Reciprocal activity of longitudinal and circular muscle during intestinal peristaltic reflex

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Grider, J. R. Reciprocal activity of longitudinal and circular muscle during intestinal peristaltic reflex. Am J Physiol Gastrointest Liver Physiol 284: G768–G775, 2003; 10.1152/ajpgi.00384.1998.—A two-compartment, flat-sheet preparation of rat colon was devised, which enabled exclusive measurement of longitudinal muscle activity during the ascending and descending phases of the peristaltic reflex. A previous study using longitudinal muscle strips revealed the operation of an integrated neuronal circuit consisting of somatostatin, opioid, and VIP/pituitary adenylate cyclase-activating peptide (PACAP)/nitric oxide synthase (NOS) interneurons coupled to cholinergic/tachykinin motor neurons innervating longitudinal muscle strips that could lead to descending contraction and ascending relaxation of this muscle layer. Previous studies in peristaltic preparations have also shown that an increase in somatostatin release during the descending phase causes a decrease in Met-enkephalin release and suppression of the inhibitory effect of Met-enkephalin on VIP/PACAP/NOS motor neurons innervating circular muscle and a distinct set of VIP/PACAP/NOS interneurons. The present study showed that in contrast to circular muscle, longitudinal muscle contraction during the descending phase and relaxed during the ascending phase. Somatostatin antiserum inhibited descending contraction and augmented ascending relaxation of longitudinal muscle. The sequence of events involves activation of sensory neurons coupled via modulatory interneurons to excitatory and inhibitory motor neurons that projected into the circular muscle layer. The excitatory neurons express acetylcholine alone or coexpress acetylcholine and the tachykinins substance P (SP) and neurokinin A (NKA) (3, 5, 6). The inhibitory neurons coexpress VIP and nitric oxide (NO) synthase (NOS) or pituitary adenylate cyclase-activating peptide (PACAP) and NOS (3, 5, 6). The sensory pathway activated by muscle stretch involves extrinsic CGRP neurons with cell bodies in the dorsal root ganglion (12, 14). The sensory pathway activated by mucosal stimuli involves intrinsic neurons with afferent terminals in the mucosa and cell bodies in the enteric nervous system. Mucosal stimuli release 5-HT from enterochromaffin cells (7, 16, 29), which, in rat and human intestine, acts on 5-HT3 receptors located on sensory nerve terminals (16); the resultant release of CGRP activates an integrated circuit of interneurons coupled to excitatory and inhibitory motor neurons (10, 12, 25). The terms excitatory and inhibitory refer to the ability of the neurotransmitters to cause depolarization or hyperpolarization of smooth muscle membrane potential and to elicit contraction or relaxation, respectively.

The integrated circuit of modulatory interneurons consists of somatostatin neurons coupled to opioid neurons; the latter are coupled to inhibitory VIP/PACAP/NOS motor neurons innervating circular muscle. During the descending phase of peristalsis, there is an increase in the activity of somatostatin neurons leading to a decrease in the activity of opioid neurons, thereby eliminating the restraint exerted by opioid neurons on inhibitory motor neurons and resulting in an increase in the release of inhibitory motor neurotransmitters (10, 13, 17). A secondary pathway appears to involve GABA neurons coupled in a reciprocal pathway to opioid neurons (10). Recent studies (11) on longitudinal muscle strips with adherent myenteric plexus but devoid of circular muscle suggest that a similar integrated circuit of somatostatin and opioid neurons regulates the activity of the longitudinal muscle and relaxes in reverse fashion to circular muscle during the peristaltic reflex. Longitudinal muscle activity is regulated by excitatory VIP/PACAP/NOS interneurons coupled to cholinergic/tachykinin motor neurons innervating longitudinal muscle.

gut smooth muscle; enteric nervous system; neuropeptides; gastrointestinal motility

