

BIOLOGICAL ACTION OF LAMPREY GONADOTROPIN-RELEASING HORMONE IN LAMPREYS

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Gonadotropin-releasing hormone (GnRH) is the major hypothalamic peptide known to control the pituitary-gonadal axis in mammals. The presence of GnRH in the hypothalamus in many different species of vertebrates signifies a functional role that has been conserved throughout vertebrate evolution. We have recently determined the structure of GnRH in the sea lamprey (*Petromyzon marinus*), as pGlu-His-Tyr-Ser-Leu-Glu-Trp-Lys-Pro-Gly-NH₂ (Sherwood et al., 1986). The structure of the lamprey GnRH differs in five amino acids compared with mammalian GnRH and chicken GnRH I and in four amino acids with salmon GnRH and chicken GnRH II.

Lampreys belong to the class of Agnathans, the oldest living vertebrates. Although lampreys lack vascular or neural connections between the hypothalamus and adenohypophysis, the control of the pituitary by the hypothalamus is probable by diffusion of GnRH across the connective tissue to the adenohypophysis (Gorbman, 1965; Nozaki et al., 1984). Physiological studies utilizing mammalian GnRH analogues which stimulated various reproductive processes (Sower et al., 1982, 1983, 1985) have provided evidence for the regulatory influence of the hypothalamus on the pituitary-gonadal axis. More recently in our first reported paper on the biological activity of lamprey GnRH, we demonstrated that ovulation had occurred in 80% of the lampreys treated with either a single injection or two injections of lamprey GnRH at 0.2 or 0.1 ug/kg (Sower et al., 1987). This present paper examines the biological activities of lamprey GnRH, a lamprey GnRH putative antagonist ([D-Phe^{2,6}, Pro³] lamprey GnRH) and a mammalian GnRH superagonist ([D-Ala⁶, Pro⁹ NEt] mammal GnRH) on steroidogenesis as an indicator of pituitary function in female and male adult sea lampreys in two different reproductive stages to further enhance our understanding of the role of hypothalamic GnRH in reproduction in lampreys.

The lamprey GnRH or the mammalian GnRH superagonist significantly stimulated plasma estradiol and progesterone in male and female lampreys undergoing the final maturational processes (Figs 1 and 2). In contrast, in male and female lampreys

in the parasitic phase, plasma estradiol decreased and progesterone increased in response to lamprey GnRH (0.1 or 0.05 ug/g) or the mammalian GnRH superagonist (0.05 or 0.025 ug/g). The putative lamprey antagonist which significantly inhibited ovulation in our earlier study (Sower et al., 1987) had no effect on estradiol levels in the present study except at a dose of 0.05 ug/g in the female lamprey in which estradiol levels were significantly higher than controls at 24 hr. However, this putative lamprey antagonist at doses of 0.3, 0.15, or 0.075 ug/g, stimulated estradiol levels but had no effect on progesterone levels in the male lampreys.

In summary, lamprey GnRH is biologically-active in stimulating the pituitary-gonadal axis and its activity is dependent upon reproductive stage of the lamprey. The lamprey GnRH molecule has retained the length and NH₂- and COOH-termini of the GnRH molecule and has been conserved in its function in terms of its ability to stimulate the reproductive system in the lamprey. Increasing our understanding of the structure and function of the vertebrate GnRHs may contribute to our understanding of the evolution of the reproductive system in vertebrates.

Acknowledgments

We thank C. Barr, C. Burne, and S. Charpentier for excellent technical assistance. This work was supported by grants from the Great Lakes Fisheries Commission and the National Science Foundation (DCB-8602907).

