51) Effect of renal denervation on hemodynamic changes induced by intracerebro-ventricular (i.c.v.) administration of 5 hydroxytryptamine (5-HT).

Akira Murakami, Nagao Kajiura, Yoshiko Kobayashi, Jun Hashida, Takashi Kita, Tateshi Tei, Toshio Kushi, Tsugio Osada, Kazushige Kuniyoshi, Yuji Ohtsuka, Hitoshi Kurumatani, Fumiaki Kobayashi, Hiroko Miyata and Michinobu Hatano.
Department of Cardiology, Surugadai Nihon Univ. Hospital, Tokyo 101.

It has been suggested that serotonergic nervous system plays an important role in blood pressure regulation in normotensive as well as in hypertensive state. We have reported that peripheral alpha-receptor stimulating mechanism is important for pressor effect observed after i.c.v. administration of 5-HT, since the pressor response was abolished by systemic phenoxybenzamine pretreatment. Among peripheral sympathetic nervous systems, renal nerve has elicited much attention since this nerve has been shown to have significant blood pressure regulatory function in various models of hypertension. To elucidate whether the renal nerve plays a role in pressor response after centrally administered 5-HT, we investigated the effect of renal denervation on 5-HT induced response.

Materials and Method: Male Wistar rats (n=20) weighing approximately 200g were used. One week before the experiment, bilateral renal denervation was performed using phenol around renal arteries (group D). Sham operated rats were prepared for control (group S). On the day before the experiment, cannulae in carotid artery and lateral cerebral ventricle were inserted. The experiment was conducted under conscious and minimally restrained state. After observation of resting MAP and HR for at least 30min. 5-HT (5µg/5µl saline) was injected i.c.v. then MAP and HR were recorded for 60min. Blood samplings of 1.5ml ea. were withdrawn through the carotid cannula before and immediately after i.c.v. 5-HT (5µg) in different subgroups of rats. The control sample was taken at least 30 min. before 5-HT injection and the same amount of blood was transfused from donor rats prepared in the same subgroup. For renal tissue NE and epinephrine (E) assay, some of the rats were decapitated before 5-HT injection. PNE and renal tissue catecholamine were measured by high performance liquid chromatography combined with electrochemical detector.

Results: Body weight of rats in both groups were similar at the time of the experiment. Resting MAP, and MAP few minutes after 5-HT when pressor response became maximum were not different between two groups; 102.9 ± 12.0 to 121.8 ± 13.8 , 101.8 ± 12.4 to 120.3 ± 30.0 mmHg in group D and group S, respectively. HR was decreased significantly, but similarly in both groups; Δ HR -27.2 ± 22.6 , -49.0 ± 44.4 /min. in group D and S, respectively. PNE was increased significantly in both groups and there was not significant difference; 0.22 ± 0.11 to 0.29 ± 0.12 , 0.24 ± 0.10 to 0.29 ± 0.11 ng/ml in group D and S, respectively. At one week after denervation, kidney weight was similar in both groups. Renal tissue NE was much lower in group D (6.8ng/g kidney) as compared with group S (57.5ng/g kidney) however tissue E was not significantly different between group D and S, 12.1 and 12.8ng/g kidney, respectively.

Discussion: Considerable regeneration of renal nerve is observed to occur in 3 to 4 weeks after denervation using phenol. In our experiment, rats were used one week after denervation and at this time, renal tissue NE was much lower in the denervated group, which suggests the denervation was successful. We have postulated that peripheral alpha-receptor stimulating mechanism is important for pressor response elicited by i.c.v. 5-HT administration, however, it has not been elucidated how the serotonergic system relate to sympathetic nervous system. In this experiment, renal denervation in Wistar rat did not affect the pressor response induced by i.c.v. 5-HT injection, which may suggest that renal nerve does not play significant role in this pressor effect.

Conclusion: We investigated the effect of renal denervation on pressor response after centrally administered 5-HT and the results suggested that renal nerve may not play significant role in this pressor response.