Stimulatory effect of β-adrenergic agonists on ileal L cell secretion and modulation by α-adrenergic activation

J Claustre, S Brechet, P Plaisancie, J A Chayvialle and J C Cuber

U 45 INSERM, Hôpital Edouard Herriot, Pavillon H bis, 69437 Lyon Cedex 3, France
(Requests for offprints should be addressed to J Claustre)

Abstract

Postprandial release of peptide YY (PYY) and glucagon-like peptide-1 (GLP-1) from L cells results from both nutrient transit in the ileal lumen and neural drive of endocrine cells. The adrenosympathetic system and its effectors have been shown to induce secretion of L cells in vivo or in vitro. Because these transmitters act through three receptors, β, α1, α2, coupled to different intracellular pathways, we evaluated the responses of L cells to specific agonists, using the model of isolated vasculantly perfused rat ileum. General stimulation of adrenergic receptors with epinephrine (10^-7 M) induced significant GLP-1 and PYY secretions (94 ± 38 and 257 ± 59 fmol/8 min respectively) which were abolished upon propranolol (10^-7 M) pretreatment and strongly decreased upon infusion with 10^-8 M prazosin. Blockade of α2-receptors with idazoxan (10^-8 M) did not alter epinephrine-induced peptide secretion. The β-adrenergic agonist isoproterenol (10^-6 M) infused for 30 min induced a transient release of GLP-1 and PYY (integrated release over the 8 min of the peak secretion: 38 ± 16 and 214 ± 69 fmol for GLP-1 and PYY respectively, P<0.05). Because terbutaline but not dobutamine or BRL 37,344 (10^-5 M) induced significant GLP-1 and PYY secretions (135 ± 30 and 305 ± 39 fmol/8 min respectively), isoproterenol-induced secretions are suggested to result mainly from stimulation of the β2-isoreceptor type. In contrast, the α1-agonist phenylephrine (10^-7 M) did not stimulate peptide release. When co-infused with 10^-6 M or 10^-7 M isoproterenol, 10^-7 M phenylephrine raised GLP-1 release to 174 ± 53 and 108 ± 28 fmol/8 min respectively (vs 38 ± 16 and 35 ± 10 fmol/8 min for isoproterenol alone, P<0.05) whereas PYY secretion was not significantly increased. Clonidine (10^-7 M), an α2-agonist, induced a moderate and delayed increase of GLP-1 and PYY but abolished the isoproterenol-induced peptide secretion. Our results showed that general stimulation of adrenergic receptors stimulates the secretory activity of ileal endocrine L cells. The net peptide secretion results from the activation of the β2-isoreceptor type. Additionally, GLP-1 and PYY secretions are positively modulated by α1-receptor stimulation and inhibited by α2-receptor activation upon β-receptor occupation.

Journal of Endocrinology (1999) 162, 271–278

Introduction

Intestinal endocrine cell secretion is under the control of nutrients in the lumen, and of nervous or endocrine mediators acting at the basolateral side (Walsh 1994). In the ileum, endocrine cells are primarily accounted for by enterochromaffin cells, and L cells that secrete peptide YY (PYY) and several pro-glucagon-derived peptides (Sjölund et al. 1983, Walsh 1994). Pro-glucagon-derived peptides are glucagon-like peptide-1 (GLP-1), GLP-2, oxyntomodulin, and glicentin. GLP-1 is a potent insulino-tropic hormone (Holst & Orskov 1994). PYY, which is co-stored with GLP-1 in L cells, induces vasoconstriction, inhibits intestinal motility and secretion, and inhibits pancreatic and gastric secretions (Walsh 1994). PYY has thus been proposed to participate in the ileal brake (Wen et al. 1995).

Whereas the effects of nutrients on PYY and GLP-1 secretions have been extensively studied in vivo and in vitro (Fu-Cheng et al. 1995, Wen et al. 1995), the modulation of these endocrine secretions by the nervous system has been poorly investigated. The sympathetic nervous system is known to control mucosal functions (Cooke 1986), and mucosal glands are surrounded by putative noradrenergic processes (Newson et al. 1979). Electrical stimulation of the splanchic nerves induced PYY release in anaesthetized dogs and pigs (Sheikh et al. 1989, Zhang et al. 1993). Epinephrine was shown to induce GLP-1 release in the isolated vasculantly perfused rat ileum (Herrmann-Rinke et al. 1995), and to stimulate the release of PYY and enteroglucagon from enteric endocrine cells in primary short-term culture (Barber et al. 1987, Aponte et al. 1988, Buchan et al. 1987). In agreement with these results, isoproterenol, a β-adrenergic agonist, was shown to
stimulate the release of the two peptides from the isolated rat ileum (Dumoulin et al. 1995). The effects of \(\alpha\)-adrenergic agonists on GLP-1 secretion have been studied in cell cultures only (Buchan et al. 1987). Because \(\beta\)- and \(\alpha\)-adrenoceptors are coupled to different intracellular transduction pathways (Summers & McMartin 1993), we assessed the effects of epinephrine in the presence of specific adrenergic blockers and of \(\beta\)-, \(\alpha\)-1– and \(\alpha\)-2-adrenergic agonists alone or associated on L endocrine cell secretions.

