Effect of Hypophysectomy and Growth Hormone Administration on Somatostatin and Gastrin Content in the Stomach of Rats

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Abstract

The effect of hypophysectomy and bovine growth hormone (GH) administration on somatostatin (SRIF) content as well as gastrin content in the rat stomach was investigated. SRIF content was determined by a specific radioimmunoassay. The total SRIF content in the stomach had decreased 4 weeks after hypophysectomy but was restored significantly in those rats which were subjected to bovine GH administration for 7 days after hypophysectomy. Furthermore, in control rats, an increase in SRIF content in the stomach was observed after 7 days of GH administration. Similar changes in total content of gastrin were observed after hypophysectomy and bovine GH administration, although these changes were not significant. These results indicate that GH may influence gastric function through changes in SRIF and gastrin content in the stomach.

It has been reported by several workers (Arimura *et al.*, 1975; Polak *et al.*, 1975) that somatostatin which was first isolated from ovine hypothalamus exists throughout the gastrointestinal tract. Somatostatin strongly inhibits the secretion of gastrointestinal hormones (Bloom *et al.*, 1974; Guenther *et al.*, 1975) and gastric acid and pepsin (Albinus *et al.*, 1977; Schrupf *et al.*, 1976). However, the functional role of somatostatin containing D cells of the gastrointestinal tract is not known. Recently it was reported that the secretion of gastric somatostatin was stimulated by exogenous gastrin administration (Barden *et al.*, 1979), or by the intragastric administration of nutrients and HCl (Schusdziarra *et al.*, 1978). On the other hand, it is well-known that GH influences gastrin content in the stomach (Creutzfeldt *et al.*, 1971; Enochs *et al.*, 1976), and gastric acid and pepsin secretion

(Schapiro *et al.*, 1970; Crean, 1963; Snapper *et al.*, 1937; Jacobson and Magnani, 1964). Therefore, in order to clarify the relationship between GH and gastric function, the present study investigated the effect of hypophysectomy and GH administration on somatostatin and gastrin content in the stomach of rats.

Materials and Methods

Male Sprague-Dawley rats aged 7 weeks were used in the present study. The animals were maintained at 24°C under controlled lighting (lights on 0700 h-1700 h) and given free access to laboratory feed (Oriental Yeast Co., Tokyo) and tap water throughout the experiments.

Six rats were hypophysectomized by the transpharyngeal technique (Institute of Animal Reproduction, Saitama). Three weeks after operation, these 6 rats and 7 control rats received injections of bovine growth hormone (NIH-GH-B18) subcutaneously at 500 µg/day/rat for 7 days at the same time each day. Another group of 6 control and 6 hypophysectomized rats received injections of 0.2 ml

Table 1. Somatostatin Content in the Stomach of Hypophysectomized and Control Rats.

	No.	ng/organ	ng/g wet weight	ng/g protein
Control	6	1060± 69 ^a	1089± 78	6797± 380
Hypox	6	427± 32 ^b	768± 62 ^c	4948± 487 ^c
Hypox+GH	6	748±133 ^d	1070±214	9270±2660
Control+GH	7	1590±149 ^e	1458±144 ^f	11480±1061 ^e

a: mean±SEM.

b: P<0.001, c: P<0.02 compared to the control values.

d: P<0.05 compared to the values for hypophysectomized rats.

e: P<0.01, f: P<0.05 compared to the control values.

Table 2. Body Weight, Stomach Weight, and Gastrin Content in Hypophysectomized and Control Rats.

	No.	Body Weight (g)	Stomach Weight (mg)	Gastrin Content (ng/organ)
Control	6	211±12.5 ^a	978±42.2	137±18.4
Hypox	6	102± 4.8 ^b	550±16.7 ^b	111±18.3
Hypox+GH	6	135± 1.8 ^c	708±15.3 ^c	152±15.1
Control+GH	7	237±17.6	1114±55.2	178±32

a: mean±SEM.

b: P<0.001 compared to the control values.

c: P<0.001 compared to the values for hypophysectomized rats.

saline in the same manner. The animals were killed 24 h after the last injection. All animals were weighed and decapitated. The stomach was quickly resected and incised along the greater curvature, washed by chilled saline, weighed and homogenized in 10 ml of chilled 2N acetic acid. The extracts were suspended in boiling water for 10 min, centrifuged at 12,000 rpm for 30 min, and a part of the supernatant was lyophilized and kept refrigerated. The rest of the supernatant was freeze-dried until assay. SRIF was measured by specific radioimmunoassay, described elsewhere (Makino *et al.*, 1977; and 1979), and gastrin was measured with a CIS gastrin kit (CEA-IRE-SORIN Association, Saclay).

