Vagal afferent input determines the volume dependence of rat esophageal motility patterns

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Dong, Haheng, Christopher W. Loomis, and Detlef Bieger. Vagal afferent input determines the volume dependence of rat esophageal motility patterns. Am J Physiol Gastrointest Liver Physiol 281: G44–G53, 2001.—The volume dependence of balloon distension-evoked esophageal rhythmic motor responses and their neural correlates was investigated in 72 urethane-anesthetized rats. With increasing balloon volume (75–200 μl), distal esophageal rhythmic contractions decreased in rate and became tonic in the range of 150–250 μl. This change in motor pattern involved only the striated musculature of the esophageal body and persisted after acute transection of the spinal cord at C2. Impulse frequency in single vagal afferents of the distal esophagus increased with intraluminal pressure over the entire range of balloon volumes tested (50–300 μl). Distension-responsive neurons in the nucleus tractus solitarii showed rhythmic burst activity (type I), tonic excitation (type II), or inhibition followed by off bursts (type III). Increasing strength of stimulation changed type I responses to nonrhythmic but intensified type II and III responses. We conclude that load-dependent changes in distal esophageal motility pattern are encoded by vagal afferents alone and do not involve a spinal afferent input even at near-noxious stimulus strengths.

IN MAMMALS, SUCH AS THE RAT, peristaltic transport of food or drink through the esophagus relies chiefly on the full-length striated muscle coat of the tunica muscularis propria and, by inference, a neural control system made up of vagovagal reflex loops and brain stem interneurons (for reviews, see Refs. 6 and 26). In the distal portion of the rat esophageal body, reflex motility is characterized by rhythmic contractions evident during sustained balloon distension in the 20- to 100-μl range. This motor pattern is effected by a bilateral uncrossed reflex arc and is strongly facilitated by refferent feedback (20). Stimulation of mechanosensory vagal endings of the rat esophagus elicits not only special visceral motor but also autonomic cardiovascu- lar responses (19). The latter increase in magnitude with inflation pressure (19) beyond the range in which secondary peristalsis is elicited (21). Thus vagal mech-}

anosensory input from the rat esophagus appears to encode information over a wide dynamic range. As yet, functional information on these primary vagal afferents is rather limited (2, 10), in particular as regards the properties of mechanosensory fibers supplying the distal esophagus. However, recent studies in the opossum have reported that esophageal vagal tension receptors possess a low threshold and low saturation pressure (27), whereas esophageal mechanosensory receptors innervated by dorsal root ganglionic (spinal or “sympathetic”) afferents have either a wide dynamic range or high threshold (28).

In exploratory experiments, we noted that the reflex contraction pattern of the distal esophageal body changes from rhythmic to tonic as balloon distension is applied at increasing volumes. This observation led us to ask whether the altered motor pattern was caused by other sensory inputs from the esophagus, specifically the spinal afferent pathway, which is believed to mediate nociceptive signals (9, 17). Furthermore, it appeared necessary to examine the involvement of the esophageal smooth muscle tunica muscularis mucosae (TMM), as the latter receives its major sensory innervation via spinal afferents (16).

The present study was undertaken to examine the hypothesis that the vagal afferent input alone determines the pattern and force of distal esophageal contractions. Our specific aims were 1) to characterize the motor response patterns evoked by distal esophageal distension at volumes exceeding physiological levels (17, 29); 2) to examine the contribution of the TMM; 3) to determine the range in which vagal afferents from the esophagus encode intraluminal pressure signals; 4) to examine the role of spinal afferent input; and 5) to demonstrate alterations in neuronal activity patterns recorded at the level of the medulla oblongata.

MATERIALS AND METHODS

All procedures in this study were approved by the Animal Care Committee of Memorial University of Newfoundland in accordance with the Guidelines of the Canadian Council on Animal Care.

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General procedures. The experiments were performed in 72 male Sprague-Dawley rats (300–400 g) anesthetized with urethane (1.2 g/kg) given intraperitoneally. After tracheal intubation, the right carotid artery was cannulated for monitoring arterial blood pressure. Rectal temperature was maintained at 37–38°C by means of radiant heat.

