

Behavioral analysis and neurogenesis in mice overexpressing erythropoietin

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Erythropoietin (Epo) is produced in the kidneys under hypoxic conditions to increase erythrocytes. Healthy volunteers, psychiatric patients and healthy mice have been treated with acute injections of Epo showing positive effects on learning, memory, attention and mood. Both, Epo and its carbamylated derivate also increased neurogenesis in healthy mice. The aim of the present study was to investigate the effect of Epo on learning, memory and neurogenesis using two animal models that overexpress endogenous Epo: Tg21 mice chronically overexpressing human Epo in the brain only without any changes in blood parameters, and Tg6 mice constitutively overexpressing human Epo in both plasma and brain. Learning and memory were assessed by means of a wide range of conventional tests and the IntelliCage. To assess adult neurogenesis we quantified proliferating cells, young neurons (or young cells of the neuron lineage) and differentiating cells and total number of granule cells in the dentate gyrus. No differences were found between transgenic (either Tg21 or Tg6) and wild type animals in learning and memory in any of the tests. We found the expected differences between younger and older animals in proliferation and neuronal differentiation, but there was no difference between transgenic and wild type animals. The total number of granule cells was also similar in Tg21, Tg6 and wild type animals. In conclusion, we could not find any positive effect of chronic endogenous overexpression of Epo in learning, memory and neurogenesis, narrowing Epo's brain impact to the previous observation in reduced impulsivity and increased anxiety.