Circumferential, not longitudinal, colonic stretch increases synaptic input to mouse prevertebral ganglion neurons

Steven M. Miller1,2 and J. H. Szurszewski1,2,3

1Department of Physiology and Biophysics, 2Enteric Neuroscience Program, and 3Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, Minnesota 55905

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Miller, Steven M., and J. H. Szurszewski. Circumferential, not longitudinal, colonic stretch increases synaptic input to mouse prevertebral ganglion neurons. Am J Physiol Gastrointest Liver Physiol 285: G1129–G1138, 2003.—The relationship between longitudinal and circular muscle tension in the mouse colon and mechanosensory excitatory synaptic input to neurons in the superior mesenteric ganglion (SMG) was investigated in vitro. Electrical activity was recorded intracellularly from SMG neurons, and muscle tension was simultaneously monitored in the longitudinal, circumferential, or both axes. Colonic intraluminal pressure and volume changes were also monitored simultaneously with muscle tension changes. The results showed that the frequency of fast excitatory postsynaptic potentials (fEPSPs) in SMG neurons increased when colonic muscle tension decreased, when the colon relaxed and refilled with fluid after contraction, and during receptive relaxation preceding spontaneous colonic contractions. In contrast, fEPSP frequency decreased when colonic muscle tension increased during spontaneous colonic contraction and emptying. Manual stretch of the colon wall to 10–15% beyond resting length in the circumferential axis of flat sheet preparations increased fEPSP frequency in SMG neurons, but stretch in the longitudinal axis to 15% beyond resting length in the same preparations did not. There was no increase in synaptic input when tubular colon segments were stretched in their long axes up to 20% beyond their resting length. The circumferential stretch-sensitive increase in the frequency of synaptic input to SMG neurons persisted when the colonic muscles were relaxed pharmacologically by nifedipine (2 μM) or nicardipine (3 μM). These results suggest that colonic mechanosensory afferent nerves projecting to the SMG function as length or stretch detectors in parallel to the circular muscle layer.

prevertebral ganglia; colonic mechanoreceptors; intestinointestinal reflex

SYMPATHETIC PREVERTEBRAL GANGLIA mediate inhibitory enteroenteric reflex pathways whereby distension of the distal colon inhibits contractions in the same or a proximal part of the colon and upper gastrointestinal tract without using central nervous system pathways (11, 12, 25). The afferent limb of the reflex consists of intestinofugal afferent neurons with cell bodies in the gut wall whose axons project to and make excitatory cholinergic synapses with prevertebral ganglion neurons (5, 6, 16, 17, 23, 25). In the mouse, rat, and guinea pig, cell bodies of colonic intestinofugal afferent (colonofugal) neurons are located exclusively in myenteric ganglia (6, 7, 13, 18, 19, 21, 23, 27), whereas in the pig, the cell bodies of colonofugal neurons are located in both myenteric and submucous plexuses (28). The afferent limb of the reflex arc consists of sympathetic postganglionic neurons whose axons project to the gut, where they terminate in myenteric ganglia to inhibit excitatory motor neurons and motility (25).

Previous studies in vitro demonstrated that colonic distension activates a cholinergic mechanosensory afferent pathway from the colon to the inferior mesenteric ganglion (IMG) in the guinea pig and superior mesenteric ganglion (SMG) in the guinea pig and mouse (3, 5, 20, 24, 26). The colonic mechanosensory afferent nerves that project to IMG neurons in guinea pig and to SMG neurons in mouse are believed to function as volume detectors, because excitatory cholinergic synaptic input to ganglion neurons increases when colonic intraluminal volume is increased during filling and decreases when colonic intraluminal volume decreases during emptying (1, 21, 25). However, it is not known whether colonic mechanosensory synaptic input to IMG and SMG neurons is a result of increased volume (stretch) per se or due to increased colonic wall tension, as would be expected as a consequence of increased intraluminal volume, according to the Law of LaPlace. On the other hand, colonic mechanosensory synaptic input to the guinea pig IMG was previously shown to increase when colonic contractions increased and to decrease when colonic contractions were reduced (26), supporting the concept of in-series tension receptors in colonic afferent nerves projecting to the IMG.