A collapsible, high-compliance balloon made from PE-60 polyethylene tubing was filled with water and placed in the distal part of esophagus (11–12 cm from upper incisors) for distending the esophagus and simultaneous recording of intraluminal pressure. When fully distended, the oval-shaped balloon had a long and a short diameter of 15 and 9 mm, respectively, and a volume of 550 µl. As confirmed by autopsy, the center of the balloon was positioned in the diaphragmatic portion of the esophagus. Inflation of the balloon with 300 µl distended the esophagus to a cylindrical shape with an outer diameter of 6 mm and a length of 13 mm. In four experiments, the balloon was inserted into the gastro-esophageal junction, and autopsy showed the tip of the balloon to protrude into the stomach. The balloon was connected to a manually operated syringe and an infusion pump (model 355, Sage Instruments), permitting graded or constant-rate incremental distension to be applied. Deflation was done manually, and the volume withdrawn was controlled closely to maintain a constant baseline. As shown in Fig. 1, the high compliance of this system enabled changes in intraoesophageal pressure to be detected at sensitivity level of 1 mmHg.

In medullary single-unit recording experiments, the animals were mounted in a stereotaxic frame. The caudal roof of the fourth ventricle and surrounding structures of the dorsal medulla were surgically exposed under a dissection microscope. Cerebrospinal fluid was drained continuously with a wick. Extracellular single-unit recordings were made by means of single barrel glass micropipettes filled with 3 M NaCl. To ensure that tracks aligned with the anatomic transverse plane of the nucleus tractus solitarii (NTS), the electrode carrier was tilted caudally by 27° out of its vertical axis. Under microscopic control, the micropipette was inserted into the ventral and dorsal medullary recording sites by means of a three-axis oil hydraulic micromanipulator (model MMO-203, Narishige). For the ventral medullary recording sites, stereotaxic coordinates were restricted to the nucleus ambiguous compact formation (800–1,000 µm rostral to the cranial edge of the area postrema, 1,800–2,000 µm lateral to the midline, and 2,200–2,500 µm ventral to the medullary surface). Deflected in our laboratory’s previous work (5, 20). In the dorsomedial medulla at the level of the intermediate and caudal NTS, the area explored was confined to a circumscribed region (0–200 µm rostral to the cranial margin of the area postrema, 600–700 µm lateral). As shown previously (6, 20), at this level the cell-dense caudal half of the NTS centralis (NTS, c) lies 400–550 µm below the dorsal medullary surface. The pipette was advanced in 5- to 10-µm steps until units were located that responded in a consistent fashion during distal esophageal distension.

Recording from vagal afferent fibers was done after exposure of the cervical vagal trunk. The left vagal trunk was explored first, followed by the right trunk in some cases. A black synthetic rubber platform was put under the nerve for better observation. Both the nerve and the platform were initially immersed in saline. After the perineural sheath of the nerve was removed by microdissection, the saline was replaced with warm mineral oil. Single afferent fibers were teased from the nerve trunk and decentralized carefully, and then they were placed on one pole of a bipolar platinum wire electrode, the other pole being connected to a ground. Nerve action potentials were initially passed through a differential preamplifier (Duo 773 Electrometer, World Precision Instruments).

In some experiments, recordings were made in the left nodose ganglion. After the cervical vagus nerve was exposed, the nodose ganglion was surgically exposed and the supranodosal vagal trunk was cut. After the nodose ganglion and infranodosal 1-cm cervical vagal trunk were dissected free, the nodose ganglion was desheathed carefully and put onto a platform to dampen movements caused by carotid arterial pulsations and respiration. Extracellular single-unit recordings were made by means of single-barrel glass micropipettes filled with 3 M NaCl.

Extracellular single unit signals were conditioned by conventional methods (NeuroLog modules NL102, NL126, NL106, NL120, Digitimer), along with arterial blood pressure and esophageal pressure signals (model 7D polygraph, Grass Instruments). All outputs were digitized at a sampling rate of 5 or 5.56 kHz, and then they were displayed and stored in a computer by means of a data acquisition system (DigiPack 1200, Axon Instruments).

For spinal cord transection, the animals were mounted in a stereotaxic frame. The cervical spinal cord (C1–C3) was surgically exposed through a dorsal midline incision and the dura was opened under the dissection microscope. The animal was artificially ventilated at 62–70 cycles/min by means of an automatic respirator (DigiPack 1200, Axon Instruments).

