Neuroendocrine Interactions: Implications for Gender Differences in Autoimmune, Inflammatory and Infectious Diseases

Esther Sternberg [1] Cherie Butts [1] Alexandra Tait [1]

[1] National Institute of Mental Health/National Institute of Health, Bethesda, Maryland, USA

Hormonal factors regulate immunity and affect susceptibility to autoimmune/inflammatory disease. Regulation of immunity by and interactions between the hypothalamic pituitary adrenal (HPA) and hypothalamic pituitary gonadal (HPG) axes contribute to the two- to ten-fold higher incidence and severity of autoimmune/inflammatory diseases in females compared to males. Activation of the HPA axis generally inhibits inflammation through the immunosuppressive effects of the glucocorticoids binding to glucocorticoid receptors (GR). Hormones of the HPG axis, particularly estrogens, can directly affect immunity at the cellular level and also interact with the HPA axis to alter glucocorticoid regulation of immunity. Interruptions of the HPA or HPG axis through surgical or pharmacological means alter host susceptibility to inflammatory disease. Differences in receptor number or sensitivity contribute to altered immune cell responsiveness to hormones. Changes in immune cell GR and ER numbers during development may contribute to gender and developmental differences in autoimmune disease. We have recently shown that dendritic cells express progesterone receptors (PR) and respond to progesterone differentially during maturation. Decreased GR sensitivity related to mutations or environmental factors may also induce glucocorticoid resistance and result in enhanced immune responses. We have recently shown that bacterial toxins selectively repress GR and other nuclear hormone receptor transactivation, including the PR and the ERβ. Understanding hormonal interactions with immune cells at multiple levels will shed light on gender differences in immunity and will lead to new avenues for therapy.