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Rapid Glucocorticoid Mediation of Suppressed Testosterone Biosynthesis in Male Mice Subjected to Immobilization Stress

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Physical and psychosocial stress challenge homeostasis, increasing glucocorticoid secretion (in rodents, corticosterone [CORT]) while decreasing testosterone (T) levels. The dynamics of stress-induced changes in T, CORT, and luteinizing hormone (LH) concentrations in mice have not been investigated previously. In particular, it remains to be established whether there is a rapid effect of CORT that is directly mediated by glucocorticoid receptors (GRs) in the testis. Therefore, serum and intratesticular T, serum CORT, and LH levels were measured during acute immobilization (IMO) stress, using the C57BL/6 strain of mice. The effects of testicular GR blockade were investigated by administration of the GR antagonist, RU486, via intratesticular (IT) or intraperitoneal (IP) injection. CORT levels increased in stressed males starting at 15 minutes, reaching a fivefold higher plateau by 1 hour compared with controls ($P < .01$). Conversely, starting from 30 minutes on, both serum and intratesticular T levels decreased in stressed males to 30% and 8% of control values, respectively, by 6 hours ($P < .01$). In contrast, LH was unchanged by IMO stress for up to 6 hours. Intratesticular treatment with RU486 partially prevented the IMO-induced decline in T levels. CORT treatment reduced intracellular cyclic adenosine monophosphate (cAMP) content in Leydig cells by 15 minutes and T production by 30 minutes in vitro. We conclude that 1) the rapid changes in T suggest a suppression of T biosynthesis by glucocorticoid through a nongenomic mechanism, lowering the production of cytoplasmic cAMP; 2) changes in gonadotropic stimulation of Leydig cells are unlikely to explain the suppression of T levels during acute stress; and 3) the results are consistent with a direct inhibitory action of CORT on Leydig cells.

Key words: Leydig cell, cyclic AMP, glucocorticoid receptor

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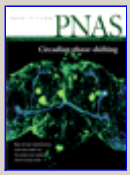
L. J Martin and J. J Tremblay
Glucocorticoids antagonize cAMP-induced Star transcription in Leydig cells through the orphan nuclear receptor NR4A1
J. Mol. Endocrinol., September 1, 2008; 41(3): 165 - 175.
[Abstract] [Full Text] [PDF]



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V. Vasta, M. Shimizu-Albergine, and J. A. Beavo
Modulation of Leydig cell function by cyclic nucleotide phosphodiesterase 8A
PNAS, December 26, 2006; 103(52): 19925 - 19930.
[Abstract] [Full Text] [PDF]