CENTRAL NERVOUS SYSTEM—I. ANIMAL MODE

Specific control of LH and FSH secretion by estrogens, androgens and progestins at the anterior pituitary level, F. LABRIE, L. LAGACE, J. DROUIN and V. RAYMOND, Medical Research Council Group in Molecular Endocrinology, Le Centre Hospitalier de l'Université Laval, Quebec G1V 4G2, Canada

In order to eliminate uncontrollable changes of LH and FSH responsiveness to LHRH secondary to sex steroid-induced modifications of LHRH secretion *in vivo*, the direct action of sex steroids at the anterior pituitary level on gonadotropin secretion was studied in rat anterior pituitary cells in primary culture. Preincubation of cells with 1×10^{-9} M 17β-estradiol (E_2) led to an increased LH and FSH responsiveness to LHRH, the concentration of the neurohormone required for half-maximal stimulation of LH release (ED_{50}) being reduced approximately 2-fold. The stimulatory effect of E_2 was also apparent on basal LH release while the maximal response to the neurohormone was not affected. The effect of E_2 on the pituitary sensitivity to LHRH was exerted at an ED_{50} value of 2×10^{-11} M, thus indicating the physiological significance of the effects observed. Progesterone (P) alone at concentrations lower than 100 nM had no effect on basal or LHRH-induced LH release. However, in the presence of E_2, P had a biphasic effect on LH release: a transient increase of the LH responsiveness to LHRH maximum (at 4 h) followed by a marked inhibition of the sensitizing effect of E_2 on the LH response to LHRH. Contrary to the findings with LH, P alone led to stimulation of basal FSH release and increased the maximal FSH response to LHRH, this effect being potentiated by E_2. On the other hand, testosterone and dihydrotestosterone led to a marked inhibition of the LH responsiveness to LHRH, the LHRH ED_{50} value being increased 3-fold. Basal LH release and the maximal LH response to LHRH were not affected by androgens. Markedly different effects of androgens were found on FSH secretion: increased basal release and maximal response to LHRH. The specific and often opposite effects of androgens, estrogens and progestins on LH and FSH secretion in pituitary cells in primary culture offer a precise model for study of biological activity(ies) of synthetic steroids. Using this system, we could find that the "progestins" currently used in the pill have potent androgen-like activity which could be, up to a large extent, responsible for their contraceptive efficiency. Better understanding of the action of sex steroids at the anterior pituitary level on gonadotropin secretion should facilitate interpretation of the site of action of these steroids *in vivo*.

OOCYTES AND STEROIDS

Recent findings related to the mechanism of action of progesterone for promoting meiotic releasing events on *Xenopus laevis* oocytes, S. SCHORDERET-SLATKINE,* M. SCHORDERET,† F. GODEAU,‡ and E. E. BAULIEU, *Station de Zoologie expérimentale, University of Geneva, †Ecole de Médecine, University of Geneva, Switzerland, ‡Laboratoire des Hormones, Bicêtre. France

Amphibian oocytes are arrested at the prophase of the first meiotic division. Meiosis is physiologically reinitiated by progesterone released by follicle cells under pituitary stimulation. During this period of "maturation" the large nucleus (germinal vesicle) breaks down and meiosis evolves up to the second meiotic metaphase where the cell remains arrested until sperm penetration or parthenogenetic activation. It has been established that a maturation promoting factor (MPF) appears in the cytoplasm of progesterone-treated oocytes whose appearance is dependent on protein synthesis but not on transcriptional activity. Progesterone is inactive when injected into the oocyte. A progesterone analogue was found able to promote oocyte maturation when linked to a macromolecule which does not enter the cell. It has been also shown that lanthanum (10^{-2} M) and various non-steroidal compounds (β receptor adrenergic antagonists, local anesthetics and antiarrythmic drugs, at 10^{-3} M) are potent inducers of maturational events. At these concentrations, the non-steroidal agents are supposed to displace membrane bound calcium and perhaps to modify calcium homeostasis within the cell. Furthermore, the inhibition of progesterone induced maturation by γ-chlorocyclohexane (gammexane) also implicates some interaction at a membrane level, possibly by interacting with phospholipid turnover and/or metabolism. All these considerations imply that this system does not fit the current models of the mechanism of action of sexual steroids which require transcriptional events mediated by an intracellular hormone receptor complex. It could lead itself to study the hypothesis that progesterone first interaction is located at the membrane level and linked to transmembrane movements of calcium.

TESTES AND STEROIDS

Occurrence and possible function of steroid receptors in the testis, H. J. VAN DER MOLEN, W. M. O. VAN BEURDEN, J. A. GROOTEGOED, E. MULDER and F. F. G. ROMMERTS, Department of Biochemistry (Division of Chemical Endocrinology), Medical Faculty, Erasmus University, Rotterdam, The Netherlands

In rat testis tissue a specific receptor for oestradiol is present in interstitial tissue, but not in seminiferous tubules, whereas a receptor, specific for androgens, can be demonstrated in seminiferous tubules but not in interstitial tissue.

The androgen receptor can be demonstrated in the nuclear and cytoplasmic fractions of testicular tissue of mature hypophysectomized rats, either *in vivo* after injection of testosterone or *in vitro* after incubation of testis tissue with testosterone. Using agar-gel electrophoresis this receptor can be distinguished from the testicular transport-like protein for androgens (androgen binding protein = ABP). After *in vivo* administration of testosterone the steroid bound to the receptor in mature rat testis is mainly unmetabolized testosterone. After dissection of testis tissue the larger part of the receptor appears to be present in the seminiferous tubules. The amount of exogenous testosterone that can be bound per mg of protein in the nuclear extract increases gradually during 20 days after hypophysectomy. Some characteristics of the receptor in the nuclear extract and of ABP have been compared: the receptor is more sensitive to temperature increases than ABP; the steroid dissociates more slowly from the receptor than from ABP; cyproterone acetate shows almost no effect on the binding of dihydrotestosterone to ABP, but does compete for the receptor binding sites in the nuclear extract. The androgen receptor appears to localize mainly in Sertoli cells, as shown by studies with Sertoli cell enriched testis tissue and with isolated Sertoli cells. With respect to the localization of the androgen receptor in seminiferous tubules it has also been attempted to detect in male germinal cells an androgen receptor with properties similar to the properties of androgen receptors which are known to be present in the seminiferous tubules of rat testis. Tubule fragments and cell preparations enriched in germinal cells and Sertoli cells were isolated from testicular tissue of rats (30–35 days of age) and these preparations were incubated with [^{3}H]-testosterone. Radioactive steroid was specifically bound to receptors extracted with 0.4 M KCl from the nuclear fractions of tubule frag-