The muscle coat of the colon is made up of an outer longitudinal muscle layer and an inner circular layer (8), the latter constricting the gut lumen during contraction, the former shortening it. It is possible that there are mechanoreceptor populations in both muscle layers that respond to changes in muscle stretch or muscle tension and relay that information to prevertebral ganglion neurons. We investigated this possibility...
by examining in vitro the relationship between colonic wall tension and colonic mechanosensory synaptic input to the mouse SMG. Changes in colonic wall tension and intracellular electrical activity from SMG neurons were simultaneously monitored during spontaneous colonic contractions, during colonic distension with fluid, and during manual stretch of the colon wall. The results showed that colonic mechanosensory fast excitatory synaptic input to mouse SMG neurons increased when muscle tension decreased before contraction and during circumferential but not longitudinal colonic stretch. In contrast, fast excitatory synaptic input to SMG neurons decreased and was often absent at peak tension of contraction. These results suggest that cholinergic mechanosensory colonofugal neurons that project to the SMG function as stretch receptors arranged in parallel to the circular muscle layer.

MATERIALS AND METHODS

Sixty-nine SJL/J male mice (15–25 g; Jackson Labs) were used. Animals were euthanized by stunning and cervical dislocation or by asphyxiation with CO₂. These methods of euthanization were approved by the Mayo Institutional Animal Care and Use Committee. From each animal a segment of colon (1 cm distal to the inferior mesenteric artery to 1 cm proximal to the superior mesenteric artery) with attached mesentery, mesenteric nerves, blood vessels, and SMG was removed as previously described (20) and was placed in a mesentery, mesenteric nerves, blood vessels, and SMG was proximal to the superior mesenteric artery) with attached mesentery, mesenteric nerves, blood vessels, and SMG was removed as previously described (20) and was placed in a dissecting dish containing oxygenated (97% O₂-3% CO₂) Krebs solution at room temperature (22–23°C). The ionic composition of the Krebs solution was in (mM) 120.7 NaCl, 5.9 KCl, 15.5 NaHCO₃, 1.2 NaH₂PO₄, 1.2 MgCl₂, 2.5 CaCl₂, and 11.5 glucose, bubbled with 97% O₂-3% CO₂.

Dissection Procedures to Make SMG-Colon Preparations

Further dissection was made to obtain a preparation consisting of a 2.5- to 3.0-cm-long segment of colon connected to the SMG via the inferior mesenteric artery, colonic nerves, inferior mesenteric artery, and vein were also secured with a row of pins, maintaining the approximate in vivo longitudinal length. A 1.5-cm-long steel pin was placed through the opposite (anal) edge and was connected via silk thread to a Statham force transducer attached to a micromanipulator. With this arrangement, contractions along the longitudinal and circular muscle axes could be recorded and stretch of the colon could be applied in both axes.

Electrical Recordings

Intracellular recordings from SMG neurons were made with glass microelectrodes filled with 3 M KCl (electrode resistances were 40–80 MΩ) and a WP M707 electrometer (World Precision Instruments) as previously described (20). Electrical and mechanical signals were simultaneously displayed on a Tektronix 5113 oscilloscope and a Gould 2400 chart recorder and were stored on FM tape (Hewlett-Packard 3964A recorder). To assess the frequency of fast synaptic potentials, tape recordings were played back to a strip chart recorder by using a chart speed of 100 mm/s. Fast excitatory postsynaptic potentials (fEPSPs) and action potentials (APs) in the traces were counted manually. “N” refers to the number of SMG-colon preparations, hence the number of ganglia studied, whereas “n” refers to the number of ganglion neurons studied.

