Learning, memory and neurogenesis under chronic overexpression of erythropoietin

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The hormone erythropoietin (Epo) is produced in the kidneys under hypoxic conditions and released into the blood stream to increase red blood cell number. Some non-hematopoietic effects have also been shown, such as positive effects on learning, memory, attention and mood in psychiatric patients and animal models (upon acute Epo treatment). Besides this, 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: Tg21 mice chronically overexpressing human Epo in the brain only (4 fold) without any changes in blood parameters, and Tg6 mice constitutively showing high human Epo values in both plasma (12-fold) and brain (26-fold). Learning and memory were assessed by means of a wide range of conventional tests and the IntelliCage. To asses adult neurogenesis (Tg21 = 16.0±0.9 months; Tg6 = 6.0±2.2 months) 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. The results on learning and memory show that there are no difference between transgenic (either Tg21 or Tg6) and wild type 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, and as expected no age differences effect. 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. Supp SNF NCCR Neuro.