

**Original Article**

**PERIPHERAL INSULIN RESISTANCE INDUCED BY STREPTOZOTOCIN AND MODIFIED DIETS: SOME IMPLICATIONS FOR HIPPOCAMPAL MORPHOLOGY AND FUNCTION**

Oluwole B. Akinola, Aminu Imam, Oluseye P. Ogunbiyi

**Abstract**

The role of insulin resistance and metabolic perturbations in the pathogenesis and progression of neurodegenerative disease is receiving increasing attention. Here, we compared hippocampal-dependent function and morphology across rat models of insulin resistance induced by streptozotocin (STZ) with and without modified diets. Rats were randomized to receive either multiple low-dose STZ (30 mg/kg; 5 successive days) with or without post-feeding with high-fructose drink (HFrD) or high-fat diet (HFD). Oral glucose tolerance test was performed 48 hours to sacrificing the rats by challenging rats with oral glucose (2 g/kg) followed by estimation of blood glucose at 0, 30, 60 and 90 minutes interval. At 30 or 60 days of feeding with modified diets, spatial memory was assessed by the Morris water maze (MWM) technique, after which the rats were sacrificed. Fasting plasma insulin and glucose were then assayed, followed by estimation of homeostatic model assessment of insulin resistance (HOMA-IR). Besides, the perfused brains of the rats were studied histologically by the Congo red technique. The use of intraperitoneal STZ with or without modified diets triggered insulin resistance with variable degrees of biochemical, neurobehavioral and hippocampal structural changes, including significant increases ( $P < 0.05$ ) in fasting blood glucose, impaired glucose tolerance, significantly increased latency time on the MWM, and dysmorphology of hippocampal CA1 field, which were most pronounced in the STZ-injected rats post-fed HFrD or HFD for 30 or 60 days, compared with those on STZ, HFD or HFrD alone. These findings have implications and relevance for studies aimed at exploring the association between insulin resistance and hippocampal structural and functional integrity.

Key words: Hippocampus, Insulin resistance, High fat diet, Fructose, Streptozotocin