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Oral Communication Abstract
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Spexin-based galanin receptor 2 agonist (NS200) improves diabetic nephropathy in type 2 diabetes

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Objectives: Spexin is a novel neuropeptide having an emerging role in metabolic diseases such as obesity and diabetes and involved in energy homeostasis and food intake. Spexin-based galanin receptor 2 agonist (NS200) has anti-depressive action and anxiolytic effect. The aim of this study is to investigate the effect of NS200 on insulin resistance and diabetic nephropathy in type 2 diabetic animal.

Methods: 8 to 10 week old *db/m* and *db/db* mice were treated with NS200 for 12weeks. NS 200 was administered by intraperitoneal injection at a dose of 1.0 mg/kg/day as reported in the previous study.

Results: There were no changes in body weight, food and water intake, urinary volume, fasting glucose level and HbA1c level by NS200 treatment in diabetic mice. Insulin tolerance test and glucose tolerance test were not also changed by treatment. NS200 lowered systolic blood pressure. Interestingly, NS200 improved urinary albumin excretion significantly in diabetic mice. Renal histology showed reduced glomerulosclerosis and tubulointerstitial fibrosis in treatment groups. Renal TGFβ and type IV collagen expressions were decreased in NS200 treated group, whereas PAI-1 and F4/80 expression were increased in treatment group. Insulin signaling pathway such as PI3K, p-AKT, and p-ERK protein expression were significantly suppressed by treatment in diabetic nephropathy. Despite there were no beneficial effects in basal metabolic parameters and insulin resistance, NS200 treatment in diabetic mice showed renoprotective effects in urinary albumin excretion and renal structural changes.

Conclusions: Our results provide the evidence that spexin-based galanin receptor 2 agonist by NS200 has renoprotective effect in diabetic nephropathy. These findings suggest the mechanism via its inhibition of renal insulin signaling pathway therefore provide a considerable promise as a new agent in diabetic nephropathy.