Central neuropeptide Y induces proximal stomach relaxation via Y1 receptors in the dorsal vagal complex of the rat

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Kobashi, Motoi, Yuichi Shimatani, Keisuke Shirota, Song-Yu Xuan, Yoshihiro Mitoh, and Ryuji Matsuo. Central neuropeptide Y induces proximal stomach relaxation via Y1 receptors in the dorsal vagal complex of the rat. Am J Physiol Regul Integr Comp Physiol 290: R290–R297, 2006; First published September 29, 2005; doi:10.1152/ajpregu.00423.2005.—Effects of neuropeptide Y (NPY) on motility of the proximal stomach was examined in anesthetized rats. Intragastric pressure was measured using a balloon situated in the proximal part of the stomach. Administration of NPY into the fourth ventricle induced relaxation of the proximal stomach in a dose-dependent manner. Administration of an Y1 receptor (Y1R) agonist [Leu31, Pro34]NPY induced a larger relaxation than NPY. The administration of an Y2 receptor agonist (NPY 13-36) did not induce significant changes in motility. Microinjections of [Leu31, Pro34]NPY into the caudal part of the dorsal vagal complex (DVC) induced relaxation of the proximal stomach. In contrast, similar injections into the intermediate part of the DVC increased IGP of the proximal stomach. Administration of NPY into the fourth ventricle did not induce relaxation after bilateral injections of the Y1R antagonist (1229U91) into the caudal DVC. These results indicate that NPY induces relaxation in the proximal stomach via Y1Rs situated in the DVC. Because bilateral vagotomy below the diaphragm abolished the relaxation induced by the administration of NPY into the fourth ventricle, relaxation induced by NPY is probably mediated by vagal preganglionic neurons. Intravenous injection of atropine methyl nitrate reduced relaxation induced by administration of NPY. Therefore, relaxation induced by NPY is likely mediated by peripheral cholinergic neurons.

NPY is a key peptide in the regulation of body energy homeostasis. Besides the role of NPY in feeding behavior, NPY is involved in several abdominal functions. Centrally administered NPY delayed gastric emptying via Y2 receptors (Y2R) (18) and inhibited gastric distension-induced pyloric relaxation via Y1Rs (19). Thus NPY contributes to the control of digestion via upper abdominal functions. Gastric contractile activities that occur in the distal stomach are particularly important for digestion. In addition, accommodation of food is important for a smooth digestion. Tack et al. (45) described impaired accommodation related to functional dyspepsia symptoms. Gastric relaxation in the proximal stomach to accommodate ingested food is achieved by the intramural nervous system and extrinsic nervous system. Receptive relaxation is a well-known response achieved by the extrinsic nervous system (4), which arises from neurons in the dorsal motor nucleus of the vagus (DMV) (42). Thus the hindbrain is involved in the control of gastric motor activities. However, the relationship between NPY and gastric relaxation of the proximal stomach, which serves as a reservoir, has never been clarified. Recently, we suggested that administration of orexin-A, which is one of the appetite-stimulating peptides produced in the hypothalamus, into the fourth ventricle induced relaxation of the proximal stomach as well as an enhancement of distal stomach contractility (26). Because NPY affects DVC neurons that receive afferent information from the stomach (44) and send efferent information through axons to the gastrointestinal tract (3), it is possible that NPY induces gastric relaxation to accommodate ingested food.

The present study was undertaken to demonstrate the role of NPY in gastric relaxation of the proximal stomach to accommodate food intake. The contribution of Y1Rs in the dorsal medulla to the relaxation of the proximal stomach induced by NPY was also examined, as well as the peripheral cholinergic contribution.

MATERIALS AND METHODS

Animals and preparations. Male Sprague-Dawley rats (280–320 g) were used. Each animal was fasted for 1 day before the start of the experiment. Each animal was anesthetized with an inhaled isoflurane.

