Stroke-prone spontaneously hypertensive rats (SHRSP), recognized as the best animal model for human essential hypertension and hypertensive stroke, in some cases also have severe myocardial degeneration and fibrosis as well as hypertrophy of the heart. It was therefore thought that SHRSP would be a useful animal model for studies on ischemic heart diseases and hypertrophied heart. As a basic experiment toward confirmation of this, myocardial changes after injection of Isoproterenol were examined and compared with those in normotensive WKY.

Male SHRSP and WKY, ranging from 1 to 5 months of age, were used in this experiment. Some of the SHRSP received antihypertensive treatment using Captopril 30mg/kg/day p.o. from 9-11 weeks of age for 4 weeks or from 6 weeks of age for 8 weeks. Isoproterenol 150-300mg/kg was injected subcutaneously, and Nicotine 1-5mg/kg and Ergometrine 16.5mg/kg were injected intravenously. After treatment, electrocardiograms were taken by chest leads from rats without anesthesia (Neuropac-II, NIHON KOHDEN) and serum α-hydroxybutyrate dehydrogenase (α-HBD) activity was measured (RaBA-Super, Chugai) chronologically. Light- and electronmicroscopical examinations on the myocardium were performed after death.

After injection of Isoproterenol, severe myocardial degeneration and necrosis were found electronmicroscopically, chiefly in the apex and the subendocardium of the left ventricle, even within 24 hours of injection. Replacement by granulation tissue and fibrosis followed in the same areas. In comparison with WKY, these changes were more predominant in mature SHRSP. In electrocardiogram, marked ST changes (elevation and/or depression) were found one day after injection and were still recognizable 5 days after injection. The incidence of ST changes in ECG's after injection was over 90% in mature SHRSP, around 50% in young SHRSP and about 25% in WKY; thus showing an extremely high incident rate in mature SHRSP. Serum α-HBD activity in mature WKY was between 40 and 160 international unit (I. U.). This was similar to that of SHRSP before injection. After injection of Isoproterenol, the α-HBD activity increased rapidly in mature SHRSP, reaching about 1,000 I. U. one day after injection but then decreasing to near the original levels 4 days after later. In young SHRSP and WKY, the α-HBD activity was significantly lower than in mature SHRSP from 1 to 3 days after injection, and no marked increase such as seen in mature SHRSP was found. Similar experiments were performed using SHRSP received antihypertensive treatment. Blood pressures of mature SHRSP administered Captopril from 9-11 weeks of age for 4 weeks were remarkably lower than those of controls. Nevertheless, α-HBD activity was similar in both groups from 1 to 4 days after injection; both groups thereby indicated a rapid increase in α-HBD activity. Blood pressures of SHRSP administered Captopril from 6 to 13 weeks of age were also lower than they were for controls. Although α-HBD activity increased rapidly, it seemed to be slightly lower for the treated group than for the controls. On the other hand, similar ST changes in ECG's were also found in mature SHRSP at 3-5 minutes after injection of Nicotine or Ergometrine while no remarkable changes were found in WKY. These changes were transient and no severe myocardial changes were recognized even after repeated injections over a 3 months period.

In this experiment, it was clearly shown that in comparison with WKY, injection of Isoproterenol easily induced severe myocardial changes in SHRSP. This effect was more predominant in mature SHRSP. Furthermore, it was suggested that hypertension and/or hypertrophy of heart must be the most important risk factors in myocardial changes, and also suggested that myocardial changes might be influenced not only by hypertension but also by other factors such as the numbers or reactivity of β-receptors in the heart, etc., which may be determined genetically. The results of this experiment indicate that SHRSP is a useful animal model for studies on human myocardial diseases as well as suggest that certain drugs be administered with care to the patient of hypertension.