Isoproterenol, as epinephrine, binds the three types of \(\beta\)-adrenergic isoreceptors (Giacobino 1995), and effects of catecholamines on the gastrointestinal tract have been attributed both to \(\beta\)-2- and \(\beta\)-3-adrenergic stimulation (Coruzzi et al. 1997, Levasseur et al. 1997). \(\beta\)-adrenergic receptors are coupled to the cAMP pathway (Emorine et al. 1989) but \(\beta\)-3-, unlike \(\beta\)-2-adrenoceptors, are not subject to desensitization (Nantel et al. 1993), which may have consequences on the pattern of response to catecholamine stimulation. We thus wished to study the effects of specific \(\beta\)-adrenergic agonists on GLP-1 and PYY secretion. This study was conducted in a model of isolated vascularly perfused rat ileum (Cuber et al. 1990).

Materials and Methods

Reagents

Chemical reagents were purchased from Merck (Darmstadt, Germany). Bovine serum albumin (BSA) was obtained from Bioalcor (Cassen, France) and the amino acid mixture hyperamine 25 (25·6 g nitrogen/l) from Braun Medical (Boulogne, France). The following reagents were from Sigma (St Louis, MO, USA): clonidine, dobutamine, idazoxan, isoproterenol, phenylephrine, prazosin, terbutaline, yohimbine, and GLP-1-(7–36) amide. PYY (porcine) was purchased from Peninsula Laboratories (St Helens, Merseyside, UK). BRL 37,344 (Welwyn Garden City, Herts, UK) was a kind gift from SmithKline Beecham Pharmaceuticals (Darmstadt, Germany). Bovine serum albumin (BSA) was purchased from Merck (Darmstadt, Germany). Bovine serum albumin (BSA) was obtained from Bioalcor (Cassen, France) and the amino acid mixture hyperamine 25 (25·6 g nitrogen/l) from Braun Medical (Boulogne, France). The following reagents were from Sigma (St Louis, MO, USA): clonidine, dobutamine, idazoxan, isoproterenol, phenylephrine, prazosin, terbutaline, yohimbine, and GLP-1-(7–36) amide. PYY (porcine) was purchased from Peninsula Laboratories (St Helens, Merseyside, UK). BRL 37,344 was a kind gift from SmithKline Beecham Pharmaceuticals (Welwyn Garden City, Herts, UK).

Surgical procedure

The dissection of the ileum and controls of viability in ex vivo conditions have been described previously (Cuber et al. 1990). Briefly, male 250–300 g Wistar rats (Dépré, Saint Doulchard, France) were anaesthetized with i.p. pentobarbitone (75 mg/kg), the abdomen was opened with a midline incision, viscera were exteriorized and, after ligation of vessels, the colon was removed. A first cannula was inserted 10 cm proximal to the ileo-colic junction and after emptying and rinsing the intestine a second one was inserted at the ileo-colic junction. After ligating its supplying vessels, the foregut was pulled apart, and steel and silicone elastomer cannulas were inserted in the mesenteric artery and the portal vein respectively. Upon catheterization, the ileum was vascularly perfused (2·5 ml/min) with a medium consisting of washed bovine erythrocytes (25%), BSA (3%), glucose (5 mM), amino acid solution (1%) in Krebs–Henseleit buffer oxygenated with gaseous O\(_2\):CO\(_2\) (95:5%). The perfused ileum was transferred to a bath at 37 °C and luminally perfused with isotonic saline (250 µl/min).