![Fig. 1](http://apjpphysiology.org/download/fig1.png)
of a small animal respiration pump (model 663, Harvard Apparatus). Spinal transection was done by cutting spinal cord with a scalpel (blade size 11) at the level of C2, and completeness of the cut was verified later at autopsy.

**Drugs.** Scopolamine methyl bromide (methscopolamine), nifedipine, and urethane were obtained from Sigma Chemical; tubocurarine chloride was purchased from Burroughs-Wellcome. All the drugs were administered intravenously in aqueous solution, except for nifedipine, which was dissolved in ethanol.

**Data analysis.** To ensure reproducibility of responses, distensions at low volume and volumes over 200 μl were applied at 3- to 5-min and at 0.5- to 1-h intervals, respectively. In the case of rhythmic contractions, intraluminal pressure was taken at the peak of each wave and averaged. When rhythmic activity was evoked by constant-rate incremental distension, the instantaneous frequency of contractions was calculated from the reciprocal of the interval between two successive waves and expressed as the number of waves per second (Hz). Data are presented as means ± SE, except where noted otherwise. Student’s paired t-tests were done with statistical software (Microcal Origin, Microcal Software). Differences were considered statistically significant at P < 0.05. Numbers (n) given in parenthesis refer to individual separate experiments and, in the case of extracellular unit recordings, to the total number of individual units. In preparing Fig. 2B, data files were imported into Microcal Origin, where digital subtraction of pressure signals could be performed.

**RESULTS**

**Volume dependence of distal esophageal motility pattern.** Distension produced both rhythmic and tonic pressure responses that varied with balloon volume and required an intact vagal innervation (Fig. 2). During constant-rate incremental distension, rhythmic contraction waves appeared at a threshold volume of 46.4 ± 2.7 μl (n = 9); they remained steady below 100 μl, slowed progressively between 100 and 200 μl, and were replaced by a tonic contraction between 150 and 250 μl (Fig. 2, B and C). A single-step distension in the range of 150–200 μl evoked an initial slow or tonic contraction that changed to rhythmic contraction waves as the intraluminal mean pressure declined gradually (Fig. 2A and see Fig. 6). Distension at volumes above 250 μl caused a persistent increase in reflex threshold, as evidenced by an increase in the minimal balloon volume required to elicit rhythmic activity (61.0 ± 2.7 μl, n = 9). Repeated testing at a volume of 300 μl demonstrated that the peak pressure evoked by subsequent distension declined by 22% and remained depressed for up to 2 h.

Placement of the balloon in the gastroesophageal junction revealed a modified response profile during constant-rate incremental distension (Fig. 2D). When the balloon volume reached 250–300 μl, intraluminal pressure appeared to level off, indicative of an increase in esophageal compliance. Bilateral vagotomy abolished this apparent relaxation response, along with rhythmic pressure wave activity preceding it (n = 4) (Fig. 2D).

Ventral medullary units (n = 31) responding to distal esophageal distension were recorded in 17 rats. All units were silent at rest and did not fire unless a distension-evoked pressure wave occurred. The mean latency between the beginning of esophageal distension and the first evoked spike was 1.06 ± 0.07 s. The pattern of evoked spike activity depended on the magnitude of balloon inflation. At balloon volumes of 50–100 μl, rhythmic activity prevailed and consisted of spike bursts associated with the rising phase of each pressure wave (Fig. 2E). The mean spike frequency of the initial burst was 29.3 ± 2.2 Hz. Three units (9.6%) had a short burst discharge 1 ± 0.5 s after rapid deflation of the balloon. Responses to 200 μl were obtained in 19 units. Evoked firing was continuous during distension (3.0 ± 0.1 s) at a mean frequency of 34.4 ± 3.4 Hz and was temporally correlated with a nonrhythmic pressure rise in the distal esophagus (Fig. 2E). About two-thirds of the units (68.4%) showed a burst discharge 0.7 ± 0.2 s with balloon deflation.