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injection of urethane chloralose (urethane, 0.8 g/kg; chloralose, 65 mg/kg body wt). Subsequent anesthesia was administered through Silastic tubing (OD, 1.0 mm; ID, 0.5 mm) inserted into the right jugular vein. Each animal had a tracheal cannula made from polyethylene tubing (OD, 2.07 mm). After an abdominal incision was made, a balloon created from thin latex rubber and plastic tubing (OD, 1.7 mm) was introduced into the proximal stomach from the tip of the fundus. The balloon was secured by purse-string sutures around the gastric wall using 4-0 silk thread. Another tube (OD, 2.0 mm) was also introduced into the stomach from the greater curvature just distal to the limiting ridge to drain gastric juices and was ligated with the gastric wall around the tubing (27, 29). After closing of the abdominal incision, each animal was mounted on a stereotaxic apparatus. The neck muscles were removed, and the ligaments between the occipital bone and the atlas were carefully removed. A small hole was made through the dura mater to administer the drugs as previously described (26). Three microliters of drugs were administered using a Hamilton syringe into the fourth ventricle. When the drugs were injected into the DVC using a microglass pipette, the occipital bone and dura mater were removed to expose the surface of the brain stem. Animals were placed in the prone position during the experiments. Body temperature was maintained at 36°C using a heating pad placed under the body (model ATB-1100; Nihon Kohden, Japan). Animal care was in accordance with the guidelines of the Physiological Society of Japan. The experimental protocols used were approved by the Okayama University Animal Use Committee (approval number: 03-002-005).

Recording of intragastric pressure. An intragastric balloon was inflated with 0.2–0.5 ml of water, maintaining the initial intragastric pressure (IGP) of 0.5–0.7 kPa. A similar volume was used in our previous studies (26, 27, 29) to measure gastric relaxation of the proximal stomach. After gastric balloon inflation, animals were left for at least 60 min until the IGP stabilized. The distal end of this tubing was connected to a strain-gauge pressure meter (model 6M82; NEC-Sanei, Japan) to measure the IGP. Gastric response data were stored on a personal computer using the Power Lab system (AD Instruments) for later analyses.

Administration of NPY and related peptides into the fourth ventricle. Dose-dependent gastric relaxation was studied with administration of NPY and related peptides to the fourth ventricle. All drugs were dissolved in Ringer solution. Because a similar administration of Ringer solution (3 µl) did not induce any response of proximal stomach motility in our previous study (26), we did not test the effect of Ringer solution on motility again. Each rat received three different NPY doses [0.3, 1.0, and 3.0 nmol (3 µl); 6 rats], or [Leu31, Pro34]NPY [a Y1R agonist; 0.1, 0.3, and 1.0 nmol (3 µl); 6 rats], or NPY 13–36 [a Y2R agonist; 0.1, 0.3, and 1.0 nmol (3 µl); 5 rats]. The gastric response was observed for at least 1 h after the administration of each drug. Drug doses were always administered in ascending order. NPY, [Leu31, Pro34]NPY, and NPY 13-36 were purchased from the Peptide Institute (Osaka, Japan).

Local administration of Y1R agonist and antagonist. Commercially prepared glass micropipettes (10 µm in tip diameter, World Precision Instruments) connected to a 50-µl Hamilton syringe were installed in a microinjector (model XF-320; Nihon Kohden, Japan) for injecting [Leu31, Pro34]NPY into the left DVC. Each glass pipette was filled with fluid paraffin beforehand. A test solution was sucked from the tip of a pipette, which was then penetrated into the caudal DVC or intermediate DVC at the left medulla by the use of a stereotaxic apparatus. The coordinates were 0.3 mm posterior to the obex, 0.25 mm lateral to the midline, and 0.9 mm ventral from the surface of the brain stem for the caudal DVC and 0.5 mm anterior to the obex, 0.5 mm lateral to the midline, and 0.4 mm ventral from the surface of the brain stem for the intermediate DVC. These locations corresponded with the boundary between the nucleus of the solitary tract (NST) and the DMV according to the atlas (37). Just after penetration, [Leu31, Pro34]NPY was injected at a dose of 6 pmol (60 nl) for 30 s. Each 60-nl volume would form a sphere of about 500 µm in diameter. The injection would therefore fill the entire DMV and the adjacent NST and hypoglossal nucleus. In preliminary experiments, we used four rats to determine the injection size. Pontamine sky blue solution (2%, 60 nl) was injected into the DVC at the same coordinates used for the test solutions. Stain covered the ventral part of NST, DMV, and dorsal part of the hypoglossal nucleus. To examine the effects of [Leu31, Pro34]NPY, each animal received injections into the caudal and the intermediate part of the DVC (7 rats). The second injection was made more than 30 min after the first injection. The first injection was made into the caudal DVC in four rats and into the intermediate DVC in three rats. Effects of vehicle solution (Ringer) injections were examined using six other rats. In this study, the part of the DVC located caudal to the obex was defined as “caudal DVC,” and the portion of the DVC located between the obex and anterior tip of the area postrema was defined as “intermediate DVC” according to a previous study (Fig. 2C) (49).

