REPRODUCTIVE BIOLOGY

REVIEW

Neuroendocrine regulation of GnRH release and expression of GnRH and GnRH receptor genes in the hypothalamus-pituitary unit in different physiological states

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SUMMARY

This review is focused on the relationship between neuroendocrine regulation of GnRH/LH secretion and the expression of GnRH and GnRH receptor (GnRHR) genes in the hypothalamic-pituitary unit during different physiological states of animals and under stress. Moreover, the involvement of hypothalamic GABA-ergic, β-endorphinergic, CRH-ergic, noradrenergic, dopaminergic and GnRH-ergic systems in the regulation of expression of the GnRH and GnRHR genes as well as secretion of GnRH/LH is analyzed. It appears that the neural mechanisms controlling GnRH gene expression in different physiological states may be distinct from those regulating GnRH/

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LH release. The hypothalamic GnRHR gene is probably located in different neural systems and may act in a specific way on GnRH gene expression and GnRH release. *Reproductive Biology 2010* ***10*** *2: 85-124.*
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INTRODUCTION

Gonadotropin cells in the anterior pituitary gland are regulated by the release of GnRH from the hypothalamus into the primarily portal capillaries in the median eminence (ME) and its delivery to the target *via* the hypophyseal portal vein [176]. The GnRH cells in the central nervous system are not segregated into neural clusters but appear as a loose network spred through many cytoarchitectonic structures. In most species, GnRH cells form a loose continuum from the diagonal band of Broca and more dorsal septal areas, to the bed nucleus of the stria terminalis and diencephalic areas. Also in this continuum there are cells lying dorsal to and within the supraoptic nucleus (SOP).

GnRH release is controlled by numerous stimulatory and inhibitory factors as well as factors with biphasic effects on GnRH neurons [64, 201]. After the isolation and sequencing of porcine and ovine GnRHs, it appeared that these peptides isolated from several classes of vertebrates showed multiple substitutions in their sequence when compared with pig or sheep GnRH [66, 117, 125, 144, 172]. Until now, more than a dozen isoforms of GnRH sharing 10-50% amino acid identity has been found in vertebrates. The conservation of the length of these peptides, NH_2 terminus and COOH terminus indicates that these features are critically important for receptor binding and activation.

It is generally thought that most vertebrates possess at least two, and usually three, forms of GnRH which differ in their amino acid sequence, localizations and embryonic origins [21]. The most ubiquitous is chicken GnRH II which is the evolutionary conserved member of the GnRH peptide family. Its form in mammals differs from GnRH I by three amino acid residues at position 5, 7, 8 [21, 117]. It has been shown that the biological