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of motor neurons innervating longitudinal smooth muscle. In rat and guinea pig, intestinal longitudinal muscle is predominantly innervated by excitatory cholinergic and tachykinin motor neurons (4–6, 26); its contraction and relaxation result chiefly from increase or decrease in the activity of these neurons. The motor neurons appear to be directly regulated by excitatory VIP/PACAP/NOS interneurons (30, 33), which, in turn, are regulated by somatostatin and opioid neurons. Our recent studies (11) indicate that an increase in the activity of somatostatin interneurons leads to a decrease in the activity of opioid neurons and thus an increase in the activity of excitatory VIP/PACAP/NOS interneurons; the latter are coupled to activation of cholinergic/tachykinin motor neurons innervating longitudinal smooth muscle. In support of this notion, exogenous VIP, PACAP, and NO stimulated acetylcholine and tachykinin release and induced contraction of longitudinal muscle strips in a tetrodotoxin-sensitive fashion (1, 2, 11, 21–23, 31, 32). Exogenous somatostatin inhibited enkephalin release and stimulated VIP and SP release (11).

The organization of interneurons and motor neurons regulating the activity of longitudinal smooth muscle suggests that this muscle layer might respond in reciprocal fashion to circular muscle during peristalsis such that descending relaxation of circular muscle is accompanied by contraction of longitudinal muscle, whereas ascending contraction of circular muscle is accompanied by relaxation of longitudinal muscle. The present study examined this notion using a compartmented, flat-sheet preparation of rat colon that enabled exclusive measurement of longitudinal muscle activity during the peristaltic reflex. The results indicate that longitudinal muscle contracts during the descending phase of the peristaltic reflex and relaxes during the ascending phase, utilizing for this purpose, the same components of the neuronal circuit that regulates circular muscle activity.

**METHODS**

Rats were killed by CO2 asphyxiation, and a 5-cm segment of middle-to-distal colon was removed and placed in Krebs-bicarbonate medium containing (in mM) 118 NaCl, 4.8 KCl, 1.2 KH2PO4, 1.2 MgSO4, 2.5 CaCl2, 25 NaHCO3, and 11 glucose maintained at 37°C and bubbled with 95% O2-5% CO2. The segment was opened along the mesenteric border and pinned as a longitudinal muscle activity was recorded (Fig. 1). Mucosal force-displacement transducer. Pins were inserted so as to prevent muscle activity in the circular direction. Longitudinal muscle activity was measured using a pulley assembly attached to a force transducer. The order of the compartments was reversed in different experiments so as to elicit either orad or caudal responses of longitudinal muscle.

The two-compartment preparation of rat colon for the measurement of longitudinal muscle activity during the peristaltic reflex. One compartment was used to apply mucosal stimulation with a fine brush or circumferential muscle stretch using a hook-and-pulley assembly with attached weights. The other compartment was used to measure longitudinal muscle response. In this compartment, pins were inserted so as to prevent muscle activity in the circular direction. Longitudinal muscle activity was measured using a pulley assembly attached to a force transducer. The order of the compartments was reversed in different experiments so as to elicit either orad or caudal responses of longitudinal muscle.

Circumferential muscle stretch was applied with weights via a hook-and-pulley assembly, as described previously (12, 16). As shown in Fig. 1, the stimuli were applied to a chamber, which was mechanically isolated by pins from the chamber where longitudinal activity was recorded.

After a 60-min equilibration period, a stimulus-response curve for longitudinal muscle was generated by application of muscle stretch (2–10 g for a 1-min period at 5-min intervals) or mucosal stimulation (2–10 strokes at a rate of 1 stroke/s at 5-min intervals). The preparation was then allowed to equilibrate for an additional 45-min period, after which muscle stretch or mucosal stimulation was repeated in the presence of a selective antagonist or a specific antiserum added to the recording compartment. The antagonist was added 15 min, and the antiserum 60 min, before applying the stimulus. Contraction in response to muscle stretch was transient, lasting 15–20 s, and was measured as the change from baseline tension (Fig. 2). Relaxation was sustained throughout the duration of the stimulus and was also measured as the change from baseline tension (Fig. 2).

Data analysis. Contraction and relaxation of longitudinal muscle was recorded in grams of force. Maximal responses elicited by a 10-g muscle stretch and eight mucosal strokes were not statistically different. Values were calculated as means ± SE of measurements obtained in n experiments. In each experiment, one stretch-response curve and one stroking-response curve were generated in the presence and absence of an antagonist. Tissues for each experiment were obtained from a different animal. Thus n represents the number of experiments and the number of animals. Statistical significance was evaluated using Student’s t-test for paired or unpaired values.