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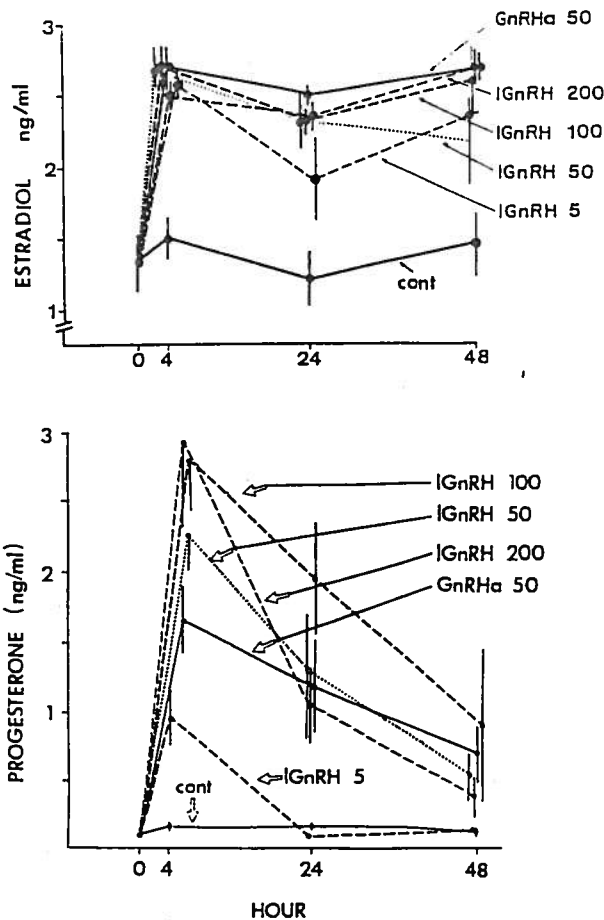


Figure 1. Plasma estradiol (ng/ml) and progesterone (ng/ml) of male lampreys injected at 0 hr with saline (cont), lamprey GnRH (lGnRH) at 200, 100, 50, or 5 ug/kg, or [D-Ala⁶, Pro⁹ NEt] GnRH (GnRHa) at 50 ug/kg. Plasma samples were taken at 0, 4, 24, and 48 hr after the injection.

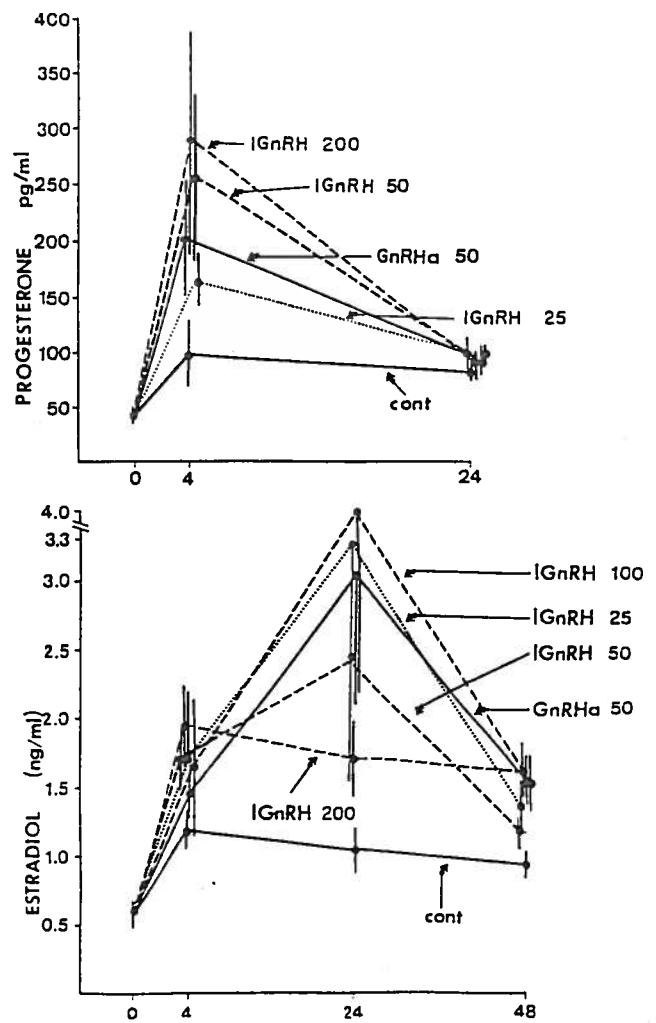


Figure 2. Plasma estradiol (ng/ml) and progesterone (pg/ml) of female lampreys injected at 0 hr with saline (cont), lamprey GnRH (lGnRH) at 200, 100, 50, or 25 ug/kg, or GnRHa at 50 ug/kg. Plasma samples were taken at 0, 4, 24, and 48 hr after the injection.