11) Role of Sympathetic Nervous System in Blood Pressure Response to Central 5-HT₁ receptor Stimulation in SHR.


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Although recent identification of several serotonin receptor subtypes and their agonists promoted investigations concerning hemodynamic regulation of the serotonergic nervous system, precise physiological roles of the system as well as their mechanisms remained to be elucidated.

The purpose of this study is to investigate the hemodynamic responses to central 5-HT₁ receptor stimulation and the role of sympathetic nervous system in its mechanism in spontaneously hypertensive rats (SHR).

MATERIALS AND METHODS: Eight-week old male SHR and age matched Wistar Kyoto rats (WKY) were used. At least 48 hours before the experiment, cannulae were inserted into unilateral carotid artery as well as into the anterior horn of the lateral cerebral ventricle. The experiment consisted of 2 protocols and was performed under conscious state. Protocol 1: After resting observation of 20 minutes, 10μg urapidil as 5-HT₁ receptor agonist was given intracerebroventricularly (icv) and mean arterial pressure (MAP) and heart rate (HR) were observed for 40 minutes (SHR n=9, WKY n=8). In different groups of rats, 10μg of urapidil was administered intravenously and MAP as well as HR were observed for 40 minutes (SHR n=7, WKY n=8). Protocol 2: Plasma norepinephrine (PNE) was measured 10 minutes either after 10μg of icv urapidil (SHR n=12, WKY n=6) or saline (SHR n=10, WKY n=8) administration.

RESULTS: Protocol 1: icv urapidil elicited a consistent decrease in MAP for 20 minutes after its administration in SHR (5 min: -9.4±1, 20 min: -5.1±2 mmHg). In WKY, there was not a significant decrease in MAP (5 min: -2.3±0.9, 20 min: -0.6±1 mmHg), and the depressor response to icv urapidil was significantly larger in SHR than that in WKY. There was not a significant change in HR in both SHR and in WKY after icv urapidil. Intravenous urapidil did not elicit a significant change in MAP born in SHR (5 min: -0.7±1, 20 min: 0.25±1 mmHg) and in WKY (5 min: -0.43±2, 20 min: +0.43±2 mmHg). Also, HR did not change significantly after intravenous urapidil both in SHR and in WKY.

DISCUSSION AND CONCLUSION: Our previous investigation that the depressor response to icv urapidil was abolished by icv pretreatment of spiroxatrine, a 5-HT₁ receptor antagonist but not by ketanserin, a 5-HT₂ receptor antagonist indicating the depressor response to icv urapidil is due to the central 5-HT₁ receptor stimulation. Since the depressor response to icv urapidil was associated with PNE decrease, the response is likely related to the suppression of the sympathetic nervous function. The enhanced depressor response to icv urapidil in SHR compared with WKY suggests that the malfunction of the central 5-HT₁ receptor and its related sympathetic system exists in SHR.