Drugs

In some experiments, nicardipine or nifedipine (both from Sigma) were added to the solution superfusing the colon to inhibit muscle contraction. Stock solutions of 10⁻² M were made in ethanol, and then they were diluted to a final concentration of 2–3 × 10⁻⁶ M in Krebs solution.

RESULTS

Relationship Between Colonic Contractions and Excitatory Synaptic Input to SMG Neurons

Tension was simultaneously measured in the longitudinal and circular muscle axes of colon segments that were connected to a fluid-filled reservoir that received fluid from the colon during contraction and returned fluid into the segment during relaxation. Intracellular recordings were made from 13 SMG neurons (N = 8). All of the neurons received ongoing fEPSPs or a combination of fEPSPs and APs. Fluid (0.05–0.10 ml) added to empty colon segments initiated
large emptying contractions that occurred at a frequency of ~1/min, with peak amplitude of longitudinal muscle contraction preceding that of the circular muscle contraction. Fluid distension also immediately increased the frequency of fEPSPs and APs in all SMG neurons tested. In the example shown in Fig. 2, synaptic input was also increased just before the onset of circular and longitudinal muscle contraction when tension either remained at baseline level or decreased before the onset of contraction. Synaptic input then decreased when muscle tension increased with contraction and was almost abolished at peak tension of contraction. The frequency of synaptic input returned to baseline levels when tension decreased after contraction.

The relationship between colonic wall tension and synaptic input to SMG neurons was further investigated in another four preparations under conditions in which the colon was prevented from emptying during contraction (isovolumetric contraction) or prevented from refilling during relaxation (Fig. 3). Similar to the previous results, the frequency of synaptic input to SMG neurons (5 out of 5 neurons tested) increased before the onset of emptying contractions, was markedly decreased at peak tension during contraction, and returned to basal levels during relaxation. However, when refilling of the colon was prevented, synaptic input to the neurons remained diminished until the colon was allowed to refill. On refilling, synaptic input to the neurons increased to basal levels. In contrast, when the colon was prevented from emptying during contraction, synaptic input to SMG neurons did not diminish until the colon was allowed to empty. These results support our previous findings that SMG neurons receive volume-sensitive colonic afferent excitatory synaptic input (21, 25) and further suggest that colonic afferent synaptic input to SMG neurons was sensitive to stretch of the colon wall but not to increases in active tension of the muscle layers accompanying colonic contraction.

To further examine the relationship between colonic muscle tension and excitatory synaptic input to SMG
neurons, an additional three SMG-colon preparations were studied. In these experiments, 0.03–0.05 ml of fluid was added to distend the colon and it was not allowed to empty its contents during contraction. Examples of results from two experiments are shown in Fig. 4. Distension of the colon with fluid resulted in a transient decrease in longitudinal muscle tension, a prolonged decrease in circular muscle tension, and an increase in frequency of synaptic input to SMG neurons (6 out of 6 neurons tested). Distension also initiated phasic contractions and increases in circular and longitudinal muscle tension. In the recording shown in Fig. 4A, excitatory synaptic input to the SMG neuron decreased when muscle tension increased, whereas synaptic input increased when the muscle layers relaxed and tension decreased. On removal of distension, there was a transient contraction of the colon and the frequency of excitatory synaptic input to the neuron decreased to the basal level seen before distension. In the other experiment, illustrated in Fig. 4B, the colon segment was distended twice with fluid. Accompanying the first distension (+0.03 ml) was a brief transient decrease in longitudinal muscle tension, a sustained decrease in circular muscle tension, and an increase in excitatory synaptic input to the neuron. The second distension (+0.07 ml) produced a transient increase in longitudinal but not circular muscle tension and a marked increase in frequency of synaptic input to the neuron that persisted for the duration of the distension. On removal of the distension, there was an increase in longitudinal and circular muscle tension and an immediate decrease in synaptic input. These results also suggest that the increased synaptic input to SMG neurons accompanying the increase in intracolonic volume was due to increased stretch (length) but not active tension (contraction) of the colon wall.

