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A correlative relationship between chronic pain and insulin resistance in Zucker fatty rats: Role of downregulation of insulin receptors

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Epidemiological studies and meta-analyses report a strong relationship between chronic pain and abnormalities in glucose metabolism, but the exact relationship between chronic pain and insulin resistance in Type-2-Diabetes (T2D) remains unclear. Using a model of neuropathic thermal and tactile hypersensitivity induced by sciatic nerve Chronic Constriction Injury (CCI) in Zucker Diabetic Fatty (ZDF) and Zucker Lean (ZL) littermates, we compared the recovery period of hypersensitivity and the progression of T2D and studied the possible involvement of insulin receptors (IR) in the co-morbidity of these two conditions. We found that, besides a lower nociceptive threshold to thermal and mechanical stimulation in a naive ZDF than in ZL littermates at 6 weeks of age, it took a longer time for CCI-induced nociceptive sensitivity to restore in ZDF rats. Meanwhile, the nerve injury accelerated the progression of T2D in ZDF rats, which was demonstrated by an earlier onset of hyperglycemia, more severe hyperinsulinemia, and a higher concentration of glycosylated hemoglobin (HbA1c) 6 weeks after CCI induction. IR-immunoreactive cells were located across the Central Nervous System (CNS) and skeletal muscles. There was a low level of IR expression in skeletal muscles of naive ZDF rats. In contrast, CCI reduced the IR expression in skeletal muscles as well as the ipsilateral spinal cord, primarily in the dorsal horn. In conclusion, our data suggest that the relationship between insulin resistance and chronic pain in ZDF rats is bidirectional and an impaired IR signaling system may be implicated in this reciprocal relationship.

Biography

Shuxing Wang has completed his PhD from Zhongshan University and Post-doctoral studies from Harvard Medical School, Massachusetts General Hospital. He has published more than 45 papers in reputed journals.

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