Changes in hippocampal neurogenesis following treatment with the glucocorticoid receptor antagonist RU486

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Depression is a serious and often fatal mental disorder with a relatively high incidence in the Western world. Although the etiology is poorly understood, chronic stress exposure has been implicated in the vulnerability to developing major depression. Indeed, clear HPA changes have been reported in a significant proportion of the major depressed patients. Although in animal studies, chronic stress was initially presumed to be causally involved in the structural damage to the hippocampal CA3 subregion, other studies have revealed a prominent stress-induced reduction in adult neurogenesis in the DG (VM Heine et al., EJN, 2004), that could, over time, contribute to the volume reductions of the entire hippocampus seen after stress. Recently, treatment with the glucocorticoid receptor anatagonist RU486 was shown to exert strikingly positive effects in a subgroup of patients with psychotic depression.
Moreover, although the working mechanism of many treatments is poorly understood, of various antidepressant drugs, it was recently shown that many, if not all of them, stimulate adult neurogenesis, often in conditions of chronic stress or corticosterone exposure. To address the possible involvement of (modulation of) neurogenesis also in this succesfull clinical application of the glucocorticoid receptor anatagonist RU486, we investigated proliferation and survival rate of adult-generated cells in the hippocampus of animals treated with corticosterone (10 mg/day during three weeks), vehicle, or Cort + RU486 (5 mg/100 mg RU486, twice daily), that were all injected with BrdU three weeks before sacrifice. Readouts included; numbers of apoptotic, Ki-67 positive, BrdU positive and doublecortin positive cells, representing dying, proliferating, late surviving and early neurogenetic cells, respectively. Results will be presented and discussed.

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