**Fig. 1.** Two-compartment preparation of rat colon for the measurement of longitudinal muscle activity during the peristaltic reflex. One compartment was used to apply mucosal stimulation with a fine brush or circumferential muscle stretch using a hook-and-pulley assembly with attached weights. The other compartment was used to measure longitudinal muscle response. In this compartment, pins were inserted so as to prevent muscle activity in the circular direction. Longitudinal muscle activity was measured using a pulley assembly attached to a force transducer. The order of the compartments was reversed in different experiments so as to elicit either orad or caudal responses of longitudinal muscle.
LONGITUDINAL MUSCLE IN PERISTALSIS

Materials. VIP10–28, PACAP6–38, and [D-Arg1, D-Trp7,9, Leu11]-SP were purchased from Bachem (Torrance, CA). Naloxone, atropine, tetrodotoxin, and all other chemicals were purchased from Sigma (St. Louis, MO). Somatostatin antibody 775 was purchased from Dr. A. Arimura, Tulane University (New Orleans, LA).

RESULTS

Longitudinal muscle activity during the peristaltic reflex. Application of circumferential muscle stretch or mucosal stimulation to the orad compartment caused a transient, 15- to 20-s contraction of longitudinal muscle in the caudad recording compartment (descending contraction; Fig. 2). Conversely, application of circumferential muscle stretch or mucosal stimulation to the caudad compartment caused relaxation of longitudinal muscle in the orad recording compartment that was sustained throughout the period of stimulation. Vertical bar represents 1 g force.

Fig. 2. Tracings of ascending relaxation and descending contraction of longitudinal muscle elicited by muscle stretch (2–10 g) applied to the caudad and orad compartments, respectively. Contraction was transient, whereas relaxation was sustained throughout the period of stimulation.

Effect of atropine and the tachykinin antagonist [D-Arg1, D-Trp7,9, Leu11]-SP on longitudinal muscle responses. In all experiments, antagonists were added to the recording compartment in which longitudinal muscle contraction or relaxation was measured. Addition of atropine (1 μM) to the caudad recording compartment decreased the magnitude of the descending contraction elicited by application of muscle stretch or mucosal stimulation to the orad compartment (83 ± 16%, P < 0.01 and 66 ± 1%, P < 0.001 inhibition of 2- and 10-g stretch stimulus, respectively; 75 ± 8%, P < 0.01 and 54 ± 3%, P < 0.01 inhibition of a 2- and 8-stroke stimulus, respectively; Fig. 4). Addition of the tachykinin antagonist [D-Arg1, D-Trp7,9, Leu11]-SP (spantide) also inhibited the magnitude of descending contraction elicited by application of muscle stretch and mucosal stimulation to the orad compartment (44 ± 6%, P < 0.01 and 26 ± 5%, P < 0.01 inhibition of 2- and 10-g stretch stimulus, respectively; 50 ± 5%, P < 0.01 and 22 ± 4%, P < 0.01 inhibition of 2- and 8-stroke stimulus, respectively; Fig. 4). The combination of atropine and tachykinin antagonist abolished the descending contraction elicited by low levels of stimulation and

Fig. 3. Ascending relaxation and descending contraction of longitudinal muscle elicited by mucosal stroking (A) and muscle stretch (B) in the presence and absence of TTX (1 μM). Values are means ± SE of 4 experiments.
strongly inhibited maximal response to muscle stretch (84 ± 1% inhibition, \( P < 0.001 \)) and mucosal stimulation (83 ± 2% inhibition, \( P < 0.001 \); Fig. 4).

Effect of VIP and PACAP receptor antagonists on longitudinal muscle responses. Addition of the VIP receptor antagonist VIP10–28 (5 \( \mu \)M) to the orad recording compartment caused an increase in ascending relaxation of longitudinal muscle elicited by application of muscle stretch or mucosal stimulation to the caudad compartment (69 ± 8%, \( P < 0.01 \) and 38 ± 7%, \( P < 0.01 \) increase in response to 2- and 10-g stretch stimulus, respectively; 66 ± 16%, \( P < 0.02 \) and 31 ± 6%, \( P < 0.01 \) increase in the response to 2 and 8 strokes, respectively; Fig. 5). Conversely, addition of VIP10–28 to the caudad recording compartment caused a decrease in descending contraction elicited by application of muscle stretch or mucosal stimulation to the orad compartment (67 ± 13%, \( P < 0.01 \) and 27 ± 3%, \( P < 0.01 \) decrease in response to 2- and 10-g muscle stretch; 70 ± 10%, \( P < 0.01 \) and 27 ± 8%, \( P < 0.02 \) decrease in response to 2 and 8 strokes; Fig. 5).

