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TNF-α: A potential molecular target in the brain against diabetes-associated male sexual behavior disorder

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Background: Sexual dysfunction, including decreased libido, sexual behavior disorder and erectile dysfunction (ED), is common in male patients with diabetes mellitus (DM). We previously demonstrated that increased peripheral tumor necrosis factor alpha (TNF-α) expression, associated with inflammation in DM, contributes to ED in the rat corpus cavernosum. However, the role of TNF-α in the central pathophysiology of DM-associated male sexual dysfunction is unknown. In this study, we examined the effects of TNF-α inhibition, i.e. etanercept (ETN) via chronic intra-cerebroventricular (ICV) infusion on nNOS expression in the hypothalamic paraventricular nucleus (PVN) and sexual behavior disorder in male diabetic rats.

Results: Male diabetic rats with ICV aCSF treatment displayed significantly severe sexual disorder accompanied with blunted nNOS expression and activity in the PVN in addition to local upregulated TNF-α and TNFR-1 expression, and increased ROS generation compared with non-diabetic controls. The sexual behavioral parameters were significantly improved in the treated group with ETN. ICV ETN significantly inhibited TNF-α and TNFR-1 expression and reduced ROS generation in the PVN in diabetic rats. In addition, ICV ETN appeared to induce marked increased in nNOS expression in the PVN of diabetic animals compared with ICV aCSF-treated diabetic rats.

Conclusion: Increased TNF-α and TNFR1 expression in the hypothalamic PVN associated with DM contributes to male sexual disorder by centrally inhibiting nNOS expression and activity in the PVN via promoting local ROS generation. Central TNF-α blockade may have beneficial effects on the male sexual disorder in diabetes through improvement of NO pathway within the PVN.

Biography

Ting Long serves as an Associate Professor in Department of Physiology at SUMC, after getting the PhD degree of Pathology and Pathophysiology in Shantou University Medical College (SUMC), China. He dedicates in diabetes associated male sexual dysfunction studies investigating the mechanism of diabetic erectile dysfunction and sexual behavior disorder. There were several TNF-α related publication recently which suggests that TNF-α is both a significant molecular biomarker and highly potential target in diabetes associated male sexual disorder.

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