Pioglitazone

Traumatic brain injury (TBI) is a leading cause of long-term disability in the United States. Even in comparatively mild injuries, cognitive and behavioral symptoms can persist for years, and there are currently no established strategies for mitigating symptoms in chronic injury. A key feature of TBI-induced damage in acute and chronic injury is disruption of metabolic pathways. As neurotransmission, and therefore cognition, are highly dependent on the supply of energy, we hypothesized that modulating metabolic activity could help restore behavioral performance even when treatment was initiated weeks after TBI. We treated rats with pioglitazone, a FDA-approved drug for diabetes, beginning 46 days after lateral fluid percussion injury and tested working memory performance in the radial arm maze (RAM) after 14 days of treatment. Pioglitazone treated TBI rats performed significantly better in the RAM test than untreated TBI rats, and similarly to control animals. While hexokinase activity in hippocampus was increased by pioglitazone treatment, there was no upregulation of either the neuronal glucose transporter or hexokinase enzyme expression. Expression of glial markers GFAP and Iba-1 were also not influenced by pioglitazone treatment. These studies suggest that targeting brain metabolism, in particular hippocampal metabolism, may be effective in alleviating cognitive symptoms in chronic TBI [1)].

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McGuire JL, Correll EA, Lowery AC, Rhame K, Anwar FN, McCullumsmith RE, Ngwenya LB. Pioglitazone improves working memory performance when administered in chronic TBI. Neurobiol Dis. 2019 Sep 9:104611. doi: 10.1016/j.nbd.2019.104611. [Epub ahead of print] Review. PubMed PMID: 31513844.