

## **Improved cognitive impulsivity and increased emotional reactivity in mice overexpressing erythropoietin in the brain**

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The renal cytokine erythropoietin (Epo) possesses neuroprotective and neurotrophic properties. Epo injections have been reported to improve memory and attention and to have antidepressant-like effects in patients with neurological problems. Exogenous acute Epo administration has also been found to positively affect learning and memory in animal models. However, the influence of endogenous Epo on cognitive functions is still unknown. The aim of this study was to investigate the effects of endogenous Epo on several behavioral and cognitive aspects in a transgenic mouse line (Tg21) that chronically overexpresses human Epo in brain, without changes in plasma levels. We run a battery of conventional tests followed by several IntelliCage test protocols. We found that motor coordination and physical performance in rotarod and water maze were significantly better in Tg21 compared to wild-type (Wt) mice. Tg21 animals also showed increased emotional reactivity in fear conditioning and open field tests as well as in the extinction phase of the nose-poke suppression protocol in the IntelliCage. Moreover, Tg21 exhibited increased activity during the initial phases of both the emergence test and the IntelliCage free adaptation module. No group difference was found in any of the short and long-term memory tests conducted using either the conventional equipment or the IntelliCage apparatus. Finally, when motor and cognitive impulsivity were tested in the IntelliCage (in a reaction time task and in a delay discounting task respectively), Tg21 and Wt mice showed similar motor impulsivity rate but different tolerance to delay with Tg21 animals having higher tolerance, therefore making fewer impulsive choices. In conclusion, chronic endogenous overexpression of Epo affects physical performance and some aspects of cognition but does not seem to play a major role in memory processes. Moreover, these results were consistently revealed by both behavioral conventional tests and IntelliCage protocols, therefore confirming the IntelliCage as a valid alternative for high-throughput phenotyping of mutant mouse lines.

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