ADRENERGIC MODULATION OF GASTRIC SOMATOSTATIN RELEASE IN RATS

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1. Introduction

β-Adrenergic agonists stimulate and α-adrenergic agonists inhibit pancreatic somatostatin release [1]. Little is known about the adrenergic modulation of the gastric D-cell. Therefore, the response of gastric somatostatin to adrenergic agonists was investigated using an isolated, perfused rat stomach preparation.

2. Materials and methods

The experimental model of the isolated, perfused rat stomach has been described in [2]. Briefly, the stomach of fasted rats was isolated with vasculature intact by division at the pylorus. Pancreas, spleen, small bowel and colon were removed. Perfusate (Krebs bicarbonate buffer, containing 0.2% human serum albumin and 3% dextran (pH 7.4) gassed with 95% O_2 and 5% CO_2) was infused into the coeliac artery (3 ml/min). Portal vein effluent was collected in 1 min intervals. Adrenergic agonists were introduced into the perfusate via a side-arm.

Somatostatin-like immunoreactivity (SLI) and immunoreactive gastrin were determined using the radioimmunoassays in [3,4]. Adrenergic stimulants used in this study did not crossreact with the antibodies.

Isoproterenol was purchased from Serva, Heidelberg; epinephrine and norepinephrine were obtained from Hoechst, Frankfurt/M.

All data are expressed as mean ± SEM. For statistical comparisons student's *t*-test for paired data was used.

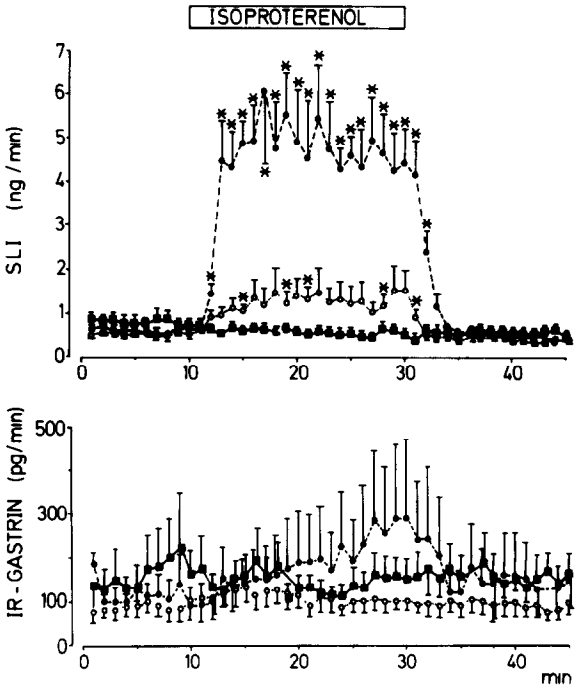

Fig.1. Effect of isoproterenol on gastric somatostatin-like immunoreactivity (SLI) and immunoreactive (IR) gastrin release. (○ . . ○) Isoproterenol 2 ng/ml (n=5); (● – –●) isoproterenol 10 ng/ml (n=6); (■——■) controls (n=5). Asteriks indicate significant changes vs basal ($p < 0.05$).

3. Results

At 2 and 10 ng/ml (9.5 and 47 nM), isoproterenol led to 2.5- and 8-fold increases in gastric SLI secretion, respectively (fig.1). Epinephrine at 2 ng/ml (11 nM) did not influence gastric SLI release whereas at 10 ng/ml (55 nM) a 2.5-fold increase was observed (fig.2). Isoproterenol and epinephrine at the low concentration did not influence gastrin secretion

