

VILDAGLIPTIN IMPROVES ANIMAL BEHAVIOR AND COGNITIVE IMPAIRMENT IN A RAT MODEL OF STREPTOZOTOCIN INDUCED DIABETES

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Increasing evidence suggests that cognitive impairment and dementia might be complications of type 2 diabetes mellitus (T2DM) (1). T2DM is a complex metabolic disease that can cause serious damage to various organs. It is a chronic disease due to an altered homeostasis of glucose and lipid metabolism characterized by insulin resistance and often followed by progressive insufficient production of insulin by the pancreatic β cells (1). GLP-1 is involved in glucose homeostasis by enhancing insulin release from pancreatic β -cells. GLP-1 receptors (GLP-1Rs) are also present in the brain mostly in the CA hippocampal regions; their activation stimulates MAPK pathway and their overexpression in the hippocampus improves learning and memory performance (1). GLP-1 has a very short half-life, as a result of its metabolism by dipeptidyl peptidase (DPP)-IV, a naturally occurring enzyme that is present in most tissues of the body and that naturally breaks down GLP-1. DPP-IV inhibitors, further than controlling blood glucose levels, possess neuroprotective effects in animal models (2, 3). Herein, we evaluated the effects of a DPP-IV inhibitor, vildagliptin, on cognitive decline associated with diabetes. Furthermore, we studied vildagliptin effects against hippocampal neurodegeneration induced by streptozotocin (STZ), a well-validated animal model of diabetes and neurodegeneration associated with cognitive decline. Diabetes and/or cognitive decline were induced in Wistar rats by intraperitoneal or intracerebroventricular injection (4) of STZ and then rats were treated with vildagliptin (3 mg/kg per day os) for 4 weeks. Rats underwent behavioral tests: Morris water maze, Passive avoidance, Forced swimming test (FST), Open field test (OF). In FST, the duration of immobility was significantly reduced by vildagliptin (3 mg/kg) in comparison to control group suggesting potential antidepressant effects. In the OF anxiogenic effects were observed in all vildagliptin-treated groups. In MWM vildagliptin improved learning and memory in STZ-treated animals. Therefore, vildagliptin has protective effects on cognitive functions in addition to its effects on blood glucose levels while it may affect mood and anxiety. Further studies are needed to disclose its clinical potential.

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