Effect of Sodium Intake on Brain Angiotensin-Converting Enzyme Activity in Spontaneously Hypertensive Rat

KENJI MIZUNO, MITSUHIRO GOTOH and SOITSU FUKUCHI

The Third Department of Internal Medicine, Fukushima Medical College, Fukushima 960

MIZUNO, K., GOTOH, M. and FUKUCHI, S. *Effect of Sodium Intake on Brain Angiotensin-Converting Enzyme Activity in Spontaneously Hypertensive Rat.* Tohoku J. exp. Med., 1981, 135 (2), 217-218 — The effect of sodium intake on angiotensin-converting enzyme activity in five areas of the brain (the cerebral cortex, midbrain, striatum, thalamus and hypothalamus) was studied in normotensive, spontaneously hypertensive and stroke-prone spontaneously hypertensive rats. The enzyme activity was significantly higher in the hypothalamus than in other areas of the brain of spontaneously hypertensive rats. Sodium intake resulted in a significant rise of the enzyme activity in the midbrain of spontaneously hypertensive rats and also in the midbrain and the striatum of stroke-prone spontaneously hypertensive rats. In normotensive rats, however, there was no significant difference in the enzyme activity in any area of brain between the control and the salt-treated group. It is likely therefore that a high circulating sodium level increases angiotensin-converting enzyme content of the brain in spontaneously hypertensive rats, and it is suggested that the increased converting-enzyme activity may play a role in development of hypertension induced by sodium loading. ——— angiotensin-converting enzyme activity; brain; sodium intake; spontaneously hypertensive rat

Angiotensin-converting enzyme, a peptidyl-dipeptide hydrolase, liberates the C terminal histidyl-leucine from angiotensin I, transforming it into the active octapeptide, angiotensin II. This enzyme has been extensively studied in peripheral tissues because of the importance of angiotensin II in hypertension (Cushman and Cheung 1971). On the other hand, there have been few papers dealing with the regional localization of the enzyme activity in the brain of spontaneously hypertensive rats. Furthermore, the effect of sodium intake on the enzyme activity of the brain is poorly described. The present study aims to clarify these points.

Female normotensive rats of the Wistar-Kyoto strain (WKY), spontaneously hypertensive rats (SHR) and stroke-prone SHR (SHRSP), aged 20-21 weeks, were used. Each of these rats was divided into two groups; a control group given stock chow containing 0.03 % NaCl (Oriental Co., Tokyo) and distilled water ad libitum, and an experimental group treated with 1.0% NaCl drinking solution for a period of 4 weeks. The rats were killed by decapitation, and the brains were separated into areas of the cerebral cortex, midbrain, striatum, thalamus and hypothalamus at 4°C. Each specimen was homogenized in 20 volumes of 0.01 M potassium phosphate buffer (pH 7.4) in a Potter-Elvehjem glass homogenizer. Angiotensin-converting enzyme activity in the homogenate from each area was measured by the spectrophotometric assay with hippurly-1-histidyl-1-leucine (Protein Research Foundation, Osaka) as substrate (Lieberman 1975). One unit of the enzyme activity was defined in terms of one nmole hippuric acid formed/min/mg of protein at

TABLE 1. *Effect of sodium intake on angiotensin-converting enzyme activity in the brain*

Brain area	Control rat			Salt-treated rat		
	WKY (n=10)	SHR (n=10)	SHRSP (n=10)	WKY (n=10)	SHR (n=15)	SHRSP (n=15)
Cerebral cortex	5.2±1.5	4.7±1.7	5.8±1.1	2.9±2.1	4.3±2.5	3.2±2.1
Midbrain	3.5±2.2	3.8±0.7	4.5±1.4	7.2±3.1	6.1±1.3†	8.2±2.7†
Striatum	5.5±3.1	4.6±2.1	3.9±1.5	6.6±1.8	5.1±2.2	13.2±2.9‡
Thalamus	6.5±3.7	2.8±0.9	1.3±1.2	6.1±2.9	2.2±1.4	1.7±0.4
Hypothalamus	4.9±3.3	10.4±2.6*	4.8±2.1	5.7±2.2	11.3±3.4	4.7±1.9

Each value is mean±s.e. for the rats. Numbers of rats are shown in parentheses.

Significance of differences: * $p<0.05$ as compared with the other areas of control SHR; † $p<0.05$, ‡ $p<0.01$ as compared with the control values.

37°C. The assay was performed in duplicate. Values are given as mean±s.e. Statistical analysis was performed with Student's *t*-test.

The results for the brain angiotensin-converting enzyme activity are summarized in Table 1. In control WKY, there was no significant difference in the enzyme activity among the five areas of the brain. In control SHRSP, the enzyme activity was relatively high (5.8±1.1 units) in the cerebral cortex, and was relatively low (1.3±1.2 units) in the thalamus. In control SHR, on the other hand, the enzyme activity in the hypothalamus was 10.4±2.6 units which was significantly higher than the values in the other areas of the brain ($p<0.05$). The enzyme activity in the midbrain of the salt-treated SHR and SHRSP was 6.1±1.3 and 8.2±2.7 units, respectively. These values were significantly higher than the corresponding values in the control rats. In the salt-treated SHRSP the enzyme activity of the striatum was also significantly higher than in the control rats. In WKY, however, there was no significant difference in enzyme activity of any area between the control and the salt-treated group.

The activity of the converting enzyme significantly increased in concomitant with an elevation of systemic blood pressure in SHR and SHRSP which were treated with salt, while the activity did not significantly change in WKY treated in the same manner. The sites where the enzyme activity significantly increased were the midbrain and the striatum. It seems likely that the enzyme production in such sites is especially sensitive to sodium in these hypertensive rats as compared with normotensive rats. Ganten et al. (1975) reported that the activated renin system in the brain might play a role in hypertension of SHR. The observed local enhancements of the converting enzyme activity may be involved in development of hypertension induced by sodium intake, through potentiating the conversion of angiotensin I into angiotensin II.

References

- 1) Cushman, D.W. & Cheung, H.S. (1971) Concentrations of angiotensin-converting enzyme in tissues of the rats. *Biochim. biophys. Acta*, **250**, 261–265.
- 2) Lieberman, J. (1975) Evaluation of serum angiotensin-converting-enzyme (ACE) level in sarcoidosis. *Amer. J. Med.*, **59**, 365–372.
- 3) Ganten, D., Hutchinson, J.S. & Shelling, P. (1975) The intrinsic brain iso-renin-angiotensin system in the rat: its possible role in central mechanism of blood pressure regulation. *Clin. Sci. mol. Med.*, **48**, 265s–268s.