b. Growth Hormone—Physiological Roles of Endogenous GRF and Somatostatin in its Regulation

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In man growth hormone (GH) secretion is affected by sleep, stress, exercise and nutrients. Although the regulation of GH secretion is accomplished by a complex neuroendocrine control system including neuropeptides and neurotransmitters, the final common pathway for the integration of these signals involves two hypophysiotropic hormones. GH-releasing factor (GRF), a 44 residue peptide, stimulates the synthesis and secretion of GH whereas somatostatin (SRIF), a tetradecapeptide, inhibits GH secretion. GH deficiency, defined as the state of impaired GH secretion, causes dwarfism if it occurs in growing children. Since the majority of children with GH deficiency respond to GRF injections with an increase in plasma GH levels, it is proposed that they have a defect in either the synthesis of hypothalamic GRF or its delivery to the pituitary. These results also suggest that some children may benefit from GRF therapy. However, certain questions remain to be not solved. Does isolated GRF deficiency induce growth failure? Can administration of GRF alone correct the growth failure attributable to hypothalamic defects? Does SRIF modify the effect of GHRH treatment in hypothalamic disorders? In the first experiment, to clarify the role of endogenous GRF and SRIF in GH production and somatic growth in normal growing rats, anti-rat GRF goat γ-globulin (GRF-ab) or anti-SRIF goat γ-globulin (SRIF-ab) was injected ip every other day for 3 weeks. Treatment with GRF-ab caused a marked decrease in GH mRNA levels in the anterior pituitary (Fig. 1). Body weight gain, tail length, anterior pituitary weight and pituitary GH content were all decreased by GRF-ab treatment. On the other hand, 3-weeks treatment with SRIF-ab tended to decrease pituitary GH mRNA and GH content but failed to affect somatic growth. Ablation of the basal medial hypothalamus by a Halász knife caused marked atrophy of the anterior pituitary and accompanied significant decrease in pituitary GH content as well as GH mRNA. To further clarify the role of GRF and SRIF in pituitary GH reduction in hypothalamus-lesioned rats, the effects of exogenous GRF and/or SRIF administration on the growth of these rats were examined. The experimental protocol is shown in Fig. 2. For the 24 days following surgery, all animals received daily subcutaneous injections of cortisol acetate, testosterone propionate and L-thyroxine sodium. Two weeks after hypothalamic ablation the rats were divided into four groups and
ACTH

The hypothalamic-pituitary-adrenal (HPA) axis is controlled by multiple factors, such as circadian rhythm, stress, and negative feedback. ACTH secretion from the anterior pituitary (AP) is mediated by multiple factors of hypothalamic (Hy) origin, including corticotropin-releasing factor (CRF), vasopressin (VP) and catecholamines (CA), which are released from nerve endings within the zona externa of the median eminence into the hypophysial portal circulation. ACTH stimulates synthesis and secretion of adrenocortical steroids which inhibit the hypothalamic-pituitary axis and complete the negative feedback loop. In this paper, we examined the interrelationship between neuropeptides and ACTH.

c. Adrenocorticotropic Hormone (ACTH)

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The hypothalamic-pituitary-adrenal (HPA) axis is controlled by multiple factors, such as circadian rhythm, stress, and negative feedback. ACTH secretion from the anterior pituitary (AP) is mediated by multiple factors of hypothalamic (Hy) origin, including corticotropin-releasing factor (CRF), vasopressin (VP) and catecholamines (CA), which are released from nerve endings within the zona externa of the median eminence into the hypophysial portal circulation. ACTH stimulates synthesis and secretion of adrenocortical steroids which inhibit the hypothalamic-pituitary axis and complete the negative feedback loop. In this paper, we examined the interrelationship between neuropeptides and ACTH.

Fig. 2. Protocol for replacement therapy with hGRF(1-29)NH₂ and/or SMS 201-995 in rats with hypothalamic ablation.

Fig. 3. Effect of 10 days-administration of hGRF(1-29)NH₂ and/or SMS 201-995 on body weight increments in rats with hypothalamic ablation.