P442

Caffeine improves central insulin sensitivity to prevent fructose-induced pressor effect through reduces superoxide production

CJ Tseng, BR Chen, LP Ger. *Kaohsiung Veterans General Hospital, Department of Medical Education and Research, 813, Taiwan*

Recent epidemiological study has reported that caffeine improves diabetic symptoms by enhancing insulin sensitivity. Caffeine consumption prevents diet-induced hypertension. The nucleus tractus solitarii (NTS) is the primary integrative center for cardiovascular control. Our previous studies have demonstrated that in the NTS, insulin can induce depressor effect. Nevertheless, the relationship between caffeine and insulin sensitivity and related modulation of cardiovascular function in the NTS has not been established. The objective of this study was to elucidate the possible signaling pathways involved in caffeine-mediated blood pressure regulation in the NTS. We used four groups of animals: control group; fructose group (10% fructose water); fructose-caffeine group (10% fructose water with caffeine 15mg/kg/day); caffeine group (15mg/kg/day). The pressor effect induced by fructose was attenuated significantly after caffeine treatment. Dihydroethidium staining showed that addiction of caffeine decreased the numbers of superoxide-positive cells in the NTS. The systemic administration of caffeine increased nitric oxide (NO) production in the NTS. Immunoblotting and immunoflurorescence analysis further showed that inhibition of fructose-induced pressor effect by caffeine significantly reduced the phosphorylation of insulin receptor substrate 1 (IRS1S307) and receptor of advanced glycation end-product, also increased AktS473, neuronal NO synthase (nNOSS1416) phosphorylation. The level of insulin in the NTS was decreased after caffeine treatment in fructose group. Central administration of insulin into the NTS induced depressor effect, and this event could be blocked by systemic administration of fructose. Treatment of caffeine could reverse the insulin-induced depressor effect. Taken together, we present a novel finding that caffeine could improve IRS1-phosphatidylinositol 3-kinase-Akt-nNOS signaling in the NTS to inhibit fructose-induced pressor effect via ameliorate superoxide production.