Hypothalamic-pituitary dysfunction in polycystic ovary syndrome

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Identifying kisspeptin as key central regulator of gonadotropin-releasing hormone (GnRH) secretion has led to a new level of understanding of the neuroendocrine regulation of human reproduction. The related discovery of the kisspeptin-neurokinin B-dynorphin (KNDy) pathway in the last decade has further strengthened our understanding of the modulation of GnRH secretion by endocrine, metabolic and environmental inputs.

Kisspeptin is a principal regulator of the secretion of gonadotropins, and thus it is critical for the onset of puberty, the regulation of sex steroid-mediated feedback and the control of adult fertility. Although there is some sexual dimorphism, both in neuroanatomical and functional sense, these functions are apparent in both men and women. Kisspeptin acts upstream of gonadotropin-releasing hormone (GnRH) and, following paracrine stimulatory and inhibitory inputs from neurokinin B and dynorphin (KNDy neuropeptides), signals directly to GnRH neurones to control pulsatile GnRH release. Depending on the isoform, route and dose in which it is administered, kisspeptin robustly stimulates the secretion and pulse frequency of luteinizing hormone (LH).

Currently, it is the primary focus of many research studies to translate the theoretical knowledge of the KNDy system into clinical expertise. Possible future clinical applications include proposed regulation of LH pulsatility, stimulation of gonadal sex steroid secretion in patients with reproductive disorders, including hypothalamic amenorrhoea and hypogonadotropic hypogonadism. Also, it seems that to some extent converse effects may be possible consisting in reducing the activity of the KNDy system to decrease LH secretion where hypersecretion of LH adds to the phenotype, such as in patients suffering from polycystic ovary syndrome (PCOS).

The main objective of the research paper is to extend the knowledge in this field with regard to PCOS patients, i.e. where hyperactivity of the KNDy system results in increased secretion of LH. In the paper, attempt has been made to determine the mechanisms, or rather the form of this increased activity, through the analysis of pulsatile secretion, with separate reference to pulse frequency and amplitude.

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