THE MANY FACETS OF INTESTINAL PERISTALIS

To the Editor: Seerden and co-workers (14) have produced an important study with impressive recordings that show many features of distension-induced electrical and motor activity in the mouse small intestine. Among the highlights of this paper are a clear demonstration of slow wave-driven propulsive contractions, further evidence that the longitudinal and circular muscle layers show the same slow-wave frequency but independent contraction patterns and the visualization of the burst-type appearance of action potentials, suggesting rhythmicity in the neural excitation (1, 11). However, the data are put into a context of peristalsis and segmentation that may lead to confusion. Hence, it is worthwhile to further discuss the existing motor patterns in the mouse due to the importance of the mouse as a current model in the study of gastrointestinal motility. Seerden and co-workers state, “In contrast to motility behavior in other animals, distension does not induce peristaltic contraction in the small intestine of mice.” Later it is stated that the observed motor pattern constitutes “a segmental pattern of contraction.” Seerden et al. show electrical and motor activity on distension of the small intestine and state that this is the first time that these contractions have been described in the mouse. However, the motor pattern they describe is the same as that described previously (11) and similar to the first observations of distension-induced motor activity. In 1898, Cannon studied gastric activity using X-ray imaging in response to the ingestion of a meal and noted “that peristaltic waves are running continuously throughout the entire digestive period” (6). On the small intestine, he wrote “peristalsis is observed. . . . as a rapid movement sweeping the food without pause through several turns of the gut,” and characterized the rhythmic contractions as myogenic (5). In addition to this motor pattern, Bayliss and Starling (2) discovered that the small intestine can evoke a peristaltic reflex, orchestrated by the myenteric plexus, in response to a local distension. Hence, right from the start, it was acknowledged that several peristaltic motor patterns exist with different underlying mechanisms. We now know that Cannon described the motor patterns governed by myogenic slow-wave activity, as described by Charles Code when he wrote in 1968 (7), “If, as the PSP (pace setter potential or slow wave) passes along the small bowel, the circular muscle fibers immediately caudal to those that just contracted are excitable and contract when the action potentials portion reaches them, then a propagated contraction results. As the process continues, a caudal-migrating band of contraction moving at the velocity of the PSP develops. This is peristalsis.” No evidence has been presented since to encourage us to deviate from this concept. The fact that contractions can be shallow, as noted by Seerden et al., has nothing to do with the principle. It just means that the neural excitation is low. The fact that the dominant pacemaker can be at different spots occasionally leading to retrograde peristalsis has always been acknowledged. The fact that the pattern appears “oscillatory” relates to the high slow-wave frequency present in the mouse small intestine. The peristaltic, propulsive nature of the slow wave-driven motor activity in the mouse small intestine has been clearly demonstrated: every propagating contraction is associated with outflow of content if flow is not blocked by an area of high pressure (8). Hence this motor pattern is peristaltic in every sense of the word, and not segmental. It should be mentioned that peristaltic activity, although leading to movement of content, does not necessarily mean that there is net transit out of the intestine. If this were to happen with every peristaltic wave, the small intestine would be empty in minutes and not in hours as required for absorption. Hence, if the peristaltic activity bumps into a quiet segment or a segment with a high intraluminal pressure, content will not proceed, just as no one denies that the peristaltic activity in the stomach may not lead to outflow of stomach content when the pylorus is closed. Also, in the small intestine in every species, the myogenic peristaltic activity is primarily aborally propagating, but essentially, a mixture of orally and anally propagating activity. This motor activity can be entirely myogenic, but in concert with neural excitation, the force of contraction increases and the propulsive nature becomes more prominent. The mixed character is most prominent in the ileum, whereas in the duodenum, propagation is almost exclusively aboral. Seerden et al. point out that the contractions in the mouse small intestine are not peristaltic, because “the contractions can propagate in oral and aboral directions.” Cannon as well as Bayliss and Starling acknowledged that the myogenic propulsive movements could occasionally propagate orally. Lammers et al. (13) also showed in the cat small intestine that waves of action potentials associated with slow waves as well as “peristaltic waves” of action potentials, independent of slow-wave activity, propagated in both directions. Seerden and co-workers proposed to identify the propagating oscillatory contractions as a segmental motor pattern. However, in a segmental motor pattern, contractions are rhythmic but stationary and not propagating.

