

Long term effects of t-cell-mediated cns inflammation on adult hippocampal neurogenesis

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Objectives: Neurogenesis is a well-characterized phenomenon within the dentate gyrus (DG) of the adult hippocampus. Aging and chronic degenerative disorders have been shown to impair hippocampal neurogenesis, but the consequence of chronic inflammation remains controversial.

Methods & Results: In this study the chronic Experimental Autoimmune Encephalomyelitis (EAE) mouse model of Multiple Sclerosis was used to investigate the long-term effects of T-cell mediated CNS inflammation on hippocampal neurogenesis. BrdU-labelled subpopulations of hippocampal cells in EAE and control mice (co-expressing Ki67, GFAP, DCX, NeuN, calretinin, calbindin, S100) were quantified at different time points, up to 1 month after BrdU administration, in order to estimate alterations on the rate and differentiation pattern of the neurogenesis process. The core features of EAE mice DG are i) enhanced cell proliferation, presumably of subgranular neural precursor cells (BrdU+ NPCs), which ii) in the long term is reversed (decline in Ki67+ NPCs), iii) increased level of immature neuronal markers (including calretinin and doublecortin) iv) trending decreases in NeuN and calbindin expression v) aberrant gliogenesis and differentiation of NPCs to mature astrocytes (BrdU+/S100+).

Conclusions: Although the inflammatory environment in the brain of EAE mice enhances the proliferation of hippocampal NPCs, in the long term neurogenesis is progressively depleted, giving prominence to gliogenesis. The discrepancy between the high number of immature cells and the low number of mature new-born cells could be the result of a caused defect in the normal maturation pathway.

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