Hypophyseal Function in SHR

Lysine Incorporation and ACTH Content

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Early morphological studies indicated that hypophyseal function in SHR was more active than that in normotensive controls (Okamoto, K ed: Spontaneous Hypertension, Springer-Igaku Shoin, New York, Berlin, Tokyo, 1972). Hypophyseal weight in SHR was proved to be increased, and this weight was closely correlated with blood pressure level in F₂ offspring obtained by SHR and normotensive Wistar rats (Yamori, Ooshima, and Okamoto: Jap Circulat J 36: 561, 1972). Moreover, recent studies on the hypophyseo-thyroidal axis in SHR indicated that TSH in the pituitary and blood was markedly increased with some reduction of T₃, T₄ level in the plasma, and that these increased TSH levels were not affected by increased plasma level of exogenous thyroid hormones (Kojima, Takahashi, Ohno, Sato, Yamada, Kubota, Yamori, and Okamoto: Proc Soc Exp Biol Med, 1975). In the present study we studied the ³H-lysine incorporation into the pituitary in SHR with or without hypertension to analyze the function, and we measured ACTH content by a radioimmunoassay technique to examine the function of the hypophyseo-adrenal axis.

Materials and Methods:

(1) Thirty SHR in the prehypertensive stage (at the age of 40 days) were divided into 3 groups: apresoline-treated rats (80 mg/L in the drink water), splanchnicotomized rats (splanchnicotomy plus mesenteric artery denervation), and nontreated rats. Eight Wistar-Kyoto (WK) rats were used as the normotensive controls in this study. On the 14th day of the experiment rats were sacrificed by decapitation 2 hours after ³H-lysine injection (0.4 μ C/Gm, i.v.). Pituitaries were homogenized and dialyzed to determine the radioactivity per mg protein of the dialysate by a scintillation counter. Or pituitaries solved in NCS solution (P₂) were counted for the radioactivity with the blood samples (B₂) collected at the sacrifice. Net pituitary incorporation (P) was calculated by correcting the counts by the radioactivity of pituitaries (Po) and blood (Bo) in the control group of rats, sacrificed immediately after ³H-lysine injection as follows: $P = P_2 - B_2 \times Po/Bo$, (2) Four and 6-month-old

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each group, stroke-prone SHR (SHRSP), stroke-resistant SHR (SHRSR), and WK, 5 in each group, were sacrificed without any pretreatment, or with dexamethasone (1 mg/Kg, i.p.) and nembutal (40 mg/Kg, i.p.) pretreatment, 2.5 and 1 hour prior to decapitation. Anterior lobes were immediately extirpated, weighed and homogenized in 1 ml of 0.05 N HCl, and the supernatant was kept frozen at -70°C until the radioimmunoassay of ACTH (Matsukura, West, Ichikawa, Jubiz, Harada, and Tyler: J Lab Clin Med 77: 490, 1971).

Results:

(1) Pituitary weights in SHRSP and SHRSR were significantly increased even at the age of 8 weeks in comparison with those in the age-matched WK. The weights of anterior lobes were also significantly increased in 4-month-old SHRSP and SHRSR. (2) ^3H -lysine incorporation into the pituitary was significantly increased in SHR at the age of 8 weeks, compared with that in WK. This increase was still marked in SHR without hypertension, that is, splanchnicotomized SHR and apresoline-treated SHR. However, the radioactivity per mg protein of the pituitary was not significantly increased in SHR. (3) ACTH content per pituitary was significantly increased in SHRSP compared with WK, but this increase was not noted when ACTH content per mg wet weight was compared. After dexamethasone pretreatment, ACTH contents per pituitary as well as per mg wet weight were decreased in SHRSP and SHRSR, but such a decrease was not noted in WK.

^3H -Lysine Incorporation into Pituitary in SHR

Experimental Groups (No. of rats)	SHR			Wistar-Kyoto
	Nontreated (10)	Apresoline- treated ⁺ (10)	Splanch- nicotomy (10)	Non-treated (8)
Blood pressure (mmHg)	168 ± 2	$136 \pm 3^{***}$	$136 \pm 3^{***}$	$131 \pm 2^{***}$
Pituitary weight (mg)	7.3 ± 0.4	7.6 ± 0.2	7.3 ± 0.3	$5.9 \pm 0.3^{**}$
Net ^3H -lysine incorporation (dpm/pituitary)	$1,555 \pm 58$	$1,869 \pm 55$	$1,853 \pm 110$	$1,164 \pm 76^{***}$

Mean $\pm$ S.E. *, **, ***: Significant differences from nontreated SHR ($p < 0.05, 0.01, 0.001$)

⁺: Apresoline treatment (80 mg/L in drinking water)

⁺⁺: Rats were sacrificed by decapitation 2 hours after ^3H -lysine ($0.4 \mu\text{Ci/Gm}$, i.v.) injection. Net pituitary counts were corrected by subtracting blood counts.

Summary with Discussion:

Pituitary weights were already increased in SHR at the young stage (8 weeks of age) compared with WK. The weights of anterior lobes were also increased at the age of 4 months. This increase in weight appeared to have

a functional significance as proved by the increased ^3H -lysine incorporation into the pituitary. As the prevention of the development of hypertension by apresoline treatment or by splanchnicotomy had no effect on the increased lysine-incorporation, the acceleration of such a metabolism did not seem to be the secondary phenomenon to hypertension, but was supposed to be a primary alteration in SHR. ACTH content in the pituitary was increased in pretreatment of dexamethasone, ACTH content was rather decreased in SHR. 4-month-old SHRSP compared with the age-matched WK. After the acute pretreatment of dexamethasone, ACTH content was rather decreased in SHR. This finding suggested one possibility that dexamethasone did not efficiently block ACTH secretion from the pituitary in SHR.

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