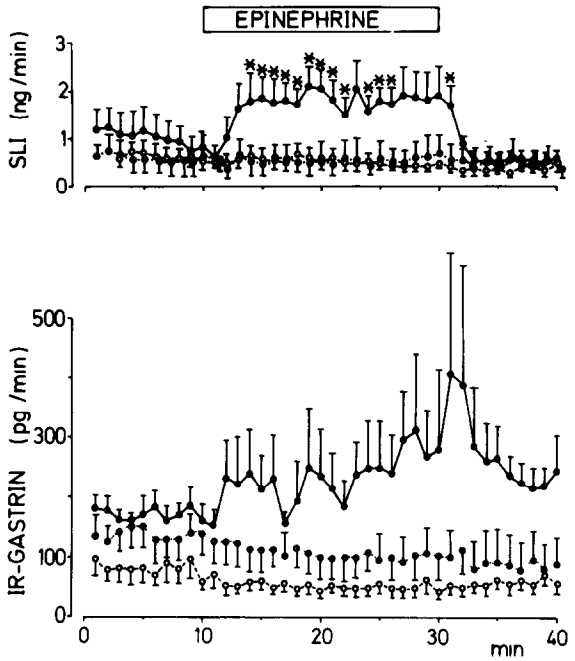

Fig.2. Effect of epinephrine on SLI and IR gastrin release. (●..●) Epinephrine 2 ng/ml (n=5); (●——●) epinephrine 10 ng/ml (n=5); (○ – – ○) controls (n=6). Asterisks indicate significant changes vs basal ($p < 0.05$).

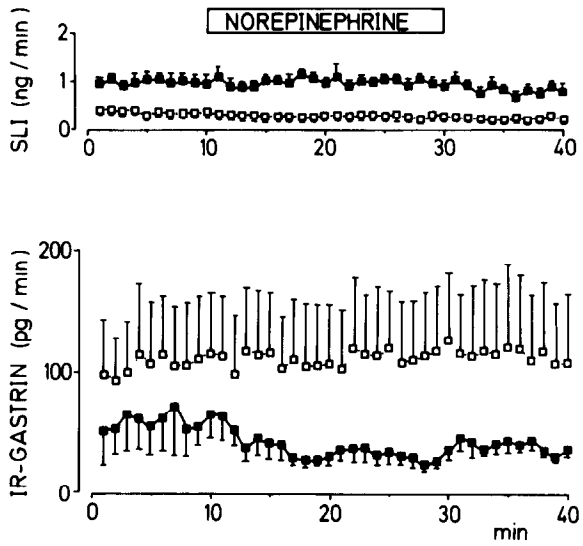

Fig.3. Effect of norepinephrine on SLI and IR gastrin release. (■——■) Norepinephrine 10 ng/ml (n=6); (□..□) controls (n=5).

while at the high concentration an enhanced gastrin release was found but this increase was not significant (fig.1,2). Norepinephrine (10 ng/ml = 59 nM) did not cause any change in the rate of gastric SLI and gastrin secretion (fig.3).

Perfusion pressure changes induced by the substances tested were small (< ± 10 mm Hg).

4. Discussion

The present results indicate that β-adrenergic agonists stimulate gastric SLI secretion whereas the α-adrenergic agonist norepinephrine in equivalent concentrations has no effect. The epinephrine levels used in this study are within, or slightly above, serum concentrations reached during exercise [5]. The concentrations reached locally following adrenergic nerve stimulation are unknown but are probably at least as high as blood levels.

Gastric acid secretion in dogs has been shown to be inhibited by β-adrenergic agonists [6–8] and stimulated by β-adrenergic blockade [9]. In cats, sympathetic nerve stimulation inhibited food-stimulated gastric acid secretion [10]. Since exogenous somatostatin inhibits gastric acid secretion [11], these results could indicate that enhanced gastric SLI release induced by β-adrenergic agonists is involved in the inhibition of gastric acid secretion.

β-Adrenergic stimuli cause an increase in gastrin secretion in vivo [12–14]. Exogenous somatostatin inhibits gastrin release [11]. Therefore, endogenous SLI released by β-adrenergic stimulation could play a role in the regulation of the G-cell. The failure of isoproterenol and epinephrine to stimulate gastrin release significantly have may be due to the large amounts of SLI released by the denervated stomach preparation used, which attenuated gastrin release.

Finally, β-adrenergic stimulating agents influence mucosal blood flow [15] and gastric motility [16] both of which are affected by exogenous somatostatin [17,18]. Therefore, the physiological role of SLI released from the stomach may involve a number of diverse functions. However, these results and the preliminary demonstration that post-prandial release of SLI is reduced by sympathectomy [19] provide evidence for an interplay between the sympathetic nervous system, release of SLI and the control of gastrointestinal function.

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