VASOACTIVE INTESTINAL PEPTIDE STIMULATES PANCREATIC SOMATOSTATIN RELEASE

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1. Introduction

Several hormones of gastrointestinal origin, including gastric inhibitory polypeptide (GIP), secretin, gastrin [1], cholecystokinin-pancreozymin [2] and pancreatic glucagon [3] stimulate the release of insulin and somatostatin from the isolated perfused pancreas. Vasoactive intestinal peptide (VIP), which has structural and biological similarities to GIP, secretin and pancreatic glucagon [4,5], has also been shown to stimulate insulin and glucagon release by the pancreas [6–8]. These studies of the effect of VIP on somatostatin release were, therefore, undertaken.

2. Method

The isolated canine pancreas preparation [9], as modified [3], was perfused using a semi-synthetic buffer medium in a non-recirculating system. The perfusate consisted of a Krebs-Ringer bicarbonate buffer with 4% Dextran T-70 (Pharmacia Fine Chemicals, Div. Pharmacia, Inc., Piscataway, NJ), 0.2% bovine serum albumin, 5 mM each of pyruvate, fumarate and glutamate and 5.5 mM glucose. The preparation consisted of the isolated pancreas and 10–12 cm adjoining duodenum. This was perfused via the coeliac artery at a constant flow rate of 18–20 ml/min and pressure between 20–40 mm Hg. The effluent of the pancreas was collected at 1 min intervals into chilled tubes containing an EDTA/benzamidine mixture (0.003 M/0.03 M) 0.1 ml/10 ml effluent and stored at −20°C until assay. Insulin and glucagon were assayed as in [10,11], and somatostatin was assayed using the method in [12] and Arimura antiserum R101.

Pure, natural VIP [13], generously provided by Dr S. I. Said, was infused (50 ng/ml) as a 9 min challenge on 1 or 2 occasions in each pancreas. An interval of 30 min hormone-free buffer perfusion preceded each challenge with VIP. In order to assess accurately the possibility of VIP-induced changes in flow, all effluent samples were weighed. There was no evidence of alterations in flow during these experiments.

All experiments were analyzed using the Mann-Whitney [14] test for nonparametric data. Data are expressed as mean ± SEM.

3. Results and discussion

Figure 1 represents a typical experiment in which 50 ng/ml VIP was infused on 2 occasions in a single experiment, resulting in a 2–3-fold increase in insulin and somatostatin release on each occasion. The mean (± SEM) of the somatostatin and insulin levels of all the experiments in which VIP was infused, a total of 7 challenges in 4 experiments are summarized in table 1. Peak response of both insulin + somatostatin occurred at 2 min or 3 min of the challenge. In all

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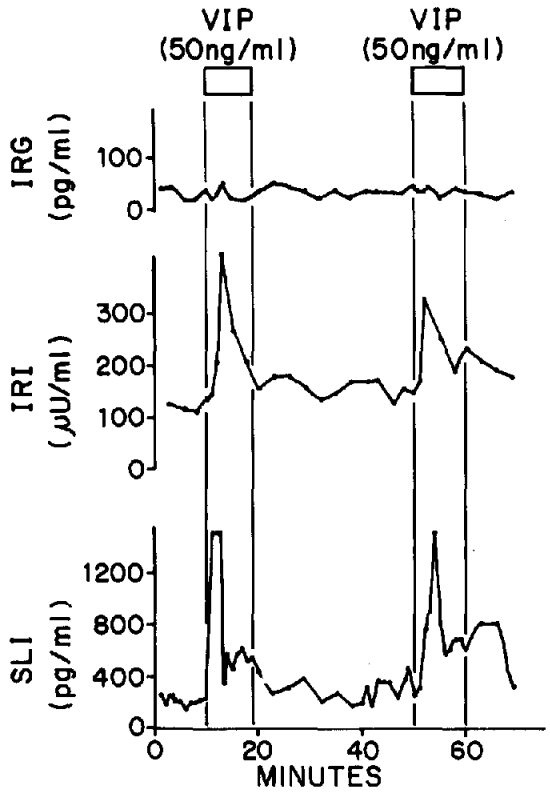

Fig.1. The effect of VIP on immunoreactive insulin (IRI), glucagon (IRG) and somatostatin (SLI) release from the isolated perfused dog pancreas.

instances a significant increase in insulin and somatostatin was observed. The rise in glucagon was not statistically significant in any of the experiments.

This demonstration of VIP-induced somatostatin release, together with its described insulin and glucagon stimulating properties, is compatible with the suggestion that VIP may play a role in modifying islet cell secretion [5–8]. Since VIP-containing nerve fibers [15] and endocrine cells [16] have been observed in the pancreas, this effect could be a local one within the islet. If so, the high concentration of VIP used in this study may be compatible with intra-islet concentrations to which the hormone secreting cells are exposed. This D-cell response of VIP may also be responsible for the noted increase in somatostatin content of islets in the nontumorous area of human pancreas in cases of VIP-producing pancreatic tumors [5].

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Table 1
The effect of VIP on immunoreactive somatostatin (SLI) and insulin concentrations[a] from the effluent of the isolated perfused dog pancreas

	SLI (pg/ml)			Insulin (μU/ml)		
Perfusate	Buffer	VIP	Buffer[b]	Buffer	VIP	Buffer[b]
Expt. 1A	72 ± 6.5	114 ± 7.7[c]	40	140 ± 9	213 ± 46	170
1B	95 ± 10.3	153 ± 6.7[c]	370	193 ± 13	232 ± 36	175
2A	206 ± 11.7	734 ± 147[c]	390	122 ± 6	247 ± 45	156
2B	325 ± 34	744 ± 108[c]	320	149 ± 9	232 ± 37	180
3A	42 ± 1.6	65 ± 7.6[d]	74	25 ± 0.2	39 ± 4.2	50
4A	67 ± 3.2	118 ± 18[d]	33	24 ± 1.5	44 ± 10.2	20
4B	64 ± 3.5	109 ± 3.3[c]	72	21 ± 0.7	30 ± 5.3	23

[a] Mean ± SEM of all samples measured during each of the 9 min perfusion periods
For SLI, $N = 9$; for insulin, $N = 5$
[b] The figures in this column represent the concentration of a single sample 9 min after cessation of the VIP stimulus
[c] $p < 0.005$
[d] $p < 0.05$

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