

## **Effects of chronic overexpression of erythropoietin in the brain on cognitive functions and physical performance**

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According to our results, chronic overexpression of human Epo has no effect on learning or memory in healthy mice. We could not detect any differences between Tg21 and control animals in any of the conventional tests or IC protocols used to test long and short-term memory, spatial recognition memory, and working memory. Taken together, the results obtained in open field, startle response and fear conditioning test and the conditioned nosepoke suppression protocol (this last one in the IntelliCage), chronic overexpression of human Epo in Tg21 animals increases anxiety-like behavior and emotional reactivity. Tg21 mice also exhibited an increased exploratory behavior during the adaptation phase to the IC, which supports this conclusion.

Chronic overexpression of human Epo has an important effect on cognitive impulsivity. Tg21 mice showed a higher tolerance to delay or a higher capacity to distinguish between immediate but small reward, and late but large reward. On the other hand, Epo seems to have no effect on motor impulsivity since no differences could be found between Tg21 and control groups.

The rotarod test and grip test demonstrated that Tg21 and control animals have similar motor skills. Interestingly, Tg21 mice were able to maintain their physical performance for a longer period and were able to swim faster, suggesting that Epo could improve aerobic performance (always considering that these are not tests to measure aerobic capacity).

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