Cross-talk of corticotropin-releasing hormone receptor subtype 1 with dopamine D₁ receptor: functional relevance in alcohol dependence

Laura BROCCOLI¹, Kay JÜNGLING², Dasiel O. BORROTO-ESCUELA³, Rainer SPANAGEL¹, Wolfgang H. SOMMER¹, Hans C. PAPE⁵, Kjell FUXE³, Jan M. DEUSSING⁴ and Anita C. HANSSON¹, *

¹Department of Psychopharmacology, Central Institute of Mental Health, Mannheim, Germany; ²Institute of Physiology I (Neurophysiology), Westfälische Wilhelms-Universität Münster, Germany; ³Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden; ⁴Molecular Neurogenetics, Max Planck Institute of Psychiatry, Munich, Germany

Upregulated corticotropin-releasing hormone (CRH) and CRH receptor subtype 1 (CRF₁) activity within the amygdala play a crucial role in the development of a chronic negative affective state, which is recognized as a major driving force for perpetuating the vicious cycle of alcohol dependence. Although the role of the neurotransmitter dopamine (DA) is mainly seen in the acquisition of alcohol reinforcement and maintenance of voluntary alcohol consumption, increasing evidences also indicate that amygdala DA receptors are highly involved in the modulation of emotional responses. Within the amygdala nuclei, GABAergic cluster of interneurons, known as intercalating cell masses (ITC). These neuronal populations are highly enriched in DA D₁ and CRH CRF₁ receptors, and exert important gating functions for intra-amygdala signal flow. We have established a functional interaction between the CRF₁ and D₁ receptor involved in the regulation of affective behavior, which represent a novel mechanism of amygdala function. Specifically, CRF₁-driven increased stress vulnerability and stress-induced alcohol seeking in dependent animals is due to the simultaneous activation of D₁ receptor. Based on these findings we suggest that CRF₁-D₁ receptor cross-talk in the amygdala neurons is involved in the hyper-responsiveness to behavioral stress that importantly adds to maintaining the dependent state.

*Submitting author e-mail: anita.hansson@zi-mannheim.de