Effect of Colonic Stretch on Excitatory Synaptic Input to SMG Neurons

**Longitudinal stretch.** The effect of longitudinally applied colonic stretch on excitatory synaptic input to

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**Fig. 2.** Relationship between LM and CM contractions of the colon and excitatory synaptic input to a mouse SMG neuron. (See Fig. 1, top, for a diagram of the experimental setup used). The colon segment was connected to a reservoir filled with Krebs solution into which the colon’s content could empty during colonic contraction. Aa and Ab: fast speed traces of portions of the electrical activity are indicated by asterisks. B: top and middle traces are of LM tension (LMf) and CM tension (CMf), respectively, and the bottom trace is intracellular electrical activity simultaneously recorded in the neuron. The dashed lines in this and subsequent figures indicate when peak tension of LM and CM contraction occurred. C: frequency of fast excitatory postsynaptic potentials (fEPSPs) and action potentials (APs) in the electrical recording in B, counted in 1-s bins. Note that adding Krebs solution to the colon caused an initial decrease in LMf and CMf, caused an immediate increase in the frequency of fEPSPs and APs, and evoked phasic colonic contractions. Note that the frequency of fast synaptic potentials increased at the onset of phasic contractions and that the frequency decreased when LMf and CMf increased during a contraction.

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**Fig. 3.** Relationship between LM and CM contractions of the colon and synaptic input to a mouse SMG neuron when the colon was prevented from refilling after contraction and from emptying during contraction. The preparation and setup used were the same as that for the experiment shown in Fig. 2. A valve connected the anal end of the colon to a fluid-filled reservoir into which colonic content could empty during contraction. Closing the valve at the peak of colonic contraction prevented it from emptying. A: top and middle traces show LMf and CMf, respectively, and the bottom trace is the simultaneously recorded electrical activity in the neuron. B: frequency of fEPSPs and APs recorded from the same neuron, counted in 1-s bins. In A, bottom, note that Krebs solution added to the colon immediately increased the frequency of fast synaptic potentials and caused phasic colonic contractions. Note that synaptic input increased at the onset of contraction but was absent when the colon contracted and emptied (asterisk in middle complex). Synaptic input was absent as long as refilling was prevented, and it was restored when the colon was allowed to refill (left complex). Under isovolumetric contraction, i.e., when the colon was prevented from emptying during contraction (right complex), synaptic input to the neuron continued during contraction until the valve was opened and the colon could empty.
SMG neuron did not increase when the colon segment was stretched to 10% of its resting length, but synaptic input to the neuron did increase on balloon distension and input remained elevated when longitudinal stretch was terminated during distension. When distension was released, synaptic input immediately decreased. Since in most of the experiments on longitudinal stretch of the colon only one or two neurons in each ganglion were tested, it is possible that neurons in a distinct location in the ganglion might receive input from longitudinal muscle afferents and were not sampled. To rule out this possibility, two additional preparations were studied in which an attempt was made to sample neurons throughout the SMG. Of 16 neurons tested, 14 showed an increase in synaptic input when the colon was distended with fluid but none showed an increase when the colon was stretched to 15–20% beyond its resting length.

Circumferential stretch. Colon tube preparations were resistant to manual stretching in the circular axis. When segments (N = 4) were stretched in the direction of the circular axis, the circular muscle immediately contracted, making it difficult to further stretch the colon without causing a marked distortion in circumferential shape of the colon. Accompanying these events, there were no increases in frequency of synaptic inputs to any of five SMG neurons tested.

