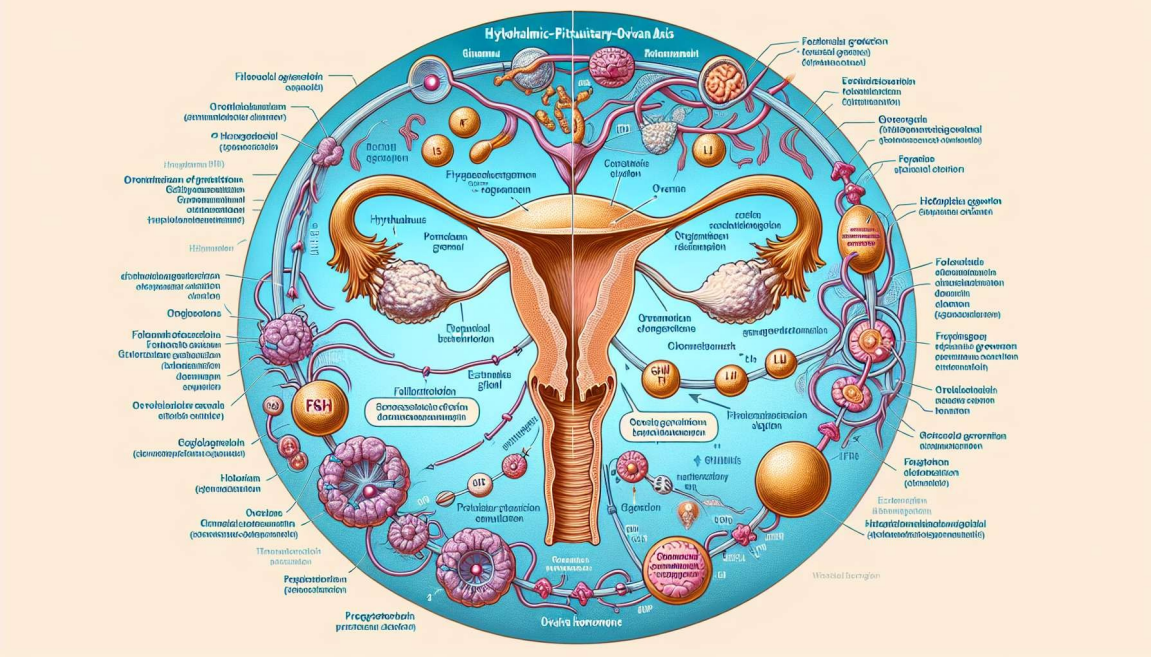

The hypothalamic-pituitary-ovarian (HPO) axis is a complex endocrine regulation system that controls the menstrual cycle and female reproductive function. It involves fine hormonal interactions between three key structures: the hypothalamus, the pituitary gland, and the ovaries. Understanding the mechanisms of regulation of the HPO axis is essential for apprehending the physiology of the menstrual cycle and the causes of ovulation and fertility disorders.

The hypothalamus is a cerebral structure located at the base of the brain, which plays a central role in the regulation of the HPO axis. It secretes in a pulsatile manner a neurohormone called GnRH (Gonadotropin Releasing Hormone), which stimulates the synthesis and release of pituitary gonadotropins, FSH (Follicle Stimulating Hormone) and LH (Luteinizing Hormone). The frequency and amplitude of GnRH pulses vary during the menstrual cycle and are modulated by endogenous (ovarian hormones, neurotransmitters) and exogenous (stress, nutrition, physical activity) factors.

The pituitary gland is an endocrine gland located just below the hypothalamus, which receives GnRH pulses via the hypothalamic-pituitary portal system. In response to GnRH, the gonadotropic cells of the adenohypophysis secrete FSH and LH, which act directly on the ovaries to regulate follicular growth, ovulation, and luteal function. FSH stimulates the recruitment and maturation of ovarian follicles, while LH triggers ovulation and the formation of the corpus luteum.