Infusion protocol

After equilibration (5 min), venous effluents were collected on EDTA (final concentration: 10 mM) every 2 min and rapidly centrifuged. Supernatants were stored frozen at −20 °C until assay. Drugs were infused (250 µl/min in isotonic saline containing 3% BSA) through a catheter connected close to the arterial input. Infusion of adrenergic agonists consisted of a 20-min control period, 30-min drug infusion, and a 10-min post-infusion control period. Blockers were infused 2 min before and during agonist infusion (i.e. after an 18-min control period).

RIA

GLP-1 and PYY were assayed directly in the supernatant from venous effluents, as previously described (Plaisancié et al. 1994, 1995). The 199D anti-GLP-1 antibody was used at a 1:250 000 dilution. This antibody reacts 100% with GLP-1-(7–36) amide, 84% with GLP-1-(1–36) amide, and less than 0.1% with GLP-1-(1–37), GLP-1-(7–37), GLP-2, and glucagon. The detection limit and ID\(_{50}\) (half maximal inhibitory dose) were 0.4 and 4 fmol/tube. PYY was assayed with the A4D anti-porcine PYY antiserum at a 1:800 000 dilution. This antibody cross-reacts less than 1% with bovine pancreatic polypeptide and neuropeptide Y. Sensitivity and ID\(_{50}\) were 1 and 7 fmol/tube respectively.

Statistical methods

Results are expressed as means ± s.e.m. obtained in five to eight experiments. Integrated responses were calculated for each animal from the sum of discharges measured during peak secretion (from the second to the ninth minute of infusion) minus the mean value of the 20-min control period. Comparisons were performed with Student’s t-test for paired or unpaired data as appropriate. Differences reaching the \(P<0.05\) level were considered significant.

Results

Effects of epinephrine alone or with specific blockers on GLP-1 and PYY secretion

Epinephrine infusion (10\(^{-7}\) M) induced GLP-1 and PYY secretions (Fig. 1, \(n=6\), \(P<0.05\)) to maximal secretion rates.
When prazosin ($10^{-8}$ M) was co-infused with $10^{-7}$ M epinephrine the resulting GLP-1 secretion was decreased (Fig. 1A) to a level of $41 \pm 5$ fmol/2 min (controls: $29 \pm 7$ fmol/2 min, $n=4$). The net integrated release over 8 min was then $4 \pm 12$ fmol (to be compared with $94 \pm 38$ fmol with epinephrine alone, $P<0.05$). PYY secretion was decreased (Fig. 1B) to a value of $63 \pm 15$ fmol/2 min (controls: $24 \pm 3$ fmol/2 min, $n=4$). The integrated release over 8 min was decreased to $94 \pm 55$ fmol to be compared with $257 \pm 59$ fmol with epinephrine alone ($P<0.05$).

Blockade of $\alpha_2$-adrenoreceptors with idazoxan ($10^{-8}$ M, Fig. 2), infused 2 min before and during epinephrine ($10^{-7}$ M), failed to modify significantly GLP-1 or PYY secretions induced by epinephrine alone.

Epinephrine and epinephrine plus propranol increased arterial pressure from 51 $\pm$ 3 to 66 $\pm$ 4 and from 50 $\pm$ 1 to 73 $\pm$ 6 mmHg respectively. Under infusion of prazosin or idazoxan, epinephrine did not alter arterial pressure any more.

Effects of isoproterenol on GLP-1 and PYY secretions

Isoproterenol, a non-specific $\beta$-agonist ($10^{-6}$ M), induced a transient increase of the output of the two peptides in the portal effluent. GLP-1 release rose within 2 min of infusion (Fig. 3A) and reached a maximal concentration of $37 \pm 12$ fmol/2 min at 6 min (vs basal $19 \pm 7$ fmol/2 min, $n=8$). The net integrated release over the 8 min of the peak was $38 \pm 16$ fmol ($P<0.05$). The $10^{-7}$ M concentration resulted in a quite similar pattern with a maximal concentration of $32 \pm 7$ fmol/2 min (net integrated release: $35 \pm 10$ fmol/8 min, $n=7$, $P<0.05$).

Isoproterenol induced a stronger, dose-dependent release of PYY in the portal effluent to $111 \pm 31$ (10$^{-6}$ M, $n=8$, Fig. 3B) and $54 \pm 14$ (10$^{-7}$ M, $n=5$) fmol/2 min ($P<0.05$, basal values: $34 \pm 7$ and $22 \pm 4$ fmol/2 min respectively). The corresponding integrated releases were $214 \pm 69$ and $77 \pm 38$ fmol/8 min for the 10$^{-6}$ M and 10$^{-7}$ M concentrations.