To examine the effects of a blockade of Y1Rs on the gastric response, microinjection of Y1R antagonist (1229F91; Sigma) into the caudal DVC was performed. After confirmation of gastric relaxation induced by the fourth ventricular administration of NPY (1.0 nmol) was studied in six rats. Atropine methyl nitrate, a peripherally acting muscarinic cholinergic receptor antagonist, was used (40). Atropine methyl nitrate (2.0 mg/kg body wt; Sigma) was dissolved in 0.15 M saline and administered intravenously. A similar dose of atropine completely blocked the increase in IGP induced by the electrical stimulation of the peripheral cut end of the cervical vagus nerve in the rat in a previous study (33). Before the administration of atropine, relaxation induced by the administration of NPY (1.0 nmol) into the fourth ventricle, the abdomen was reopened, both vagi were cut, and the abdominal incision was closed. More than 30 min after the vagotomy, the response to NPY (1.0 nmol) was again examined.

Intravenous administration of atropine. To demonstrate that the peripheral cholinergic neurotransmission was involved in the gastric response, the effects of atropine on the gastric relaxation induced by fourth ventricular administration of NPY (1.0 nmol) was studied in six rats. Atropine methyl nitrate, a peripherally acting muscarinic cholinergic receptor antagonist, was used (40). Atropine methyl nitrate (2.0 mg/kg body wt; Sigma) was dissolved in 0.15 M saline and administered intravenously. A similar dose of atropine completely blocked the increase in IGP induced by the electrical stimulation of the peripheral cut end of the cervical vagus nerve in the rat in a previous study (33). Before the administration of atropine, relaxation induced by the administration of NPY was confirmed. Response to NPY was again examined 10–15 min after the administration of atropine. Preliminary experiments in six rats revealed that the mean magnitude of the relaxation induced by the administration of NPY after the atropine injection was significantly smaller than the relaxation before the atropine injection (data not shown). However, the atropine injection significantly decreased the basal IGP before administration of NPY. To obtain sensible results, IGP should be restored to preatropine values before testing effects of NPY administration. Therefore, we additionally inflated the balloon to restore IGP to preatropine values after the administration of atropine.

Data analyses. To analyze relaxation of the proximal stomach, the minimum value of the IGP wave was measured every minute as previously described (26). All numerical values are represented as means ± SE. To analyze responses to administration to the fourth ventricle, differences were examined between the mean values just before the administration of solutions and those 19–20 min after the administration using the paired Student’s t-test (P < 0.05 for significance). For analyzing the response to microinjection of the Y1R agonist, mean values just before the injection of solutions and those 5–6 min after the injection, were used for statistical analysis.
RESULTS

NPY induced relaxation of the proximal stomach via Y1Rs. Effects of administration of NPY, [Leu\textsuperscript{31}, Pro\textsuperscript{34}]NPY and NPY 13–36 to the fourth ventricle were examined. Administration of NPY produced relaxation in a dose-dependent manner. Low dose (0.3 nmol) administration of NPY did not induce a significant reduction in IGP ($t$ = 1.22, $P$ = NS (not significant), $n$ = 6); however, administration of 1.0 nmol ($t$ = 5.50, $P$ < 0.05, $n$ = 6) and 3.0 nmol ($t$ = 3.23, $P$ < 0.05, $n$ = 6) NPY induced a significant relaxation (Fig. 1A). The degree of relaxation depended on the dose of NPY (Fig. 1D).

Administration of [Leu\textsuperscript{31}, Pro\textsuperscript{34}]NPY, which is a known Y1 receptor (Y1R) agonist, also induced gastric relaxation. The low dose (0.1 nmol) administration of [Leu\textsuperscript{31}, Pro\textsuperscript{34}]NPY did not induce a significant reduction in IGP ($t$ = 1.29, not significant); however, administration of 0.3 nmol ($t$ = 3.66, $P$ < 0.05, $n$ = 6) and 1.0 nmol ($t$ = 7.16, $P$ < 0.05, $n$ = 6) [Leu\textsuperscript{31}, Pro\textsuperscript{34}]NPY induced a significant relaxation (Fig. 1B). The mean magnitude of [Leu\textsuperscript{31}, Pro\textsuperscript{34}]NPY-induced relaxation was almost twice as high as that induced by NPY (Fig. 1D). Administration of three different doses of NPY 13-36, which is a known Y2R agonist, did not induce a significant response (Fig. 1, C and D). Table 1 shows the mean values before and after administration of NPY and related peptides.

