Growth Hormone Resynthesis in the Pituitary after Depletion Induced by a Hypothalamic Extract[1]

It has recently been observed that growth hormone (GH) is dynamically involved in rapid adjustments to metabolic needs. The dynamic role of GH was suggested by the detection of a rise of its plasma levels after hypoglycaemia, fasting or exercise[2,3].

The increased GH titres in plasma are probably paralleled by a depletion of GH pituitary content as indicated by previous experiments in which a substantial reduction of pituitary GH was observed after insulin hypoglycaemia[4,5].

Since GH secretion appears to be subject to the whim of moment-to-moment metabolic needs[6], it seemed of special interest to study the rate of its resynthesis in a pituitary almost completely depleted, as is that of an animal submitted to the intracarotid injection of a stalk median eminence (SME) region extract[7-9]. An experimental device such as this appears to be the best at present available for evaluating the rate of GH resynthesis.

Materials and methods. Hypothalamic extracts from 30-day-old Sprague-Dawley female rats were used. The stalk median eminence region and adjacent ventral hypothalamus of 80 rats were removed, weighed, pooled and homogenized with 0.1 *N* HCl. The diluted extract was centrifuged at 3000 rpm for 15 min at 4°C. The pH of the supernatant was adjusted to 7.4 by addition of $NaHCO_3$ solution. The final volume was made up so that the acid extract from 5 mg of rat hypothalamus (nearly equivalent to the hypothalamic tissue of one rat) was contained in 0.2 ml of medium. As recipient animals, 30-day-old Sprague-Dawley female rats were used. All recipient animals were injected in the carotid with 5 mg/0.2 ml of hypothalamic extract. The recipient animals, divided into four groups of 15 animals each, were killed by decapitation 15 min and 1, 3, and 5 h after treatment, respectively. Their pituitaries were removed, weighed on a torsion balance, pooled by groups and homogenized with saline. Dilutions were made in order to provide two dosage levels in the same volume of injected fluid (0.5 ml). The same procedure was followed in preparing the homogenates with control pituitaries taken from 30-day-old rats treated only with 0.2 ml of saline. Growth hormone bioassay of pituitary homogenates was performed following the method of GREENSPAN[10] as modified by REICHLIN[11]. 7–10 female rats hypophysectomized by transauricolar approach[12] were used to assay each of the two doses of the samples. NIH preparation of growth hormone (GH-B7) was used as the reference standard. The GH potencies of the pituitary homogenates were calculated on the basis of the results of the four-point assay according to FINNEY[13].

Results and discussion. From the results (see Table) it appears that 15 min after the intracarotid injection of SME extract, GH content in the pituitary is reduced to extremely low values. 1 h after SME extract administration, the pituitary GH content corresponds to 60% of the normal value, while after 3 h and 5 h it rises to values of 80% to 100% respectively.

Thus the resynthesis of GH in the pituitary, after the experimentally induced depletion, takes place at a relatively rapid rate. This suggests that the pituitary may rapidly reestablish its normal storage of the hormone.

The results of the present experiments seem to agree with the observations of ROTH et al.[2], who pointed out that GH plasma levels in man fluctuate rapidly during the day in response to nutritional factors, being depressed by feeding and progressively elevated during fasting[14].

Growth hormone resynthesis in rat pituitary after the depletive effect of an intracarotid injection of stalk median eminence extract (SME)

No. of rats	Treatment	Time interval from treatment to death	Growth hormone pituitary content (μg/mg)	Fiducial limits $P = 0.95$
15	Saline (0.2 ml/100 g body weight)	15 min	160.1	135.2–206.1
15	SME (5 mg/0.2 ml/100 g body weight)	15 min	too low to be determined	
15	SME (5 mg/0.2 ml/100 g body weight)	1 h	97.0	72.6–128.0
15	SME (5 mg/0.2 ml/100 g body weight)	3 h	123.0	95.0–158.2
15	SME (5 mg/0.2 ml/100 g body weight)	5 h	180.0	170.1–230.6

Riassunto. Lo studio della velocità di resintesi dell'ormone somatotropo nella ipofisi di ratto dopo la massiva deplezione indotta dalla somministrazione endocarotidea di un estratto di eminenza mediana dell'ipotalamo, ha messo in evidenza che 1 ora dopo la somministrazione il contenuto dell'ormone viene ricostituito in misura del 60%, 3 ore dopo sale all'80%, 5 ore dopo corrisponde ai valori normali.

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