lease in an atherosclerotic plaque as well as formation of autoimmune complexes *in situ* require further investigations.

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State of the Myocardium in Rats of a New Hypertensive Strain

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Study of the heart in a new strain of rats with hereditary stress-induced hypertension (NISAG) reveals a complex of structural and functional changes which are analogous to the manifestations of essential hypertension. These changes are shown to be adaptive-compensatory in nature and indicative of limited functional reserves of the hypertrophic myocardium.

Key Words: *arterial hypertension; stress; myocardium; hormones; electrolytes*

The role of emotional stress in the development of hypertensive reactions has been extensively studied [3]. It was hypothesized that hereditary predisposition largely contributes to the etiology and pathogenesis of essential hypertension. However, there are no data on the interaction between the hereditary factor and stress in the realization of potential pathology.

Recently, a new strain of rats with hereditary stress-induced arterial hypertension (NISAG) has been obtained at the Institute of Cytology and Genetics (Siberian Division of the Russian Academy of Sciences) [10]. These rats are characterized by high sensitivity to stress. The information regarding NISAG rats can be found in the literature [2,4,6]; however, no complex morphological and functional studies have been performed.

Our objective was to study structural and functional organization of the myocardium as the target organ in hereditary stress-induced arterial hypertension and to prove the adequacy of this experimental model for studying the role of the relationship between genotype and environment in the etiology and pathogenesis of essential hypertension.

MATERIALS AND METHODS

Experiments were carried out on six 6-month-old male NISAG rats (35th generation) weighing 370± 25 g. Normotensive male Wistar rats of the same age and weight served as the control. Morphological study was performed at the tissue, cellular, and subcellular levels. Cardiomyocytes (CMC) and stroma were studied by histomorphometric analysis [1]. Electron microscopy and stereomorphometry of

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TABLE 1. Comparative Morphometric Characteristics of the Myocardium in Wistar and NISAG rats (*M±m*)

Parameter	Wistar (*n*=5)	NISAG (*n*=6)
Diameter of CMC, μ	14.7±0.29	21.1±0.37*
Volume density of stroma, %	15.0±0.59	18.6±0.72*
Volume density of CMC, %	85.0±0.59	81.4±0.72*
Stroma/parenchyma volume ratio	0.179±0.01	0.234±0.01*
Numerical density of CMC profiles, mm^{-2}	5071±275	2405±311*
Diameter of arterial lumen, μ	21.7±1.65	12.5±0.80*
Thickness of arterial wall, μ	14.4±0.62	18.4±0.66*
Wall/lumen ratio	0.80±0.041	1.66±0.091*
Thickness of myofibrils, μ	3.3±0.07	4.0±0.08*
Mitochondria/myofibrils volume ratio	0.70±0.02	0.64±0.03
Sarcoplasmic reticulum/myofibrils volume ratio	0.094±0.01	0.124±0.01*

Note. *$p<0.01$; *n*: number of animals.

TABLE 2. Hormones and Electrolytes in Wistar and NISAG rats (*M±m*)

Parameter	Wistar (*n*=5)	NISAG (*n*=6)
Aldosterone, nmol/liter	1.0±0.15	1.5±0.02*
Insulin, μU/ml	29±1.3	14.5±3.4*
K, % of dry substance	1.5±0.005	0.7±0.003*
Na, % of dry substance	0.39±0.02	0.25±0.01*
Ca, % of dry substance	0.006±0.0008	0.002±0.0003*
Mg, % of dry substance	0.06±0.0003	0.08±0.0008*

Note. *$p<0.05$.

CMC were performed using conventional techniques. The intracellular contents of K, Na, Ca, and Mg were determined in dry heart tissue by plasma photometry. Cardiac function was evaluated by ECG. Concentrations of aldosterone (nmol/liter) and insulin (μU/ml) were determined by the radioimmunological method. Systolic arterial pressure (AP) was measured by the indirect method.

RESULTS

The mean AP in NISAG rats at rest exceeded that in control rats: 160±3.3 *vs.* 130±3.5 mm Hg, respectively.

A comparative histomorphometric study revealed structural changes in the heart of NISAG rats at various levels of organization: the mean diameter of CMC from the left ventricle was 1.5-fold greater, while the number of CMC per square unit of the myocardium was 2-fold lower than in Wistar rats (Table 1). Such a marked hypertrophy of muscle cells is consistent with the scheme of the development of left ventricle concentric hypertrophy [9]. This phenomenon was accompanied by thickening of the muscular layer and narrowing of intramural myocardial arteries, and consequently, by a higher wall/lumen ratio in comparison with the control (Table 1). Electron microscopy revealed ultrastructural alterations typical of activated plastic processes in CMC: thickened myofibrils, proportionally enlarged myofibrillar and mitochondrial apparatuses (judging from their unchanged ratio in enlarged CMC), increased volume of sarcoplasmic reticulum and its ratio to myofibrils (Table 1), and hyperplasia of membrane structures of the Golgi apparatus. These changes point to adaptive and compensatory rearrangement of the myocardium during the onset of hypertension [5].

Our findings correlate with the data on the myocardial electrolyte balance and plasma hormonal profile in hypertensive rats. In NISAG rats, the basal aldosterone level was considerably higher, while the insulin level was lower compared with the controls (Table 2). At the same time, the electrolyte balance (an important parameter of myocardial function) was impaired in these rats, which manifested itself as lowered K, Na, Ca, and Mg levels (Table 2). The low potassium content may indirectly reflect insufficient protein synthesis in hypertrophic heart [11]. A parallel and more pronounced decrease in the

Na content indicates, on the one hand, impaired ion transport and Na,K-ATPase function, and, on the other, can be considered as a compensatory reaction aimed at maintaining the myocardial contractile function [13]. This holds true for the decrease in the Ca level, since it can serve as an indirect criterion of myocardial energy supply under conditions of hypertrophy [8,12]. However, these changes are unlikely to be adaptive and adequate, since each of them modulates the levels of all the cations and gives rise to pathogenetic changes in electrophysiological and structural parameters of the myocardium [6].

In fact, structural adaptive-compensatory modifications in the myocardium of NISAG rats are accompanied by pathological shifts. For example, changes in the stroma/parenchyma ratio indicate increased proportion of the connective tissue in the myocardium, decreased numerical density of CMC (Table 1), and destructive-degenerative processes in CMC. These changes are attended by relative coronary insufficiency revealed by ECG (inversion of T_{aVR} and decreased amplitude of $T_{II,\ aVL,\ aVR}$) and may create conditions for the development of cardiopathy.

Thus, comparative morphophysiological study of the heart of NISAG and Wistar rats revealed structural and functional changes induced by elevated AP, which are adequate to the manifestations of essential hypertension. These changes are adaptive and compensatory in nature, as evidenced by electrolyte balance and hormonal profile, but point to exhaustion of functional reserves of the hypertrophic myocardium. Our findings suggest that the new strain of hypertensive rats provides a specific model of stress-induced arterial hypertension. This model is useful for evaluation of the role of interactions between genetic and environmental factors in the etiology and pathogenesis of essential hypertension and its correction.

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