37) Delayed Neuronal Death by Transient Ligations of Bilateral Carotid Arteries in SHRSR, SHRSP and WKY.

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Introduction

Experimental studies on the pathogenic mechanisms of stroke up to the present clarified that the age-related development of severe hypertension over 200 mmHg in stroke-prone SHR (SHRSP) induced the reduction of cerebral blood flow which resulted in hypoxic and hyponutritional medial smooth muscle degeneration and necrosis in intracerebral small arteries with blood brain barrier. On the other hand, the survival rate after bilateral ligation of carotid arteries was usually lower in SHRSP than in Wistar-Kyoto rats (WKY) and SHRSP are regarded to be more vulnerable to hypoxia. However, the results of ligation experiments are known to be affected by the kinds and depth of anaesthesia. Recently, it was reported that the transient ligations of carotid arteries in rats and Mongolian gerbils caused degeneration and necrosis of neuronal cells in hippocampus which is called delayed neuronal death.

In this study we applied the experimental method for inducing delayed neuronal death to observe pathological changes of cerebral ischemia in SHRSP which is more vulnerable to hypoxia than in stroke-resistant SHR (SHRSR) and WKY.

Materials and Methods

Male SHRSR, SHRSP and WKY, 5 rats for each strain, were used at the age of 5 months. Blood pressure and body weight were shown in the table.

The bilateral carotid arteries of rats were surgically separated and ligated with metal clips for 5 minutes under constantly regulated Halothane anaesthesia. After the rats woke up, they were fed as usual. On the 5th day after the operation, the rats which had been fasted for 20 hours were perfused for the fixation of the brain under anaesthesia with sodium pentobarbital. The fixation was performed by transcardiac perfusion at a pressure of 120 cm H₂O. The time of fixation was 60 seconds for normal saline containing heparin (20 u/ml) and then 20 minutes for 10% formalin solution. Then the brains were removed, kept in the formalin solution for 1 week, dehydrated and embedded in paraffin. Neuronal cells in hippocampus were microscopically observed after the brain sections were stained with cresylviolet.

Results and Discussion

Some neurons in hippocampus were stained darker and showed shrinkage after bilateral carotid ligation. These damaged neurons were increased in number in SHRSR and SHRSP in comparison with WKY. Such degeneration and death of neuronal cells were more severe in SHRSR, especially in SHRSP than in WKY, suggesting that there may be a strain difference in the hypoxic neuronal damages.

Strain	Blood Pressure (mmHg)	Body Weight (g)	Incidence of degeneration and death of neuronal cells in hippocampus (No. of rats)
SHRSR	227 ± 12	354 ± 6	4/5
SHRSP	248 ± 4	291 ± 11	4/5
WKY	131 ± 1	388 ± 14	2/5

The delayed neuronal death has been well documented in Mongolian gerbils. Our present study first reported the delayed neuronal death in SHR which appeared more marked compared with WKY. Especially SHRSP may be possibly useful for the research on the mechanism of pathological hypoxic changes in neuronal cells and also on the prevention against or protection of neurons from ischemic damages.