Isoproterenol ($10^{-6}$ M, $10^{-7}$ M) decreased very moderately the arterial pressure during the entire perfusion period (from 60 $\pm$ 2 to 55 $\pm$ 3 mmHg, and from 65 $\pm$ 6 to 58 $\pm$ 4 mmHg, $P<0.05$ respectively).

Stimulation of GLP-1 and PYY secretions by specific $\beta$-adrenergic agonists

The $\beta_1$-adrenergic agonist dobutamine ($10^{-5}$ M) did not alter GLP-1 or PYY secretion (Fig. 4). In contrast, terbutaline ($10^{-5}$ M), a $\beta_2$-agonist, strongly and transiently stimulated ($P<0.05$) GLP-1 and PYY secretions (Fig. 4), to maximal secretions of $76 \pm 10$ fmol/2 min (control values: $19 \pm 2$ fmol/2 min) and $120 \pm 4$ fmol/2 min (control values: $25 \pm 4$ fmol/2 min). The corresponding integrated releases during the 8-min peak were
135 ± 30 and 305 ± 39 fmol for GLP-1 and PYY respectively. As shown in Fig. 4, the β3-agonist BRL 37,344 (10⁻⁵ M) did not significantly alter GLP-1 secretion and moderately increased PYY secretion to a maximal secretion of 67 ± 13 fmol/2 min (integrated release: 105 ± 36 fmol/8 min, n=4, P<0·05).

Of the three β-specific adrenergic agonists only BRL 37,344 induced a slight decrease of the arterial pressure (from 65 ± 1 to 60 ± 1 mmHg, P<0·05).

**Effects of phenylephrine alone or combined with isoproterenol**

Infusion of the α1-agonist phenylephrine (10⁻⁷ M) did not alter GLP-1 or PYY secretions (Fig. 3). Peptide release progressively rose however by the end of the infusion and during the post-infusion period. Phenylephrine moderately increased the arterial pressure in the preparation, from 64 ± 6 to 72 ± 5 mmHg (n=8, P<0·05).
Infusion of $10^{-7}$ M phenylephrine plus isoproterenol ($10^{-6}$ M) resulted in a transient peak of GLP-1 secretion (maximum release: $58 \pm 16$ fmol/2 min, integrated peak release: $55 \pm 6$ fmol/8 min, $n=4$).

Phenylephrine ($10^{-7}$ M) plus isoproterenol ($10^{-6}$ M) infusion did not raise the integrated peak PYY response ($246 \pm 71$ fmol/8 min, $n=6$) over isoproterenol alone ($214 \pm 69$ fmol/8 min, $n=8$, Fig. 3B). Accordingly, blockade of $\alpha_1$-adrenoreceptors with prazosin had little effect on phenylephrine plus isoproterenol-induced PYY secretion. Likewise, $10^{-7}$ M isoproterenol-induced PYY release was not altered by $10^{-7}$ M phenylephrine ($107 \pm 16$, $n=8$ vs $77 \pm 38$ fmol/8 min, $n=5$, not significant).

The phenylephrine and isoproterenol co-infusions did not alter the arterial pressure. Additional infusion of prazosin decreased arterial pressure from $56 \pm 1$ to $51 \pm 1$ mmHg ($P<0.05$).

**Effects of clonidine, alone or with isoproterenol**

The $\alpha_2$-adrenergic agonist clonidine ($10^{-7}$ M) did not result in significant GLP-1 and PYY secretions, but only elicited a sluggish rise of secretion of the peptides by the end and after the drug infusion (Fig. 5). When co-infused with isoproterenol, clonidine abolished isoproterenol-induced GLP-1 and PYY secretion peaks (Fig. 5). Blockade of $\alpha_2$-adrenoreceptors with $10^{-7}$ M yohimbine reversed the inhibitory effect of clonidine on isoproterenol-induced peptide release (Fig. 5).

Under clonidine and clonidine plus isoproterenol infusion, blood pressure increased progressively to $92 \pm 7$ and $76 \pm 9$ mmHg (vs controls: $61 \pm 9$ and $63 \pm 4$ mmHg). Upon additional infusion of yohimbine, blood pressure decreased from $59 \pm 2$ to $54 \pm 1$ mmHg.

