Changes in adult proliferation in low and high aggressive mice in relation to inborn alterations in HPA axis activity

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Male wild house-mice, selected for long attack latency (LAL) and short attack latency (SAL), differ in stress coping strategies, with the LAL mice showing passive strategies and the SAL mice displaying active strategies. This genetic trait was associated with a differential regulation of the hypothalamic-pituitary-adrenal (HPA) axis under basal and stress conditions, with LAL mice showing higher HPA reactivity. LAL mice further show signs of a hypo-reactive serotonergic system. Thus, LAL mice show some characteristics that are also seen in depressed patients. Since stress suppresses newborn cell proliferation in the hippocampal dentate gyrus, we tested the hypothesis that line differences in stress coping and HPA regulation are reflected by the rate of cell proliferation. Cell proliferation in the subgranular zone (SGZ) of the dentate gyrus, assessed by bromodeoxyuridine (BrdU) numbers, was two-fold lower in LAL than in SAL mice, and was paralleled by higher plasma corticosterone concentrations in LAL mice. To estimate *basal* cell proliferation rate in LAL and SAL mice, the endogenous proliferation marker Ki-67 was used. Under basal conditions, LAL mice had significantly lower numbers of Ki-67-positive cells in the SGZ than SAL mice. Furthermore, forced swim stress induced 24 h later a significant reduction in BrdU-positive cell numbers in the SGZ of LAL but not of SAL mice. In conclusion, dentate gyrus proliferation rate was shown to reflect a genetic trait in coping style and stress responsiveness. Granule cell proliferation is suppressed by stress in LAL mice, whereas it is resistant to stress in SAL mice. These results may suggest line differences in hippocampal plasticity under conditions of chronic stress.

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