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News & Comments

Tofacitinib: Potential Agent in Diabetes-Induced Cognitive Dysfunction

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Impairment in glucose metabolism is a hallmark of the lifestyle disease known as diabetes mellitus. Diabetes patients' declining cognitive abilities are becoming more widely known, and they place a heavy cost on the healthcare system. A key intracellular signalling system called Janus Kinase (JAK) must be activated for the body to perform critical physiological processes. As a selective JAK inhibitor, Tofacitinib is effective in treating a variety of disorders, including liver damage, asthma, vascular damage, atherosclerosis, psoriasis, and other inflammatory conditions. An essential member of the neurotrophic family, brain-derived neurotrophic factor (BDNF), has been found to have positive effects on memory impairments caused by a variety of aetiologies. The present study was designed to explore the role of Tofacitinib in long-standing diabetes-induced cognitive impairment in rats along with the possible involvement of BDNF, neuroinflammation and oxidative stress.

In this investigation, sixty Wistar Albino rats (250-280 g) were used. The rats were housed in the department's animal house, where they were given conventional laboratory care. Using five trials of the Morris Water Maze test, the last (10th) week's learning and memory were evaluated. Rats had to be killed to separate the brain, which was then homogenized in phosphate-buffered saline. Ten rats each made up each of the six experimental groups that were used. For statistical analysis, GraphPad Prism version 8 was used. The present study's data were given as Mean±SD.

All experimental animals' baseline glucose levels did not significantly rise. The difference between day 1 and day 4 ELT in non-diabetic rats was significant, and this difference shows that rats are capable of learning. When compared to non-diabetic rats, STZ-injected animals had significantly lower brain BDNF levels, which could be measured in brain homogenates. In this investigation, STZ injection caused a considerable rise in plasma glucose levels and the onset of diabetes mellitus. Additionally, there was a considerable impairment in learning in long-term diabetic rats (no significant decline in day 4 ELT), which was used to measure cognitive function impairment.

In the current study, Tofacitinib (15 and 30 mg kgG1) treatment significantly enhanced the cognitive capabilities of STZ-injected rats as measured by a significant decline in day 4 ELT (increase in learning) and increase in day 5 TSTQ (increase in memory). JAK inhibitor Tofacitinib has been demonstrated to lessen neurological impairments in rats injured by ischemia-reperfusion. In the current study, there were notable changes in biochemical parameters in the brains of long-term diabetes rats in addition to the impairment in learning and memory. The neurotrophic factor known as BDNF has been shown to

have positive effects on memory and learning. Additionally, it has been demonstrated that chronic diabetes lowers BDNF expression in the brain.

In rats with chronic diabetes, learning and memory problems are the main signs of cognitive impairment. A JAK inhibitor called Tofacitinib may lessen chronic diabetes-related learning and memory deficits.

JOURNAL REFERENCE

Fan S. and R. Song, 2022. Beneficial effects of tofacitinib in long-standing diabetes-induced cognitive impairment in rats through BDNF-TNF-"-Nrf2 signalling pathway. Int. J. Pharmacol., 18: 856-863.

KEYWORDS

Learning, memory, inflammation, oxidative stress, diabetes, tofacitinib, brain homogenates, BDNF