

64. INHIBITION OF OVARIAN ESTROGEN BIOSYNTHESIS BY PROLACTIN

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During lactation and hyperprolactinemia, ovulation is inhibited. To determine whether prolactin has a role in controlling ovarian estrogen biosynthesis, groups of rats (28 days old) primed with 20 IU pregnant mares' serum gonadotropin (PMSG) were injected with one of the following treatments: (1) saline, (2) prolactin (6 IU/rat) 48h later, (3) LH (10 µg /rat) 51h later or (4) prolactin followed by LH. All rats were sacrificed 52h after PMSG (just prior to the LH surge). Aromatase activity was determined in ovarian microsomes by incubating [1,2³H]-androstenedione (0.1 µC/0.1 µM) for 30 mins and quantitating the ³H₂O released during aromatization. Prolactin decreased aromatase activity 50%, whereas LH increased enzyme activity by 25%. Treatment with prolactin as well as LH, prevented the LH-induced increase and caused 36% decrease in aromatase activity compared to controls. When the largest preovulatory follicles removed from normal 4-day cycling rats on proestrus morning prior to the LH surge, were incubated with prolactin (1 µg/0.5 ml), LH (10 µg/0.5 µl), or prolactin + LH, prolactin prevented the 2-fold increase in aromatase activity observed with LH alone. In these studies [1 β³H]-androstenedione (0.1 µC/0.2 µM) was added after 2h and the incubation continued for 2h. These results suggest that prolactin interferes with the action of LH on aromatase.

65. IS TAMOXIFEN AN IDEAL ANTAGONIST OF ESTROGEN ACTION?

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Tamoxifen is a non-steroidal antagonist of estrogens and is used as the only specific medical treatment in breast cancer. Its association with the estrogen receptor (ER) would mean that tamoxifen should be physiologically active in all those tissues that are endowed with ER. Liver ER is said to mediate sex hormone induced synthesis of proteins. The influence of tamoxifen on rat liver function was evaluated here. Estradiol and testosterone derivatives both decreased liver glycogen and impaired triamcinolone mediated gluconeogenesis in male, adrenalectomized rats, without affecting the binding of the glucocorticoid to its specific cytoplasmic receptor. Neither sex steroid altered the induction of liver enzymes. Tamoxifen acted as a weak agonist of gonadal hormones at the level of liver glycogen but did not exert an additive effect with either testosterone or estradiol. Chromatography revealed that, at comparable concentrations, estrogens and tamoxifen did not saturate the same species of protein. Tamoxifen binders were furthermore distinct from transcortin on both Sephadex G-200 and DEAE-Cellulose-52 columns. One hundredfold excess of glucocorticoids did not displace the binding of sex steroids to liver vectors. These studies emphasize the need to reconsider the mechanisms of action of tamoxifen which is said to be an ideal estrogen antagonist. Aided by grants from the CNRS (AI 03 1917) and UER Broussais Hotel-Dieu.

7. STEROIDS AND DIFFERENTIATION

66. ANDROGEN EFFECTS ON NEUROTRANSMITTER SYNTHESIS IN THE DEVELOPING RAT BRAIN

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Gonadal steroids exert diverse and extensive effects in the central nervous system. Testosterone acts during a limited period of perinatal development in male animals to influence permanently the development of reproductive behaviour and neuroendocrine function. This study has examined the role of androgens in the production of the catecholamine neurotransmitters during development. Four day old female rats were treated with testosterone propionate and catecholamine synthesis measured by a radioenzymatic assay of tyrosine hydroxylase (TH) activity in discrete regions of the brain. Androgen-treated animals were compared with control female and male litter mates. In the hypothalamus-preoptic area, TH activity increased by 50% on day 6 (2 days steroid treatment), decreased slightly up to day 10 and increased to greater than 300% of pre-treatment values by day 16. Similar patterns of increase were observed in control female and male animals. TH activity in the brain stem was not altered by androgen treatment and remained constant in all experimental groups from day 4 to 20. In the cortex, TH activity was very low during the first few days of life but increased rapidly between day 6 and 9 before decreasing on day 10 to levels similar to days 1-4. The role of androgens in the development of the cortex is under investigation.