The magnitudes of the increase in ascending relaxation and the decrease in descending contraction elicited by the PACAP antagonist PACAP6–38 (5 \( \mu \)M) were very similar to those elicited by VIP10–28 (Fig. 6).

Effect of the opioid antagonist naloxone on longitudinal muscle responses. Addition of the mixed \( \mu /\delta \)-opioid receptor antagonist naloxone (10 \( \mu \)M) to the orad recording compartment caused a decrease in ascending relaxation elicited by application of muscle stretch or mucosal stimulation to the caudad compartment (100 ± 5%, \( P < 0.001 \) and 76 ± 10%, \( P < 0.01 \)

![Fig. 4. Descending contraction of longitudinal muscle elicited by mucosal stroking (A) and muscle stretch (B) in the presence and absence of atropine (1 \( \mu \)M), the tachykinin antagonist (antag) spantide (10 \( \mu \)M), or a combination of atropine and spantide. The antagonists were added for a period of 15 min before responses were measured. Values are means ± SE of 4 experiments.](image)

![Fig. 5. Ascending relaxation and descending contraction of longitudinal muscle elicited by mucosal stroking (A) and muscle stretch (B) in the presence and absence of VIP10–28 (5 \( \mu \)M). The antagonist was added for a period of 15 min before responses were measured. Values are means ± SE of 4 experiments.](image)
Effect of somatostatin antiserum on longitudinal muscle responses. Addition of the specific somatostatin antiserum 775 (1:100 final dilution) for 1 h to the orad recording compartment caused an increase in ascending relaxation elicited by application of muscle stretch or mucosal stimulation to the caudad compartment (80 ± 14%, P < 0.01 and 18 ± 2%, P < 0.01 increase in response to 2- and 10-g muscle stretch, respectively; 93 ± 5%, P < 0.001 and 12 ± 4%, P < 0.05 increase in response to 2 and 8 strokes, respectively; Fig. 8). Conversely, addition of somatostatin antiserum to the caudad recording compartment caused a decrease in descending contraction elicited by application of mus-

Fig. 6. Ascending relaxation and descending contraction of longitudinal muscle elicited by mucosal stroking (A) and muscle stretch (B) in the presence and absence of the pituitary adenylate cyclase activating peptide (PACAP) antagonist PACAP6–38 (5 μM). The antagonist was added for a period of 15 min before responses were measured. Values are means ± SE of 4 experiments.

decrease in response to 2- and 10-g muscle stretch, respectively; 100 ± 3%, P < 0.001 and 72 ± 8%, P < 0.01 decrease in the response to 2 and 8 strokes, respectively; Fig. 7). Conversely, addition of naloxone to the caudad recording compartment caused an increase in descending contraction elicited by application of muscle stretch or mucosal stimulation to the orad compartment (147 ± 12%, P < 0.01 and 22 ± 9%, P < 0.05 increase in response to 2- and 10-g muscle stretch, respectively; 177 ± 10%, P < 0.001 and 20 ± 3%, P < 0.01 increase in the response to 2 and 8 strokes, respectively; Fig. 7).
cle stretch or mucosal stimulation to the orad compartment (83 ± 17%, P < 0.01 and 22 ± 2%, P < 0.01 decrease in response to 2- and 10-g muscle stretch, respectively; 92 ± 8%, P < 0.01 and 16 ± 4%, P < 0.02 decrease in the response to 2 and 8 strokes, respectively; Fig. 8).

