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nNOS neuron- and Ang II neuron-mediated sympathomodulatory effects in heart-failed Dahl rats with chronic salt-sensitive hypertension.

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Summary

Background: We have demonstrated that the nNOS neuron-mediated sympathoinhibition is up-regulated in salt-sensitive hypertensive Dahl rats, based on the 7-nitiroindazole i.v. experiments and the S-methyl-L-thiocitrullin (SMTC) icv experiments using conscious rats, the immunohistochemical studies, and the tissue enzyme assay studies.

Objective: To investigate the endogenous nNOS-mediated or angiotensin II-mediated effects on overall sympathetic outflow in heart-failed Dahl rats with chronic salt-sensitive hypertension.

Design and methods: Dahl salt-sensitive or Sprague-Dawley rats were fed either a high-salt (8% NaCl) or regular diet from 6-week-old to 15-week-old for 10 weeks. Arterial pressure (AP), heart rate and renal sympathetic nerve activity (RSNA) were measured in conscious and free-moving rats. Baroreceptor (baro)-unloaded RSNA was measured when AP was decreased to produce the maximum RSNA with a perivascular occluder in the inferior vena cava. SMTC of 10 mg/kg was intravenously injected. About 40 min later after SMTC, losartan of 10 mg/kg was intravenously injected. The brain-tissue nNOS activities were determined by the citrulline method with tritiated L-arginine after partial purification by the affinity chromatography with 2', 5'-ADP Sepharose. The amount of partial purified enzyme was determined by the Bradford method.

Results: Chronic hypertensive Dahl rat fed high-salt diet for 10 weeks showed decreased body weight from 396 ± 5 to 308 ± 8 g, increased heart weight from 1.3 ± 0.02 to 1.7 ± 0.03 g, and increased end-diastolic left ventricular pressure from 3.6 ± 1.2 to 12.1 to 1.8 mmHg. SMTC did not significantly alter resting RSNA or the baro-unloaded RSNA in high-salt SD rats, but decreased resting RSNA to 68 ± 8% and the baro-unloaded RSNA from 280 ± 57 to 210 ± 24% in heart failed Dahl rats. SMTC plus losartan did not significantly alter resting RSNA but increased the baro-unloaded RSAN from 337 ± 75 to 424 ± 92% in high-salt SD rats, but reversed resting RSNA and the baro-unloaded RSNA to 283 ± 39% in heart failure rats. Tissue nNOS activity in the brainstem did not significantly alter but that in the diencephalon decreased from 11.3 ± 0.2 to 8.4 ± 0.4 kcpm/min/μg.

Conclusions: These findings suggests that endogenous nNOS system may be down-regulated but enhance slightly sympathetic outflow at the level of pre-motor neurons but endogenous AT1 receptor-mediated effect on sympathetic outflow was suppressed in heart-failed Dahl rats with chronic salt-sensitive hypertension.