Relationship Between Muscle Tension, Intracolonic Volume, and Excitatory Synaptic Input to SMG Neurons

Intraluminal pressure, volume of intraluminal content, longitudinal or circular muscle contractions, and synaptic input to SMG neurons (n = 44) were recorded simultaneously in 26 preparations in which the colon segment was connected to a fluid-filled reservoir, allowing it to empty on contraction and refill with fluid on relaxation. Figure 6A shows results from 1 of 17 preparations in which tension was measured in the longitudinal axis, and Fig. 6B shows tension measured in the circular muscle axis in 1 of 9 preparations. In all of the preparations, longitudinal or circular muscle tension and colonic intraluminal pressure increased during contraction, whereas colonic intraluminal volume decreased as fluid was expelled from the colon into the reservoir. Peak longitudinal muscle tension preceded peak colonic intraluminal pressure (Fig. 6A), whereas peak circular muscle tension coincided with peak intraluminal pressure (Fig. 6B). In all 44 neurons tested, synaptic input increased just before contraction, and input then decreased and was sometimes completely abolished as colonic muscle tension and intraluminal pressure increased and intracolonic volume decreased during contraction. In the traces illustrated in Fig. 6B, two successive spontaneous colonic contractions are shown with tension recorded from the circular axis. Note that an increase in synaptic input to the neuron coincided with a decrease in colonic intraluminal pressure and an increase in intraluminal volume before the onset of circular muscle contraction. Note
also that the peak tension of the second contraction was larger than the first and that synaptic input to the neuron was less at the peak of the higher-amplitude second contraction compared with the first. These results suggest that increased synaptic input to SMG neurons was associated with stretch of the colon wall that occurred during increases in intracolic volume. This hypothesis was tested in 9 of the 26 preparations in which the colon segments were manually stretched in the longitudinal direction while synaptic input to SMG neurons was simultaneously recorded. In 11 of 11 SMG neurons tested, synaptic input did not increase when colon segments were stretched in the longitudinal axis up to 20% increase of resting length, similar to the previous results that longitudinal stretch of the colon did not increase synaptic input to SMG neurons. On the other hand, attempts to manually stretch three colon preparations in the circular muscle axis were unsuccessful, because the colon contracted when stretch was applied and further stretch unevenly distended the shape of the colon. These manipulations were not accompanied by an increase in synaptic input to any of six SMG neurons tested, similar to the previous results.

Colonic Muscle Tension and Synaptic Input to SMG Neurons in Flat Sheet Preparations

Flat sheet preparations of the colon were made to directly test whether synaptic input to SMG neurons increased during stretch of the longitudinal muscle, circular muscle, or both. The flat colon sheets, unlike the tubular segments of colon, could be readily stretched in both the circular and longitudinal axes. For these experiments, the sheet was pinned out to its approximate resting in vivo length in both axes and the colon was stretched 1–2 mm (10–15% beyond resting dimensions) in the circular axis and 3–4 mm (15% beyond resting length) in the longitudinal axis. The effect of longitudinal and circular stretch of the colon on synaptic input to SMG neurons was examined in three flat sheet preparations. All five neurons tested exhibited ongoing fEPSPs and APs before the colon was stretched, and synaptic activity increased when the colon sheet was stretched in the circular axis but not when it was stretched in the longitudinal axis (Fig. 7A). During maintained stretch in the longitudinal axis, there was no increase in fEPSP frequency until manual stretch in the circular axis was applied (Fig. 7B). In these experiments, circumferential stretch of the colon sheet produced a small increase in tension in the longitudinal muscle layer in addition to the large increase in circular muscle tension (Fig. 7). However, the increase in longitudinal tension produced by circumferential stretch was much smaller than the increase in longitudinal tension produced when the colon was stretched in the longitudinal axis, the latter being insufficient to cause an increase in synaptic input to SMG neurons. These results suggest that circumferen-

