

### **Distribution of the glucocorticoid receptor in the human amygdala; changes in mood disorder patients.**

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

Exposure to stress activates the hypothalamic-pituitary-adrenal (HPA) axis that stimulates glucocorticoid (GC) release from the adrenal. These hormones exert numerous effects in the body and brain and bind to a.o. glucocorticoid receptors (GR) expressed in the limbic system, including the hippocampus and amygdala. Hyperactivity of the HPA axis and disturbed stress feedback are common features in major depression. GR protein is present in the human hypothalamus and hippocampus, but little is known-neither in healthy subjects nor in depressed patients-about GR expression in the amygdala, a brain structure involved in fear and anxiety. Since chronic stress in rodents affects GR expression in the amygdala, altered GR protein level in depressed versus healthy controls can be expected. To test this, we investigated GR- $\alpha$  protein expression in the post-mortem human amygdala and assessed changes in ten major or bipolar depressed patients and eight non-depressed controls. Abundant GR immunoreactivity was observed in the human amygdala, both in neurons and astrocytes, with a similar pattern in its different anatomical subnuclei. In major depression, GR protein level as well as the percentage of GR-containing astrocytes was significantly higher than in bipolar depressed patients or in control subjects. Taken together, the prominent expression of GR protein in the human amygdala indicates that this region can form an important target for corticosteroids and stress, while the increased GR expression in major, but not bipolar, depression suggests possible involvement in the etiology of major depression.