

## Effects of erythropoietin on neuronal apoptosis and neurogenesis in hippocampal dentate gyrus in the rat model of Alzheimer's disease

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**Background and Aims:** Alzheimer's disease is a prevalent disorder with severe neurodegeneration. Because it has been demonstrated that erythropoietin (EPO) has positive effects on central nervous system, the aim of this study was to evaluate the effect of EPO on neuronal apoptosis and neurogenesis in hippocampal dentate gyrus (DG) in a well defined model for Alzheimer's disease.

**Methods:** A rat model of sporadic dementia of Alzheimer's type was established by a bilateral intracerebroventricular injection of streptozotocin (STZicv). Impairment of learning and memory was confirmed two weeks after STZ icv injection by passive avoidance learning test and then the rats were divided into 4 groups; control, control-EPO, STZicv and STZicv-EPO. Erythropoietin was injected intraperitoneally every other day with a dose of 5000 IU/kg and finally rats were anesthetized and decapitated for immunohistochemical study; neuronal apoptosis by TUNEL Test and neurogenesis by Ki67 method in granular layer of hippocampal DG.

**Results:** The results showed a significant increase in neuronal apoptosis in hippocampal DG in the STZicv group ( $p < 0.05$ ); however EPO decreased neuronal apoptosis in Alzheimer's rats, as there wasn't any significant difference between STZicv-EPO and control groups. Although, STZicv and EPO alone did not change neurogenesis in granular layer of hippocampal DG, but EPO significantly increased neurogenesis in this layer in the STZicv-EPO group comparing to the control ( $p < 0.001$ ) and STZicv groups ( $p < 0.001$ ).

**Conclusions:** In this study, we report that treatment of EPO significantly reversed the neuronal apoptosis induced by STZicv and also significantly increased neurogenesis. Results suggest neuroprotective and neurotrophic effects of erythropoietin in neurodegenerative conditions.

**Keywords:** Alzheimer's; Erythropoietin; Streptozotocin; Neuronal apoptosis; Neurogenesis