Disruption of primary and secondary esophageal peristalsis by afferent stimulation

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Bardan, Eytan, Pengyan Xie, Muhammad Aslam, Mark Kern, and Reza Shaker. Disruption of primary and secondary esophageal peristalsis by afferent stimulation. Am J Physiol Gastrointest Liver Physiol 279: G255–G261, 2000.—Recent studies have shown that afferent signals originating from the pharynx inhibit progression of primary esophageal peristalsis. Our aim was to further elucidate the effect of esophageal and pharyngeal afferent stimulation on primary and secondary esophageal peristalsis. We studied the effect of esophageal air distension and pharyngeal water stimulation on progression of primary and secondary peristalsis in nine healthy volunteers aged 27 ± 2 yr (4 men, 5 women). At a threshold volume, rapid injection of water into the pharynx, directed posteriorly, resulted in complete halt of the progressing secondary and primary esophageal peristalses in both the proximal and distal esophagus. The threshold volume of injected water for inducing inhibition was similar for secondary (0.6 ± 0.2 ml) and primary (0.5 ± 0.1 ml) esophageal peristalsis. Progression of primary peristalsis induced by a dry swallow and secondary peristalsis induced by intraesophageal air distension were completely inhibited by intraesophageal injection of 15 ± 2 ml of air in 70% and 75% of the trials, respectively. We conclude that afferent signals induced by esophageal air distension and pharyngeal water stimulation inhibit propagation of both primary and secondary esophageal peristalsis, suggesting a shared neural control mechanism for these types of peristalsis.

METHODS

Nine healthy young volunteers (age 27 ± 2 yr; 4 men, 5 women) were studied in the supine position after overnight fasting. The studies were approved by the Human Research Review Committee of the Medical College of Wisconsin, and volunteers gave written informed consent before the studies. Before each study, the presence of primary and secondary peristalsis was verified in each subject. A total of 16 volunteers were originally enrolled in the study and underwent screening studies. For evaluation of primary peristalsis, the subjects performed ten dry and ten 5-ml water swallows. For evaluation of secondary peristalsis, incrementally increasing volumes of air were injected into the mid esophagus. We started with a 5-ml volume, and, if secondary peristalsis was not stimulated, subjects were asked to swallow once to clear the air residue and the next injected volume was increased by 5 ml. We tested up to 60-ml air injections. Only subjects who had fully propagated primary peristalsis and produced secondary peristalsis in response to all three trials of a given volume of air injection were included in the study. With these strict criteria, 9 of 16 volunteers qualified and enrolled in the study.

The upper esophageal sphincter (UES), esophageal body, lower esophageal sphincter (LES), and gastric pressures were recorded concurrently using two sleeve assemblies, each passed through one nostril and positioned such that the LES sleeve device (6 × 0.5 × 0.4 cm; Arndorfer Specialties, Greendale, WI) straddled the LES and the UES sleeve device (6 × 0.4 × 0.3 cm; Dentsleeve, Bowden, Australia) straddled the UES. With this arrangement, the esophageal body pressures were recorded at the top of the LES sleeve and 3, 6, 9, in patients with motility disorders or reflux-induced injuries (9, 13). The mechanism for these clinical observations has not been fully elucidated. In addition, it is not known whether secondary esophageal peristalsis is affected similarly by the inhibiting influence of pharyngeal and, potentially, esophageal afferent stimulation. The aim of the present study, therefore, was to investigate the effect of esophageal and pharyngeal afferent stimulation on primary and secondary esophageal peristalsis.

Recent studies have shown that afferent signals originating from the pharynx exert an inhibitory effect on primary esophageal peristalsis and prevent its propagation (3, 4, 21). These findings raise the possibility that afferent signals originating from other areas of the deglutitive axis, such as the esophagus, may exert a similar effect and may explain the mechanism of some of the failed esophageal peristalsis. Failed esophageal peristalsis is reported to occur after 5–15% of dry and water swallows in apparently healthy individuals (7, 18). This occurrence is significantly more prevalent

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DISRUPTION OF ESOPHAGEAL PERISTALSIS

A

10 ml Air

Eso Inj Port

Pharyn Inj Port

UES

E15

E12

E9

E6

E3

LES

Gastric

Sub EMG

Time in seconds

B

DS

DS

DS

0.9 ml Water

UES

E15

E12

E9

E6

E3

LES

Gastric

Sub EMG

Time in seconds
12, and 15 cm proximally. The upper sleeve assembly incorporated an injection port located 2 cm proximal to the sleeve device. This manometric assembly was positioned so that the injection port faced posteriorly, to avoid injecting water into the larynx. The subjects were monitored for 10 min after positioning of the two manometric assemblies for adaptation and were studied thereafter.