The ovaries are the target organs of pituitary gonadotropins, which exert a feedback on the HPO axis via the secretion of steroid hormones, mainly estrogens and progesterone. During the follicular phase of the cycle, the growth of ovarian follicles stimulated by FSH is accompanied by a progressive increase in estradiol secretion by the granulosa cells.

Estradiol exerts a negative feedback on the hypothalamus and the pituitary gland, slowing down the secretion of FSH and allowing the selection of the dominant follicle.

When estradiol levels reach a critical threshold late in the follicular phase, they exert a positive feedback on the HPO axis, triggering a peak of LH secretion responsible for ovulation. After ovulation, follicular cells transform into luteal cells under the action of LH, forming the corpus luteum which mainly secretes progesterone. Progesterone exerts a negative feedback on the HPO axis, inhibiting the secretion of GnRH and LH and preventing the recruitment of new follicles during the luteal phase.

In the absence of fertilization, the corpus luteum involutes, causing a drop in progesterone and estradiol levels. This hormonal deprivation lifts the brake on the HPO axis, allowing a new increase of FSH secretion and the start of a new menstrual cycle. In case of pregnancy, the embryo secretes hCG (chorionic gonadotropin hormone) that maintains the corpus luteum and the secretion of progesterone, thus ensuring the maintenance of pregnancy.

Disturbances in the regulation of the HPO axis can lead to menstrual cycle and fertility disorders. A deficiency in the secretion of GnRH, for example in the context of mental anorexia or hypercorticism, can block the secretion of gonadotropins and induce hypothalamic amenorrhea. A prolactinoma can also slow down GnRH secretion due to an inhibitory effect of prolactin on GnRH neurons, leading to amenorrhea and infertility due to gonadotropic insufficiency.

On the other hand, an oversupply of LH, observed in polycystic ovary syndrome (PCOS), can disrupt follicular maturation and ovulation, leading to chronic anovulation and infertility. In PCOS, hyperandrogenism fosters an increase in the frequency of GnRH pulses, preferentially stimulating the secretion of LH at the expense of FSH. This imbalance in the FSH/LH ratio is responsible for disordered folliculogenesis and absence of ovulation.

Understanding the mechanisms of regulation of the HPO axis is therefore essential for the diagnosis and management of endocrine disorders of reproduction. Exploration of the HPO axis relies on dynamic hormonal assays (GnRH test, clomiphene citrate test) and on pituitary imaging (MRI) in case of suspected pituitary adenoma. Treatments aim to restore a physiological pulsatile secretion of GnRH (GnRH pump in hypogonadotropic hypogonadism) or to directly stimulate ovulation by exogenous gonadotropins (FSH, hCG) in assisted reproduction protocols.

Key points:

1. The hypothalamic-pituitary-ovarian (HPO) axis is a complex endocrine regulation system that controls the menstrual cycle and female reproductive function, implying hormonal interactions between the hypothalamus, pituitary gland, and ovaries.

2. The hypothalamus secretes GnRH in a pulsatile manner, which stimulates the synthesis and release of pituitary gonadotropins, FSH, and LH.

3. In response to GnRH, the pituitary gland secretes FSH and LH, which act on the ovaries to regulate follicular growth, ovulation, and luteal function.

4. During the follicular phase, FSH-stimulated growth of ovarian follicles is accompanied by a progressive increase of estradiol secretion, which exerts a negative feedback on the HPO axis.

5. High levels of estradiol at the end of the follicular phase exert a positive feedback effect on the HPO axis, triggering a peak secretion of LH responsible for ovulation.

6. After ovulation, the corpus luteum mainly secretes progesterone, which exerts a negative feedback on the HPO axis, inhibiting the secretion of GnRH and LH during the luteal phase.

7. Disturbances in the regulation of the HPO axis can result in menstrual cycle and fertility disorders, such as hypothalamic amenorrhea, hyperprolactinemia, or polycystic ovary syndrome.

8. The examination of the HPO axis depends on dynamic hormonal assays and pituitary imaging in case of suspected pituitary adenoma.

9. Treatments aim to restore a physiological pulsatile secretion of GnRH or to directly stimulate ovulation with exogenous gonadotropins in the context of assisted reproductive techniques.