Hong Yang, J Diabetes Metab, 2:8
doi: http://dx.doi.org/10.4172/2155-6156.S1.06

OMICS Group Conferences
Accelerating Scientific Discovery

2nd World Congress on
Diabetes & Metabolism

6-8 December 2011 Philadelphia Airport Marriott, USA

TITLE

Brainstem Thyrotropin-Releasing Hormone (TRH) triggered Sympathetic overactivation in Type 2 Diabetes

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Autonomic control of visceral functions is critical for maintaining metabolic homeostasis. Enhanced sympathetic drive and impaired vagal function play important roles in multisystemic pathophysiology of type 2 diabetes (T2D), including reduced insulin secretion, gastroparesis, hypertension, and high cardiovascular mortality. TRH is a three amino acid neuropeptide originally discovered in the hypothalamic paraventricular nucleus. Brainstem raphe nuclei are another major locus of TRH neurons, which project TRH-containing fibers to innervate brainstem and spinal sympathetic and vagal motor/premotor nuclei. TRH acts at these nuclei to control sympathetic and vagal descending pathways involved in regulating food intake, blood pressure, heart beat, pancreatic insulin secretion, and gastrointestinal secretion/motility. Our recent studies revealed the autonomic dysregulation by brainstem TRH in Goto-Kakizaki (GK) rat, a polygenetic T2D model with basal hyperglycemia and hypertension. TRH analog injected intracisternally or microinjected into the rostral ventrolateral medulla, a sympathetic center, induced sympathetic-overactivation in GK rats, shown as a complete inhibition of gastric acid secretion, suppression of insulin response to hyperglycemia, and uncounterbalanced sympathetic drive to increase blood pressure and accelerate heart beat, leading to cardiac mortality. The fasting and re-feeding associated neuronal activation in brainstem dorsal vagal complex observed in non-diabetic rats was totally absent in GK rats, which is associated with lower levels of vagal-regulated gut hormones ghrelin, insulin, amylin, glucose-dependent insulinotropic polypeptide, and pancreatic peptide. The vagal stimulatory action of brainstem TRH is suppressed by hyperglycemia. Targeting on restoring a balanced sympathetic-vagal regulatory function of brainstem TRH could be a new direction for the prevention and therapy of T2D.

Biography

Dr. Yang completed medical school and doctorate in Digestive Physiology in Beijing Medical University (Medical School of Peking University), followed by postdoctoral training on Brain-Gut Interactions in Dr. Taché lab at UCLA, where she studied vagal-mediated regulation on gastric functions by brainstem thyrotropin-releasing hormone (TRH). Since 1995, she is the Principal Investigator in studies funded by NIH, VA, and UCLA. Her research interest is focused on the autonomic disorders in endocrine disease, especially the role of brainstem TRH in sympathetic-vagal dysfunction in type 2 diabetes and thyroid diseases. She has published 67 original research papers and 15 book chapters/reviews.