**Differentiation of striated and smooth muscle components.** Acute blockade with methscopolamine (0.2 μmol/kg iv) of parasympathetic cholinergic efferents to the TMM smooth muscle tunic (5) did not result in a measurable change in the amplitude and pattern of distension-evoked esophageal responses (Fig. 3A). Dur-
VAGAL CONTROL OF ESOPHAGEAL MOTILITY PATTERN

A

B

C

D

E

 ESA

 DE

 BP

 Pump infusion time (s)

 Intraluminal pressure (mmHg)

 Frequency of contractions (Hz)

 Distension volume (μl)

 Distension volume (μl)

 Intraluminal pressure (mmHg)
neuromuscular paralysis with tubocurarine (0.15 μmol/kg iv), both rhythmic and tonic contractions were completely inhibited for 10 min, and the pressure-volume relationship was indistinguishable from that obtained after vagotomy (not illustrated). In vagotomized rats, esophageal compliance increased significantly at distension volumes ≥250 μl. This apparent increase in compliance was augmented by nifedipine (0.8 μmol/kg iv), as evidenced by a further reduction in intraluminal pressure high-volume distension were chosen for this study. All of these afferents fired tonically at rest, without any evidence of cardiac or respiratory modulation. The resting discharge rate varied from 0.4 to 34 Hz (mean 9.7 ± 2.8 Hz). During distal esophageal distension, the firing frequency increased linearly with the logarithm of esophageal inflation pressure in the test range and did not show saturation even at balloon volumes as large as 300 μl. As suggested by the rate of resting and distension-evoked discharge, these fibers appeared to fall into three subgroups (Fig. 5C). When impulse frequencies obtained at 300 μl were arbitrarily set as the maximum, the fractional increase in firing frequency as a function of applied pressure showed a similar slope in all the fibers tested (Fig. 5D).

Extracellular single-unit recordings from the nodose ganglion were done in 20 animals. Most units in the 23

Fig. 3. Differentiation of striated and smooth muscle components. A: representative example illustrating the absence of change in esophageal compliance and motility pattern after intravenous methscopolamine (MSCP). B: subtraction of distension-evoked pressure increase after vagotomy from control response reveals the reflex neurogenic component of intraluminal pressure increase. Vagus-dependent response reaches its peak at a balloon volume between 150 and 200 μl. A second, nifedipine-sensitive component is evident at large balloon volumes (250–300 μl; n = 6 animals) after vagotomy. Values are means ± SE. *P < 0.05.

Fig. 4. Failure of C2-level spinal cord transection to alter volume-dependence of reflex motility in distal esophagus. Response to constant-rate (15 μl/s) incremental inflation of intraluminal balloon placed at 11.5 cm from upper incisors is shown before and 1.5 min after the transection.
units obtained had respiratory rhythm \((n = 14)\); others were firing with a cardiovascular rhythm \((n = 2)\), tonically \((n = 6)\), or had an unknown rhythm \((n = 1)\). Only one neuron responded to distal esophageal distension. This unit was not activated until the distension pressure exceeded 90 mmHg, and the largest increase in firing frequency occurred in a pressure range above 200 mmHg (not illustrated).

**Volume dependence of dorsal medullary neuronal activities.** Sixty-seven units that responded to distal esophageal distension were recorded in the intermediate and caudal NTS region. These unit discharges corresponded to the three types described previously (13), in terms their spontaneous background activity, firing patterns, and responses to balloon inflation or deflation (Table 1). Average depths below the extraventricular surface of the NTS for type I, II, and III units were 471.6 ± 38.9 (SD), 460.0 ± 44.9, and 482.3 ± 43.0 μm \((P > 0.05)\), respectively. Within a given track, type I units were separated by as little as 10–30 μm from type II and III units.

Type I units responded to 50- to 100-μl distensions with rhythmic spike bursts that coincided with the rising phase of the distal esophageal pressure waves. When balloon volume was increased to 200 μl, type I units produced high-frequency tonic spiking with an increased incidence of burst discharges after deflation (Table 1, Fig. 6). However, on deflation, most units showed a silent period that varied directly with balloon volume \((7.5 ± 0.9 \text{ s at } 200 \mu l \text{ vs. } 5.1 ± 0.8 \text{ s at } 50–100 \mu l; P < 0.05)\).

