**Fig. 1.** LH plasma concentration of long-term ovariectomized rats treated with EB and P (closed circles) and injected with naloxone (open circles). $B_{\text{max}}$ (hatched bars) and $K_d$ values (open bars) of $^3$H-naloxone binding to membrane fractions of distinct brain areas obtained from ovariectomized rats before and after the surge of LH induced by estradiol.

* = $p < 0.01$ vs. 10.00 h on day 5
+ = $p < 0.01$ vs. control

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222. **The effect of $\beta$-endorphin-infusion on releasing hormone-stimulated anterior pituitary hormone secretion in normal human subjects**

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$\beta$-Endorphin (β-endo) and ACTH derive from the same precursor hormone, proopiomelanocortin. Administration of β-endorphin as well as of other opioid peptides exerts significant endocrine effects. The existence of a short-loop feedback inhibition of pituitary ACTH release by β-endo has been postulated, and a stimulatory influence on PRL and GH secretion could be demonstrated. However, data on the effect of peripherally administered β-endorphin in humans are highly controversial.

To further investigate this issue, we infused human synthetic β-endorphin at a constant rate of 1 μg/kg × min or normal saline as control to 7 male normal volunteers for 90 min with a one-week interval in random order. 30 min after starting the β-endo or placebo infusion, a releasing hormone cocktail was administered as a bolus injection (oCRH, GRH 1 μg/kg, GnRH 100 μg, TRG 200 μg). Blood was drawn at −60 min, prior to the endo-infusion and up to 180 min for measurements of β-endorphin, all other anterior pituitary hormones and cortisol by RIA. The protocol was reviewed by the clinical Ethics Committee and written informed consent was obtained from all participants.

Infusion of β-endo resulted in high plasma levels (33,600 ± 3,300 pg/ml) with a rapid decrease after the infusion was stopped. During the control infusion, β-endo plasma levels rose in response to CRH from 95 ± 12 pg/ml to 172 ± 12 pg/ml ($\bar{X} \pm \text{SEM}; p < 0.05$). Plasma ACTH and serum cortisol levels in response to the releasing hormone with and without β-endo- or placebo-infusion are shown in Fig. 1. There was no significant difference between the peak values or the area under the
stimulation curve (Ai). The PRL response to TRH was significantly higher after β-endo-infusion compared to placebo (Δi 1,209 ± 183 ng/ml × h vs 834 ± 104 ng/ml × h; p < 0.05). The GH response to GRH was also higher after β-endo-infusion (Δi 391 ± 212 ng/ml × h vs 218 ± 64 ng/ml × h; p < 0.05). There was no difference in the response of LH, FSH and TSH to their releasing hormones. Our data on ACTH and cortisol secretion do not support the concept of a short-loop negative feedback acting at the site of the pituitary. However, although β-endo does not cross the blood-brain barrier, it has been reported that high levels of peripheral β-endo do influence β-endo CSF levels. A modulating effect on hypothalamic neurons can therefore not be excluded. The exaggerated response of PRL and GH to their releasing-hormones after β-endo-infusion may be due to direct opioid receptor stimulation.

References