Genetic Subgrouping of Stroke-prone SHR and Stroke-resistant SHR

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The establishment of SHRSP has contributed to the elucidation of the relationship between hypertension and hypertensive diseases such as stroke (Yamori et al: Stroke 7: 46, 1976, Yamori and Horie: Stroke 8: 456, 1977). For analyzing the relationship among stroke incidence, life span, and developmental course of blood pressure in young age, we firstly obtained the frequency distribution of stroke incidence in relation to life span. As it was proven to be bimodal, the histogram was presumed to consist of 2 different components. Secondly, the regression equation of blood pressure from 50 days to 100 days of age about 6 substrains in SHR indicated that there were some differences in the developmental course of blood pressure among these substrains (Yamori et al: Jap Circulat J 42: in press).

From these findings, we attempted the selection of SHR substrains with different developmental courses and levels of hypertension in order to analyze the genetic mechanism of hypertensive diseases, such as cerebral hemorrhage and infarction.

Materials and Methods:
(1) From among stroke-prone SHR (SHRSP), A1-sb substrains were used for the further selection of more and less severe hypertension. SHRSP which showed a rapid or slower development of hypertension were selected respectively and mated with the litter mate with similar characteristics in blood pressure development at each generation. (2) The similar upward and downward selection of blood pressure was also attempted in stroke-resistant SHR (SHRSR). (3) The selected A1-sb with more severe hypertension was mated with a SHRSR substrain to obtain F1 generation. Blood pressure was repeatedly checked from 30 days to 100 days of age by an indirect tail-pulse-pickup method.

Results and Discussions:
(1) The substrain obtained by an upward selection for 6 generations developed severe hypertension over 200 mmHg before the age of 90 days, while those obtained by downward selection developed hypertension more slowly and reached 190 mmHg in average at the age of 90 days. Regression equations of blood pressure increase from 50 days to 100 days were \( Y=1.85X+62.6 \) in the former and \( Y=0.808X+113.5 \) in the latter, where \( Y \) is blood pressure in mmHg and \( X \) is days after birth \( (50 \leq X \leq 100) \) and these selected groups did differ from each other not only in the development of hypertension but also in the nature and the incidence of cerebrovascular lesions. The ratios of cerebral hemorrhage to infarction were in a clear contrast between the upward-selection group (SP-1) and the downward-
selection group (SP-2); high (37:63) in the former and low (3:97) in the latter. Life spans, the incidence of stroke and the percentage of hemorrhage and infarction in stroke in these selected substrains are indicated in the table.

(2) Regression equations of blood pressure increase in 2 selected SHRSR subgroups were \( Y = 1.60X + 49.2 \) and \( Y = 0.92X + 90.0 \), respectively.

(3) The regression equation of blood pressure in the \( F_1 \) generation obtained by crosses between SP-1 and SHRSR was \( Y = 1.25X + 97.0 \). This regression equation was roughly intermediate between those of SP-1 and SHRSR (\( Y = 0.85X + 110.5 \)).

**Summary:**
From these results, we can conclude that the developmental pattern of hypertension in the young age is genetically determined and closely related to the incidence of hemorrhage or infarction. These newly selected substrains of SHRSP with higher incidences of cerebral infarction (SP-2) or hemorrhage (SP-1) are regarded as the better models for studying the pathogenesis, treatment, and prevention of infarction or hemorrhage, respectively.

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