DISCUSSION

The mechanical responses of longitudinal muscle during the ascending and descending phases of the intestinal peristaltic reflex were measured in the present study using a two-compartment, flat-sheet preparation of rat colon that enabled exclusive measurement of longitudinal muscle activity. This was made possible by immobilizing circular muscle while allowing longitudinal muscle to contract or relax. The reverse was done in earlier studies (12, 16) that examined the activity of circular muscle during the two phases of the peristaltic reflex.

Both circumferential muscle stretch and mucosal stimulation caused contraction of longitudinal muscle caudad (descending contraction) and relaxation orad (ascending relaxation) to the site of stimulation. The pattern was exactly the reverse of that observed in circular muscle, which contracted orad and relaxed caudad to the site of stimulation (12, 17). The effect of neurotransmitter antagonists or antisera was consistent with blockade of the activity of motor neurons or interneurons that regulate circular or longitudinal muscle function. Previous studies (9, 15, 17) had shown that descending relaxation of circular muscle was mediated by the combined activities of VIP/PACAP/NOS motor neurons. In some species, these neurons coexpress VIP and NOS and/or PACAP and NOS (5); in rat intestine, they appear to coexpress VIP, PACAP, and NOS (20). Consistent with this notion, VIP, PACAP, and NO are released during the descending phase of the peristaltic reflex (9, 15, 17). VIP and PACAP antagonists or antisera block descending relaxation of circular muscle (9, 15, 17). In the rat myenteric plexus, VIP, PACAP, and NOS are also coexpressed in interneurons that project caudad within the plexus (20). These interneurons also contribute to release of VIP, PACAP, and NO during the descending phase of the peristaltic reflex, but their function is excitatory (30, 33) and involves activation of cholinergic and tachykinin motor neurons innervating longitudinal muscle. Previous studies (1, 2, 21–23, 31, 32) using myenteric plexus-longitudinal muscle preparations devoid of circular muscle have shown that exogenous VIP, PACAP, and NO stimulate the release of acetylcholine and SP and induce contraction of longitudinal muscle that is sensitive to tetrodotoxin, atropine, and tachykinin antagonists. Our recent studies (11) using the same myenteric plexus-longitudinal muscle preparation have shown that endogenous release of VIP, PACAP, and NO from these interneurons stimulates the release of SP. Accordingly, release of VIP, PACAP, and NO from these interneurons during peristaltic activity would be expected to elicit descending contraction of longitudinal muscle that is sensitive to blockade by 1) VIP and PACAP antagonists, 2) NOS inhibitors, and 3) muscarinic and tachykinin antagonists. This, in effect, was the pattern observed in the present study (see Figs. 4–6).

It is worth noting that in guinea pig and rat intestine, the majority (>50%) of myenteric neurons express both SP and NKA (3–6); most are motor neurons innervating circular muscle. A relatively small number (~10%) innervate longitudinal muscle and coexpress acetylcholine; an equal number of motor neurons innervating longitudinal muscle expresses acetylcholine only (3–5). Very few motor neurons (<3%) innervating longitudinal muscle are inhibitory (3–5); thus contraction of longitudinal muscle in rat and guinea pig intestine is mediated by activation of excitatory cholinergic/
peristaltic reflex, the increase in VIP, PACAP, and NO is accompanied by increase in somatostatin release and decrease in enkephalin release. Somatostatin antiserum increases enkephalin release and decreases VIP, PACAP, and NO release. Conversely, the opioid antagonist, naloxone, enhances VIP, PACAP, and NO release. The increase or decrease in VIP, PACAP, and NO is accompanied by corresponding increase or decrease in descending relaxation of circular muscle (9, 15, 17). The present study shows that somatostatin antiserum decreases, and naloxone increases, descending contraction of longitudinal muscle (Figs. 7 and 8). The pattern is consistent with the notion that the same circuit of somatostatin and opioid interneurons regulates VIP/PACAP/NOS motor neurons innervating circular muscle as well as VIP/PACAP/NOS interneurons coupled to cholinergic/tachykinin neurons innervating longitudinal muscle.