Fig. 5. Relationship between LMx, CMx, and synaptic input to SMG neurons during longitudinal stretch of the colon. In A, a colon tube preparation filled with fluid was used. A diagram of the setup is shown in Fig. 1, top. In B, a colon tube with an intraluminal balloon inserted into the anal end was used (see diagram of experimental setup in Fig. 1, middle). In both A and B, the colon was stretched from the anal end by moving the force transducer and cannula backward (see MATERIALS AND METHODS for details). The numbers below the CMx trace are the average frequencies (fEPSPs per second) in the intervals between arrows. A: stretch of the colon in the longitudinal direction, first to 10% beyond its initial resting length (Lx) and then to 15% beyond Lx, did not result in an increase in synaptic input to the neuron. B: during longitudinal stretch of the colon to 10% beyond Lx, there was only a slight increase in frequency of synaptic inputs to the neuron. However, balloon distension (ΔVbh) during longitudinal stretch was accompanied by a large increase in frequency of synaptic inputs to the neuron. Synaptic input frequency further increased when the longitudinal stretch was released to Lx and distension was maintained. When distension was released, synaptic input frequency decreased to a basal level similar to that which occurred before distension.
tial but not longitudinal colonic stretch activated mechanosensory input to SMG neurons.

Effect of Muscle Relaxants on Stretch-Induced Increase in Synaptic Input to SMG Neurons

Contractile activity in flat sheet preparations of the colon was inhibited by adding the L-type Ca\(^{2+}\) channel antagonists nifedipine (2 \(\mu\)M) or nicardipine (3 \(\mu\)M) to the superfusate. In the presence of nifedipine (6 neurons tested in 3 preparations) or nicardipine (1 neuron tested in 1 preparation), circumferential stretch of the colon sheet to 15% beyond resting length resulted in increased synaptic input to the neurons, similar to the response of cells to the same circumferential stretch before relaxing the colon (Fig. 8).

DISCUSSION

In the present study, the relationship between colonic wall tension and colonic mechanosensory synap-
tic input to SMG neurons was investigated during spontaneous colonic contractions, colonic distension with fluid, and manual stretch of the colon wall. The results showed that excitatory synaptic input from the colon to SMG neurons 1) increased when colonic wall tension decreased during relaxation, 2) decreased when colonic wall tension increased during colonic contraction, 3) increased during circumferential but not longitudinal stretch of the colon wall, and 4) increased during circumferential stretch when the colonic smooth muscle was pharmacologically relaxed by L-type Ca\(^{2+}\) channel blockers. These results support our hypothesis that mechanosensory colonofugal nerves projecting to the SMG monitor changes in intracolonic volume by sensing changes in circumferential stretch of the colon wall.

Muscle tension receptors in abdominal viscera are defined as slowly adapting mechanoreceptors whose discharge rate is related to the amount of tension in the muscle layers of the viscus (15). Through an analogy to muscle spindles and Golgi tendon organs in skeletal muscle, muscle tension receptors in abdominal viscera are similarly classified into two types, depending on their response to distension and active contraction of the viscus (10, 14). “In-series” receptors (e.g., Golgi tendon organs) increase their firing frequency during active contraction and passive distension of the viscus. “In-parallel” receptors (e.g., muscle spindles) increase their discharge rate when the viscus is passively distended but decrease their discharge rate when they are “unloaded” during contraction. In the present study, it was found that afferent excitatory synaptic input to SMG neurons increased during colonic relaxation, decreased during colonic (isotonic) contraction, and increased during circumferential stretch of the colon. This behavior is what would be predicted from an in-parallel tension receptor. Thus we interpret our results to indicate that cholinergic mechanosensory
afferent nerves from the colon to the SMG function as in-parallel receptors.