Seerden et al. suggested that the mouse intestine does not exhibit the “peristaltic reflex.” The reason that the peristaltic reflex was not seen was likely due to the fact that it was not evoked. The peristaltic reflex is initiated by local mechanical stimulation of the mucosa or by local muscle stretch. The major features of this reflex involve activation of sensory neurons, polarized activation of interneurons, and release of excitatory and inhibitory neurotransmitters from motoneurons to mediate “oral” muscle contraction and “caudal” muscle relaxation. This pattern is not likely to occur very often under physiological conditions of general distension (15). It is often suggested that the peristaltic reflex can be studied using the “Trendelenburg” preparation. However, Trendelenburg showed that in an isolated segment of the guinea pig small intestine, when the intraluminal pressure is kept constant at a level above that which induces peristalsis, extremely regular, rhythmic peristaltic activity occurs (16), likely, in many circumstances, at the slow-wave frequency. Derived from Trendelenburg’s study, the regular rhythmic phasic contractile frequency is between 7 and 20 cycles/min (17), dependent on experimental conditions, which is similar to the slow-wave frequency observed under similar conditions (8a), or after cholinergic stimulation (4) or recorded in vivo (9). The phasic nature of the guinea pig intestinal peristalsis is not always obvious in experimental protocols that use the Trendelenburg preparation, because unlike in Trendelenburg’s study, the experiments are often terminated immediately after the first emptying of the segment of intestine. As Tonini et al. (15) pointed out, it is likely that large distensions in the small intestine required to generate intestinal peristalsis would make sensory neurons fire repetitively, evoking slow excitatory synaptic potentials in other sensory nerves leading to massive
synchronous activation of motoneurons. This would cause general excitation of the musculature leading to phasic propulsive contractions associated with slow-wave activity in the mouse and likely in the guinea pig as well (13a, 14a). Hence, peristalsis in the “Trendelenburg” preparation should not be regarded as a simple reflex but as an all-or-nothing motor pattern triggered by mechanical stimulation of the intestine (14a, 15) and involving both neurogenic and myogenic mechanisms. Not all distension-induced motor patterns show contratctions that last for the duration of the slow wave. One pattern was described by Bercik et al. (3) in the rat intestine where, on distension, in addition to slow wave-driven peristaltic activity, a propagating wave of contraction occurs that leaves the circular muscle layer of the intestine contracted for some time. This can also be observed in the guinea pig intestine (10). In this case, the contraction pattern does not remain phasic at the slow-wave frequency; hence, this is a condition where the enteric nervous system overrules slow-wave activity, probably by fully depolarizing the musculature.

In future studies of the various motor patterns of the intestine under different conditions, the mapping of the electrical activity of the gastrointestinal smooth muscle as developed and involved by Lammers and co-workers (12) will be of great utility of the gastrointestinal smooth muscle as developed and involved by Lammers and co-workers (12) will be of great utility. The movement and innervation of the smallest intestine. *J Physiol* 24: 99–143, 1899.


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DISCUSSION (8). It could well be that other methods of eliciting the peristaltic reflex (bolus distension or chemical or electrical stimulation) may induce a peristaltic reflex in mice, but we have not tested these. It could also well be that distension would have evoked the peristaltic reflex if these had not been overruled by the much more frequent propagating oscillations. We have classified these propagating oscillations as segmental because of the close relationship between the duration of the contraction and the interval of the slow wave (Fig. 6 in Ref. 8), again a relationship that does not occur in the peristaltic reflex. We believe that some contractions are not only related to the timing of the slow wave but are also limited by the duration of the slow-wave interval, and propagating oscillations are such an example. Yes, in some situations, we also think that segmental contractions could be stationary, but that does not preclude the possibility that other types of segmental contractions could propagate.

In his letter, Huizinga describes a multitude of peristaltic contractions as analyzed by many in the course of gastrointestinal motility research, and we have no problem with this exposition. We are also convinced that the type of distension-induced contraction we described in the mice is part of this “library” of contractions. But it is also clear that terminology can only go so far and that motility can be amazingly complex. Therefore, arguments derived from experiments performed in one part of the intestine, under one set of circumstances, in one species, cannot be used, without testing, in other parts, in another species, under another set of circumstances.

At the end of the day, studies of the mechanism of intestinal contractions require high-resolution recording and description of the electrical, mechanical, and intraluminal activities; preferably simultaneously. This is not a very revolutionary statement, because this has been stated many times by others including by Dr. Huizinga himself (4). On the shoulder of previous work (1–5, 7, 9–11), we hope with this publication (8) to have progressed a bit further into a fuller understanding of the fascinating complexity of small intestinal motility.

REFERENCES


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