Role of Splanchnic Nerves in Spontaneously Hypertensive Rats

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IT is an almost established fact that the hypertensive state in spontaneously hypertensive rats (SHR) is maintained for the most part by a hyperactivity of the sympathetic nerves at least in the early stage of the hypertension. The following nerve severance and stimulation experiments were done in order to quantitatively study to what extent the splanchnic nerve activity contributes to the elevation of arterial pressure.

Nine SHR's (mean age; 16 weeks old) and

nine normotensive control rats (NCR) (18 weeks old) were anesthetized with pentobarbital. The left femoral artery was cannulated for recording arterial pressure. Laparotomy was done by a median incision. First the right splanchnic nerve and then the left splanchnic nerve were cut. Each time the change in arterial pressure was recorded and the peripheral cut end of the nerve was stimulated with square pulses of 10 V and 5 msec, to observe what frequency of stimulation

Fig.1. Decrease in arterial pressure by severance of right splanchnic nerve (R) and left splanchnic nerve. Filled circles: SHR; open circles: NCR. Each mean with SD from 9 rats. Numerical values are ESF's (mean ± SD), frequencies of splanchnic stimulation needed to restore pressure drop by severance. P's are significance levels of difference in ESF between SHR and NCR.

Key Words:

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was required to compensate for the drop in arterial pressure induced by the severance. This frequency is referred to as equivalent stimulation frequency (ESF). It is thought that ESF represents mean discharge rate of the vasoconstrictor fibers of the splanchnic nerve, which has been present before the nerve severance.

By cutting the right splanchnic nerve, arterial pressure in SHR was decreased from 148 ± 7.5 (SD) mmHg to 127 ± 14.5 mmHg. To restore the decrease, the frequency needed to stimulate the peripheral cut end of the nerve (ESF) was 3.4 ± 2.8 /sec. On the other hand in NCR, the severance of the right splanchnic nerve induced a pressure drop from 113 ± 19.7 to 103 ± 25.3 mmHg and the ESF was only 0.67 ± 1.63 /sec.

When the left splanchnic nerve was further severed, arterial pressure dropped to 85.3 ± 22.1 in SHR. The ESF needed to bring the pressure back to the level before the left nerve severance by stimulating the left nerve was 3.7 ± 1.1 /sec. In NCR arterial pressure dropped to 78.8 ± 24.6 mmHg on severance of the left splanchnic nerve and the corresponding ESF was 0.86 ± 0.52 /sec.

These experimental results are graphically summarized in Fig 1.

ESF was significantly higher in SHR than in NCR at $P < 0.025$ for the right splanchnic nerve and at $P < 0.001$ for the left splanchnic nerve. This result is in agreement with the action potential study made by Okamoto, Nosaka, Yamori and Matsumoto¹ that efferent impulses in the splanchnic nerve are increased in SHR. They compared total numbers of impulses between SHR and NCR and obtained a ratio about 3 to 1. The corresponding ratio for the ESF's was close to this value, being 4-5 to 1.

Under normal resting conditions, the tonic sympathetic activity is said to correspond to a discharge below or around 1 to 2 impulses/sec. The present study revealed that the average splanchnic discharge rate was within normal range in NCR and far above it in SHR.

Mean arterial pressure was significantly higher in SHR than in NCR at $P < 0.001$ before the nerve severance. After the unilateral severance, the difference in arterial pressure was already insignificant ($0.10 < P < 0.25$). The difference was further diminished after bilateral severance of the splanchnic nerves ($0.25 < P < 0.50$). These results indicate that the splanchnic nerves play an important role in maintaining the hypertensive

state in SHR.

REFERENCES

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Discussion:

Chairman: YOSHIHIRO KANEKO, Tokyo Univ.

Dr. YAMORI (Kyoto Univ.): We are pleased to learn your results, since they are consistent with our previous report that the sympathetic discharge in the splanchnic nerve was increased in SHR. Dr. Folkow formerly suggested that an adaptive medial hypertrophy of the resistance vessels may largely account for the increased resistance in SHR. Recently he reported that this structural change of the vessels occurs quite early in SHR. How old were the SH rats you used?

Dr. IRIUCHIJIMA: These experiments were done on 4 month old SH rats. In other experiments on 7 month old SH rats, we found, however, no significant increase in total peripheral resistance as compared to NCR, following ganglion blockade.

Dr. IIZUKA (Tokyo Univ.): I have two questions. Was the stimulation frequency-pressure response curve identical in both SHR and NCR groups? You have shown that section of both splanchnic nerves decreased arterial pressure to almost same levels in both groups. Then, how do you think of the activity and role of the sympathetic nerves to other areas, especially to the heart, in SHR?

Dr. IRIUCHIJIMA: In our experiments, heart rate was always higher in SHR than in NCR. But, after ganglion blockade, there was no difference in heart rate between both groups. The results suggest that the sympathetic nerve activity to the heart may also be increased.

Dr. SOKABE (Toho Univ.): The cardiac function of SHR seems to be inhibited in some way. Dr. Albrecht recently reported that cardiac output is decreased in SHR, and your data indicates a tendency of decrease in cardiac output in SHR. The decrease may become significant if the number of experiments increases. The turnover

rate of cardiac norepinephrine seems also decreased in SHR as reported by Lois et al. (Circ. Res. 24: 85, 1969).

Dr. YAMORI: We think that the cardiac function show a tendency to increase in the early developmental stage of hypertension in SHR. When hypertension is established after one year old, however, the indices related to the cardiac function tend to decrease. At this stage, hypertension seems to be maintained by increased total peripheral resistance.

Dr. KIKUIRI (Sapporo Univ.): Do you think that an increase in sympathetic activity occurs in other vascular areas as well?

Dr. IRIUCHIJIMA: I imagine that an increase in sympathetic activity occurs in other vascular areas in parallel at least qualitatively.

Dr. YAMORI: We investigated the problem in hindquarter limbs preparations of SHR. We found that there was an increased neural dependency in peripheral resistance of SHR. We concluded that this resulted from both increased sympathetic tone and increased vascular reactivity to norepinephrine? There might be some difference in the sympathetic nerve activity between the splanchnic areas and the hindquarter limb areas.

Dr. FUKIYAMA (Kyushu Univ.): Do you think

that comparison of the rate of the sympathetic nerve impulses is possible between two individual animals?

Dr. IRIUCHIJIMA: I do not know between two individual animals. However, between two groups of animals, it may be possible if we use computers.

Dr. KANEKO: I have three questions. Your experiments were done under anesthesia with pentobarbital. This drug sometimes affects arterial pressure levels of rats considerably. Did you control the depth of anesthesia? Do you think that the higher equivalent stimulation frequency you observed in SHR is specific to SHR? It appears possible that ESF was higher in SHR as compared to NCR simply because levels of arterial pressure were higher in SHR. Did you measure ESF of the splanchnic nerve in rats with hypertension of other types too?

Dr. IRIUCHIJIMA: I have no experience with other hypertensive rats, but I am thinking of studying in future.

Dr. KANEKO: Do you know whether the sympathetic discharge in the splanchnic nerves is tonic or intermittent in unanesthetized conditions? I think we have to be careful about the role of the splanchnic nerve activity in maintenance of hypertension until this question is answered.