### Contribution of Y1Rs in the DVC to relaxation.

Effects of local administration of [Leu\textsuperscript{31}, Pro\textsuperscript{34}]NPY into the left intermediate or the left caudal DVC were examined. A schematic representation of the injection sites is shown in Fig. 2C. Injection of [Leu\textsuperscript{31}, Pro\textsuperscript{34}]NPY (6 pmol) into the caudal DVC induced relaxation (Fig. 2Aa). Mean IGP after the injection of [Leu\textsuperscript{31}, Pro\textsuperscript{34}]NPY was significantly lower than that before the injection ($t$ = 3.82, $P$ < 0.05, $n$ = 7). The injection of the vehicle solution into the caudal DVC did not induce a significant change in IGP ($t$ = 0.73, $P$ = NS, $n$ = 6) (Fig. 2Ab). In

### Table 1. Effects of fourth ventricular administration of NPY and related peptides on the intragastric pressure

<table>
<thead>
<tr>
<th>Dose, nmol</th>
<th>NPY, $n$ = 6</th>
<th>[Leu\textsuperscript{31}, Pro\textsuperscript{34}]NPY, $n$ = 6</th>
<th>NPY 13–36, $n$ = 5</th>
</tr>
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<tbody>
<tr>
<td>0.1</td>
<td>0.59±0.029</td>
<td>0.58±0.027</td>
<td>0.55±0.011</td>
</tr>
<tr>
<td>0.3</td>
<td>0.64±0.035</td>
<td>0.59±0.035*</td>
<td>0.57±0.026</td>
</tr>
<tr>
<td>1.0</td>
<td>0.65±0.039</td>
<td>0.58±0.052*</td>
<td>0.58±0.025</td>
</tr>
<tr>
<td>3.0</td>
<td>0.58±0.009</td>
<td>0.55±0.023</td>
<td>0.56±0.024</td>
</tr>
</tbody>
</table>

Data are mean intragastric pressure ± SE (kPa). NYP, neuropeptide Y. *Significant difference ($P$ < 0.05) compared with that of preinjection of drugs.
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Fig. 2. Effects of microinjection of [Leu<sup>31</sup>, Pro<sup>34</sup>]NPY (Y1R agonist) into the 2 different sites of the dorsal vagal complex (DVC) on the IGP. Aa: typical response of the proximal stomach induced by microinjection of [Leu<sup>31</sup>, Pro<sup>34</sup>]NPY into the caudal DVC. Ab: mean IGP pre- and postinjection of [Leu<sup>31</sup>, Pro<sup>34</sup>]NPY or vehicle solution are presented. Bb: typical response of the proximal stomach induced by microinjection of [Leu<sup>31</sup>, Pro<sup>34</sup>]NPY into the intermediate DVC. Bb: mean IGP pre- and postinjection of [Leu<sup>31</sup>, Pro<sup>34</sup>]NPY or vehicle solution are presented. *Significant changes in IGP induced by microinjection of drugs. C: schematic representation of injection sites. Two different sites are plotted on the horizontal plane of the medulla.

contrast, the injection of [Leu<sup>31</sup>, Pro<sup>34</sup>]NPY (6 pmol) into the intermediate DVC increased IGP (Fig. 2Ba). Mean IGP after the injection of [Leu<sup>31</sup>, Pro<sup>34</sup>]NPY was significantly higher than that before the injection (t = 3.25, P < 0.05, n = 7). Injection of the vehicle solution into the intermediate DVC did not induce a significant change in IGP (t = 0.65, P = NS, n = 6) (Fig. 2Bb).

Effect of local injection of 1229U91, which is known as a Y1R antagonist, on the relaxation induced by the administration of NPY to the fourth ventricle was examined. Administration of NPY (1.0 nmol) induced relaxation before injection of 1229U91 (Fig. 3Aa, left). A significant decrease in IGP was observed after the administration of NPY (t = 4.06, P < 0.05, n = 8) (Fig. 3Ab). After the injection of 1229U91 into the bilateral DVC (10 pmol on each side), administration of NPY showed a slight, but not significant, increase in IGP (t = 2.30, P = NS, n = 8) (Fig. 3Aa, right and Ab, right). A similar injection of vehicle solution into the bilateral DVC (100 nl on each side) did not affect the relaxation induced by NPY (Fig. 3Ba). A significant decrease in IGP induced by the administration of NPY was observed before the administration of vehicle solution (t = 7.36, P < 0.05, n = 6) and after administration (t = 5.99, P < 0.05, n = 6) (Fig. 3Bb).

