51) Effect of High Protein Diet on Cerebral Blood Flow and Cerebrovascular Reactivity in Rats. Ryoichi Horie*, Yukio Yamori°, Michiya Ohtaka°, Akira Ooshima° and Hajime Handa*. Japan Stroke Prevention Center, Department of Pathology, Shimane Medical University°, Izumo 693 and Department of Neurosurgery, Faculty of Medicine, Kyoto University*, Kyoto 606.

INTRODUCTION The successful establishment of Stroke-prone SHR (SHRSP) (OKAMOTO, K., YAMORI, Y. and NAGAOKA, A.: *Circ. Res.* 34 and 35 (suppl. 1):143, 1974) suggested the existence of some genetic factors for stroke indifferent to hypertensive genetic factors, and also made it possible to confirm great importance of hypertension in the development of cerebral stroke. As specific genetic factors for stroke were concerned, the qualitative difference in the degree of cerebrovascular permeability between SHRSP and stroke-resistant SHR (SHRSR) was first reported by YAMORI in 1978. And the first semi-quantitative evidence of an essential difference between SHRSP and SHRSR was obtained by YAMORI'S PREPARATION-II (HORIE, R. and YAMORI, Y.: *Jap. Heart J.*, 19(4), 1978). On the other hand, the importance of severe hypertension for stroke was also proven by prophylactic experiments (YAMORI, Y. and HORIE, R.: *Jap. Circ. J.*, 39:616, 1975) and successively the initiation mechanism of stroke was reported based on the experimental facts concerning severe hypertension and cortical cerebral blood flow (rCBF) (HORIE, R.: *Jap. Circ. J.*, 41:915, 1977), i.e., "severe hypertension in SHRSP causes functional reduction of rCBF, especially in the areas fed by recurrent branches from main cerebral arteries. Long-term duration of moderate ischemic hypoxia due to rCBF reduction results in increased cerebrovascular permeability. This then causes arterionecrosis which was regarded as a pathological finding common to cerebral bleeding and cerebral infarction." Further, emphasis has been placed on cerebrovascular reactivity (CVR) in the development of stroke (YAMORI, Y. and HORIE, R.: In factors influencing vascular reactivity, Igaku-Shoin, Tokyo, 1977) and the necessity of careful selection of drugs for long-term therapy of hypertension was reported from the view point of the effect of antihypertensive agents on cerebrovascular reactivity (HORIE, R., YAMORI, Y., OHTAKA, M., AKIGUCHI, I. and FUKASE, M.: *Stroke* 9:98, 1978), i.e., ideal antihypertensive agents maintain the normal range of rCBF by controlling blood pressure without reduction of cerebrovascular reactivity. For example, in contrast to such ideal antihypertensive agents, apresoline reduces cerebrovascular reactivity, although it maintains the normal range of rCBF.

On the other hand, prophylactic effect of high protein diet on stroke was reported (YAMORI, Y., HORIE, R., NARA, Y. and IKEDA, K.: *Jap. Heart J.*, 18:551, 1977).

In the present study, effect high protein diet on rCBF and CVR were investigated.

MATERIALS AND METHODS SHRSP used in this study were the F₄₄ generation of SHR maintained at Japan Stroke Prevention Center (Izumo, Japan) and controls were normotensive Wistar-Kyoto rats (WK). These male rats (including 12 WK and 34 SHRSP) were fed on various diets, i.e., normal laboratory stock diet, high protein diet (containing 50% of soybean protein) and high fat-cholesterol (HFC) diet (including 20% suet, 5% cholesterol and 2% cholic acid) at the age of 40 days and thereafter. In these conscious rats, rCBF was repeatedly measured by the hydrogen clearance method and chemical cerebrovascular reactivity was also examined by detecting an increase in rCBF in response to 10% CO₂ inhalation. At the same time, body weight and blood pressure (by the tail pickup method) was continuously checked.

RESULTS SHRSP fed on the HFC diet showed moderate hypertension similar to that in SHRSR, while SHRSP fed on the normal and high protein diet developed severe hypertension over 200mmHg. Control WK were normotensive.

As for CBF, SHRSP fed on the normal diet showed marked reduction and SHRSP fed on the HFC diet showed moderate reduction, while SHRSP fed on the high protein diet maintained the normal range at the age of 8 months. Chemical cerebrovascular reactivity in SHRSP fed on the high fat-protein diet also maintained the normal range in contrast to marked reduction in SHRSP fed on the normal diet

and SHRSP fed on the HFC diet, in both absolute values and percent increase (Table 1).

Diets (Rats)	Normal (WK)	Normal (SHRSP)	High Protein (SHRSP)	High Fat-Cholesterol (SHRSP)
Body Weight (g: M $\pm$ SE)	333 $\pm$ 18	260 $\pm$ 33	292 $\pm$ 21	302 $\pm$ 11
Blood Pressure (mmHg: M $\pm$ SE)	146 $\pm$ 4	233 $\pm$ 6**	231 $\pm$ 6**	183 $\pm$ 5**
CBF (ml/min/100gm) M $\pm$ SE	88.9 $\pm$ 10.6++	43.2 $\pm$ 3.8**	79.1 $\pm$ 3.6++	67.0 $\pm$ 5.1++
C CBF Increase to CO ₂ Inhalation (ml/min/100gm) M $\pm$ SE	142.1 $\pm$ 14.0++	42.6 $\pm$ 5.6**	161.1 $\pm$ 6.7++	29.2 $\pm$ 15**
V R CBF Increase to CO Inhalation (% M $\pm$ SE)	284 $\pm$ 30	208 $\pm$ 0.2	308 $\pm$ 0.15++	151 $\pm$ 15***

** : Significant difference from Wistar-Kyoto rats on a normal diet ($p < 0.01$)

+, ++ : Significant difference from SHRSP on a normal diet ($p < 0.05, 0.01$)

SUMMARY AND DISCUSSION As we previously reported and reconfirmed, SHRSP fed on the normal diet developed stroke, in average, at the age of 9 months in males. However, in the present study, SHRSP fed on the high protein (soybean protein in this study) diet maintained the normal range in both rCBF and chemical cerebrovascular reactivity in spite of the development of severe hypertension at the age of 8 month. These experimental results substantiated prophylactic effect of high protein diet on stroke from the view point of mechanism of stroke mentioned above in the introduction.

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