**Discussion**

The peptide responses to the three adrenergic agonists, epinephrine, isoproterenol and terbutaline, were transient and lasted for about 8 min. This pattern recalls the 3-min spike of insulin release from isolated perfused canine pancreas upon isoproterenol stimulation (Iversen 1973). Whether the swift fading of adrenergic stimulation of endocrine cells results from receptor desensitization or from interference by adrenergic-sensitive modulators of hormone release remains to be established. It is noteworthy that bombesin and calcitonin in gene related peptide, two enteric neuropeptides, induced a transient increase of GLP-1 and PYY secretion from the isolated rat ileum (Dumoulin et al. 1995). These observations favour the hypothesis that neurotransmitters and neuropeptides are scheduled to modulate intestinal endocrine cell secretion for brief time-periods only. Actually, the
The adrenosympathetic system is primarily devoted to short-term adaptations (Chrousos & Gold 1992). Under infusion of the \( \beta \)-adrenergic blocker propranolol, epinephrine-induced peptide secretion was abolished (GLP-1) or nearly abolished (PYY). Propranolol was previously found to inhibit epinephrine-induced entero-glucagon secretion from canine isolated endocrine cells in short-term culture (Buchan et al. 1987). Isoproterenol induced the same pattern of secretion of GLP-1 and PYY as epinephrine, in agreement with a prominent \( \beta \)-adrenergic effect in epinephrine-induced peptide secretion.

\( \beta \)-receptor stimulation may proceed through the \( \beta_1 \), \( \beta_2 \) - and \( \beta_3 \)-isoreceptors (Emorine et al. 1989). The \( \beta_1 \)-adrenergic agonist dobutamine failed to induce a significant peptide secretion. \( \beta_1 \)-receptors are not strongly involved in \( \beta \)-adrenergic activation in the gastrointestinal tract, and are located to ganglia only (Ek et al. 1986). Our results suggest that \( \beta \)-adrenergic stimulation-induced GLP-1 and PYY secretions result from a predominant \( \beta_2 \)-receptor stimulation, although \( \beta_3 \)-adrenoceptors could be involved to a minor extent. The concentration of the \( \beta_3 \)-adrenergic agonist BRL 37,344 that we used was unable to meaningfully stimulate peptide secretion, but was sufficient, in contrast, to decrease arterial pressure. Ileal smooth muscle relaxation is predominantly mediated by \( \beta_3 \)-adrenoceptor stimulation (Manara et al. 1995) but few studies have dealt with the involvement of \( \beta \)-adrenoceptor (sub)types in endocrine secretion. Secretion of gastrin and somatostatin from isolated gastric antral cells of rat was shown to result from \( \beta_3 \)-adrenergic stimulation (Levasseur et al. 1997), whereas inhibition of gastric acid secretion in the cat (putatively through somatostatin secretion) could be mediated through stimulation of both \( \beta_2 \)- and \( \beta_3 \)-adrenoceptors (Coruzzi et al. 1997). Our results are in agreement with a binding study showing that in the ileal mucosa of old Brattleboro rats, \( \beta \)-adrenoergic receptors are accounted for by \( \beta_2 \)-receptors (Yu & Ouyang 1997). These results would require further experiments with specific blockers, however.

Specific stimulation of \( \alpha_1 \)-receptors did not evoke peptide release. In contrast, when epinephrine was infused with the \( \alpha_1 \)-adrenergic blocker prazosin, the GLP-1 as well as the PYY secretion peaks were strongly decreased, thus showing the involvement of \( \alpha_1 \)-adrenoceptor stimulation in GLP-1 and PYY secretions. At variance with our results, prazosin did not decrease epinephrine-induced enteroglucagon secretion from canine isolated endocrine cells (Buchan et al. 1987). A likely hypothesis is that the peptide secretion was already maximal under the remaining \( \beta \)-adrenergic stimulation alone in this latter study. Actually, the epinephrine concentration was 100-fold higher than the concentration presently used. Species to species variations could also explain these differences.

Interestingly, the \( \alpha_1 \)-agonist phenylephrine co-infused with isoproterenol induced a threefold increase of GLP-1 release over isoproterenol alone. The specificity of this effect is demonstrated by its disappearance after blockade of \( \alpha_1 \)-adrenoceptors with prazosin. The PYY response to isoproterenol was not enhanced by phenylephrine to the same extent as the GLP-1 response. This is surprising because PYY and GLP-1 are considered to be co-stored in and released by the same population of ileal L cells (Walsh