During the ascending phase of the peristaltic reflex, the pattern of neurotransmitter release and muscle activity is the reverse of that observed during the descending phase. Thus somatostatin release decreases, whereas enkephalin release increases. The changes in neurotransmitter release are accompanied by ascending contraction of circular muscle and relaxation of longitudinal muscle. During the ascending phase of the reflex, VIP release reverts to basal or below basal levels and tachykinin release increases (8, 17); the increase in tachykinin release reflects predominant activity of tachykinin motor neurons innervating circular muscle. Consistent with the pattern of somatostatin and enkephalin release during the ascending phase, somatostatin antiserum increased and naloxone decreased ascending relaxation of longitudinal muscle (Figs. 7 and 8).

A model depicting myenteric interneurons and motor neurons regulating circular and longitudinal muscle activity during the peristaltic reflex is shown in Fig. 9. The model is an expansion of previous models (8, 10, and 17) that is designed to take into account pathways involved in the regulation of longitudinal muscle activity. It is worth emphasizing that the results of the present study are supported by our earlier measurements of neurotransmitter release on the projections of myenteric interneurons and motor neurons as determined by immunocytochemistry and on the predicted effects of specific neurotransmitter antagonists and antiserum.

In his extensive early studies of peristaltic activity in guinea pig small intestine using the Trendelenburg preparation, Kottegoda (24) concluded that “while the contraction of circular muscle proceeds, the longitudinal muscle relaxes.” He asked presciently whether the “nervous pathways for excitation and inhibition of the two muscle layers are arranged so that the muscles do not contract simultaneously,” concluding that this would otherwise defeat the purpose of the peristaltic reflex, that is, the propulsion of the contents of the gut. In more recent studies of guinea pig small intestine using a digitized imaging technique, Hennig et al. (19) noted that contraction and relaxation of longitudinal muscle were not synchronous with those of circular muscle. Sarna (27) came to a similar conclusion using strain gauges oriented along the long axes of circular and longitudinal muscle of canine small intestine in vivo. Sarna (27) showed that, whether in the fasting or fed state, when circular muscle contracted, longitudinal muscle underwent passive elongation, i.e., relaxation.

Smith and Robertson (28) used a different preparation, the modified Trendelenburg preparation of guinea pig distal colon, and arrived at a different conclusion. The mechanical recordings were made using separate transducers attached to circular muscle and to an immediately aboral segment of longitudinal muscle (1.5 cm in length) from which the underlying circular muscle and mucosa had been removed. Thus recordings were made from adjacent segments, with the longitudinal segment aboral to the circular muscle segment. These segments were mechanically isolated from each other by pins. When the circular muscle underwent contraction, the aboral circular muscle would have undergone relaxation and the overlying longitudinal...
muscle would have undergone contraction. Thus con-
traction would have been measured in both the circular
muscle segment and in the aboral longitudinal muscle
segment and would be in accordance with those ob-
tained in the present study.

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REFERENCES

1. Bartho L and Lefebvre R. Nitric oxide induces acetylcholine-
mediated contractions in the guinea-pig small intestine. Naunyn

2. Bartho L and Lefebvre R. Nitric oxide-mediated contraction of
enteric smooth muscle. Arch Int Pharmacodyn Ther 329: 53–66,
1995.

3. Brookes SJH and Costa M. Enteric motor neurons. In: Inner-
vation of the Gut: Pathophysiological Implication, edited by
Tache Y, Wingate DL, and Burks TF. Boca Raton, FL: CRC,

4. Brookes SJH, Song ZM, Steele PA, and Costa M. Identifica-
tion of motor neurons to the longitudinal muscle of the guinea pig

5. Costa M, Brookes SJH, Steele PA, Gibbins I, Burcher E,
and Kandiah CJ. Neurochemical classification of myenteric
neurons in the guinea-pig ileum. Neuroscience 75: 949–967,
1996.

6. Ekblad E, Ekman R, Hakanson R, and Sundler F. Projec-
tions of peptide-containing neurons in rat colon. Neuroscience 27:

7. Gershon MD, Kirchgesner AL, and Wade PR. Intrinsic
reflex pathways of the bowel wall. In: Innervation of the Gut:
Pathophysiological Implication, edited by Tache Y, Wingate DL,

8. Grider JR. Tachykinins as transmitters of ascending contrac-
tile component of the peristaltic reflex. Am J Physiol Gastrointest

9. Grider JR. Interplay of VIP and nitric oxide in the regulation of
the descending relaxation phase of peristalsis. Am J Physiol

