Distribution of the CRHR1 and CRHR2 mRNAs in the brain of transgenic mice overexpressing CRH

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Corticotropin-releasing hormone (CRH) and urocortin (Ucn) fulfill prominent roles in the regulation of the stress response. In human, hypersecretion of CRH has been implicated in stress-related disorders, including major depression. To study more in detail the brain mechanisms causing these disorders, we developed a transgenic mouse line overexpressing CRH (CRH-OE) exclusively in neural tissue. CRH-OE mice show hypothalamo-pituitary-adrenal (HPA)-axis disregulation reminescent of changes reported for major depression and, moreover, changes in neuroendocrine and autonomic functions resembling symptoms of human chronic stress. Previously, we showed that in this model levels of CRH and CRH-mRNA are increased in various brain areas including centres involved in the functioning of the HPA-axis.Furthermore, we demonstrated downregulation of Ucn in the main urocortinergic center, the Edinger-Westphal nucleus. To know more about the regulation of the stress response it is important to identify the changes occurring in the expression of the CRHR1 and CRHR2 receptors that binds CRH and the Ucn respectively, with very high affinity. mRNA distribution of CRHR1 and CRHR2α were assessed by *in situ* hybridization with Dig-labelled RNA probes. Remarkably, compared to wild type mice, CRH-OE mice reveal no difference in distribution of the CRHR1 but do show an increased expression of CRHR2α mRNA in the lateral septal nucleus, bed nuclei of the stria terminalis, medial nucleus of the amygdala, ventromedial hypothalamus, lateral hypothalamus, arcuate nucleus and dorsal raphe nucleus. In addition, expression of CRHR2α mRNA was observed inthe cerebral cortex and medial septal nucleus, which were completely lacking CRHR2α mRNA in the wild type mice. Recently, we developed radioactive in situ hybridization technique to detect these receptors that we are using now to quantify the receptors` expressions. In view of these results, CRH-OE mice appear to be a valuable tool to explore the roles of the CRH receptors in the genesis of stress-induced and HPA-axis-mediated human brain disorders.

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