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# The Influence of Hypophysectomy on the Stores of Somatostatin in the Hypothalamus and Pituitary Stem[1] (39268)

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Utilizing immunocytochemistry on the rat, somatostatin (somatotropin-release-inhibiting hormone) has been demonstrated in the organum vasculosum of the lamina terminalis (OVLT), throughout most of the cephalocaudal extent of the median eminence, and in the upper segment of the infundibular stem (1, 2; Baker, unpublished). The significant storage of somatostatin in the median eminence and infundibular stem has been confirmed by radioimmunoassay performed on the tissue of this area (3). Similarly, by means of immunofluorescence, somatostatin has been demonstrated in the median eminence of the guinea pig (4).

Because of the probability that pituitary somatotropin exerts a short-loop feedback effect on hypothalamic somatostatin, an examination of the influence of hypophysectomy on the content of somatostatin in the OVLT, median eminence, and infundibular stem is of special interest. This paper reports the results of such a study in which immunocytochemistry was used for the demonstration of somatostatin.

*Materials and methods.* Of 20 young-adult female Sprague-Dawley rats, 10 were hypophysectomized by the parapharyngeal approach and 10 served as controls. The rats were maintained on a lighting schedule of 14-hr light/10-hr darkness. They ate *ad libitum*. Twenty-eight to 133 days after hypophysectomy, operated rats paired with nonoperated control rats were killed by decapitation. An area of the brain encompassing the OVLT, the hypothalamus, and pituitary stem was excised, fixed in Bouin's fluid, embedded in Paraplast, and sectioned. Immunocytochemistry was performed with the peroxidase-antiperoxidase (PAP) method of Petrali-Sternberger (5) using an antiserum to synthetic somatostatin (B 173) prepared by us according to the Vaitukaitis *et al.* (6) procedure. Specificity of the antiserum was demonstrated by absence of labeling when normal rabbit serum was substituted for antisomatostatin and by complete loss of labeling capacity after prior absorption of the antiserum with synthetic somatostatin. On the other hand, labeling capacity was not lost after absorption with gonadotropin-releasing hormone, thyrotropin-releasing hormone, arginine-vasopressin, or oxytocin. For these procedures, antisoma-

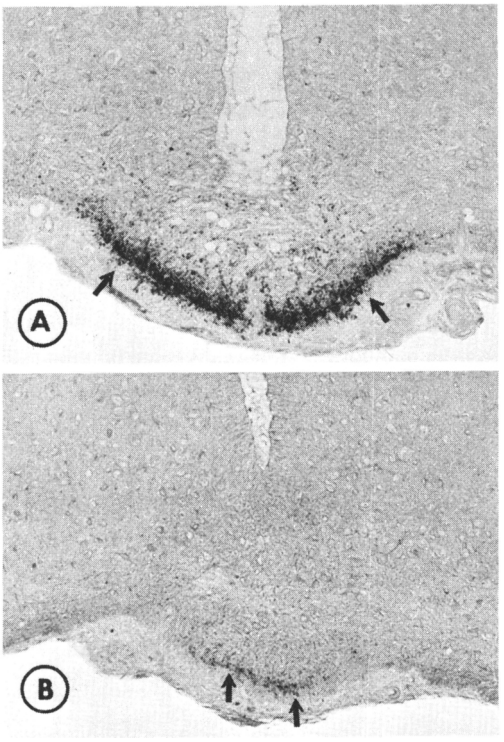


FIG. 1. Somatostatin (arrows) in the cephalic segment of the median eminence from a control rat (A) and from a rat 133 days after hypophysectomy (B) (× 110). The content of somatostatin is reduced in (B).

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tostatin was diluted 1/50, and the absorbants were prepared in 1% solutions. Antiserum and solutions of absorbants were mixed 1:1 by volume and incubated overnite.

The effect of hypophysectomy was evaluated by direct comparison of sections from each hypophysectomized rat with sections from its nonoperated control considering transverse planes through the OVLT; the median eminence at its cephalic, broad central, and caudal levels; and the superior segment of the infundibular stem. Two criteria were used as indicators of completeness of hypophysectomy: (a) the body weight at termination of the experiment was lower than at the time of operation and (b) the internal reproductive organs were atrophic.

*Results.* The amount of somatostatin present in the OVLT of control rats was so small that it was difficult to ascertain whether hypophysectomy elicited a change in quantity. Certainly a great increase or decrease did not occur. In the cephalic zone of the median eminence, the amount of stored somatostatin was reduced by hypophysectomy (Fig. 1A, B) in all animals except one, which was paired with a rat that had an exceptionally small amount in this region. Somatostatin was depleted severely from the broad central zone of the median eminence (Fig. 2A, B). A similar situation obtained in the caudal zone of the median eminence where the infundibulum forms the infundibular stem by closure of the infundibular recess (Fig. 3A, B). Although traces of somatostatin still appeared in the upper stem, the peripheral region, where neoformation of nervous tissue had occurred, was totally devoid of the hormone.