**Figure 5** Effects of \( 10^{-6} \) M isoproterenol (●), \( 10^{-7} \) M clonidine ( ViewBag), and \( 10^{-6} \) M isoproterenol plus \( 10^{-7} \) M clonidine (▼) on GLP-1 (A) and PYY (B) release by the rat ileum (means ± S.E.M.). Restoration of the isoproterenol-induced peptide secretion peak by \( 10^{-7} \) M yohimbine after its suppression by clonidine (open circles with broken lines).
1994). Contrasting with this belief, a portion (15%) of L cell granules from rabbit colon was found to be labelled with PYY but not enteroglucagon antibodies, thus putatively explaining specific PYY or enteroglucagon secretions upon luminal stimulations (Nilsson et al. 1991). Conversely, in human ileum, some granules from L cells were found to contain GLP-1 but not PYY (Eissele et al. 1992). The specific mobilization of GLP-1-containing granules by our phenylephrine plus isoproterenol infusion might be responsible for the potentiation of GLP-1, but not PYY release, under these circumstances. Nevertheless, blockade of α1-adrenergic receptors with prazosin strongly decreased the epinephrine-induced secretion of both peptides. Thus, the possibility of a potentiating effect of α1-receptor stimulation on β-receptor stimulation-induced secretion of PYY should also not be rejected. Such a potentiation has been observed in other cell systems. In the pineal gland, β-adrenergic stimulation of N-acetyl transferase activity is potentiated by α1-agonist stimulation (Klein et al. 1983). In adipoocytes, α1- and β-adrenergic agonists synergistically increase the expression of the uncoupling protein thermogenin, whereas α1-agonists alone have very limited effects (Rehnmark et al. 1990). β- and α1-adrenergic agonists act via the adenylate cyclase and the phospholipase C–protein kinase C–calcium pathways respectively (Summers & McMartin 1993). Activation of both pathways was shown to induce the release of PYY and GLP-1 or enteroglucagon from isolated intestinal rat cells (Brubaker 1988, Saïfa et al. 1994, 1998), but the direct stimulation of second messenger systems did not show any evidence of synergism between these pathways on GLP-1 release (Brubaker 1988).

The α2-adrenergic receptor antagonist idazoxan (10⁻⁸ M) did not alter epinephrine-induced GLP-1 or PYY secretion. In agreement with our findings, the α2-antagonist yohimbine did not significantly alter the enteroglucagon responses to epinephrine in isolated ileal canine cells (Buchan et al. 1987). Thus, the stimulation of α2-adrenergic receptors does not appear to be significantly involved in epinephrine-induced peptide secretion. When infused alone, clonidine induced a modest and delayed rise of GLP-1 and PYY concentrations in venous effluent. As compared with the increase of perfusion pressure, this time-course suggests that the present effects on peptide release resulted from alteration of mucosal blood flow. In agreement with this statement, when the clonidine-induced rise of blood pressure was blocked by a simultaneous infusion of the vasodilator hydralazine, peptide secretion was no longer observed (authors’ unpublished results). Such a mechanism could obviously not be at work in ileal cell cultures, in which clonidine did not alter enteroglucagon release (Buchan et al. 1987). Clonidine abolished the isoproterenol-induced GLP-1 and PYY secretion. This effect was reversed by blockade of α2-adrenergic receptors with yohimbine, thus showing that activation of α2-receptors may exert an inhibitory modulation of β-adrenergic receptor-induced peptide secretion. We failed, however, to disclose this effect in our epinephrine experiments. The potency of clonidine is greater than that of epinephrine or norepinephrine upon α2-receptor occupation (Langer 1981). Thus, the inhibitory effect of clonidine as here recorded was a true but probably amplified image of the impact of α2-receptor occupation by natural transmitters in control conditions. α2-receptors are negatively coupled to adenylate cyclase (Watson & Girdlestone 1996). Inhibition of cyclic adenosine monophosphate production is also induced by somatostatin, which was found to inhibit epinephrine-induced enteroglucagon release from isolated canine cells (Barber et al. 1987). The effect of α2-adrenergic receptor stimulation that we observed here is in agreement with the inhibitory function of α2-adrenoceptors in the gastrointestinal tract (Tanila et al. 1993).

Our results show that adrenergic activation of endocrine ileal L cells in rats may result from combined activation of the three types of receptors. The level of secretion of GLP-1 and PYY thus appears to be controlled very accurately. Activation of β-receptors, most probably of the β2-subtype, induces a rapid, short-lived GLP-1 and PYY secretion. This response is synergistically increased by α1-receptor stimulation. α2-adrenergic stimulation is liable to modulate the peptide release induced by β-receptor stimulation.

References

Adrenergic control of ileal L cells


Received 6 January 1999
Accepted 29 March 1999