15) The Effect of a Calcium Channel Blocker, NC-1100 on Ischemic Neuronal Damage in SHR. Satoshi Iida, Fumihiko Kashiwagi, Rinnosuke Obo, Tatsushi Kamiya, Shunsuke Kimura, Kazuhiro Usuda, Jun Shimizu, Yasuo Katayama, and Akiro Terashi. Second Department of Internal Medicine, Nippon Medical School, Tokyo, 102.

It has been assumed that ischemia causes loss of calcium homeostasis and subsequent rise in intracellular calcium leads to neuronal damage. Some reports have indicated that calcium channel blockers may decrease ischemic neuronal damage, while others could not. The effect of a calcium channel blocker, NC-1100 on delayed neuronal death incurred on hippocampus was investigated using two vessel occlusion model.

<Material and methods> Male 18-week-old SHR were used. The animals were anesthetized with 3% halothane in a nitrous oxide/oxygen mixture (70%/30%) and ventilated mechanically through out the procedure. A silicon catheter was inserted into the vena cava through the right jugular vein. Tail artery was cannulated to monitor blood pressure and blood gases. Cerebral ischemia was induced for 10 min by bilateral carotid artery occlusion in combination with lowering of blood pressure to 50 mmHg by infusion of trimethaphan camphor sulphonate and exanguination. Treated group was given NC-1100 (3 mg/kg) i.v. just before the induction of ischemia. Control group was given normal saline. The local cerebral blood flow of hippocampal CA1 region was measured by hydrogen clearance method before and after ischemia in treated and control group as well as in non-ischemic group. The number of normal neurons (neuronal density) in hippocampal CA1 region were counted at day 1,2,3,4,7 after ischemia in treated and control group.

<Results> Neuronal density of CA1 region was not significantly decreased at day 1,2,3,4, but markedly decreased at day 7 after ischemia. Pre-treatment of NC-1100 (3 mg/kg) significantly increased neuronal density at day 7 after ischemia, compared to control group. No significant difference in local cerebral blood flow was seen between before and after injection of NC-1100 (3 mg/kg) in non-ischemic group. NC-1100 did not significantly increase local cerebral blood flow both in ischemia and in reperfusion, compared to control group.

<Conclusions> Delayed neuronal death at day 7 after ischemia was improved by pre-treatment of NC-1100. Local cerebral blood flow was not increased by NC-1100 both in ischemia and in non-ischemic group. This indicates that the effect of NC-1100 on delayed neuronal death may be mediated by suppression of calcium influx to neurons, not by improvement of local cerebral blood flow.