

What is the relationship among the various endocrine components of the male reproductive system?

Hypothalamic-Pituitary-Testicular Axis-feedback loops

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The hypothalamic-pituitary-testicular unit is an integrated system that assures the adequate and appropriate secretion of male hormones and the production of sufficient sperm for the propagation of the species. Each anatomical site is integrated with the others in a classic endocrine-feedback manner, with ample local paracrine and intracrine modulation required for its most effective function.

Testes

The Leydig cells of the testes are the site of production and secretion of the hormone testosterone. Through its direct action and that of its metabolites, dihydrotestosterone and estradiol, the hormonal milieu required for male sexual development and function is created; there is also a wide range of androgen- and estrogen-mediated effects on critical target organs such as the brain, bone, muscle, liver, skin, bone marrow, adipose tissue and immune systems. The Leydig cells are regulated by circulating levels of luteinizing hormone (LH), a hormone produced in the pituitary gland under the control of a hypothalamic hormone, gonadotropin releasing hormone (GnRH). GnRH in turn is modulated by neurotransmitters produced in the brain and circulating hormones. The spermatogenic compartment consists of Sertoli cells and germ cells in the seminiferous tubules, that act in an integrated fashion with one another and Leydig cells to result in normal germ cell production. The Sertoli cells are stimulated by intratesticular testosterone and follicle stimulating hormone (FSH). The testes, through their production of steroid and peptide secretory substances, also provide the regulatory feedback control of the hypothalamic and pituitary components of the axis.

Hypothalamic regulation of gonadotropin-releasing hormone

Hypothalamus

The hypothalamus is the principal integrative unit responsible for the normal pulsatile secretion of GnRH, that is delivered through the hypothalamic-hypophyseal portal blood system to the pituitary gland. The

pulsatile release of GnRH provides the signals for the timing of the release of LH and FSH, which under normal circumstances occurs approximately every 60–90 minutes.

Pituitary

GnRH acts by binding to the GnRH receptors on the surface of the pituitary LH and FSH secreting cells. The secretion of GnRH is regulated in a complex fashion by neuronal input from higher cognitive and sensory centers and by the circulating levels of sex steroids and peptide hormones such as prolactin, activin, inhibin, and leptin. The local effectors of GnRH synthesis and release include a number of neuropeptides, opioids, catecholamines, indolamines, nitric oxide and excitatory amino acids, γ -aminobutyric acid (GABA), dopamine, neuropeptide Y, vasoactive intestinal peptide (VIP), corticotropin-releasing hormone (CRH), and kisspeptin. Catecholamines, excitatory amino acids, and nitric oxide in physiologic amounts are stimulatory, whereas kisspeptin, opioid peptides and β -endorphin are inhibitory. Testosterone, either directly or through its metabolic products (estradiol and dihydrotestosterone), has predominantly inhibitory effects on the secretion and release of GnRH, LH, and FSH in the male. The inhibitory effects of testosterone and estradiol on gonadotropin secretion is mediated by inhibition of kisspeptin production in the hypothalamus. Prolactin is a potent inhibitor of GnRH secretion, thus explaining its role in inhibiting LH and testosterone secretion in the clinical condition of hyperprolactinemia.

Integration of the hypothalamic-pituitary gonadal axis

The normal pulsatile secretion of LH and FSH is principally driven by the pulses of GnRH from the hypothalamus. Regulation of LH and FSH is the result of feedback inhibition of the hypothalamic-pituitary component by the secretory products of the Leydig cells and Sertoli cells. Testosterone, directly and through its metabolites, regulates LH and FSH. Thus, if serum testosterone is elevated, LH and FSH will be inhibited; if testosterone is low due to Leydig cell dysfunction, LH and FSH will be increased. This is referred to as primary hypogonadism. FSH is also regulated by other Sertoli cell products; inhibin is a suppressor of FSH. If Sertoli cells are dysfunctional, spermatogenesis may be hindered and an elevated FSH may be a marker for such injury. Some patients with infertility will have reduced inhibin and isolated elevations of serum FSH. If the defect in steroidogenesis or spermatogenesis is the result of decreased LH and FSH secretion, then low serum levels of testosterone will not be accompanied with elevated gonadotropins.

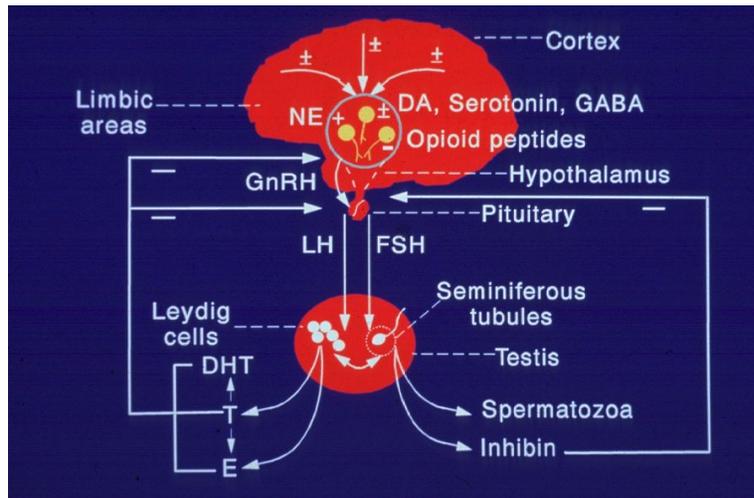


FIG. 1. Schematic representation of the components of the hypothalamic-pituitary-testicular axis and of its feedback regulators.

Suggested reading

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