Type II units showed a sustained increase in activity during esophageal distension and fired continuously at rest, with the exception of two units that had a rhythmic basal discharge in phase with expiration. In the latter, distension-evoked tonic activity reverted to an expiratory rhythm 2–3 s after deflation of the balloon. Type II units showed a volume-dependent poststimu-
lation silent period before resuming their spontaneous discharge (4.2 ± 0.7 s for 200 μl vs. 2.9 ± 0.4 s for 50–100 μl; P < 0.05). Both the increase and decrease in firing rate were volume dependent (Table 1).

Type III units had a resting discharge significantly higher than that of type I units and were inhibited by esophageal distension. On deflation of the balloon, they showed a rebound burst discharge (Table 1). Intraburst

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**Table 1. Characteristics of esophageal distension-responsive units recorded in rat NTS caudal central subnucleus area**

<table>
<thead>
<tr>
<th>Type</th>
<th>n</th>
<th>Resting Discharge, Hz</th>
<th>Activity Evoked at Balloon Volume of</th>
<th>“Off” Response at Balloon Volume of</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>50–100 μl</td>
<td>200 μl</td>
</tr>
<tr>
<td>I</td>
<td>26</td>
<td>Rhythmic bursts</td>
<td>24.3 ± 2.3 Hz</td>
<td>34.3 ± 3.3 Hz</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.9 ± 0.3</td>
<td>(n = 25)</td>
<td>(n = 23)</td>
</tr>
<tr>
<td>II</td>
<td>28</td>
<td>Tonic</td>
<td>6.0 ± 1.0 Hz</td>
<td>14.2 ± 2.5 Hz</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(n = 1)</td>
<td>(n = 3)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>13</td>
<td>Complete cessation</td>
<td>2.6 ± 1.0 Hz</td>
<td>19.2 ± 2.6 Hz</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(n = 7)</td>
<td>(n = 3)</td>
<td>(n = 3)</td>
</tr>
</tbody>
</table>

Values are means ± SE; n, no. of units recorded. *Spike frequency in leading burst. NTS, nucleus tractus solitarii. “Off” response denotes change in firing caused by balloon deflation. †P < 0.05 vs. type I units (8–12 rats per unit type). ‡P < 0.05 vs. 50 to 100-μl distension.

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**Fig. 6.** Representative type I distension-sensitive units recorded in the caudal half of the nucleus tractus solitarii centralis region. A: moderate distension of esophagus evokes rhythmic bursting discharge in phase with intraluminal pressure wave of the distal esophagus. B: strong distension induces high-frequency tonic discharge of the neuron, with nonrhythmic pressure rise. The bin width of spike-frequency histogram (SFH) was set at 0.25 s. C: in another unit at intermediate volume, distension evokes initial nonrhythmic discharge that becomes rhythmic 15 s later as intraluminal pressure falls gradually. Note correlation between unit activity and esophageal contractions as response changes from tonic to rhythmic pattern.
spike frequency and burst latency depended on the magnitude of the stimulus.

*Esophageal distension evoked rise in blood pressure.* Distal esophageal distension was accompanied by a measurable arterial pressor response at every balloon volume tested. At 50–100 μl, systolic and diastolic pressure increased by 7.2 ± 0.9 and 8.9 ± 0.9 mmHg, respectively. At 200 μl, the respective increases were 12.6 ± 1.4 and 14.6 ± 1.4 mmHg. The volume dependence of the pressor response was statistically significant (P < 0.05).

**DISCUSSION**

In the rat esophagus, motor control of the striated muscle tunica propria involves segmental vagovagal reflex circuits composed of primary vagal afferents, esophageal premotoneurons in the NTSp, and esophageal motoneurons in the nucleus ambiguous compact formation (1, 4, 6, 7, 11, 20, 31). As demonstrated in the present study, brain stem esophagomotor control entails the generation of different motility patterns. Thus the distal esophagus executes rhythmic or sustained (tonic) contractions depending on the level of afferent impulse activity. Our data not only confirm vagal input as the principal determinant in esophageal motor pattern control but also militate against a direct involvement of spinal afferent input. This idea agrees with previous work by Renihan et al. (24) showing that after vagotomy rat NTS neurons do not respond to intestinal distension, although neurons in the dorsal motor nucleus of the vagus (DMV) continue to do so through a spinal afferent pathway. As discussed below, the volume dependence of esophageal motor patterns and their central neuronal correlates need to be considered in relation to the dynamic range of vagal afferent input from the esophagus.