To study the effect of pharyngeal stimulation on secondary esophageal peristalsis, the predetermined threshold volume of air that consistently induced secondary peristalsis was injected into the mid esophagus and the subject’s pharynx was stimulated by water injection timed to coincide with the arrival of pressure waves at the proximal (sites 12 or 15 cm above the LES) or distal (sites 6 or 9 cm above the LES) esophageal recording sites.

To study the effect of pharyngeal water stimulation on the progression of esophageal primary peristalsis, subjects were asked to swallow on command, and their pharynx was stimulated by injections of minute amounts of water. Water injections were timed to coincide with complete UES relaxation or arrival of the peristaltic pressure wave at the proximal or distal recording site described above.

Pharyngeal water stimulation was initiated by rapid pulse injection of 0.1 ml of water directed toward the posterior pharyngeal wall. The volume of injected water was increased by 0.1-ml increments until either the progression of the peristaltic wave was halted or an irrepressible swallow occurred. Each volume was repeated three times for each recording site, and the subjects withheld swallowing after water injection for as long as they could. Occurrence of the swallow was judged by typical deglutitive UES relaxation, submental electromyograph signal, subject’s signal using a hand-held marker, and observer’s marks on the polygraph paper. Each swallow tested by pharyngeal stimulation was done 25–30 s after a control swallow or a secondary peristalsis and was followed 25–30 s later by a second control swallow or secondary peristalsis. Inhibition of progressing primary or secondary peristalsis after each pharyngeal water injection was accepted when the pressure wave was completely abolished after the injection. For this criterion, we evaluated the pressure phenomenon at all of the recording sites distal to the peristaltic pressure wave, during which the water was injected into the pharynx. Rate of occurrence of inhibition after each water injection was scored as percentage of the trials for each site.

To determine the effect of esophageal afferent stimulation by distension on the progression of the primary and secondary peristalsis, the above-mentioned sequences were repeated, with the exception that instead of pharyngeal water injection, esophageal air distension was used as the afferent stimulus. The volume of air injected into the esophagus was the same as the threshold volume for stimulation of secondary peristalsis.

We also evaluated the effect of swallowing on secondary esophageal peristalsis. For this evaluation, after stimulation of the secondary peristalsis by injection of predetermined threshold volume, subjects were asked to swallow coincident with the arrival of the peristaltic pressure wave at the stated recording site.

Using these techniques, we determined 1) the threshold volume of air injected into the mid esophagus that stimulated a secondary peristaltic pressure wave, 2) the threshold volume of water injected into the pharynx that inhibited the progression of primary and secondary esophageal peristalsis, 3) the development, or lack thereof, of a new peristaltic pressure wave after each inhibited peristaltic wave, 4) the effect of pharyngeal water injection on the amplitude and duration of the pressure wave at the onset of which water was injected into the pharynx, 5) the presence or absence of...

**Fig. 1.** Inhibition of secondary (A) and primary (B) esophageal peristalsis by pharyngeal water stimulation. A: pharyngeal injection of 1.1 (middle) and 1.2 (right) ml of water results in complete inhibition of secondary esophageal peristalsis induced by intravesophageal injection of 10 ml of room air. In both cases the inhibitions are followed by a command of dry swallow (DS) to clear the air from the esophagus. An uninhibited secondary esophageal peristalsis induced by intravesophageal injection of 10 ml of air in the same subject is shown on left. The contraction waves during which the pharyngeal stimulation were perfused are attenuated in both examples. B: inhibition of primary esophageal peristalsis as a result of a dry swallow after pharyngeal stimulation by injection of 0.9 ml of room temperature water (middle). Normally propagated primary peristalsis is seen on right and left of the example. Note the attenuation of the contraction wave during which the pharyngeal water injection was performed. UES, upper esophageal sphincter; LES, lower esophageal sphincter; EMG, electromyograph; E3–E15, esophageal recording site distance from LES; 1°P, 2°P, primary and secondary peristalsis, respectively.
DISRUPTION OF ESOPHAGEAL PERISTALSIS

