24) The effects of the administration of methysergide before or after intra-cerebroventricular(i.c.v.) administration of 5-hydroxytryptamine(5-HT) on hemodynamics in conscious rats.

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We have reported that i.c.v. administration of 5-HT elicited pressor response which was accompanied with increase in plasma norepinephrine and this pressor response was abolished by phenoxybenzamine pretreatment in conscious rat. The purpose of this experiment is to investigate the relationship between the serotonergic nervous system and the sympathetic nervous system.

Materials and Methods:

Male Wistar rats(WR) and SHR weighing approximately 250g were used. On the day before the study, the carotid artery and jugular vein were cannulated to facilitate mean arterial pressure(MAP) observation and drug administration. Also, cannula was inserted stereotaxically into the anterior horn of lateral cerebral ventricle. All the experiments were performed under conscious and minimally restrained state. Exp I: After the observation of resting MAP and heart rate(HR) for at least 30 minutes, 5-HT was administered i.c.v. then MAP and HR were observed for 50 minutes. Then 1 μ g of methysergide was given i.c.v. and 10 minutes after the methysergide injection, the same amount of 5-HT was given i.c.v.. MAP and HR were observed for 30 minutes. Exp II: Instead of i.c.v. pretreatment of methysergide, either 0.1mg/kg or 1mg/kg of methysergide was given intravenously.

Results:

Five-HT elicited consistent pressor response in both SHR and WR. The pressor response immediately after 5-HT was significantly larger in SHR than that of WR, however, pressor response lasted longer in WR. Whereas HR increased significantly immediately after 5-HT in SHR, it decreased significantly in WR. Pretreatment of i.c.v. methysergide abolished the pressor effect of 5-HT in both SHR and WR. Intravenous pretreatment of methysergide of 0.1mg/kg did not preclude the pressor effect of 5-HT, however, 1mg/kg i.v. abolished the pressor effect of 5-HT in both SHR and WR. Also, pretreatment of i.c.v. or i.v.(1mg/kg) methysergide abated the effect of 5-HT on HR response. Table shows the effect of methysergide pretreatment on 5-HT induced changes in MAP and HR.

Table:

		Methysergide			
		1 μ g i.v.c.		1mg i.v.	
		Before	After	Before	After
WR	Δ MAP mmHg	28.2 $\pm$ 3.3	-0.3 $\pm$ 2.6	31.5 $\pm$ 4.2	5.0 $\pm$ 1.8
(n=13)	Δ HR/min	-40.6 $\pm$ 8.6	13.1 $\pm$ 11.9	-51.0 $\pm$ 13.9	3.5 $\pm$ 6.2
SHR	Δ MAP mmHg	34.0 $\pm$ 2.2	-1.3 $\pm$ 1.4	36.8 $\pm$ 3.0	-0.5 $\pm$ 0.5
(n=14)	Δ HR/min	20.7 $\pm$ 6.9	2.3 $\pm$ 2.4	31.8 $\pm$ 5.5	0 $\pm$ 5.1

Discussion:

Since methysergide is serotonin receptor antagonist, the observed effects of methysergide on 5-HT induced pressor response suggest that this pressor response is evoked by the stimulation of the serotonergic nervous system.

It has been suggested that i.c.v. administered 5-HT could nonspecifically stimulate the sympathetic system, but this may not be a feasible mechanism of the pressor effect of 5-HT. The effect of large amount i.v. methysergide may be resulted from the central penetration of the drug.

Conclusion:

Central pressor effect of 5-HT was abolished by pretreatment of methysergide. Since the pressor response was inhibited by peripheral alpha antagonist, our data suggest the close relationship between the serotonergic and the sympathetic nervous system.