Contribution of vagal efferent neurons. To examine the contribution of parasympathetic preganglionic neurons, the effect of anterior and posterior subdiaphragmatic vagotomy on relaxation induced by administration of NPY (1.0 nmol) was examined. Vagotomy abolished relaxation induced by the administration of NPY into the fourth ventricle (Fig. 4A). A significant decrease in IGP observed before sectioning of the vagi (t = 3.40, P < 0.05, n = 6) was not observed after sectioning (t = 0.54, P = NS, n = 6) (Fig. 4B). A significant difference was observed (t = 2.85, P < 0.05, n = 6) between the mean decreases in IGP induced by the administration of NPY before vagotomy (0.093 ± 0.027 kPa) and after vagotomy (0.007 ± 0.013 kPa).

Peripheral cholinergic contribution to the relaxation. To examine the contribution of peripheral cholinergic transmission, effects of intravenous injection of atropine (2.0 mg/kg) on the relaxation induced by administration of NPY into the fourth ventricle (1.0 nmol) were examined. Magnitude of relaxation after the injection of atropine was lower than that before injection of atropine (Fig. 5A). A significant decrease in IGP, observed before injection of atropine (t = 5.07, P < 0.05, n = 6), was not observed after injection of atropine (t = 2.25, P = NS, n = 6) (Fig. 5B). A significant difference was observed (t = 2.54, P < 0.05, n = 6) between the mean decreases in IGP induced by the administration of NPY before the injection of atropine (0.101 ± 0.020 kPa) and after the injection of atropine (0.036 ± 0.016 kPa).
DISCUSSION

The present study demonstrates that NPY induced the relaxation of the proximal stomach via Y1Rs situated in the caudal DVC. Relaxation induced by NPY was achieved by vagal preganglionic neurons that connect to cholinergic myenteric neurons.

Gastric relaxation by way of Y1Rs. To demonstrate the contribution of Y1Rs to gastric relaxation, we used [Leu31, Pro34]NPY as an Y1R agonist and 1229U91 as an Y1R antagonist. Strictly speaking, [Leu31, Pro34]NPY acts on the Y5 receptor in addition to the Y1R (39). In addition to Y1 antagonistic properties, 1229U91 has some Y4 agonistic activity (36). Injections of [Leu31, Pro34]NPY into the caudal DVC induced gastric relaxation and injections of 1229U91 into the caudal DVC attenuated NPY-induced relaxation. Therefore, we concluded that the Y1R mediated NPY-induced gastric relaxation in the present study.

Several studies revealed that the Y1R subtype plays a prominent role in mediating feeding induced by NPY (22, 23, 47). Because gastric relaxation was also achieved by the Y1R in the present study, this gastric relaxation might be closely associated with food intake. Fasting is usually followed by feeding; therefore, gastric relaxation achieved by the actions of NPY, which is released by fasting, to enhance smooth accommodation of food is rational. Reflex relaxations, induced by the activation of esophageal and/or pharyngolaryngeal receptors before food reaches the stomach, are well known (1, 4, 28, 42). Centrally released NPY might cooperate with the acute reflex relaxation just after swallowing to facilitate accommodation of the stomach to a meal.

Possible sites of action of NPY to induce gastric relaxation. Hypothalamic arcuate nucleus contains a high density of neurons that produce NPY (10). Fasting markedly increases NPY protein and mRNA levels in the hypothalamic arcuate nucleus (20) and also augments NPY release in the paraventricular hypothalamic nucleus (PVN) (25). The NPY containing neurons project to various parts of the brain, including the PVN (21). PVN neurons also project to parasympathetic and sympathetic preganglionic neurons in the brain stem and spinal cord (35). Furthermore, PVN stimulation excites the NST neurons, which receive input from the stomach (41). Therefore, it is possible that NPY in the forebrain affects the gastric motility by way of the PVN. In the present study, however, fourth ventricular administration of NPY and/or microinjection
of an NPY agonist into the DVC induced gastric relaxation. The more preferable explanation is that NPY release in the DVC affects gastric motility. NPY immunoreactive neurons are localized in the area postrema and the NST (16). NPY neurons in the NST are activated under restricted daily feeding (20). Thus the NST neurons that contain NPY might be the source of the gastric response observed in the present study.

