

ERYTHROPOIETIN PROMOTES THE RECOVERY OF GENETICALLY INDUCED SHORT-TERM
MEMORY DEFICIENCY IN MICE

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ABSTRACT

The production of new neurons in the adult mammalian brain is mainly restricted to the olfactory system and the hippocampal formation. However, its physiological and behavioural role is still debated. We have developed transgenic mice expressing permanently activated Ras under the direction of the neuronal promoter for synapsin-1 (1) (named synRas mice). In these mice the proliferation of adult progenitor cells is dramatically reduced in the dentate gyrus of the hippocampus but not in the subventricular region generating precursor cells for olfactory neuron turnover. Impaired hippocampal progenitor proliferation in synRas mice is associated with a reduced spatial short-term memory assessed in the 8-arm radial maze while long-term memory is not affected as measured in the mouse Morris radial maze (2). The growth factor erythropoietin (EPO) and erythropoietin receptors (EPOR) are expressed in the nervous system and peripherally administered EPO, crosses the blood-brain barrier, stimulating injury-induced neurogenesis and neuronal differentiation (3). When breeding synRas with mice overexpressing EPO in the brain the reduction in spatial memory capacity was completely reverted to the level of wt animals as judged from the 8-arm radial maze assay. Wt and EPO-expressing mice showed identical levels of short term memory performances. After peripheral injections of erythropoietin protein in wt animals doublecortin positive neuronal precursor cell numbers were enhanced and improvements in performance in the short term memory assay were found. These results suggest that erythropoietin is involved in the recovery of genetically induced deficiencies of hippocampal progenitor cell proliferation and short term memory in mice.

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2) M Manns, Z Bichler, O Leske and R Heumann³ Gender modulated down-regulation of adult hippocampal precursor cells by transgenic expression of Ras in neurons: impact on short term memory processes, 2009 GBM-Meeting abstract

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