A

Eso Inj Port
12 ml Air

Pharyn Inj Port
UES
E15
E12
E9
E6
E3
LES
Gastric
Sub EMG

Time in seconds

B

Eso Inj Port
10 ml Air 10 ml Air 10 ml Air

UES
E15
E12
E9
E6
E3
LES
Gastric
Sub EMG

Time in seconds
trials. Likewise, these inhibitions were followed by intraesophageal injection of 15 ml of room temperature air. This air injection resulted in stimulation of a secondary peristaltic wave that propagated to the LES. As seen, the amplitude of the pressure wave coincident with air injection was attenuated compared with the pressure wave at the same site during a second primary peristaltic pressure wave (shown on right).

**Results**

**Effect of pharyngeal stimulation on esophageal peristalsis.** At a threshold volume, rapid injection of water into the pharynx directed posteriorly resulted in complete halt of the progressing secondary esophageal peristalsis induced by intraesophageal injection of the predetermined threshold volume (15 ± 2 ml) (Fig. 1). Similar to our earlier reports (4), at a threshold volume intrapharyngeal water injection also resulted in complete halt of the progressing esophageal primary peristalsis induced by a dry swallow. The threshold volume of injected water into the pharynx that inhibited the progression of a secondary peristalsis (0.6 ± 0.2 ml) was similar to that required to inhibit the progression of the primary esophageal peristalsis (0.5 ± 0.1 ml). Pharyngeal water injection resulted in significant reduction in the amplitude and duration of the primary and secondary pressure waves during which the injections were made (Fig. 2).

Inhibition of the primary and secondary peristaltic pressure waves by pharyngeal stimulation was not associated with generation of a subsequent peristaltic wave, with the exception that inhibition of the secondary peristaltic pressure wave in one subject was followed by regeneration of a completely propagated secondary peristaltic pressure wave. In two additional volunteers, the inhibition was followed by a partially propagated pressure wave limited to the proximal three recording sites (1 and 2 episodes, respectively).

**Effect of esophageal stimulation on esophageal peristalsis.** The progression of the primary peristalsis induced by a dry swallow was completely inhibited by intraesophageal injection of 15 ± 2 ml of air in 70% of the trials. These inhibitions, in contrast with inhibitions induced by pharyngeal water stimulation, were followed by generation of a peristaltic pressure wave that propagated from the proximal to the distal esophageal recording sites (Fig. 3A). Similarly, progression of the secondary esophageal peristalsis was inhibited by intraesophageal injection of 15 ± 2 ml in 75% of the trials. Likewise, these inhibitions were followed by development of a new secondary peristaltic pressure wave (Fig. 3B).

**Discussion**

The inhibitory effect of sensory signals originating from the pharynx on primary esophageal peristalsis (3, 4, 21) and LES resting tone (17, 22) have been documented previously. The present study confirms the existence of a similar inhibitory influence on secondary esophageal peristalsis in humans. The findings of the present study also demonstrate for the first time the inhibitory effect of the afferent signals originating from the esophagus on progressing primary and secondary esophageal peristalsis.

In contrast to universal inhibition of both primary and secondary peristalsis by pharyngeal stimulation, inhibition of primary and secondary peristalsis by esophageal stimulation was achieved in only 70–75% of trials. This discrepancy may be caused by the fact that we used only one volume of air for esophageal distension, and this volume may not have been adequate for inhibitory stimulation in all instances.

To elucidate the role of central deglutitive inhibition on the progression as well as the parameters of the primary peristaltic pressure wave induced by closely timed swallows has been reported previously (2, 10, 16, 23). The inhibitory effect of closely timed swallows on the progression of secondary esophageal peristalsis shown in this study suggests the presence of a central control mechanism for secondary esophageal peristalsis similar to that for primary peristalsis. The findings of the present study also indicate that the secondary esophageal peristalsis is subject to the same inhibitory effect resulting from the peripheral stimulation of the deglutitive axis as the primary esophageal peristalsis.