The volume injected into the DVC was 60 nl. As stated previously (see MATERIALS AND METHODS), we observed that the injected dye stained the ventral part of the NST, the DMV, and the dorsal part of the hypoglossal nucleus. These areas are realistic, because 60 nl of solution makes a sphere 500 μm in diameter. These observations strongly suggest that the test solution affected neurons in both the ventral NST and the DMV. Therefore, we could not determine whether NPY acted on just the NST or the DMV neurons.

Microinjection of the Y1R agonist into the caudal DVC, but not intermediate DVC, induced gastric relaxation. Microinjections into the intermediate DVC increased the IGP. This was not surprising, because the intermediate and caudal DMV contain different groups of preganglionic neurons (32, 49). It is well known that the caudal part of the DMV is involved in gastric relaxation (15, 32, 49) and that injection of L-glutamate into the caudal DMV induced relaxation (32). Microinjection of prolactin-releasing peptide into the caudal DMV induced gastric relaxation, whereas a similar injection into the rostral DMV increased IGP (15). Thus the caudal DMV is intimately involved in gastric relaxation. Therefore, the caudal DMV is the most probable area to induce relaxation of the proximal stomach, which is also shown in other studies.

Contribution of vagal preganglionic neurons and peripheral cholinergic neurons in the induction of NPY responses. The result of the subdiaphragmatic vagotomy revealed that relaxation induced by NPY was achieved by vagal preganglionic neurons. The NST sends a descending projection to the sympathetic preganglionic neurons in the spinal cord and also projects into several sympathetic premotor nuclei, including the rostral and caudal ventrolateral area (43). Therefore, a sympathetic contribution to the NPY response in the present research should be considered. However, bilateral subdiaphragmatic vagotomy completely abolished the NPY response of the stomach in the present study. Therefore, the proximal stomach relaxation observed in the present study was probably
achieved by the activation of parasympathetic preganglionic neurons.

Central effects of NPY and peptide YY (PYY) on antrum motility are well investigated (7). A high dose of NPY facilitates the basal contractility of the antrum via the Y1R. In contrast, a low dose of NPY or PYY decreases motility with increased levels of gastrointestinal motility via the Y2R. Extracellular recordings revealed that Y2R agonists or PYY inhibited the firing rate of the majority of DMV neurons (6). These studies revealed that the contractile activities of the antrum is facilitated by the activation of the Y1R and is suppressed by the activation of the Y2R, suggesting a contribution of cholinergic vagal efferent outflow. Our observations as to the blockade of peripheral muscarinic transmission seem to indicate that NPY reduced the levels of IGP in the proximal stomach. Activation of the Y1R decreased IGP of the proximal stomach, inhibiting the cholinergic vagal efferent outflow. This effect seems to be different from the results obtained from the antrum motility experiments. It could be that the role of the Y1R in the relaxation of the proximal stomach differs from that in antrum motility. An electrophysiological study in in vitro slice preparations showed that excitatory postsynaptic currents of DMV neurons induced by the electrical stimulation of the NST were partly inhibited by presynaptic actions of NPY via the Y1R (3). This result corresponds with our observations where the activation of the Y1R decreased activity of vagal excitatory preganglionic neurons that connect with cholinergic myenteric neurons. To investigate the effects of peptides on antrum motility, peptides were injected into the DVC anterior to the caudal (7), on the other hand, relaxation of the proximal stomach observed in the present study occurred by injection of peptides into the DVC posterior to the caudal. Thus the regional difference might induce different results. That is, activation of the Y1R in the intermediate DVC and those in the caudal DVC induced phasic contraction of the distal stomach and relaxation in the proximal stomach, respectively. It was concluded that certain parts of the relaxation induced by centrally administered NPY should mediate inhibition of vagal excitatory preganglionic neurons via the Y1R in the proximal stomach.

Differences between appetite-enhancing agents and anorexics on gastric motility. The effect of appetite-enhancing peptides on the phasic contractions of the distal stomach is dramatically opposite to that of anorexics agents. Appetite-enhancing peptides facilitate phasic contractions and gastric emptying (2, 13, 26, 31). On the contrary, anorexic agents depress phasic contractions (11, 30). These phenomena are to be expected, because enhanced appetite facilitates digestion and anorexia induces dyspepsia. Our previous study (26) in the proximal stomach revealed that administration into the fourth ventricle of orexin-A, an appetite-enhancing peptide produced in the hypothalamus like NPY, induced gastric relaxation. On the contrary, anorexic agents, such as apomorphine, increased the IGP of the proximal stomach (30). We infer that IGP in the proximal stomach, which works as a reservoir, might be an appropriate index to ascertain the appetite of an animal.

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