Introduction

Erythropoietin (Epo) is produced in the kidneys under hypoxic conditions to increase erythrocytes.

- Healthy volunteers, psychiatric patients and healthy mice have been treated with
  either an acute injection or a longer treatment of Epo showing positive effects on
  learning, memory, attention and mood.
- Healthy mice treated with Epo and its carbamylated derivative also increased
  neurogenesis in the dentate gyrus.
- The studies suggest that Epo could modulate plasticity, synaptic connectivity and
  activity on memory-related neuronal networks.

Aim of the study: to investigate the effect of the overexpression of endogenous Epo on
learning, memory and neurogenesis.

Methods

Two transgenic mouse lines: Tg21 chronically overexpressing Epo in the brain (4-fold
times more than a wild-type (Controls) without changes in blood parameters, and Tg6
systemically overexpressing Epo (26-fold increased of Epo levels in the brain and 12-fold
in plasma). A total number of sixty-five female animals were tested (Tg21, n=17; Control,
n=16; Tg6, n=16; Control, n=16).

Behavioral tests: Morris Water Maze, 8-Radial Maze, T-Maze and Fear Conditioning.
Behavioral tests in the IntelliCage (www.newbehavioral.com): Conditioned Noisepoke
Suppression, Place Learning, Serial Reversion, Patrolling and Chaining.

The right hemisphere of the brain was cut in forty-um thick sagital sections. Proliferating
cells were stained with Ki67, differentiating cells were stained with DCX and the total
number of granule cells were visualized with a Giemsa staining. A total number of twenty-
four female animals were tested (Tg21, n=6; and Control, n=6; 14 months old; Tg6, n=6; 6
months old; Control, n=6; 6.5 months old).

IntelliCage protocols: During Serial Reversion (A), Patrolling (B) and Chaining (C) mice can drink from one correct corner that changes according to different patterns. In both, acquisition and reversal phase control and transgenic animals showed a similar performance level at learning and memory. Tg6 animals could not carry out these tests.

Neurogenesis: We found the expected differences between younger and older animals
in proliferation and neuronal differentiation, but there was no difference between
transgenic and control animals.

Conclusion

1. As opposed at acute models chronic overexpression of Epo did not have any effect on
   learning and memory in any of the behavioral tests performed.
2. We did not observe any changes in proliferating cells, differentiating cells or total
   number of granule cells in the dentate gyrus of the hippocampus.
3. These results narrow Epo’s brain impact to the previous observations in reduced
   impulsivity and increased anxiety.

References

2. Miliou A, Dionisio MM, Stith PJ, Reid SR. Erythropoietin improves spatial learning and