Results

The sensitivity of the assay of SRIF was 7.8 pg/tube and the displacement curve of the gastric extracts was found to be parallel to the standard curve (data not shown). There was no interference by various pituitary, pancreatic and gastrointestinal hormones as described elsewhere (Makino *et al.*, 1977). The displacement curve of the gastric extracts was also seen to be parallel to the standard curve of gastrin, although

extraction rate of gastrin in acetic acid was lower than that in water (data not shown). As shown in table 1, the gastric SRIF content of hypophysectomized rats decreased significantly compared with control rats. The SRIF content in hypophysectomized rats increased after the administration of bovine GH for 7 days to near control levels. In control rats SRIF content increased significantly after GH administration. In hypophysectomized rats, the gastrin content decreased, but after the administration of GH was restored to near control levels (Table 2). In control rats gastrin content increased after GH administration (Table 2). However, these changes in gastrin content were not significant. The body weight and stomach weight of hypophysectomized rats significantly decreased and were restored to control levels by the administration of bovine GH (Table 2).

Discussion

The present study has shown that SRIF and gastrin content increased after GH administration and decreased after hypophysectomy. These changes in SRIF after hypophysectomy were consistent with our earlier work on the hypothalamus (Kanatsuka *et al.*, 1979). In the hypothalamus, SRIF content per organ as well as per mg wet weight decreased significantly after hypophysectomy. On the other hand total SRIF content in the pancreas had not changed or decreased but its content per mg wet weight as well as per mg protein was markedly increased after hypophysectomy (Kanatsuka *et al.*, 1977). The reason for this discrepancy remains to be determined. The result for SRIF after GH administration was compatible to the observation for the hypothalamus (Kanatsuka *et al.*, 1979) and the pancreas (data was not shown). Although the changes in gastrin content of the stomach were not significant in the present study, our results were not inconsistent with the observation of Enochs *et al.* (Enochs and Johnson, 1976). Since it was reported that SRIF secretion in the gastric vein decreased after hypophysectomy (Yamamoto *et al.*, 1979), it is possible that GH may affect SRIF secretion as well as its synthesis in the gastric D cells. In the hypothalamus we assumed that GH acted directly or indirectly through somatomedins on the somatoneuric cell bodies, and increased the SRIF content (Kanatsuka *et al.*, 1979). In the stomach it is also possible that GH acted directly or indirectly through somatomedins on gastric D cells as well as G cells, and increased the SRIF and gastrin content. Since this effect of endogenous GH was absent following hypophysectomy, it seemed likely that SRIF and gastrin content decreased in the hypophysectomized rats. Furthermore it was reported that hypophysectomy resulted in the atrophy of chief

cells as well as parietal cells associated with decreased secretion (Schapiro *et al.*, 1970; Crean, 1963; Snapper *et al.*, 1937; Jacobson and Magnani, 1964). The atrophy of gastric mucosa was reversed by GH administration (Crean, 1963). These findings suggest that GH acts directly on chief cells as well as parietal cells. A second possibility is that GH acts first on gastric G cells and this increased gastrin in turn affects the D cells as well as other cells. This is supported by reports that gastrin enhanced gastric SRIF release (Barden *et al.*, 1979) and had a trophic effect on parietal cells (Johnson, 1974). A third possibility is that GH acts first on the parietal cells and causes acid secretion and this hyperacidity in turn affects the function of D cells and G cells. However, this is unlikely because hyperacidity inhibits gastrin secretion (Jordan and Garcia-Rinald, 1969), but stimulates SRIF secretion (Schusdziarra *et al.*, 1978). It is also unlikely that GH acts first on D cells and that increased SRIF affects on other cells, because SRIF inhibits action of G cells and parietal cells.

Therefore it was suggested that GH affects D cells directly or indirectly through the changes in G cells' function.

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