
Bilateral carotid artery occlusion (BCAO) caused severe ischemic damage of the brain in spontaneously hypertensive rat (SHR), but not in normotensive Wistar Kyoto rat (WKY). In SHR cerebral blood flow is markedly reduced and anaerobic metabolites are increased and adenosine triphosphate (ATP) is decreased. These facts suggested that hypertension accelerates cerebral ischemia following BCAO. In the present study, neurologic deficit and cerebral metabolites were measured following BCAO in SHRSP, stroke-resistant SHR (SHRSR), WKY, and the F1 and F2 hybrids in order to investigate the involvement of genetic factors in the increased susceptibility to cerebral ischemia.

Male SHRSP, SHRSR, WKY, F1(SHRSP X SHRSR), F1(SHRSP X WKY), F2(SHRSP X SHRSR), and F2(SHRSP X WKY), at 10 weeks of age, were used. The animals were anesthetized with ether and both common carotid arteries were ligated with silk sutures. Neurological symptoms were examined at 0, 0.5, 1, 2, 3, 5, 8, and 24 hrs after BCAO. Brain samples for measuring metabolites were obtained after inactivation by microwave irradiation. A piece of parieto-frontal cortex and adjacent white matter of the brain was cut out and homogenized in 0.3 N perchloric acid. After neutralization lactate and ATP were measured by standard enzymatic method.

Systolic blood pressure in the tail artery of conscious animal was measured the day before the experiment using a pulse-pick up method.

The blood pressure was in the following order: SHRSP, F1(SHRSP X SHRSR), SHRSR, F1(SHRSP X WKY), and WKY. The incidence of acute-stroke (jumping and/or seizure) in SHRSP was 100% at 3 hrs after the occlusion. In SHRSR and WKY, no acute-stroke was observed within 8 hrs. The incidence of acute-stroke in F1 hybrids was intermediate between their parental strains. The pattern of the time course of mortality rate following BCAO in each strain was similar to that of the acute-stroke. The neurological sensitivity to BCAO decreased in the following order: SHRSP, F1(SHRSP X SHRSR), F1(SHRSP X WKY), SHRSR and WKY. F1(SHRSP X WKY) is more sensitive than SHRSR, although the blood pressure of the F1 rats is lower than that of SHRSR.

Cerebral lactate increased to 10 times of the control level at 2 hrs after the occlusion in SHRSP. In SHRSR, the lactate increased slightly; 4 hrs after the occlusion the increase was only 3 times. No change of lactate level was observed in WKY. In F1 hybrids, the increase of lactate was intermediate between the parental strain. Cerebral ATP in SHRSP decreased greatly and reached 10% of the control level 2 hrs after the occlusion. The value of lactate at 2 hrs after BCAO in each strain decreased in the same order as neurological changes.

Blood pressure value in F2(SHRSP X SHRSR) and F2(SHRSP X WKY) was distributed over the range of the parental strains. There was no correlation between the blood pressure and the onset time of acute-stroke in these F2 hybrids; 6 of F2 (SHRSP X WKY) having the the blood pressure lower than 150 mmHg developed acute-stroke, and 16 out of 22 F2(SHRSP X SHRSR), that showed the same level of blood pressure as SHRSP, developed acute-stroke. No correlation between blood pressure and cerebral lactate or ATP was observed in the F2 hybrids.

These results indicate that genetic factor(s) as well as blood pressure is involved in the susceptibility to brain ischemia in SHRSP.