DISSECTING THE CENTRAL STRESS RESPONSE USING SITE-SPECIFIC GENETIC MANIPULATION IN ADULT MICE

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The biological response to stress is concerned with the maintenance of homeostasis in the presence of real or perceived challenges. This process requires numerous adaptive responses involving changes in the central nervous and neuroendocrine systems. When a situation is perceived as stressful, the brain activates many neuronal circuits linking centers involved in sensory, motor, autonomic, neuroendocrine, cognitive, and emotional functions in order to adapt to the demand. However, the details of the pathways by which the brain translates stressful stimuli into the final, integrated biological response are presently incompletely understood. Nevertheless, it is clear that dysregulation of these physiological responses to stress can have severe psychological and physiological consequences, and there is much evidence to suggest that inappropriate regulation, disproportional intensity, or chronic and/or irreversible activation of the stress response is linked to the etiology and pathophysiology of anxiety disorders and depression.

Understanding the neurobiology of stress by focusing on the brain circuits and genes, which are associated with, or altered by, the stress response will provide important insights into the brain mechanisms by which stress affects psychological and physiological disorders. The CRF/Urocortin system is fundamental in orchestrating the organisms stress response. In addition to its hypophysiotropic action, CRF integrates the behavioral responses to stress within the central nervous system. This lecture will present an integrated multidisciplinary approch from gene to behavior using mouse genetics and animal models aim in elucidating the contribution of different members of the CRF/Urocortin family of peptides and receptors to the central stress respone. Defining the contributions of known and novel gene products to the maintenance of stress-linked homeostasis may improve our ability to design therapeutic interventions for, and thus manage, stress-related disorders.