Overexpression of erythropoietin in the brain improves cognitive impulsivity and increases emotional reactivity

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Recently, it has been reported that erythropoietin (Epo) treatment in schizophrenic patients improves memory and attention, but there was no effect on psychopathology or social functioning. In addition, some studies suggested that Epo may have antidepressant-like properties as it improves mood and reverses neurocognitive dysfunction in patients with treatment resistant depression or bipolar illness. In healthy subjects, Epo treatment leads to mood improvement and enhances the processing of emotions, but not cognitive performance. Furthermore, some experiments in animal models suggested that Epo and its carbamylated derivative (CEPO) improve learning and memory. These studies imply that a single high-dose Epo injection or a 3 months weekly treatment with the same high-dose of Epo has an effect on cognition. However, nothing is known on Epo’s impact in mice chronically overexpressing Epo in the brain. Thus, the aim of the present study was to investigate how Epo affects cognitive performance using a transgenic mouse line (Tg21) that chronically overexpresses Epo in the brain (4-fold times more than wild type), without any changes in blood parameters. We used a comprehensive battery of tests to assess short and long-term memory, exploratory behavior, motor and cognitive impulsivity (or tolerance to delay), and anxiety. Overall, Tg21 mice showed a higher tolerance to delay. Tg21 animals also showed an increased in emotional reactivity during fear conditioning and open field tests and better physical performance in water-maze and rotarod test. However, no difference in motor impulsivity between Tg21 and Wt groups could be found. Moreover, there was no improvement in the short and long-term memory in the transgenic mice. In conclusion, chronic endogenous overexpression of Epo might have an effect on physical performance and some aspects of cognition.