Effect of Cervical Sympathectomy on Cerebrovascular Atherogenesis in SHR

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After the new method (Yamori's barium-contrasted Sudan staining method: YBCSS method) for macroscopical detection of cerebrovascular fat deposition was successfully devised, new experimental systems (Yamori's preparation I, II, and III) and a new experimental model (Yamori's arteriolipidosis-prone rats: ALR) were established (Yamori et al: Clin Exp Pharmacol Physiol, Suppl 3, 199, 1976). These experimental methods, systems, and models have been expected to throw light on the mechanisms in atherogenesis, thus to obtain some new clue to the prophylaxis of stroke and cerebral athero- or arteriosclerosis. As we previously reported, in the cerebral arteries and arterioles of rats, fat deposition was producible (Yamori et al: Jap Heart J 16: 332, 1975). The most important factor for such a cerebrovascular atherogenesis in rats was hypertension (Yamori et al: Stroke 7: 120, 1976). Yamori's preparation II proved producibility of fat deposition without hypertension (Yamori et al: Stroke 6: 385, 1976), and Yamori's preparation III and establishment of ALR verified the significance of the genetic factor for atherogenesis. These results suggested the existence of some relationships among hypertension, hemodynamic derangement, and the genetic factor, i.e., existence of probable common mechanisms to these factors in the initiation of cerebrovascular atherogenesis in rats. In the present studies, we tried to analyze the role of innervation as one of these common mechanisms.

Materials and Methods:

Forty male SHRSP (A₃ stain), at the age of 60 days were applied to Yamori's preparation I (Yamori et al: Jap Heart J 17: 387, 1976). On half of them, bilateral cervical sympathectomy was performed by microsurgical technique using a microscope for microneurosurgery to avoid irritation or injury to surrounding vessels or attached nerves and tissues. We were especially careful in the area of bifurcation of the carotid artery. All rats were fed on a high cholesterol diet (HFC diet) of 20% suet, 5% cholesterol, and 2% cholic acid for 3 weeks. Blood pressure (tail-pulse-pickup method), body weight and serum cholesterol level (Zurkowski method) were repeatedly checked during the experimental period. After physiological saline preperfusion (at 38°C with systolic pressure of rats through an aortic cannula), the rats were perfused by 75% barium sulfate with 10% gelatin. This was followed by Sudan staining of the brain fixed with 10% formalin (i.e., YBCSS method).

In order to confirm reliability of surgical sympathectomy and to observe the appearance of innervation in the basilar artery, fluorescence microscopic study was

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also performed. I.e., after decapitation, basilar arteries were dissected out by microneurosurgical technique using a microscope, carefully avoiding damage to the adventitia of arteries, especially when stripping the arachnoid membranes surrounding the vessels. Then these arteries were immersed into ice-cold Krebs-Ringer bicarbonate buffer containing 14% glyoxylic acid for 10 min. Finally, the vessels were stretched flat on slide glass, quickly dried, and mounted in liquid paraffin for fluorescence microscopy.

Results:

No respiratory disturbances were recognized in any of the rats after the operation, and reliability of surgical sympathectomy was confirmed with the facts that denervated groups showed no noradrenaline varicosities. This was in contrast to the clear appearance in control groups of such varicosities at the inner part of the adventitia adjacent to media in the basilar arteries.

As shown in the table, no fat deposit was detected in the cerebrobasal arteries of the denervated group, as compared with the presence of clear ring-like fat deposits in all cases of the control group. The mean values of the number of sudanophilic rings in the control group were 3.2 ± 0.7 . Blood pressures, gain in body weight and serum cholesterol levels showed no statistically significant differences among the 2 groups.

Our fluorescence microscopic studies with highly concentrated glyoxylic acid immersion revealed that innervation in the basilar arteries appeared in ring-like or spiral form, i.e., such NA varicosities were detected, although meshworks of NA varicosities existed in part.

Table I. Effect of Innervation on Atherogenesis in the Cerebrovascular System in SHR (A_3 Strain)

	Control Group	Denervated Group
Fat deposition (%)	100	0 ($p < 0.05$)
Number of sudanophilic rings ($M \pm SE$)	3 $\pm$ 0	0 ($p < 0.01$)
Blood pressure (mmHg, $M \pm SE$)	182 $\pm$ 5	187 $\pm$ 5
Gain in body weight (Gm, $M \pm SE$)	31 $\pm$ 4	30 $\pm$ 2
Serum cholesterol level (mg/100 ml, $M \pm SE$)	484.8 $\pm$ 36.3	493.9 $\pm$ 31.3

Summary with Discussion:

Denervated groups clearly showed low susceptibility to fat deposition in the cerebrovascular system, as compared with the control group. However no significant differences were noted in blood pressure, gain in body weight and serum cholesterol levels. These results suggested the important role of innervation on fat deposition.

On the other hand, our fluorescence microscopic study with concentrated glyoxylic acid immersion revealed that appearance of innervation in the basilar artery seemed to be spiral or ring-like, just as the fatty deposition produced by Yamori's preparation I, II, and III was detected as clear ring-like form.

Further investigation into the relationship between innervation and ring-like sudanophilic rings in the cerebrovascular system should be required. However,

the results reported here support and substantiate our previous assumption about the initiation mechanism of arterio- or atherosclerosis based on our experiments. I.e., the vicious circle of repeated vasodilatation and vasoconstriction—probably under the influence of nervous control—might be the basis for fatty degeneration resulting in cerebral arterio- or atherosclerosis.

This study was supported by the Science and Technology Agency of Japanese Government, Ministry of Education, National Institutes of Health, USA (Grant HL 17754), Japan Tobacco and Salt Public Corporation, and Japan Heart Foundation.