HPG Axis and the Gonadal Hormones

Hypothalamus

GnRH, synthesized by neuroendocrine neurons in the hypothalamus, is released in a pulsatile manner into the hypophyseal portal circulation supplying the pituitary gland. The GnRH pulse generator is considered to be comprised of KISS1 neurons in the arcuate/infundibular nucleus of the hypothalamus. Many central (neurotransmitters, neuropeptides, glial factors) and peripheral signals influence GnRH secretion.

↓ GnRH

Anterior pituitary

Pulsatile GnRH release stimulates the synthesis of LH and FSH by the gonadotrophs and pulsatile release from these pituitary cells into the systemic circulation. Note in some species prolactin also serves important gonadotrophic functions.

↓ LH, FSH

Gonads

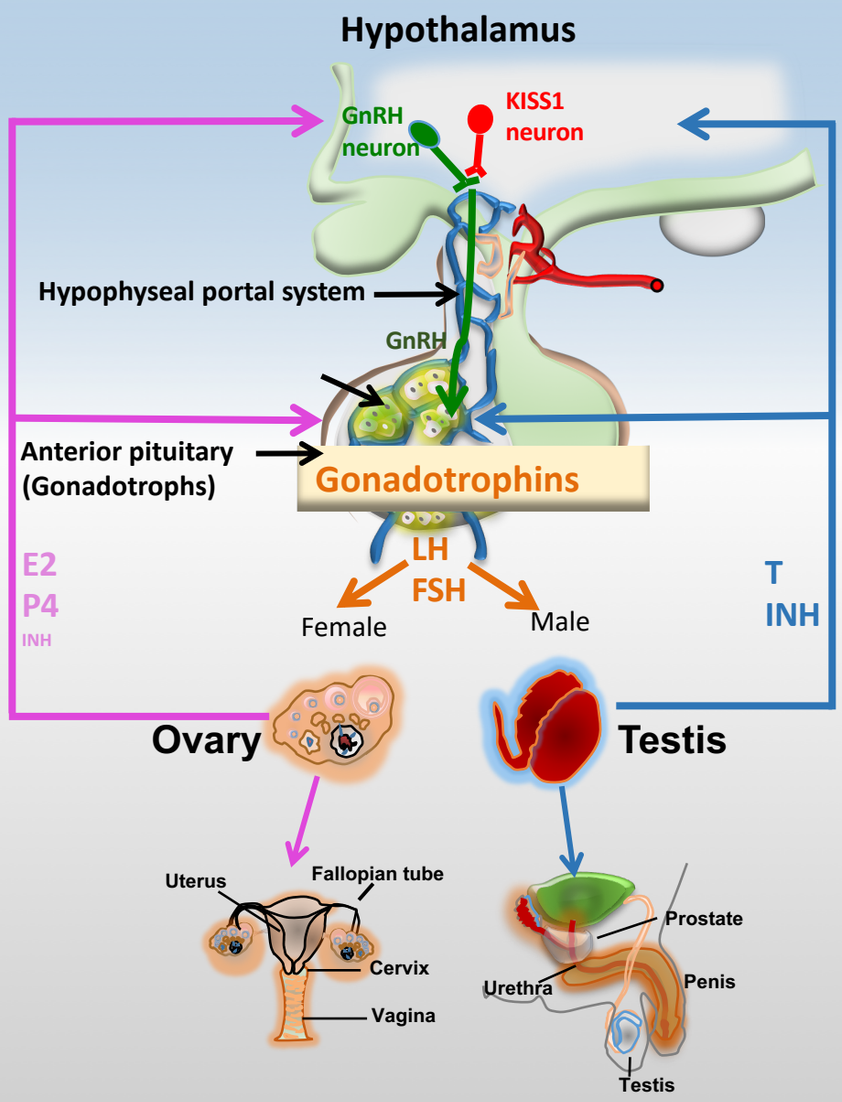
LH and FSH drive gametogenesis and sex steroid production In the adult male and female (premenopausal). In the female, both gonadal functions are subserved by the ovarian follicle, but in the male spermatogenesis takes place in the seminiferous tubule while testosterone production occurs in the Leydig cell of the interstitial spaces. Gonadal steroids (and gonadal protein hormones) regulate LH and FSH secretion by feedback actions that are exerted directly at the pituitary or indirectly via the hypothalamus.

E2, P4 - female ↓ ↓ T - male

Target Tissues

Gonadal steroids target several tissues, most notably reproductive tract, brain and bone. A major component of steroid signaling is mediated via nuclear steroid receptors that regulate gene expression in target tissues.

GnRH: Gonadotropin releasing hormone; KISS1:Kisspeptin
FSH: Follicle stimulating hormone; LH: Luteinizing hormone
E2: Estradiol , P4: Progesterone, INH: Inhibin
T: Testosterone, INH: Inhibin



The brain plays a critical role in governing the ovarian cycle in females (menstrual cycle in women) and spermatogenesis and testosterone secretion in males. Gonadal steroids in turn contribute to the control of sexual, aggressive and risk-taking behaviors.

Dr. Plant spent his academic career spanning four decades studying the control of the HPG axis in the rhesus monkey, a representative higher primate. His research contributed to the elucidation of the GnRH pulse generator, the timing of puberty and the neural mechanisms governing menstrual cyclicity and testicular function.

Drs. Cooper, Simpkins and Breckenridge have extensive experience identifying and characterizing the molecular events associated with development and aging of reproductive mechanisms and the effects of xenobiotics on reproductive function in males and females.

Drs. Grattan and Hovey are experts in the physiology and pathophysiology of prolactin, the later includes inhibitory actions on the HPG axis.

Dr. Handa has years of experience studying neuronal circuitry in the hypothalamus and performing and interpreting results from RIA, LC-MS-MS and mRNA analyses of HPG, HPA, HPG, HPT hormones.