

Stress and glucocorticoids: companions in health and disease

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The effects of stress and glucocorticoids on brain and cognitive function are dependent upon a number of factors, including the specific characteristics of the stressor, the context as well as individual differences in the vulnerability to stress. The central action of corticosteroids is mediated by mineralocorticoid (MR) and glucocorticoid receptors (GR), which coordinate distinctly different responses to stress. Through MR corticosteroid facilitates permissively the selection of the most appropriate behavioural strategy to cope with a challenge. High corticosteroid concentrations activate additional GR, which drives gene networks underlying energy mobilization and recovery from stress-induced changes. Through GR, corticosteroid promotes the consolidation of new information and the storage of energy resources in preparation for future needs. Despite the obvious importance of the stress hormones for mental health and homeostasis, the potentially disruptive effects of corticosteroids in the control of brain function and behaviour have received much attention. Why some individuals develop cognitive deficits after stress, while other individuals improve their cognitive performance under similar adverse conditions is still unresolved. (i) Stress in early life (maternal deprivation) as well as (ii) later life (exposing mice to rats) differentially affects endocrine regulation and cognitive performance. (iii) Acute intracerebroventricular (icv) administration of the GR antagonist mifepristone in ng amounts blocks the protective and memory promoting effects of corticosteroid. Chronic mifepristone icv improves cognitive performance and enhances circadian corticosteroid amplitude, like anti-depressants do. We proposed and demonstrated that the action of stress and glucocorticoids depend on the context and the genetical background of individuals. MR/GR imbalance reflects neuroendocrine dysregulation and behavioural maladaptation, while increasing the risk for a predisposing stress-related disorder.

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