Distension-sensitive mechanosensory nerves in visceral muscle that are found in the vagus, splanchnic, and pelvic nerve trunks are mostly of the in-series type (9, 14). They appear to be arranged in series with the longitudinal muscle, because their rate of firing increases during longitudinal stretch of the viscus or when longitudinal muscle tension increases during contraction. These afferent nerves, whose cell bodies are located in vagal ganglia and dorsal root ganglia of the spinal cord, connect the abdominal viscera with the central nervous system. In-series longitudinal muscle tension receptors are believed to act as sensors of the degree of distension and level of contractile activity in the viscus (15). They are often referred to as tension receptors because they encode information about the degree of tension in the gut wall. In contrast, the present study suggests that the mechanosensory colonofugal nerves that project to the SMG monitor changes in intracolonic volume during filling and emptying of the colon by sensing the degree of stretch or length of the circular muscle, not the longitudinal muscle layer. They appear to encode information about the diameter of the colon wall. Thus colonofugal nerves projecting to SMG neurons appear to carry a qualitatively different message about the mechanical state of the colon from that conveyed from the colon to the central nervous system by extrinsic primary mechanosensory afferent nerves.

Gastrointestinal distension-responsive afferent nerves are generally considered to be muscle afferent nerves (14, 22) because their endings are in the muscularis, as demonstrated functionally by showing that removal of the mucosa does not impair responses to distension (4) and anatomically by anterograde tracing studies (2). To determine the functional location (longitudinal muscle layer, circular muscle layer, or both) of mechanosensory colonofugal afferent nerves, we used a flat sheet preparation of the colon wall and measured tension in the direction of the long axis of the circular muscle layer and in the direction of the long axis of the longitudinal muscle while recording mechanosensory afferent synaptic input to SMG neurons. When the colon wall was stretched in the circular muscle direction, afferent input to SMG neurons increased. In contrast, stretch of the colon wall in the direction of the long axis of the longitudinal muscle did not increase mechanosensory afferent synaptic input to SMG neurons. We infer from these results that cholinergic mechanosensory colonofugal neurons that project from the colon to the SMG are mechanically connected in parallel with the circular muscle layer. Mechanosensory nerves in parallel with the circular muscle would be excited by stretch of the circular muscle but would be offloaded when that muscle layer contracts. Accordingly, we speculate that the colonic mechanosensory afferent pathway to the SMG might operate as follows during filling and emptying of the colon: an increase in colonic intraluminal volume during filling increases the circumference of the colon, causing a tangential lengthening of the circular muscle layer, which in turn activates mechanosensory afferent nerves that are mechanically connected to it, resulting in an increased frequency of afferent synaptic input to SMG neurons. Contraction and emptying of the colon decreases the circumference of the colon and unloads the mechanoreceptor endings of the colonofugal nerves, resulting in a diminished synaptic input to the SMG. This conclusion is tentative because the anatomic location and arrangement of the mechanosensory endings within the muscle layers have not been determined and because SMG neurons receive mechanosensory synaptic input indirectly from secondary or higher-order neurons in the mechanosensory pathway (20, 21). Additional studies are also needed to determine the mechanism(s) by which stretch of the colon wall is transduced to excite the mechanosensory endings.

A major function of the distal colon is to store and evacuate feces. As the colon wall is stretched during filling of the colon with feces, stretch-induced depolarization and AP generation in smooth muscle cells as well as stretch-induced peristaltic reflex activity result in contractions to empty the colon. Noradrenaline release from sympathetic nerves can inhibit colonic contractions by inhibiting excitatory motor neurons and perhaps also by a direct effect on the smooth muscle cells. An increase in excitatory synaptic input to SMG neurons during stretch of the colon would be expected to increase the probability of AP firing in the neurons and to increase noradrenergic output to the colon. In addition, inhibitory sympathetic reflexes, in which distension of a portion of the colon results in inhibition of contraction in adjacent or more proximal parts, are important in tonic inhibition of colonic motility. Thus the physiological function of stretch-sensitive mechanosensory information relayed from the colon to SMG neurons might be to dampen the tendency of the colon to contract as it fills and thus to allow it to fill more completely.

In summary, the present results suggest that mechanosensory afferent nerves projecting from the colon to the sympathetic prevertebral ganglion neurons provide information about changes in diameter of the colon wall, not colonic wall tension.

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DISCLOSURES

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