40) Developmental change of Left Ventricular Action Potential and Sympathetic Effect in SHR. Sadayuki Sato, Tomoe Nakata, Souichirou Sekiya,* Takeshi Tsutsumi,* Hirofumi Osada*. Department of Clinical Physiology, Kanagawa Prefectural College, Yokohama; *Division of Cardiology, Showa University Fujigaoka Hospital, Yokohama.

Purpose

We have reported the alteration of electrophysiological, pathological and biochemical change in heart of SHR in the development of high blood pressure and left ventricular hypertrophy and we found that the electrophysiological property of heart muscle has changed already even before the development of hypertension. In this report, it was investigated the developmental alterations in the electrophysiological differences of heart muscle between in SHR and WKY, from prenatal stage to postnatal stage, mainly by the measurement of action potential, and also investigated the role of the sympathetic function on these differences.

Method

In SHR and WKY of 18 and 20 days of prenatal gestation age, and of 1, 3, 7 and 15 days after birth, the following parameters were analysed.

1) RR and QT intervals in A-B lead of ECG were calculated in rats of 1~15 days after birth.

2) The epicardial action potential (AP) of left ventricle were recorded in both prenatal rats and postnatal rats of 1~15 days after birth. AP were recorded from 30~70 sites on the specimen from epicardium of left ventricle with conventional microelectrode method, under normal Tyrode solution kept at 37°C. The heart muscle was electrically stimulated with rectangular pulse wave of 4 msec at frequency of 1 Hz. In prenatal rats, the mother rats were anesthetized and their abdomen was opened. After the incision of their uteruses, the embryonic heart was excised and isolated. From the record of AP, action potential duration 30, 50, 90 (APD30, APD50, APD90), amplitude of AP, max rate of rise of AP were calculated.

3) In order to investigate the mechanism of alteration of APD50 in SHR, the effect of the following drug on APD50 of embryonic rat heart in SHR and WKY.

- (1) β -isoproterenol (ISO, 2.4 mg/kg/day)
- (2) de-norepinephrine (NE, 2.4 mg/kg/day)
- (3) propranolol (Prop., 5 mg/kg/day)
- (4) prazosin (Praz., 5 mg/kg/day)

ISO, NE and Prop were administered using mini-osmotic pump and Praz. was administered orally to their maternal rats for 12~14 days from 6th day of gestation.

Result

1) QT duration was prolonged in SHR of 1, 3 days after birth, as compared to WKY, but this difference was disappeared in 15 days after birth.

2) The max rate of rise of AP in SHR of 18 and 20 days of gestation was not different from that of WKY. The amplitude of AP were greater in SHR of 20 days of gestation than in WKY.

3) The APD50 in the embryonic heart and in heart of juvenile rat in SHR were more prolonged than that in WKY.

4) The APD50 in WKY rat heart treated with ISO or NE revealed elongation tendency, as compared to non-treated WKY and this prolonged APD50 were almost similar to that in non-treated SHR.

5) The APD50 in heart of SHR treated with Prop. or Praz. showed shortening tendency, as compared to that in non-treated SHR.

6) The effect of NE. or ISO. on APD50 was more remarkable in SHR than in WKY, from 20 days of gestation to 10 days after birth.

Conclusion

1) In SHR, the prolongation of APD50 and the increase of amplitude of AP were observed in embryonic stage and juvenile stage after birth. From these findings, it was assumed that the electrophysiological alteration of heart muscle in SHR began before the development of hypertension.

2) It was also assumed that the sympathetic hyperactivity, both α and β effect, might be one of factors for these alteration of AP in heart of SHR.