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MET-ENKEPHALIN ENHANCES STEROIDOGENESIS OF CULTURED GRANULOSA CELLS

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Peptides related to the three opiod-systems have been detected in human follicular fluids. Since opiate receptors have been demonstrated on oocytes, we tested the effects of various opioid agonists and antagonists on FSH-dependent progesterone(P) secretion from cultured granulosa cells.Follicular fluids were aspirated in periovulatory period and the size of the follicles was at least I5mm.After centrifugation,the pellet was washed three times with colture medium (RPMI I640,Flow,UK).In order to establish a primary colture,they were incubated in Petri dishes at 37°C in humidified 95% air /5%CO_2 atmpsphere for 48 hours.At that time the medium was collected and renewed adding IOOmM/ml purified FSH(Metrodin,Serono,I)and various opioidagonists and antagonists.Incubation lasted other 48 hours.
μM to nM Naloxone hidrocloride(Nalx) inhibit FSH-induced P-secretion,indipendently from the line(Met-Enk) stimulated P production in both μM(I60.3±39.8,%)on control and nM concentration(82.3±44.2%).This effect was reversed by adding Nalx.On the contrary,uM Leucine-Enkephaline (Leu-Enk) reduced P production(-5I+13.8%).This effect desappeared in nM range.K-receptor agonist U-50,488H,seemed to induce an inhibition,which was reversed by k-antagonist MR 2266.
In conclusion, almost everyone of the opioid peptides fisiologically present in follicular fluid are able to interfer with steroidogenesis of granulosa cells.Interestingly enough, Met-Enk stimulation is Nalx reversible and dose dependent, suggesting the mediation of an opiate-receptor.

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B-EP changes in pharmacologically induced-menstrual cycles

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Several studies suggest the involvement of the opioid system in the physiological cyclic regulation of gonadotropin release.The arcuate nucleus is the main source of B-endorphin(B-EP) in the brain.Pituitary represents the most important source of plasmatic B-EP and it has been shown that in the pre-and/or post-ovulatory days a significant peak of plasma B-EP levels occurs.The aim of this study was to evaluate the effects of menstrual cyclicity on plasma B-EP levels,measuring the concentrations of circulating B-EP in women affected by primary or secondary amenorrhea and in control healthy subjects.15 nulliparous women(23-31 yrs) affected by hypothalamic primary(7)or secondary amenorrhea(6)or anovulatory oligomenorrhea(2)before and during treatment with purified FSH+HCG(9)or with hMG+hCG(6)at doses related to the ovarian response,evaluated by estradiol levels and ecographic evaluation of follicular maturation.A group of 12 healthy women(22-26 yrs)were also studied for the regularity of their menstrual cycles.Amenorrheic patients' basal levels were similar to healthy control women.In spontaneous and pharmacologically-induced ovulatory cycles a significant preovulatory peak of plasma B-EP levels occurs while it does not in oligomenorrheic patients and in unsuccessfully treated amenorrheic subjects.In the other period of the cycle B-EP levels don't show significant variations.These results suggest that when ovulation occurs,plasma B-EP levels show a relevant rise the physiological significance of which remains to be scanned.