The findings of this study have both clinical and physiological implications. From a clinical perspective,
Failed esophageal peristalsis is reported to occur after 5–15% of dry and water swallows in healthy individuals (7, 18). The mechanism for this failure is duration and frequency of the efferent vagal discharges to the esophagus (20). In humans, the amplitude and duration of the peristaltic pressure wave increases and its velocity decreases with the presence of a bolus (7, 11). These effects can also be seen from a stimulus originating outside the esophagus, such as during raised intra-abdominal pressure (8). The findings of the present study demonstrating the inhibition of progression of peristalsis by esophageal air distension and the reduction in amplitude and duration of contraction wave coincident with distension confirm the possibility of the negative influence of esophageal afferent stimulation on peristalsis.

Peristaltic contraction of the striated portion of the esophagus is controlled by lower motor neurons of the brain stem. Peristalsis in this region is induced by sequential firing of these somatic nerves that results in sequential activation of muscle motor units in a cranio-caudal direction (1). Inhibition of primary and secondary peristalsis in this region by pharyngeal and esophageal stimulation suggests a direct inhibitory effect on these brain stem lower motor neurons.

Peristalsis in the smooth muscle esophagus is controlled by both the central and enteric nervous systems as well as the intrinsic properties of smooth muscle (6, 10, 19). In this segment of the esophagus, peristalsis persists after extrinsic denervation (5, 12, 20). The mechanisms of integration of the central and peripheral control of peristalsis in the smooth muscle esophagus have not been completely elucidated. Central control of secondary peristalsis, although suggested (15), has received little attention. Our finding of inhibition of propagation of secondary peristalsis in both striated and smooth muscle esophagus strongly suggests the existence of a central control mechanism for secondary peristalsis in intact human esophagus.

The inhibitory effect of pharyngeal and esophageal stimulation on the progression of peristalsis in the smooth muscle segment of the esophagus is difficult to explain. However, it may be suggested that pharyngeal and esophageal stimulation somehow inhibit the expected depolarization and/or spike potential of the smooth muscle that was to occur after the hyperpolarization associated with original peristalsis. The mechanism of this possible interference is not known. Whether the inhibitory effect of pharyngeal and esophageal stimulation on primary and secondary esophageal peristalsis is another manifestation of previously reported (1, 14, 16, 23) deglutitive inhibition, simply represents the isolated stimulation of inhibitory function of the brain stem swallowing center through an unrelated pathway, or suggests the presence of a different inhibitory pathway or a combination thereof is not determined. Inhibition of peristalsis by pharyngeal stimulation as reported in this study, however, is different from deglutitive inhibition observed by closely timed coupled swallows in humans because it does not induce a second peristaltic wave after the inhibition.

Failed esophageal peristalsis is reported to occur after 5–15% of dry and water swallows in healthy individuals (7, 18). The mechanism for this failure is

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**Fig. 4.** Progression of the primary peristaltic pressure wave, induced by a dry swallow (left), and secondary peristaltic pressure wave, induced by intraesophageal injection of 20 ml of air (right), were completely inhibited by closely timed dry swallows.
not completely understood. In addition, esophageal dysmotility, including nonpropagated and low-amplitude peristaltic sequences, is frequently observed among esophagitis patients (9, 13). The mechanism for this phenomenon is not clearly elucidated; however, the effect of peptic injury on esophageal neuromuscular apparatus is generally suggested as a possible mechanism. Whether inhibition of the peristaltic wave by distention of the esophageal body, described in this paper, plays any role in the development of nonpropagated peristalsis in normal and gastroesophageal reflux disease patients remains to be studied.

In conclusion, afferent signals induced by esophageal air distension, as well as pharyngeal water stimulation, inhibit the propagation of both primary and secondary esophageal peristalsis, suggesting a shared neural control mechanism for both types of esophageal peristalsis. This finding indirectly supports the notion of central control of secondary peristalsis in intact human esophagus. The findings of the present study may explain the mechanism of some of the failed esophageal peristalsis.

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