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Beneficial neuroprotective effect of GSK-3 β inhibitors against brain stroke and associated cognitive impairments in diabetic rats

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Recent studies have investigated that Insulin Resistance (IR) is a strong risk factor for diabetes and cerebral stroke, which are leading causes of death and long term disability. In the recent past, various studies reported that impaired GSK-3 β activity was found in IR and cerebral stroke. The present study was designed to investigate the neuroprotective role of GSK-3 β inhibitors against cerebral stroke and cognitive deficits in diabetic rats. IR was induced by high fat diet (HFD) and cerebral stroke was achieved by 60 min ischemia followed by 24 hours of reperfusion. To estimate motor coordination rotarod performance, actophometer test has been performed. Cognitive impairment was assessed using Y-maze task and acetylcholinesterase (AChE) activity. Biochemical estimations were done to estimate oxidative and inflammatory markers, brain insulin levels, serum glucose levels. Molecular estimation of brain derived neurotrophic factor (BDNF) levels and GSK-3 β levels were also estimated. Histopathological estimation was done using hematoxylin and eosin staining. The rats subjected HFD and cerebral stroke, showed increased serum glucose and insulin levels, reduced brain insulin levels, altered motor coordination and cognition along with elevated oxidative stress and AChE activity. In addition reduced BDNF levels and high GSK-3 β activity has been observed. In contrast, rats treated with GSK-3 β inhibitor after IR and stroke, significantly improved behavioral and memory performance, reduced oxidative stress and inflammation, improved BDNF levels and attenuated GSK-3 β activity. The current study suggest neuroprotective effect of GSK-3 β inhibitor against cerebral stroke and associated cognitive deficits in diabetic rats.

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