*Discussion.* In addition to somatostatin, gonadotropin release-inhibiting hormone (GnRH) is also depleted from the median eminence following hypophysectomy (Baker, unpublished) and in both cases the greatest depletion occurs in the central and caudal segments of the median eminence. A common explanation for the similar effects of pituitary ablation on two hypophysiotrophic hormones may lie in the degeneration and subsequent repair of the median

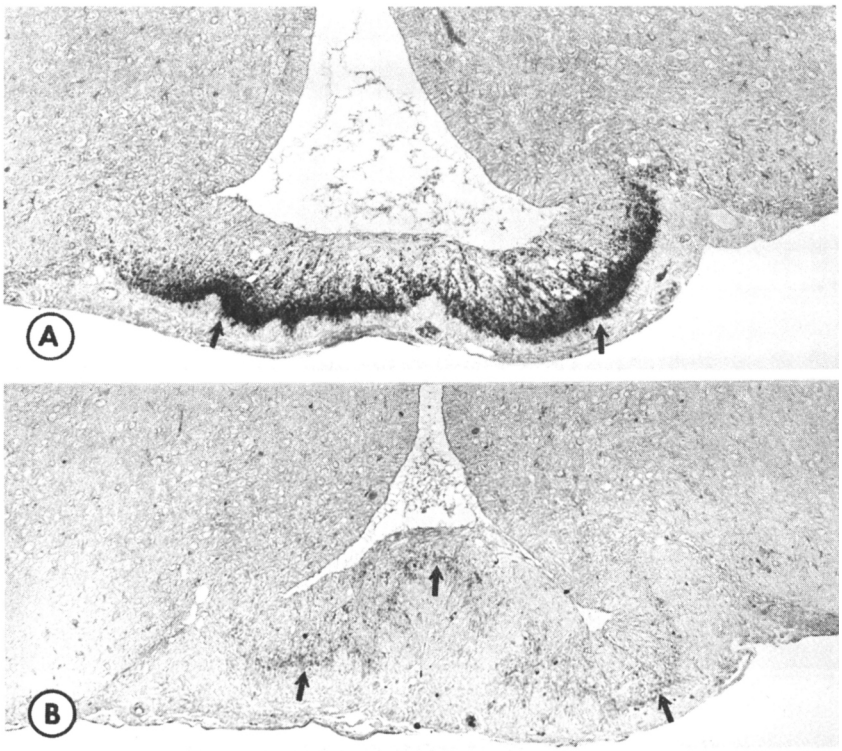


FIG. 2. Somatostatin (arrows) in the broad central segment of the median eminence from a control rat (A) and from a rat 133 days after hypophysectomy (B) (× 110). The content of somatostatin is reduced in (B).

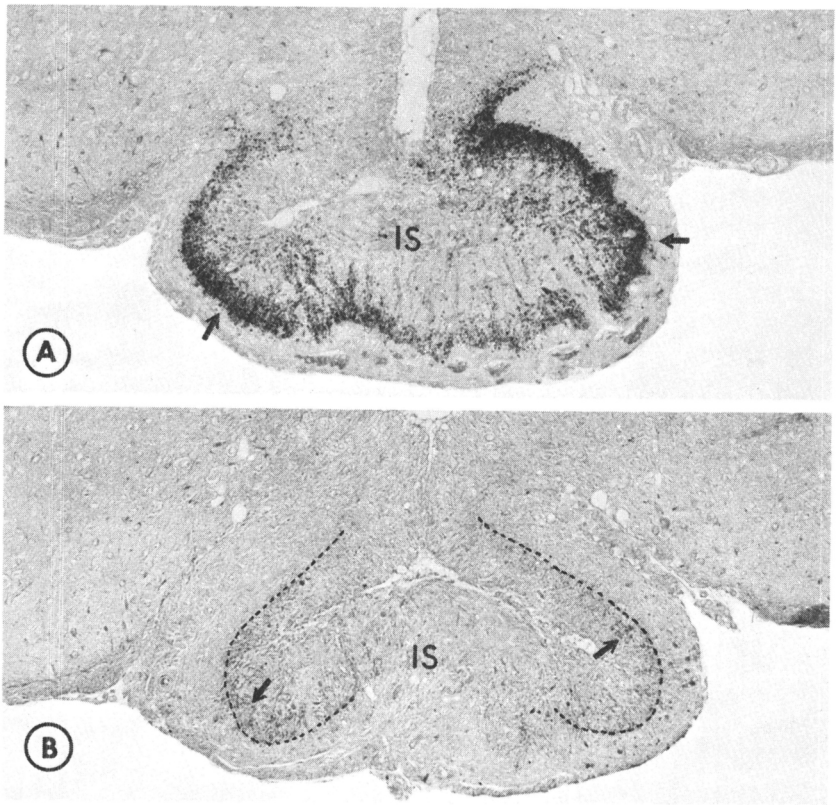


FIG. 3. Somatostatin (arrows) at the site of junction of infundibular stem (IS) and median eminence from a control rat (A) and from a rat 133 days after hypophysectomy (B) (× 110). Somatostatin is absent from newly formed nervous tissue that has formed external to the interrupted line in (B) and is depleted greatly from the infundibulum after hypophysectomy.

eminence-pituitary stalk that ensues after hypophysectomy. Primarily involved are the magnocellular neurons of the supraoptico-hypophysial system (7–10). Present evidence indicates that somatostatin is not associated with the magnocellular nerve fibers (11) and, therefore, it would not be expected to appear in the regenerated areas of the median eminence and stalk. This expectation is confirmed by our finding that somatostatin is barely detectable or totally absent from this regenerated tissue.

There are two other possible explanations for the reduced somatostatin content in the median eminence and infundibular stem after hypophysectomy. First, either interruption of the stalk, or the regenerative processes described above, might interfere with the function of other neurons that synthesize and transport somatostatin. Second, if secretion of somatostatin depends on positive feedback by pituitary somatotropin, the loss of somatotropin by hypophysectomy might reduce the production and secretion of somatostatin. Since somatostatin has been available for such a short time, no evidence is available that will permit evaluation of these possibilities.

*Summary.* Twenty-eight to 133 days after hypophysectomy of the rat, somatostatin as revealed immunocytochemically was depleted from all segments of the median eminence and from the proximal part of the infundibular stem. A consistent change in the store of somatostatin in the OVLT could not be demonstrated.

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