sokolova, T. P. Storozhevykh,
and V. B. Koshelev

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One of the leading factors in the raised blood pressure (BP) of spontaneously hypertensive rats (SHR) of the Okamoto-Aoki strain is increased activity of the sympathetic nervous system [7]. There is not only electrophysiological evidence of increased activity in the renal, splanchnic, and cervical sympathetic nerves in SHR [10], but also morphological evidence of hyperfunction of sympathetic ganglia. An increase in volume of the celiac ganglion, in the diameter of the neurons, and of their nuclei has been found [3] in SHR aged 8 weeks. Neurons of SHR rats are more resistant to chemical desympathization than neurons of Wistar rats [2, 9]. Autoradiography using ^{3}H-lysine has revealed increased protein biosynthesis in superior cervical and stellate ganglia of newborn SHR, compared with Wistar–Kyoto (WKY) rats [11]. All these features are regarded as the result of increased functional activity of nerve cells [3]. We have suggested that not only hypertrophy of neurons, but also an increase in their total number are found in sympathetic ganglia of SHR. The investigation described below was conducted to test this hypothesis.

EXPERIMENTAL METHOD

Male rats of three lines were used: normotensive Wistar (WR), WKY, and SHR, aged from 8 to 10 months. The animals were killed, the right and left superior cervical sympathetic ganglia (SCSG) were removed and fixed in Carnoy's fluid for 1 h in the cold and, after appropriate histological treatment, they were embedded in paraffin wax. Serial sections were cut 8 μ thick, oriented parallel to the long axis of the ganglion, and these were stained with Carazzi's hematoxylin. All nerve cells in which the nucleus was distinctly outlined were counted in every fifth section. The total number of nerve cells in all sections taken for analysis from a given ganglion was used as an indicator of the number of neurons in it. The neurons were counted by four independent workers by a blind method.

In another series rats of these three strains were tested for resistance to hypobaric hypoxia by a modified method [1]. Each animal was "raised" for 1 min to an altitude of 12,000 m and the time until the second agonal inspiration (t_1) was measured [1]. After descent in 1 min from the "high altitude" the time until restoration of posture (t_2) was measured. Resistance to hypoxia was assessed according to the value of t_1/t_2..

Department of Physiology of Man and Animals, Faculty of Biology, Moscow University. Laboratory of Pathophysiology, Research Institue of Pediatrics, Academy of Medical Sciences of the USSR. Department of General Biology, N. I. Pirogov Second Moscow Medical Institute.
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TABLE 1. Number of Neurons in SCSG and Resistance to Hypoxia in WR, WKY, and SHR Rats (M ± m)

Parameters	Strain of animals		
	WR	WKY	SHR
Number of neurons counted in ganglion	6357±402	8991±746*	7718±507*
n	5	5	9
Criterion of resistance to hypoxia (t_1/t_2)	5,05±2,1	18,2±6,1*	15,2±4,1*
n	18	18	27

Legend. n) Number of animals. *$p < 0.05$ compared with WR rats.

EXPERIMENTAL RESULTS

The systolic BP in the group of WR rats was 110 ± 3.4 mm Hg, in the WKY rats 117.0 ± 2.3, and in SHR rats 194 ± 4.3 mm Hg. No significant differences were found in the number of neurons between the right and left ganglia taken from the same animal, in each of these groups, and accordingly when the mean parameters were calculated, data obtained on both right and left ganglia were used. During analysis of interlinear differences, data for 10, 10, and 18 ganglia respectively were averaged (Table 1). The number of neurons in SCSG of SHR animals was greater than in WR rats, but the number of sympathetic neurons in normotensive WKY rats also was significantly greater than in the WR animals (Table 1). No statistically significant differences in the number of cells were found between SHR and WKY rats. The increased number of neurons in the ganglion evidently simply provides a basis for the raised BP, but it is not sufficient itself to cause the development of arterial hypertension.

Hyperplasia of the cranial cervical sympathetic ganglia is thus a reality in SHR, but these differences are not linked with arterial hypertension, but present genetic differences between inbred lines SHR and WKY. It has repeatedly been stated in the literature that in the pathogenesis of arterial hypertension, only their genetic precursors, namely WKY rats, can be used as an adequate control for SHR [7, 12]. We know that behavioral reactions, the distribution of the cardiac output to different organs, and other parameters of the hemodynamics in WKY rats differ from those in rats of other normotensive lines: WR and Sprague–Dawley [5, 6]. We have established yet another difference between WR and WKY lines: differences in the number of neurons in SCSG.

Neurons of SCSG have been shown [14] to exert a trophic influence on the thickness of the media of small cerebral arteries, especially those with a lumen of under 100 μ. It is interesting that the ratio of the media to the internal radius is greater in arterioles of the brain with a lumen of under 50 μ in WKY than in WR rats [12]. An increase in the ratio of the media to the internal radius in WKY rats cannot be explained by an increase of intravascular pressure, as in SHR. Hypertrophy of the media in the arterioles in this case is based on genetic features of WKY rats. Since the trophic influence of the sympathetic nervous system on blood vessel walls is well known, it can be tentatively suggested that the number of neurons in the ganglion plays a definite role in hypertrophy of the arterioles in WKY rats.

Besides the number of neurons in SCSG, we also found similar differences between the different lines with respect to yet another parameter, namely resistance to hypoxia, which was greater in SHR and WKY than in WR rats. It must be emphasized that assessment of resistance to hypoxia is a fairly sensitive method of analysis of interlinear differences. This criterion can be used to detect even population differences within the same Sprague-Dawley strain [11]. According to this criterion [1], the longer an animal can exist under conditions of extremal hypoxia, and the faster its subsequent recovery takes place under normoxic conditions, i.e., the greater the ratio t_1/t_2, the more resistant the animal is to hypoxia. It will be clear from Table 1 that resistance to hypoxia in SHR and WKY rats is significantly higher than in WR animals. Since we know that the sympathetic nervous sytem and its cranial cervical ganglia affect the resistance of rats to high altitude hypoxia [4], it can be tentatively suggested that the increase in resistance of SHR and WKY rats to hypoxia may be con-

nected with hyperplasia of the neurons in SCSG. Consequently, the greater resistance of SHR than of WR rats to hypoxia, described in the literature [8] is not necessarily linked with arterial hypertension, but is due to genetic differences between SHR and WKY lines of rats.

The interlinear differences discovered between WR rats, on the one hand, and SHR and WKY on the other, are further confirmation that when spontaneous hypertension is studied, not simply normotensive rats can be used as an adequate control, but their genetic precursors, i.e., WKY rats.

There is no doubt that WKY rats differ from WR. In the WKY line there are evidently genetically determined features by which they resemble SHR rats, and which are essential but not sufficient to cause the development of a raised BP. On the basis of the facts described above it can be tentatively suggested that one of these features is an increased number of cells in the sympathetic ganglia (possibly creating a basis for hyperactivity of the sympathetic nervous system). Clearly, however, there exist certain other factors determining the development of arterial hypertension besides the number and size of cells in the ganglia of the sympathetic system.

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