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Activity of Angiotensin-Converting Enzyme in Hereditary Stress-Induced Arterial Hypertension

O. P. Cherkasova, V. I. Fedorov, and A. L. Markel'*

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We measured activity of angiotensin-converting enzyme in plasma and tissue of NISAG and normotensive WAG rats. In different organs of NISAG rats, activity of this enzyme did not differ from the corresponding values of WAG rats, although enzyme activity in the plasma of NISAG rats was significantly lower than that of WAG rats. Since NISAG rats are characterized by low activity of renin in the renal cortex, it is hypothesized that NISAG rats simulate the low-renin hypertension, in which inhibition of activity of the angiotensin-production system results from elevation of arterial pressure of central origin.

Key Words: *angiotensin-converting enzyme; stress-sensitive arterial hypertension*

Angiotensin-converting enzyme (ACE, dipeptidyl carboxypeptidase, EC 3.4.15.1) catalyzes production of vasoactive angiotensin II and promotes inactivation of vasodilator bradykinin, which explains its key role in the control of renin-angiotensin (RAS) and kallikrein-kinin systems actively involved in blood pressure regulation. The psychoemotional stress belongs to risk factors provoking the development of arterial hypertension. For studying of the effect of stress on the development of hypertension, an inbred rat strain with hereditary stress-induced hypertension (NISAG) was reared at the Institute of Cytology and Genetics. These rats are characterized by signs specific of essential hypertension in humans: left ventricular and arterial wall hypertrophy, morphological alterations of renal glomerular apparatus, and endocrine dysfunction such as enhancement of sympathoadrenal and adrenocortical reactivity [4].

The components of RAS (ACE included) were not examined comprehensively.

Institute of Laser Physics, *Institute of Cytology and Genetics, Siberian Division of the Russian Academy of Sciences, Novosibirsk. ***Address for correspondence:*** chrom@laser.nsc.ru. O. P. Cherkasova

More that 90% ACE is localized in various tissues and organs. The dominant role in the level of circulating ACE is played by the lungs [1]. ACE plays a significant role in the development of cardiovascular diseases and in the renal pathology [9].

Our aim was to compare ACE activity in blood plasma and various tissues in rats with hereditary stress-sensitive arterial hypertension and in control normotensive WAG rats.

MATERIALS AND METHODS

Experiments were carried out on mature (5-6 month) male rats of two inbred strains: hypertensive NISAG rats (body weight 290-320 g, blood pressure BP= 171±3 mm Hg) and normotensive WAG rats (body weight 270-290 g, BP=118±4 mm Hg) kept on balanced food and water *ad libitum* under standard vivarium conditions in Institute of Cytology and Genetics. Stress was modeled by placing the rats into tight cylindrical wire cages. Immediately after stress, the rats were decapitated. The blood was drawn and the following tissue specimens were isolated: cortical layer of the left kidney, left adrenal gland, the lower lobe

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TABLE 1. Effect of Stress on ACE Level in Blood Plasma and Tissue Specimens in Rats ($M \pm m$, n=8)

Strain and group		Blood plasma, nmol×ml^{-1}×min^{-1}	Tissue specimens, μM×g^{-1}×min^{-1}				
			lung	kidneys	adrenal glands	liver (10^{-3})	heart
WAG	control	84.44±7.02	7.21±1.01	0.318±0.079	0.138±0.010	41.00±3.79	0.110±0.008
	stress	102.71±6.42	6.60±0.81	0.357±0.094	0.166±0.031	37.40±6.63	0.123±0.017
NISAG	control	29.74±1.10*	6.03±0.39	0.402±0.051	0.132±0.022	44.9±3.3	0.085±0.038
	stress	36.78±3.10^{+}	11.09±2.19^{+}	0.405±0.094	0.142±0.033	44.60±1.27	0.087±0.020

Note. p<0.05 compared to *WAG and $^{+}$NISAG control rats.

of the left lung, heart, and liver. The blood and tissue specimens were processed routinely [6].

Activity of ACE in plasma and tissue specimens was determined by micro-HPLC [5]. The data were presented in concentration of hippuric acid produced over 1 min in 1 ml blood plasma (nmol×ml^{-1}×min^{-1}) or in 1 g tissue (μmol×g^{-1}×min^{-1}). The control groups comprised intact NISAG and WAG rats.

The data were processed statistically using Student's t test for small samples.

RESULTS

In WAG rats, initial activity of ACE in blood plasma coincided with published data for normotensive animals [11,13]. In NISAG rats, initial ACE activity coincided with the data obtained on spontaneously hypertensive rats (SHR) [14]. In NISAG rats, baseline ACE activity in the plasma was 2.8-fold lower than in WAG rats. In SHR, baseline ACE activity in the plasma was 2-fold lower than in normotensive rats [3,10]. Stress significantly increased ACE in NISAG rats, although it remained almost 2-fold below the corresponding value in intact WAG rats. ACE activity in stressed WAG rats tended to increase, but this effect was insignificant (Table 1).

In lung tissue of intact NISAG and WAG rats, ACE activity was virtually identical and coincided with published data [11]. Stress significantly increased ACE in NISAG rats, but produced no effect on this parameter in WAG rats.

No significant differences in the ACE level were found in the renal cortex of control and stressed NISAG and WAG rats, and the corresponding data coincided with the previous reports [10, 11].

The level of ACE was practically equal in the adrenal glands of intact NISAG and WAG rats. In both strains, stress slightly increased ACE activity. We found no data on ACE level in adrenal glands measured by a similar method. However, the ratio of ACE activity in adrenal glands and lung in our experiments coincided with that obtained by other method [12].

In the liver ACE activity was similar in NISAG and WAG rats, being significantly lower than in other tissues. In this organ, stress produced no significant effect on ACE level.

In the myocardium, ACE activity in intsct NISAG rats was lower than in intact WAG rats. Stress produced no effect on ACE level in the heart.

Thus, ACE activity in various organs was similar in NISAG and WAG rats, but plasma level of this enzyme was significantly lower in NISAG rats. Since activity of renin in renal cortex is low, it can be hypothesized that NISAG rats reproduces the low-renin type of arterial hypertension, where inhibition of the angiotensin-production system results from primary blood pressure elevation of central origin. This view is corroborated by changes in noradrenergic cerebral regulatory system in the rats of this strain, their stress reactivity [4], and low aldosterone level in the blood [8]. During stress, significant ACE activation in the lung and blood of NISAG rats can be related to pronounced up-regulation of corticosterone secretion [7], because glucocorticoids are the inducers of ACE synthesis in the lung tissue [2].

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