Stress, emotion and cognition : role of mineralo- and glucocorticoid receptors

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"The more emotional an event, the better it will be remembered". Stress hormones such as cortisol (man) and corticosterone (rodent) are crucial for this intricate link between emotion and cognition. The hormones enhance motivation, mood and emotions, and have a profound influence on cognitive processes. This action exerted by the steroids is of evolutionary advantage and promotes health, but if dysregulated the cognitive-emotional changes become detrimental eventually precipitating stress-related diseases like Post-Traumatic Stress Disorder (PTSD). Why only some individuals experience the detrimental effects of stress, while and others remain healthy under similar conditions is a key question in cognitive neurobiology

The objective of this thesis is to identify the contribution of corticosteroids and their receptors to the integration of emotional and cognitive processes.

Corticosteroids are secreted from the adrenals in response to stress, and act in the brain via mineralo- (MR) and glucocorticoid receptors (GR). Emotional and cognitive performance of mice with genetically different MR and GR or pharmacologically-induced differential activation of these receptors was assessed in a variety of behavioural paradigms specifically designed to study the integration between emotional and cognitive domains. In this thesis I describe studies performed with two strains: the stress-susceptible BALB/c mouse strain and the stress-resistant C57BL/6J. We found that:

- Emotional arousal and cognitive performance are optimally integrated in mice with predominant MR- and additional moderate GR activation.
- The stress-susceptible BALB/c mice have an emotionally biased superior memory performance as compared to the resistant C57BL/6J mice; cognitive performance correlates with MR and GR expression in limbic brain areas.
- BALB/c mice generalize their fear responses to context and cue while C57BL/6J mice discriminate between context and cue.
- Injection of corticosterone before or after fear conditioning destabilizes the memory consolidation and facilitates extinction in BALB/c mice; C57BL/6J respond with augmented fear memory and lack of extinction.
- Mutant $MR^{CaMKCre}$ mice with forebrain-specific ablation of the MR gene display increased fear responses during all phases of memory formation and retrieval.

In conclusion, corticosteroids modulate the integration of emotional arousal and cognitive performance via a combined MR- and GR-mediated central action. It is proposed that C57BL/6J mice provide an animal model for PTSD and that the MR is a novel target for treatment of anxiety-related symptomatology.