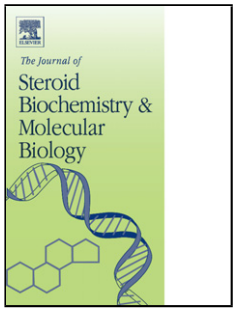

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STRESS-INDUCED MECHANISMS IN MENTAL ILLNESS: A ROLE FOR GLUCOCORTICOID SIGNALLING

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Highlights ►
► Exposure to stress can determine permanent changes in glucocorticoid signalling ► Dysfunctional glucocorticoid signalling may contribute to psychopathology susceptibility. ► GR signalling represents a convergence point for mechanisms altered in stress disorders ► SGK1 may link exposure to ELS with life-long changes in glucocorticoid function ►
► ►

Abstract

Stress represents the main environmental risk factor for mental illness. Exposure to stressful events, particularly early in life, has been associated with increased incidence and susceptibility of major depressive disorders as well as of other psychiatric illnesses. Among the key players in these events are glucocorticoid receptors. Dysfunctional glucocorticoid signalling may indeed contribute to psychopathology through a number of mechanisms that regulate the response to acute or chronic stress and that affect the function of genes and systems known to be relevant for mood disorders. Indeed, exposure to chronic stress early in life as well as in adulthood has been shown to reduce the expression of glucocorticoid receptors (GR), also through epigenetic mechanisms, and to up-regulate the expression of the co-chaperone gene FKBP5, which restrains GR activity by limiting the translocation of the receptor complex to the nucleus. Another mechanism that contributes to changes in GR responsiveness is the state of receptor