Interaction between nNOS neuron- and Ang II neuron-mediated sympathomodulatory effects in Salt-sensitive Hypertensive Dahl Rats.

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Summary

Background: We have demonstrated that the nNOS neuron-mediated sympathoinhibition is upregulated 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 study, and the tissue enzyme assay study.

Objective: To investigate the endogenous angiotensin II-mediated effects on the overall sympathetic outflow in normotensive Sprague Dawley (SD) rats and salt-sensitive hypertensive Dahl rats, under the condition of reduced nNOS-mediated inhibition.

Design and methods: Arterial pressure (AP), heart rate and renal sympathetic nerve activity (RSNA) were measured in conscious and free-moving SD rats. Baroreceptor-unloaded RSNA was measured when AP was decreased to produce the maximum RSNA with an intravascular balloon in the inferior vean cava. Endogenous angiotensin II-mediated effects on the baroreceptor-unloaded RSNA was measured with an AT1 receptor antagonist, losartan (10 mg/kg, i.v.), after nNOS-mediated sympathoinhibition was blocked with a selective nNOS inhibitor, SMTC (10 mg/kg, i.v.). SD rats were fed either a high-salt (8% NaCl) for 4 weeks or a low-salt (0.04% NaCl) for 1 or 2 weeks. Dahl salt-sensitive rats were fed a high-salt (8% NaCl) for 4 weeks. The distribution and number of nNOS neuron in the Brain of SD rats were examined with the immunohistochemical staining methods.

Results: After blocking of the nNOS-mediated sympathoinhibition, the losartan significantly increased the baroreceptor-unloaded RSNA in SD rats fed a high-salt diet, while did not significantly altered the baroreceptor-unloaded RSNA in SD rats fed a low-salt diet. The distribution of nNOS neurons in SD rats was similar to that in salt-sensitive hypertensive Dahl rats. Unexpectedly, the number of nNOS neurons in the whole brain of SD rats was also similar to that of salt-sensitive hypertensive Dahl rats.

Conclusions: These findings suggest that the endogenous Ang II suppresses overall tonic sympathetic outflow in normotensive SD rats which has lower plasma angiotensin concentration. However, the effect was masked when plasma angiotensin concentration was high. The high number of brain nNOS neurons was not represented by the inhibition experiment with a SMTC. These data leads to the possibility of the existence of other important factors for modulation of sympathetic outflow except for the nNOS neuron- or angiotensin II neuron-mediated actions.