19) The effect of intravenous 6-hydroxydopamine pretreatment on hemodynamic response with intracerebroventricularly administered 5-hydroxytryptamine in conscious rats.

Hirofumi Hayashi, Yoshiko Kobayashi, Akira Murakami, Jun Hashida, Toshio Kushiro, Kazushige Kuniyoshi, Yoshio Yamamoto, Hitoshi Kurumatani, Fumiya Kobayashi and Nagao Kajiura. Department of Cardiology, Surugadai Nihon University Hospital Tokyo 101.

We previously reported that intracerebroventricular(i.c.v.) administration of 5-hydroxytryptamine(5-HT) in conscious rats elicited pressor response, which was accompanied with increase in plasma norepinephrine and the pressor response was abolished by either phenoxybenzamine or methysergide pretreatment. For further investigation of the relationship between the serotonergic nervous system and the sympathetic nervous system, the effect of intravenous(i.v.) 6-hydroxydopamine(6-OHDA) pretreatment on hemodynamic response with centrally administered 5-HT was studied.

Materials and Methods:

Male Wistar rats(WR) weighing approximately 200g were used. The rats were divided into 2 groups. One group received 6-OHDA from tail vein(200mg/kg) on 10 day, 2 day and the day before the experiment(treated group, n=16). The other group did not receive 6-OHDA(control group, n=19). On the day before the study, carotid artery was cannulated(PE-50) to facilitate mean arterial pressure(MAP) observation. Also a cannula(PE-10) was inserted stereotactically into the anterior horn of lateral cerebral ventricle. After the observation of resting MAP and heart rate(HR) for at least 30 minutes, 5 µg of 5-HT was given i.c.v. in both groups, then MAP and HR were observed for 30 minutes. The experiment was performed under conscious and minimumly restrained state.

Results:

Resting MAP and HR in the treated group and in the control group did not differ significantly, 101.8 ± 1.7 mmHg, 428.7 ± 15.7 /min and 102.8 ± 2.3 mmHg, 414.4 ± 10.4 /min, respectively. Five-HT elicited consistent pressor response in both groups, however, the pressor response immediately after 5-HT was significantly smaller in the treated group than that of the control group, 117.5 ± 4.4 mmHg and 132.8 ± 2.9 mmHg, respectively. Ten minutes after 5-HT administration, MAP was still significantly higher than the baseline in the control group(116.6 ± 4.1 mmHg), however, MAP returned to the baseline in the treated group(105.0 ± 2.6 mmHg) and there was significant difference in two groups. HR was similar in the two groups before 5-HT administration. Only the control group showed significant decrease in HR at 2 minutes after 5-HT administration, and there was significant difference between two groups.

Discussion:

The serotonergic nervous system has been shown to play an important role in arterial pressure and heart rate regulation, however, the effects of centrally administered 5-HT on hemodynamics have been shown to vary among species and/or experimental conditions. We have reported that centrally given 5-HT in conscious rat evokes pressor response, and the peripheral sympathetic nervous system is important in the pressor mechanisms. Since 6-OHDA inhibits the sympathetic nervous system, the observed effects of 6-OHDA on 5-HT induced pressor and heart rate responses further confirm that the serotonergic nervous system exerts its effects on hemodynamics through the peripheral sympathetic nervous system.

Conclusion:

Central pressor effect of 5-HT was suppressed by 6-OHDA pretreatment and that suggests the close relationship between the serotonergic and the sympathetic nervous system.