

Glucocorticoid receptor protein expression in human hippocampus in relation to age.

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(see also overlap with projects from Van Dam, vdBerg, Swaab)

The glucocorticoid receptor (GR) exerts numerous functions in the body and brain. In the brain, it has been implicated, amongst others, in feedback regulation of the hypothalamic-pituitary-adrenal axis, with potential deficits during aging and in depression. GRs are abundantly expressed in the hippocampus of rodent, except for the Ammon's horn (CA) 3 subregion. In rhesus monkey however, GR protein was largely absent from all hippocampal subregions, which prompted us to investigate its distribution in human hippocampus. After validation of antibody specificity, we investigated GR α protein distribution in the postmortem hippocampus of 26 human control subjects (1-98 years of age) and quantified changes with age and sex. In contrast to monkey, abundant GR-immunoreactivity was present in nuclei of almost all neurons of the hippocampal CA subfields and dentate gyrus (DG), although neurons of the CA3 subregion displayed lower levels of immunoreactivity. Colocalization with glial fibrillary acidic protein confirmed that GR was additionally expressed in approximately 50% of the astrocytes in the CA regions, with lower levels of colocalization (approximately 20%) in the DG. With increased age, GR expression remained stable in the CA regions in both sexes, whereas a significant negative correlation was found with age only in the DG of females. Thus, in contrast to the very low levels previously reported in monkey, GR protein is prominently expressed in human hippocampus, indicating that this region can form an important target for corticosteroid effects in human.