13) A Model for Delayed Neuronal Death-Electrophysiological and Biochemical Studies in SHR. Kazuhiko Suyama, Masaki Kurihara, *Choichiro Miyazaki, *Kenji Matsuyama, **Masami Niwa, and Kazuo Mori. Department of Neurosurgery, *Hospital Pharmacy, **Pharmacology 2, Nagasaki University School of Medicine, Nagasaki 852

Introduction: The CA₁ pyramidal cells in the hippocampus are particularly susceptible to transient ischemia. Although selective vulnerability of these neurons is well established morphologically in ischemic animal models, such as gerbils with occlusion of bilateral carotid arteries, or rats with 4-vessel-occlusion, the pathogenesis of selective vulnerability remains unclear. In the present study, we attempted to establish a suitable model for delayed neuronal death (DND) using spontaneously hypertensive rats (SHR) and examined alterations in contents of the extracellular amino acids pre, during and after ischemia.

Material and Methods: Animals (male SHR, at 12-15 weeks old, BP: 180-200 mmHg) were divided into two groups. In group A, the vertebral arteries were occluded bilaterally by electrocauterization one day before, and in group B, no pretreatment was done. Each group was anesthetized with 2% halothane under controlled ventilation. Temperature on the temporal muscle was maintained at 37±0.5°C and PaCO₂ was kept 35-40 mmHg. Cortical blood flow (CoBF) was measured by Laser Doppler flowmetry through the frontal bone window in all animals. EEG and slow potential (SP) were recorded from CA₁ pyramidal layer with a glass microelectrode inserted stereotactically (n=10). The extracellular amino acids in the dorsal hippocampus were collected through a microdialysis probe (2 mm membrane, BAS) and analyzed using HPLC equipped with a fluorescence detector (n=14). Rats were subjected to global ischemia by temporary clipping of bilateral carotid arteries for 20 min. Seven days after ischemia, pathological examination was performed.

Results and Discussion: In group A, CoBF was dropped to 7.8±2.5% (mean ± SEM) of the preischemic values at the end of ischemia. EEG was flattened soon after occlusion and SP showed about 20 mV negative shift within 10 min. These parameters indicate the occurrence of energy failure during ischemic period in this group. After recirculation, SP was normalized within few minutes, and EEG recovered within 30-60 min. The contents of extracellular amino acids (glutamate, aspartate, taurine and GABA) were significantly increased during ischemia, and returned to baseline by 30 min of recirculation. These changes were in good agreement with previous reports (Benveniste et al. 1984). Although all parameters were normalized after recirculation, pathological examination performed later revealed the presence of selective neuronal death in CA₁ pyramidal cells in this group. On the other hand, in group B, CoBF at the end of ischemia was remained to 53.3±6.1% of preischemic values. EEG activity was suppressed moderately, while no significant alteration was observed in the content of extracellular amino acids and in SP recording during ischemic period. There was no neuronal death in CA₁ pyramidal layer of hippocampus in all animals 7 days after ischemia. We established two different transient-ischemia model. In severe ischemia, it seems that small structural or functional change in the early ischemic phase will lead to DND in CA₁ pyramidal cells.