No. 1321

The Role of Salt-Sensitivity and Sympathetic Nerve Activity in Obesity

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Summary

Metabolic syndrome, a highly predisposing condition for cardiovascular disease caused by visceral obesity, requires appropriate management. However, the detailed mechanisms have not been fully elucidated. High salt intake increases blood pressure to a greater degree in patients with metabolic syndrome than in those without it. We have shown previously that sympathoexcitation by brain oxidative stress mediates arterial pressure elevation in salt-sensitive and obesity-induced hypertension. We have also shown that aldosterone-mineralocorticoid receptor (MR) activation mediates oxidative stress-induced cardiac and renal dysfunction. Then, we hypothesized that brain aldosterone-MR activation could mediate arterial pressure elevation through brain oxidative stress-induced sympathoexcitation in metabolic syndrome-related hypertension. We used Dahl-S.Z-Lepr(fa)/Lepr(fa) rats（DF）derived from a cross between Dahl salt-sensitive and Zucker rats as the salt-sensitive metabolic syndrome model. Sgk-1 mRNA expression in the isolated hypothalamus, evaluated by real-time quantitative RT-PCR was significantly higher in DF than in Dahl salt-sensitive rats, which suggested that MR activity in the brain was upregulated in DF. Then, we examined effects of chronic intracerebroventricular eplerenone, mineralocorticoid receptor blocker or FAD 286, an aldosterone synthase inhibitor, on sympathetic nerve activity, arterial pressure, and the hypothalamic oxidative stress level. In DF, chronic intracerebroventricular eplerenone significantly reduced sympathetic nerve activity and arterial pressure. Chronic intracerebroventricular FAD 286 also significantly reduced sympathetic nerve activity and arterial pressure as well as hypothalamic oxidative stress level. In conclusion, brain aldosterone-mineralocorticoid receptor activation can be a possible pathogenic background of arterial pressure elevation through brain oxidative stress-induced sympathoexcitation in metabolic syndrome.