10. Grider JR. Interplay of somatostatin, opioid, and GABA neu-
rons in the regulation of the peristaltic reflex. Am J Physiol Gastrointest

11. Grider JR. Regulation of excitatory neural input to longitudinal
intestinal muscle by myenteric interneurons. Am J Physiol

12. Grider JR. CGRP as a sensory transmitter in the sensory
pathway that mediates the peristaltic reflex. Am J Physiol

13. Grider JR, Arimura A, and Makhlouf GM. Role of somatosta-
tin neurons in intestinal peristalsis: facilitatory interneurons in
descending pathways. Am J Physiol Gastrointest Liver Physiol 253:

14. Grider JR and Jin JG. Distinct populations of sensory neurons
mediate the peristaltic reflex elicited by muscle stretch and

15. Grider JR, Katsoulis S, Schmidt WE, and Jin JG. Regu-
lation of the descending relaxation phase of intestinal peristalsis

16. Grider JR, Kuenmerle JF, and Jin JG. 5-HT released by
mucosal stimuli initiates peristalsis by activating 5-HT1A/5-HT1p
receptors on sensory CGRP neurons. Am J Physiol Gastrointest
Liver Physiol 270: G773–G782, 1996.

17. Grider JR and Makhlouf GM. Colonic peristaltic reflex: iden-
tification of VIP as mediator of descending relaxation. Am J
Physiol Gastrointest Liver Physiol 251: G40–G45, 1986.

18. Grider JR and Makhlouf GM. Enteric GABA: mode of action and
role in the regulation of the peristaltic reflex. Am J Physiol

19. Hennig GW, Costa M, Chen BN, and Brookes SJH. Quan-
tative analysis of peristalsis in the guinea-pig small intestine

20. Hannibal J, Ekblad E, Mulder H, Sundler F, and Fahren-
krug J. Pituitary adenylate cyclase activating polypeptide
(PACAP) in the gastrointestinal tract of the rat: distribution and
effects of capsaicin or denervation. Cell Tissue Res 291: 65–79,
1998.

21. Jaffer SS, Farrar JT, Yau WM, and Makhlouf GM. Mode of
action and interplay of vasoactive intestinal peptide (VIP), se-
cretin, and octapeptide of cholecystokinin on duodenal and ileal

22. Katsoulis S, Clemens A, Schworer H, Creutzfeldt W, and
Schmidt WE. PACAP is a stimulator of neurogenic contraction
in guinea pig ileum. Am J Physiol Gastrointest Liver Physiol 265:

23. Katsoulis S, Schmidt WE, Clemens A, Schworer H, and
Creutzfeldt W. Vasoactive intestinal polypeptide induced neu-
genic contraction of guinea pig ileum. Involvement of acetyl-

24. Kottegoda SR. An analysis of the possible nervous mechanisms

25. Pan H and Gershon MD. Activation of intrinsic afferent path-
ways in submucosal ganglia of the guinea pig small intestine.

26. Pompolo S and Furness JB. Sources of inputs to longitudinal
muscle motor neurons and ascending interneurons in the

27. Sarna S. Gastrointestinal longitudinal muscle contractions.

28. Smith TK and Robertson WJ. Synchronous movements of the
longitudinal and circular muscle during peristalsis in the iso-

29. Wade PR, Chen J, Jaffe B, Kassem IS, Blakely RD, and
Gershon MD. Localization and function of a 5-HT transporter
in crypt epithelia of the gastrointestinal tract. J Neurosci 10: 107,
1985.

30. Williams JT and North RA. Vasoactive intestinal polypeptide
excites neurones of the myenteric plexus. Brain Res 175: 174–
177, 1979.

31. Yau WM, Dorsett JA, and Parr EL. Characterization of ac-
etylylcholine release from enzyme-dissociated myenteric ganglia.

32. Yau WM, Dorsett JA, and Youther ML. Inhibitory peptidergic
neurons: functional difference between somatostatin and en-
kaphalin in myenteric plexus. Am J Physiol Gastrointest Liver

33. Zafirov DH, Palmer JM, Nemeth PR, and Wood JD. Bomb-
esin, gastrin-releasing peptide, and vasoactive intestinal peptide