**Volume dependence of distal esophagomotor pattern.**

Both amplitude and pattern of distal esophageal contractions were found to depend on the volume of the intraluminal balloon and, hence, the magnitude of sensory input. The pressure-volume relationship obtained would be expected to result from the interplay of four factors: reflex contraction of the striated muscle tunica muscularis propria, neurogenic or myogenic tension of the smooth muscle TMM, neurogenic inhibition in the TMM, and the passive viscoelastic properties of both muscle tunics. Because muscarinic acetylcholine receptor blockade failed to change distension-evoked esophageal motility responses at methscopolamine doses likely to suppress vagal efferent transmission in the TMM, any centrally mediated reflex contraction of the TMM was evidently too small to be detected. Accordingly, the active neurogenic component of the intraluminal pressure change could be attributed to the muscularis propria, a conclusion corroborated by the complete loss of this response seen after vagotomy or curarization. At large balloon volumes (≥250 μl), a local myogenic contraction of the TMM occurred, as inferred from the decrease in intraluminal pressure induced by nifedipine, a blocker of smooth muscle L-type calcium channels (30). The active neurogenic component attained peak amplitude at balloon volumes between 150 and 200 μl.

Although the possibility that high-intensity vagal input inhibits motor output cannot be ruled out, the observed decline in the active neurogenic component at balloon volumes ≥250 μl (Fig. 3B) is possibly due to excessive stretching of the striated muscle tunica. Indeed, distension at this volume resulted in a long-lasting decrease in esophageal contractility, suggestive of structural damage. This interpretation is consistent with other work in rats, in which esophageal distension with 1.25-ml air boluses was considered to be noxious (29). Inflation of the Swan-Ganz catheter used in the cited study with air at a volume of 1.25–1.5 ml would distend the esophagus to an outer diameter of 6 mm (17), which is equivalent to a distension produced by a balloon filled with 300 μl water (present study).

As reflected by the evoked activity of neurons in the region of the rostral nucleus ambiguus, that is, presumptive esophageal motoneurons innervating the tunica muscularis propria, a balloon volume of 200 μl resulted in a submaximal activation of the striated muscle component. This volume evoked a tonic discharge at an average frequency of 34 Hz. Unpublished experiments (D. Bieger) on in vitro vagus nerve-esophagus preparations in our laboratory show that stimulus frequencies between 40 and 50 Hz cause a maximal tetanic contraction of the esophageal tunica muscularis propria.

At the level of the gastroesophageal junction, an apparent relaxation was evoked by high but not low to moderate volume distension. Because this relaxation was abolished by vagotomy, it appeared to be neurogenic. A recent report suggests that the gastric relaxation evoked by esophageal distension is dependent on a vagovagal reflex (25). Conceivably, the same neural control system extends to the gastroesophageal junction.

**Dynamic range of vagal afferents.** To date, very few studies have dealt with esophageal vagal afferents in the rat (2, 10), and information concerning the activity elicited at high intraluminal pressures is lacking. In this study, single-fiber recording of vagal afferents revealed that all units sampled had a wide dynamic range. Thus, at balloon volumes of 250–300 μl, the firing frequency continued to increase, whereas the active vagovagal component of the evoked intraluminal pressure rise appeared to decrease. Because unilateral damage to the vagal innervation of the esophagus impairs rhythmic reflex peristalsis (20), we were unable to record the vagal afferent activity during reflex-evoked esophageal rhythmic contraction. Our findings differ from those reported in the opossum, in which esophageal vagal afferents were shown to have both a low threshold and low saturation pressure and, hence, to encode information only in the low pressure range (27).

**Responsivity of NTS interneurons.** As reported before (13), single-unit recordings in the NTSp area revealed three different neuron groups that responded to distal
esophageal distension. Although these units were obtained in a narrowly restricted region, the ventralmost recording sites in some tracks may have encroached on the DMV. However, the firing pattern of the neurons concerned is clearly different from that of units recorded in the DMV that respond to esophageal distension (25). These DMV units were shown to fall into two types and to be activated or inhibited by esophageal distension (25). In the present work, although type III units showed a burst discharge and superficially resembled the excitatory DMV units, the burst discharge of our type III units occurred well after deflating the esophagus, whereas excitatory DMV units displayed a burst discharge before deflation of the esophagus. During high-volume distension, our type I units changed their firing pattern from rhythmic bursting to a tonic discharge, type II units were further activated, and type III units fell silent but rebounded with enhanced deflation bursts. These results demonstrate that the pattern and strength of NTS interneuron activity are dependent on the level of vagal afferent input. Because the type I units and esophageal motoneurons had corresponding firing patterns over the entire pressure range tested, and because both reflected the motility pattern recorded in the esophagus, the present results corroborate our previous inference that the type I unit represents a premotoneuron (13). The functions of type II and type III units are currently not clear; however, it is reasonable to believe some of type II units represent interneurons mediating esophageal distal inhibition (13) or esophageal cardiovascular reflex responses (19). Recordings in the rat NTS, described by others (25) have shown that most units are silent at rest and do not fire rhythmically during esophageal distension. This discrepancy could be attributable to differences in the depth of anesthesia; moreover, in the rat thoracic esophagus, distension may evoke a single phasic motor response (20).

In summary, the evidence obtained in the present study suggests that the reflex motor response pattern and contractile force in the rat esophagus vary with the strength of vagal afferent input. The role, if any, of spinal afferent input in esophageal motor control is yet to be defined. The responsiveness of vagal afferent neurons and NTS interneurons to high-volume distension indicates that this system has the ability to encode information in a high-pressure, noxious range.

**Perspectives**

Anatomically, vagal afferent terminal endings are located in esophageal myenteric ganglia, whereas relatively sparse innervation is found in the muscularis mucosae or striated musculature (16, 18). Vagal afferent neurons innervating the distal esophagus have smaller cell bodies and less or no staining intensity for calretinin and calbindin than do neurons projecting to other parts of the esophagus (16, 18). Because the presence of the calcium-binding proteins in the terminal structures is a characteristic of low threshold and rapidly adapting sensors (15), vagal afferents from the distal esophagus must have other properties. According to our data, the majority of this fiber population innervates slowly adapting receptors. Furthermore, the observed distension-evoked firing frequencies were much lower than those reported for afferents supplying the cervical esophagus (2). Thus regional response patterns may differ significantly in esophageal vagal afferents.

In the present and previous (14, 19) studies, the magnitude of arterial blood pressure responses correlated with esophageal intraluminal pressure, functionally implying the similarity in dynamic range of vagal afferents mediating esophageal cardiovascular and motility responses. This dynamic range agrees with that observed in vagal fiber recordings. Our previous work implies that different populations of rat esophageal afferents in the vagus mediate distension-evoked reflex motility and two types of cardiovascular responses (14). Furthermore, anatomic studies suggest that substance P exists in some esophageal vagal afferents in the rat (18). Because of the limited number of esophageal vagal afferent fibers from which successful recordings were obtained, we cannot as yet discern different populations clearly. However, our data suggest that, although all fibers showed an overlapping dynamic range, individual activity levels differed. Clearly, more work is needed to classify mechanosensory vagal afferents of the rat esophagus in functional terms.

By virtue of their wide dynamic range, rat esophageal vagal afferents may represent sensory neurons that have the ability to generate both normal motility-regulating and nociceptive signals depending on the intensity of stimulation (9). Esophageal distension in humans is known to evoke pain (12), and esophageal spasm and intense peristaltic contractions are considered to be painful (8). In humans, distension-evoked pain has been reported to wax during relaxation and to wane during contraction; invariably, however, isometric contraction on an incompressible balloon was noted to be painful (23). Accordingly, the slow wave tonic contractions in the rat esophageal body that result from high-volume distension by means of a water-filled incompressible balloon may be equivalent to a “pain spasm” (23). Although it is generally believed that esophageal pain is mediated by spinal afferents (8, 22), there is evidence implicating an involvement of vagal afferent pathways (3, 19, 29). The present work supports the idea that esophageal vagal afferents contribute to nociceptive processing.

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**REFERENCES**